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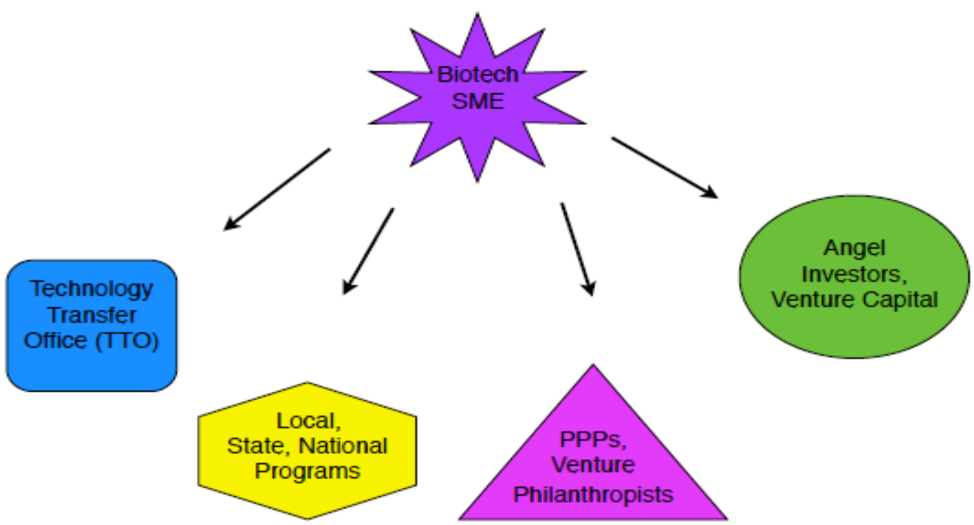
Access to Early Capital

In the United States and globally, commercial development of biotechnology relies on the continuing availability of capital to translate basic research into innovative products such as cures and therapies, seeds, foods, and medical tests and devices, as well as environmental restoration and bioremediation. Government programs and private foundations make important contributions to translational science, and inventors frequently rely on critical support from private sector funders for advanced research and development of new biotechnology products and services. This paper highlights factors that contribute to enabling environments for promising technologies to gain access to early capital.[1]

Small biotechnology companies in search of early capital rely on a variety of sources of support, monetary and otherwise:

- Government programs and incentives
- Technology Transfer Office (TTOs) licensing programs
- Angel investors and venture capital (VC)
- Venture philanthropy and public-private partnerships

Successful biotechnology entrepreneurs, or bio-preneurs, may rely on some or all of these resources, sequentially or concurrently, to bridge their capital needs on the road to successful commercialization of science to create economic and social value.



[1] Access to early capital is one of many challenges facing biopreneurs trying to bring new products and services to the market. For more information on related issues, see the BayhDole25, Inc. Biotechnology Toolkit, available online at http://www.bayhdole25.org

Government Programs and Incentives

Both developed and developing country governments around the world provide important sources of funding for early-stage companies. This paper provides a very brief overview of some of the funding mechanisms available in the United States at the federal, state, and local level. Across a range of sectors and subsectors, the Department of Energy (DOE), National Institutes of Health (NIH), Department of Defense (DOD), the U.S. Agency for International Development (USAID), and the National Science Foundation (NSF) all provide substantial support for biotech R&D:

- DOE supported a great deal of the international research on the Human Genome Project and remains the single biggest funder at the federal level for basic science and biofuel research.
- In the biopharmaceutical area, NIH remains the number one source of funds for R&D targeting diseases of the developing world,[2] and the single largest overall funder for biopharmaceutical R&D.
- Other important sources of early-stage funding are provided by the DOD through the Defense Advanced Research Project Agency (DARPA), which provides funds for early-stage research, and the Office of Naval Research (ONR) and the U.S. Army who provide major funding for many projects, including the congressionally-mandated cancer prevention/therapy projects.
- Historically, USAID provided critical support for the Green Revolution, which improved agricultural productivity in the developing world, and continues to support a range of global programs.

Other important U.S. federal programs include the Small Business Innovation Research (SBIR) program[3], administered by the National Science Foundation (NSF), as well as Cooperative Research and Development Agreements (CRADAs) available from a range of federally-funded research institutions that provide additional grants, matching funds, soft-loans, or other research assistance to academics and entrepreneurs at the early stages of commercial biotechnology R&D. On an annual basis, the SBIR alone awards $2 billion dollars to research-intensive start-ups across the spectrum of high-technology industries.

The recent U.S. health care reform legislation also included a number of new initiatives for new grant programs for qualifying biotech companies, including tax credits for qualifying R&D investments that may be converted to grant money for companies that do not have tax liability.[4] It also established the Cures Acceleration Network or CAN, to create a new office in NIH to advance basic research to the product development stage

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[2] Moran M, Guzman J, Ropars AL, McDonald A, Sturm T, Jameson N, Wu L, Ryan S, Omune B (2009) "Neglected disease research and development: how much are we really spending?" The George Institute for International Health. February 2009, p. 5, available online http://www.thegeorgeinstitute.org/iih/media-and-publications/reports/2009.cfm, accessed March 23, 2010.

[3] Details about the SBIR program are available online at http://www.sbir.gov/, accessed 23 March 2010.

[4] The Grant in Lieu of New Qualifying Discovery Project Tax Credit is modeled on existing tax credit programs and would provide a credit equal to 50% of a company's investment in qualifying therapeutic discovery projects in 2010 and retroactively in 2009, including for expenditures relating to pre-clinical research, employment of scientists and researchers, capital equipment, and clinical research for companies with up to 250 employees.

through a fully integrated process, starting with research grant funding, through accelerated access to clinical research, and facilitated FDA review for priority products.[5]

At the state level, individual U.S. states, regional consortia, and localities provide a long-standing range of general incentives for R&D intensive industries as well as support to meet the unique needs of life sciences companies:

- Corporate tax credits for research and development (R & D)
- Matching funds for SBIR programs, VC funds, or other grant programs
- Job training expenditures
- Property tax credits for building facilities and acquiring equipment and machinery
- Sales tax exemptions for equipment and machinery acquisition
- Low-interest loans or other forms of financing for construction and product development
- A 10% corporate tax credit for corporate investment in unrelated small high-technology companies
- A 6% corporate tax credit for investment in building “special purpose rooms” such as clean rooms (California)
- Access to wet-labs or other specialized research services and/or physical space at state or local incubators[6]

Technology Transfer Office (TTOs) Licensing Programs

Licensing programs supported by Technology Transfer Offices (TTOs) in universities and other research institutions provide key assistance to academic scientists and budding bio-entrepreneurs. While specific policies may vary between institutions, TTOs provide a range of services to promote and facilitate licensing activities between universities and other research institutions and private companies. In the United States, most public land-grant universities, private colleges, and government research institutes have established TTOs to assist in commercialization of promising inventions.

By counseling research scientists or other inventors at the earliest stages, on issues ranging from protection of IP rights to matchmaking with potential funders, TTOs help to ensure that economically and socially important breakthroughs reach the commercialization stage. Ensuring that IP rights are pursued appropriately and that licensing rights are evaluated appropriately, TTOs increase the likelihood that patented[7]

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[5] Implementation of the CAN Office, Review Board and related grant funding was authorized for FY 2010 at the level of $500 million.

[6] "OLR Research Report", January 28, 2000, http://search.cga.state.ct.us/dtsearch.asp?cmd=getdoc&DocId=15872&Index=I%3A\zindex\2000&HitCount=0&hits=&hc=0&req=&Item=50, accessed on January 21, 2010. See also "Strengthening New York City’s Biotechnology Industry," Issue Paper No. 5, August 2009, http://www.davidyassky.com/page/content/biotechnology/, accessed on January 21, 2010.

[7] For a fuller discussion of the IP protections important for nascent biotechnology companies, see the BayhDole25 Intellectual Property Toolkit, available online at http://www.bayhdole25.org.

technologies can gain the needed financing for the lengthy and complex development process that may lead eventually to a commercially successful product.

Licensing: Exclusive or Non-Exclusive?

Licensing by TTOs, whether in the university, research institute, or government setting, may be done on an exclusive or non-exclusive basis. Universities and government agencies granting licenses for patented technologies weigh a number of factors in determining whether an exclusive or non-exclusive license would most likely result in successful commercialization to meet the public interest. These include the potential social and commercial value of the patented invention, time, and investment needed for applied research and product development, and associated risk, which in the life-sciences is extraordinarily high.

Also, patents for basic science or a broad-based technology platform will be much more likely to be licensed on a non-exclusive basis than a narrow application, as outlined by the Council on Governmental Relations, an association of research universities: “Patents which are broad in scope and can be used in multiple industries, or patents that are so basic that they form the building blocks for new technologies, are most likely to be licensed non-exclusively, or by fields of use . . . Non-exclusive licensing is preferred by universities when the technology can be used to foster product development in many fields of use,"[8] such as the non-exclusive licenses Stanford started giving in the mid seventies for the recombinant DNA technology. Conversely, for a narrowly focused patent, or where a TTO believes that considerable financial resources, time, or both may be required to commercialize an invention, there could be a greater tendency to allow exclusive licensing in order to ensure that a product can be developed from the patented technology.[9] In 2007, the Association of University Technology Managers (AUTM) formulated best practices to ensure broad access to latest medical technologies.[10]

The availability of TTO support at an early stage may be critical for a fledgling company to attract the financial support needed for continuing growth and ultimate commercial success. Based on the support provided to biotechnology spin-offs, TTO activities also spur regional economic development. One recent study estimates that university licensing contributed to the creation of nearly 280,000 jobs between 1996 and 2007.[11]

Angel Investors and Venture Capital

While government agencies and private foundations may fund the lion’s share of basic research in the United States and Europe, private capital markets remain critical for the continued research needed for successful commercial development of biotechnology, including advanced pre-clinical and clinical trials, product prototypes, formulation, manufacturing ramp-up, and ultimately successful launch, marketing, and distribution of

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[8] http://www.ucop.edu/ott/faculty/tech.html#6, accessed online on 11 March 2010 (reprinted from COGR 1996 brochure).

[9] Ibid.

[10] AUTM’s “Statement of Principles and Strategies for the Equitable Dissemination of Medical Technologies,” has been endorsed by 70 universities and is available online at http://www.autm.net/Technology_Transfer_Resources1/3875.htm, accessed 27 May 2010.

[11] David Roessner, Jennifer Bond, Sumiye Okubo, Mark Planting, “The Economic Impact of Licensed Commercialized Inventions Originating in University Research, 1996-2007,” September 3, 2009, available online www.bio.org/ip/techtransfer/BIO_final_report_9_3_09_rev_2.pdf, accessed March 23, 2010.

new products and services. In 2008, the private sector provided more than two-thirds of total funding for R&D focused on the spectrum of commercial biotechnology.[12]

Angel Investors and institutional venture capital (VC) funds remain critical sources of investment for start-up (SU) or early-stage (ES) life sciences companies in the United States and Europe, forming the backbone of early-stage commercial investment.

Angel investors are independent investors willing to take risks with their own financial resources. Because angel investors typically fund companies at earlier stages of development than VC funders, they are important for biotechnology start-ups.[13] Prior to the 2008-2009 recession, angel investors allocated $4.6 billion to SU/ES biotechnology companies in calendar year 2006 alone.[14]

Venture capital investments are made by professionally managed funds that may have anywhere from $25 million to $1 billion to invest in emerging growth companies across a range of industries, frequently based on specialized areas of expertise. VC investors also may provide direct support and management expertise for companies that they fund. Many companies that are now "household names" once benefitted from VC funding, including Apple, Inc., Medtronics, Inc., Whole Foods Market, Inc., and notably Google.[15] In the biotech space, "in the 1970s, VCs helped found the biotechnology industry through their investments in pioneering companies like Genentech and Amgen."[16] Industry expert J. Leslie Glick cited increasing VC investments in U.S. biotech companies as a major factor in funding for the innovative life sciences, with venture funding growing "from $0.83 billion to $5.2 billion (a 527% increase.)."[17]

VC funders in particular are looking for what are called highly innovative "disruptive technologies" that are likely to create major impact in their respective field of operation, and therefore bring high value to early investors. In this context, patents provide lifescience funders with the short-hand explanation of technology breakthroughs as a key indicator of future success, and remain the currency of choice for both VCs and angel investors.

Increasingly, successful global biopharmaceutical companies like Eli Lilly, Roche, and GSK also have established their own venture capital arms to look for novel technologies

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[12] National Science Foundation (NSF) Key Science and Engineering Indicators 2010 Digest http://www.nsf.gov/statistics/digest10/funding.cfm#1 accessed on January 20, 2010.

[13] Across all industries "close to 90% of angel investment dollars target SU/ES companies, in contrast to 20% of VC funds committed to SU/ES investments." J. Leslie Glick, PhD., "VC Funding for Biotech Firms: Past Performance and Future Prospects," Wall Street BioBeat GEN-Genetic Engineering & Biotechnology News, October 15, 2008 (Vol. 28, No. 18), available online at http://www.genengnews.com/articles/chitem.aspx?aid=2632, accessed January 20, 2010.

[14] Ibid., *National Science Board's Science and Engineering Indicators 2008 -*

[15] Venture Capital 101: Venture Impact—The Economic Importance of Venture Capital Backed Companies to the U.S. Economy, available online at http://www.nvca.org/index.php?option=com_content&view=article&id=141&Itemid=133, accessed on January 20, 2010.

[16] Ibid., p. 11

[17] J. Leslie Glick, PhD., "VC Funding for Biotech Firms: Past Performance and Future Prospects," Wall Street BioBeat GEN-Genetic Engineering & Biotechnology News, October 15, 2008 (Vol. 28, No. 18), available online at http://www.genengnews.com/articles/chitem.aspx?aid=2632, accessed January 20, 2010.

under development by early-stage biotech start-ups.[18] In addition to direct funding of biotech start-ups and young companies, U.S. and foreign companies also fund R&D out of their own capital stocks, and increasingly also directly acquire or fund promising biotechnology start-ups.[19]

Biotechnology start-up and early-stage companies face intense competition for scarce investment funds not only from other biotech companies but also from other high-technology sectors with faster product development cycles and/or lower-risk profiles. With increased attention to climate change and adaptation technologies since 2008, there has been heightened interest by VC funds in emerging technologies like clean energy, as well as latest generation internet technologies and social media (e.g., Twitter, FaceBook, etc.). Looking forward in 2010, VC investment strategies project continued increases in funding in these areas, with relatively little to no growth likely in funding for biotechnology.[20]

As noted, well-established innovative life sciences companies fund commercial R&D funding internally, and may also support basic research conducted by universities or enter into collaborative R&D agreements with smaller biotechs. The National Science Foundation reports that U.S.-based global companies expended an estimated $216.3 billion in 2006 on R&D activities. Globally, foreign-based multinationals are increasingly conducting R&D in the United States, spending an estimated $34.3 billion on U.S. R&D in 2006.

U.S. multinationals also are shifting foreign R&D spending away from Canada, Europe and Japan to Asia, with beneficiary countries including China, India, Singapore, and South Korea. Growth of R&D by U.S. foreign affliates increased from less than $10 million in both China and India in 1984 to $804 and $310 million respectively in 2006,[21] reflecting the value placed by industry on R&D conducted in these growing knowledge economies.

Venture Philanthropy and Public Private Partnerships

Venture philanthropy and related public-private partnerships (PPPs) have grown to play an increasingly important role in supporting life sciences research and product development over the past decade. Growing from a base level of less than 0.2% of all public health grants in 2001,[22] philanthropic support reached 21% of total spending for R&D focused on diseases of the developing world in 2007.[23] With assets estimated at

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[18] "Eli Lilly's Venture Arm Spins Out With $200M Fund," http://blogs.wsj.com/venturecapital/2009/08/03/eli-lillys-venture-arm-spins-out-with-200m-fund/, accessed online at 27 May 2010.

[19] Ibid.

[20] "Venture View: 2010, NVCA Predictions Survey Results," National Venture Capital Association (NVCA), available online at www.nvca.org/predictions2010_presentation.pdf, accessed June 10, 2010.

[21] Statistics on U.S. and foreign MNC investment in R&D are drawn from the National Science Foundation's Key Science and Engineering Indicators for 2010 available for download at http://www.nsf.gov/statistics/digest10/funding.cfm#1 accessed on January 20, 2010.

[22] "Does Venture Philanthropy Work?" CNET News, May 8, 2004, http://news.cnet.com/2030-1030_3-5206330.html, accessed March 22, 2010.

[23] Moran M, Guzman J, Ropars AL, McDonald A, Sturm T, Jameson N, Wu L, Ryan S, Omune B, "Neglected disease research and development: how much are we really spending?," The George Institute for

approximately $33 billion,[24] the Bill and Melinda Gates Foundation has had a singular impact on development of new vaccines, therapies, and diagnostic devices, donating $800 million annually to global public health research and related programs.[25] The Gates Foundation's recently announced $10 billion, 10-year vaccine initiative may spur a new golden age for vaccine development to combat diseases of the developing world. Other prominent examples of venture philanthropists that have made signifcant contributions to advance development of therapies and cures in specific therapeutic areas include the Lance Armstrong Foundation (testicular cancer), the Michael J. Fox Foundation (Parkinson's disease), the Multiple Myeloma Foundation, the Melanoma Alliance, The American Cancer Society, The Cystic Fibrosis Foundation, and others.

Public-private partnerships (PPPs) are equally dynamic, conceptually and in operation. PPPs allow foundations or other philanthropic organizations, governments, and private companies to work together on creative solutions to address pressing public health R&D priorities.[26] These may also include research collaborations, post-marketing pilot programs, and studies for rollout of therapies in emerging markets to improve access to medicines. Looking ahead, new models for grant-makers in private foundations and additional hybrid PPP models continue to evolve, providing important opportunities for early-stage life sciences companies in the United States and globally for funding from foundations and innovative non-profit and/or non-government organizations.

Conclusions

Biotechnology remains among the highest-risk sectors for capital investment, and like other high-risk sectors was adversely affected by the capital crisis of 2008. While the first quarter of 2008 remained strong, the sector suffered in the second quarter, both domestically and internationally: "The number of biotechnology venture backings fell by nearly 50%, and the dollar amount invested fell by more than 40% from the first quarter, according to Thomson Financial. Outside the U.S., the venture financing value fell nearly 50% in the same period."[27]

As we approach the second half of 2010 and the world economy faces continuing challenges in the capital markets, life sciences has continued to demonstrate a capacity for high-stakes returns that has attracted near-record levels of investment for companies

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International Health. February 2009, p. 5. The 2009 George Institute study ranks Bill and Melinda Gates Foundation as the second highest funder of global R&D, surpassed only by spending by the U.S. National Institutes of Health (NIH).

[24] The Gates Foundation's funds for global health increased geometrically via Warren Buffet $30 billion donation. "Warren Buffett gives away his fortune," Fortune, June 25 2006, available at http://money.cnn.com/2006/06/25/magazines/fortune/charity1.fortune/ accessed March 23, 2010.

[25] Donation of just 5% of the Gates Foundation's net assets annually, the minimum requirement to retain non-profit status, amounts to nearly $1.5 billion in grants.

[26] See generally, Irina A. Nikolic and Harald Maikisch, "Public-Private Partnerships and Collaboration in the Health Sector," The World Bank (2006), available online at siteresources.worldbank.org/.../HNPDiscussionSeriesPPPPaper.pdf, accessed on 23 March 2010.

[27] Robert Dellenbach, "VC Funding for Biotech Companies Withering," Wall Street BioBeat GEN-Genetic Engineering & Biotechnology News, Sept. 1, 2008 (Vol. 28, No. 18), available online at http://www.genengnews.com/gen-articles/vc-funding-for-biotech-companies-withering/2578/

with truly innovative technologies.[28] In fact, year-end figures for 2009 show a significant increase in terms of both the number of deals and the value per deal.

It remains open to question whether funding organizations are seeking less risky, so-called "low hanging fruit," or whether more funding is going to riskier, pre-clinical research where it is needed.[29] All told, the continued strength of a broad range of funding mechanisms and the renewed health of private angel and VC investors augurs well for continued innovation in the global knowledge economy, and to the continued creation of social and economic value, including new products like vaccines, therapies, cures for the world's pressing public health challenges, agricultural products, and environmental restoration.

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[28] http://www.fiercebiotech.com/special-reports/top-20-biotech-venture-capital-deals-2009?utm_medium=nl&utm_source=internal

[29] Cynthia Robbins-Roth, "Year-end 2009 Figures Show Private Biotech Trending Up," BIOWorld, February 25, 2010 (citing a "significant increase in dollars heading into early financing rounds, with preclinical R&D-stage companies dominating the scene; in 2009, Series A rounds gathered up $849.4 million, a 38 percent increase over 2008, and more deals were done in 2009 – 57 vs. 43 for 2008, with a significantly larger median deal size), available online at

http://www.bioworld.com/servlet/com.accumedia.web.Dispatcher?next=bioWorldHeadlines_article&forceid=53684, accessed March 23, 2010.