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Acumen Fund Concepts

Socially Responsible Licensing: Model Partnerships for Underserved Markets

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Since 1980, when the United States Senate passed the Bayh-Doyle Act, publicly funded American research institutions have been encouraged to patent and license their intellectual property (IP) in order to collaborate with and receive royalties from the private sector.[1] While this model of technology transfer from universities to the commercial sector has become the traditional approach for many, a handful of academic institutions have looked beyond profit maximization and have developed new operating models. These models allow universities to both maintain their intellectual property rights and ensure that their innovations create lasting societal change by reaching large numbers of underserved people in developing countries.

In 2002, Acumen Fund[2] was involved in an investment supporting an immunosensor diagnostic device developed by scientists at University of California at Berkeley. The intellectual property licensing agreement for the immunosensor device became one of the first instances of what has now been termed 'socially responsible licensing.' This pioneering deal has since served as the gold standard for the many universities seeking to pursue similar social returns through the creative licensing of their intellectual property.

Traditional Approaches to Technology Transfers

Traditionally, universities patent and license their research to private companies for the further development, distribution and sales of their medical technology. In the mid-1990s, several universities went a step further and agreed to receive substantial funding from top-tier pharmaceutical and biotechnology companies in exchange for granting those companies exclusive licensing rights to their future discoveries. For instance, Massachusetts Institute of Technology (MIT) stood to receive $30 million over the span of 10 years from Amgen, a biotechnology company based in Cambridge, MA. This deal granted Amgen the patent rights over new technologies developed by MIT's biology, brain and cognitive science departments. Similar deals were structured at the University of Michigan with Fisher Pharmaceuticals and University

[1] Crispin Littlehales, *After 25 years in the biz, universities still working at tech transfer,* LabPulse.com, October 26, 2005.

[2] For more information on Acumen Fund please refer to http://www.acumenfund.org.

of California, Berkeley with Novartis Pharmaceuticals. These agreements sparked controversy in the academic community; many who were critical of the deals warned of the potential dangers of industry influence on the quality and impartiality of scholarship. While these exclusivity agreements have since fallen out of favor, other problems have plagued the universities' ability to collaborate with investors.[3]

For example, as the economic considerations of potential investors have evolved, a gap has emerged in the collaboration between the public and private sector. Over the past decade, the rate of scientific discovery has rapidly increased. With more innovative choices for venture capital firms and biotechnology companies to select from, investors have become more risk averse.[4] Before providing an up-front investment in any technology, private sector investors now demand that such technology be at more advanced stages of development. Consequently, universities are forced to incubate their research ideas for longer periods of time and are desperate to find further financing for development.[5] Universities have responded to this new investment climate by providing technology management support for the timely filing of patents and assistance to faculty in securing licensing agreements. In addition, many university technology transfer offices will now only file patents after a future licensee has offered to reimburse the cost of the patent.[6]

While the prospect of reaping significant financial rewards from a new discovery is enticing, scientists have also become increasingly motivated by the opportunity to address public health issues in underserved populations. The controversy that occurred in 2001 over the distribution of 'd4t', a frequently prescribed reverse transcriptase inhibitor for the treatment of AIDS, is a prime example of growing tensions around the Bayh-Doyle Act, and of increasing demands coming from the academic community to retain influence in determining the use and accessibility of intellectual property. Under the provisions of the act, Yale University held the patent rights to the d4t and had exclusively licensed its production and distribution to Bristol Meyers Squibb. With 20 percent of the population of South Africa infected by the HIV virus and 50 percent of the population falling below the poverty line, Médecins Sans Frontières (MSF) requested that Bristol Meyers Squibb grant them permission to import a generic version of d4t into South Africa. Bristol Meyers Squibb advised MSF to approach Yale, since the university held the patent for d4t and at the time was receiving $40 million a year in royalties. Yale responded by citing the terms of their licensing agreement, claiming that, as the exclusive distributor of d4t, Bristol Myers Squibb ultimately was responsible for making the decision. While this back and forth continued, the Yale student body, with the endorsement of the inventor of d4t, petitioned the school to relinquish d4t patent rights in South Africa. Under public scrutiny, Yale and Bristol Meyers Squibb allowed for generic entry of d4t into South Africa, citing the potential social value of the decision as one rationale.[7]

Research and development of new drugs and technologies that primarily target diseases prevalent in the developing world (such as malaria, HIV/AIDS, dengue fever and tuberculosis) are often perceived by private pharmaceutical companies as too risky to invest in without the promise of large financial returns. Unless there is a shift away from traditional technology transfer models, where both the university and corporation seek to gain financial success, there is a high risk that many technologies, including many of great potential social value, will continue to languish in the gaps between the needs and interests of public and private entities.

Socially Responsible Licensing

The concept of socially responsible licensing was developed at University of California, Berkeley in 2002. Eva Harris, an associate professor at the School of Public Health, and her colleagues were developing a portable technology to quickly diagnose dengue fever in the field. The leading cause of death in

[3] Crispin Littlehales, *After 25 years in the biz, universities still working at tech transfer,* LabPulse.com, October 26, 2005.
[4] Ibid.
[5] Ibid.
[6] Ibid.
[7] Julian Borger & Sara Boseley, *Campus Revolt Challenges Yale over $40m AIDS Drug,* The Guardian (Manchester, U.K.), March 13, 2001.

developing countries can be attributed to infectious diseases, particularly lower respiratory infections, tuberculosis, malaria and HIV/AIDS.[8] An essential element of the fight against infectious diseases is the capacity for early and accurate diagnosis, which is mandatory for effective treatment, case management, and the control of outbreaks. The present state-of-the-art diagnostic technology uses Immunoassays, such as Enzyme-Linked Immunosorbant Assays (ELISA), which require costly equipment and many hours of work by a skilled technician. This technology is typically only available in a few tertiary care hospitals in developing nations. Harris's innovation, the ImmunoSensor, is a user-friendly, point-of-care device that can detect antibodies or infectious agents in clinical samples rapidly and accurately.

At the time, Acumen Fund was looking for healthcare technologies with the potential for large-scale impact in developing countries, and it agreed to invest in the development of the ImmunoSensor. Harris was convinced that the ImmunoSensor had the potential to become a tool for diagnosing multiple infectious diseases in developing countries. With Acumen Fund's collaboration, Harris proposed a licensing agreement to Berkeley that would allow the non-profit Sustainable Sciences Institute to develop and distribute the technology to underserved countries for free or at cost, while maintaining the university's right to earn future royalties from derivative technologies distributed in developed countries. Harris' proposal was a radical departure from standard licensing models, but it was surprisingly well received by the university.

Harris' proposal also encouraged Berkeley's technology transfer management office to restructure their valuation process to include the double bottom line concept.[9] Carol Mimura, the head of Berkeley's Office of Intellectual Property and Industry Research Alliances (IPIRA), describes the concept as a two pronged evaluation of the financial bottom line and the scope of social impact, both being equally important to Berkeley.[10] This new idea of incorporating social impact into considerations around intellectual property rights opened the door to a broad range of IP-management models. From the university's standpoint, the additional revenue that would be gained from marketing in developing countries is not significant, given that they already receive over $50 million in royalties from current licensing agreements.[11] In fact, because sub-Saharan Africa accounts for only 1.3 percent of the global pharmaceutical market, as the CEO for Eli Lilly put it, even losing that market altogether (as opposed to competing in it with generic entry) would cost at most "about three days' fluctuation in exchange rates."[12] Ultimately, Harris' licensing proposal proved to be mutually beneficial to the public and private sectors, achieving the university's social goals without eliminating the profit drivers for a potential private sector partner. Through this legal innovation, Harris was able to safeguard the potential distribution of her invention in developing countries on a not-for-profit basis.[13]

The ImmunoSensor proposal established a precedent for Berkley, and since then the university has entered into 15 more agreements that adhere to the same structure. The most prominent of these agreements is Jay Keasling's development of an anti-malaria drug, artemisinin.[14] The artemisinin license was the fourth license to be developed under Berkeley's program. Keasling, a professor of chemical engineering, received a grant of $42.6 million from the Gates Foundation to develop, manufacture and distribute artemisinin in developing countries. Under the agreement, the anti-malaria treatment would be provided free of cost and would be freely accessible to any population in need. The grant allowed for the seamless integration of all steps in the research and development process:

[8] World Health Organization, *50 Facts: Global Health situation and trends*: 1955-2025, 1998.

[9] Barry Bergman, *Research patently in the public interest*, Berkeleyan, December 2, 2005.

[10] Ibid.

[11] Ibid.

[12] Gellman, Barton, *A Turning Point that Left Millions Behind: Drug Discounts Benefit Few While Protecting Pharmaceutical Companies' Profits*, The Washington Post, 2000.

[13] Barry Bergman, *Research patently in the public interest*, Berkeleyan, December 2, 2005.

[14] Bennet Daviss, *Malaria, Science, and Social Responsibility*, The Scientist (Vol.19, Issue 6) March 28, 2005.

Keasling is working to perfect a method to synthesize an inexpensive version of the medicine; Amyris Biotechnologies will develop the commercial process to manufacture artemisinin; and the Institute for One World Health (a non-profit drug development company) will pass the drug through equivalency trials and FDA approval, ultimately making the drug more cheaply available to a drug manufacturer.[15]

According to Mimura, the Gates Foundation's funding made it possible for the seamless hand-off from one stage of research to the next, a critical component for the successful completion of this project. Under most circumstances, there exist many gaps in the drug development pipeline that stall projects indefinitely. Keasling plans to genetically engineer a version of artemisinin by the end of 2010 and hopes to then apply the same process to develop an anti-AIDS compound found in the bark of the mamala tree.[16]

Expansion to Other Universities

Not only have scientists and philanthropists alike applauded Keasling's collaboration with the Gates Foundation, but its success has triggered the development of new models for constructing public-private partnerships (PPP) at other American research institutions such as Emory University, Yale University, Harvard College, the University of Washington, the University of California at Santa Barbara, the University of Michigan and MIT.[17]

A recent report from the Senate Joint Economic Committee found that 15 out of the 21 drugs with the most therapeutic impact were derived from federally funded projects at academic institutions. In fact, over 50 percent of basic science research in the United States originates from universities.[18] As drug developers, universities are finding that they have incredible leverage to negotiate for open access and less costly treatment in developing countries.[19]

Recently, scientists at Emory University developed emtricitabine (Emtriva), a once-daily HIV antiretroviral, which in combination with tenofovir (Viread) compose the combination pill Truvuda. Emtricitabine is also used in a newly approved triple combination pill, marketed under the brand name Atripla. Emory believes that these therapies have the potential to become the first-line treatment for HIV/AIDS in developing countries. Accordingly, in July 2005, Emory entered a deal with Gilead Sciences, a pharmaceutical company that paid them $525 million for royalties and future global sales of emtricitabine. In exchange for Emory waiving its royalties, Gilead's Access Program agreed to make the drug available at-cost in 97 developing countries, along with Truvuda and Viread (also developed at Emory).[20]

While the deal is groundbreaking, the university has encountered a number of challenges. As of February 2006, Gilead had registered Truvada in only four countries and had only filed for registration in 43 countries. Of the 97 target countries, 50 had not yet been registered. Gilead claimed that in-country resources and unexpected registration requirements slowed down the registration process.[21] However, by June 2006 Gilead had responded to growing criticism surrounding its access program by filing for registration of Truvuda in 61 countries.[22] As of May 2008, according to Gilead's International Access Operations published list, Truvada has been successfully registered in 49 countries, filed for registration

[15] Ibid.

[16] Gellman, Barton, *A Turning Point that Left Millions Behind: Drug Discounts Benefit Few While Protecting Pharmaceutical Companies' Profits*, The Washington Post, 2000.

[17] Crispin Littlehales, *After 25 years in the biz, universities still working at tech transfer*, LabPulse.com, October 26, 2005.

[18] National Science Foundation, *Science and Engineering Indicators*, Washington DC: National Science Foundation, 2004.

[19] Bowler., Doan., Hughes., Thomas., Beeson., Churchman., Lubbock., Gallant., *Ensuring access through university technology transfer: A case study of the Emory-Gilead emtricitabine deal*, 2006.

[20] Ibid.

[21] Ibid.

[22] Gilead Sciences, *Gilead offers Voluntary Licenses for Manufacturing of Viread in Developing World*, Press Release. Foster City (CA), May 10, 2006.

in 49, and pending submission in 32 countries. The company has also announced that it will provide non-exclusive licenses and technical information to South African and Indian generic manufacturers.[23] These initiatives, if successful, could create a new model for increasing access to new medical innovations.

Emory has also learned from this first experience with socially responsible licensing and plans to improve its licensing strategies to avoid the same stumbling blocks in the future. The university's case study of the Truvuda deal revealed the importance of structuring specific conditions at the time of the licensing agreement in order to monitor progress of the private company's access programs. In the Truvuda case, Emory's influence and ability to pressure Gilead's access program decreased substantially after the licensing deal had been brokered.

These lessons learned in socially responsible licensing are also valuable learning opportunities for other universities to streamline and refine the practices of their respective technology transfer management offices. Since the initial days when Harris' royalty-free license was approved for the ImmunoSensor, universities have made significant progress individually, as well as together through a unified body of academic institutions. In September 2002, an initiative led by Yale University to assemble a group of experts in public health, IP management and university policy helped to create the Universities Allied for Essential Medicines (UAEM).[24] The organization stresses the need to create and promote access to essential medicines in developing countries. UAEM realizes that many of the world's important drugs have been researched at universities and recognizes that because the development of medicines is almost entirely profit driven, investment in R&D related to the health needs of people in developing countries has come to a near standstill.[25] In view of these challenges, UAEM has adopted a mission that is two-fold: first, UAEM pushes universities to ensure that life-saving medical products developed in campus labs are accessible in developing countries, and, second, UAEM aims to facilitate and promote research on neglected diseases, or diseases that predominantly affect populations too poor to attract private-sector R&D investment.[26]

Currently there are over 25 UAEM chapters established at research institutions across the United States and Canada, and many have made great strides in guiding their universities to adopt UAEM principles. For example, in January 2007 the University of Washington's Intellectual Property Management Advisory Committee (IMPAC) passed a resolution that values the distribution of the university's intellectual property and the societal impact that it may create over the revenue that might be generated by licensing through exclusive agreements.[27] The committee adopted this policy after a visit from members of the University of Washington's UAEM chapter.

Redefining "Successful" Innovations

The Berkeley and Yale licensing initiatives started a movement whereby developed-country medical innovations are shared with large, underserved populations in countries lacking the domestic resources and pharmaceutical industries to serve themselves. Individuals and companies in industrialized countries hold 97 percent of the patents filed worldwide, and residents of industrialized countries hold 80 percent of the patents granted in developing countries.[1] The challenge for socially conscious universities, especially in industrialized countries, is whether their intellectual property can be distributed in such a way that will benefit large populations in a safe, regulated manner.

[23] Kottle, M. L., *Gilead gives up trade secrets to get AIDS drugs to poor nations,* Bloomberg.com News, August 7, 2006. AND: http://www.aidsmap.com/en/news/9C80024F-7788-4F7E-BD98-9295268D1599.asp

[24] Ellen 't Hœn, *The Responsibility of Research Universities to Promote Access to Essential Medicines,* Yale Journal of Health Policy, Law, and Ethics III:2, pp. 293-300, September 2003.

[25] Patrice Trouiller et al., *Drug Development for Neglected Diseases: A Deficient Market and a Public-Health Policy Failure,* 359 The Lancet 2188, 2002.

[26] Universities Allied for Essential Medicines, http://www.essentialmedicine.org

[27] Peter Kelley, *Choosing the greater good in promotion of UW intellectual properties,* UW Faculty and Staff Newspaper (Vol. 24, No.16), February 18-14, 2007.

[1] U.N. Development Programme, Human Development Report 68, 1999.

[2] Kottle, M. L., *Gilead gives up trade secrets to get AIDS drugs to poor nations,* Bloomberg.com News, August 7, 2006.

In addition, universities will need to rethink how they recognize faculty members for their discoveries and innovations. Traditionally, researchers are rewarded only for publication or patenting. Universities will have to recognize researchers' social impact in order to shift this competitive focus.[2] Just as universities seek out opportunities for financial returns by patenting new technologies developed by their scientists, they can value social returns by backing the scientists who develop innovative, scalable approaches to solving social problems. The sector must work to understand the long-term institutional benefits of such a social return strategy in terms of reputation and their ability to attract and retain leading talent. Universities and other research institutions must also engage in partnerships to define, measure and evaluate social returns as a component of scientific progress. Millions of people do not have access to drugs and services that exist elsewhere, and where market forces alone are unable to address these problems, universities can have a tremendous impact.

Royalty-free licensing agreements preserve economic incentives for pharmaceutical companies, allowing them to leverage manufacturing capacity and infrastructure in order to have a much greater impact on public health issues worldwide. Biotechnological intellectual property has already driven significant improvements in the lives of underserved populations. Royalty-free licensing can ensure that these improvements reach a larger proportion of the underserved market worldwide. Social returns are increasingly important to the identities and reputations of leading universities and pharmaceutical companies. By combining positive financial and reputational returns, royalty-free licensing creates a mutually beneficial relationship between universities and pharmaceutical companies, allowing both to draw on their wealth of expertise to bring affordable biotechnology innovations to the developing world.

Acumen Fund is a 501(c)3 social venture fund that invests in enterprises that offer access to critical, affordable products and services to the poor through scalable, market oriented approaches. Our investments currently focus on four key areas: water, health, housing, and energy.

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