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Nonprofit Biomedical Companies

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Abstract

Nonprofit biomedical firms are an integrated market-based solution to improve incentives for investment in promising scientific areas that have high social value but minimal potential for profit. We briefly review the current market with an emphasis on the financing of innovative product development and propose ideas for new nonprofit companies centered on the health concerns of developed countries. We conclude with a suggestion that opportunities exist for nonprofit firms focused on cancer diagnostics, given the limitations of current financing incentives and ripe scientific opportunity.

The current biotechnology market and incentives for R&D investment

Biotechnology firms are critical drivers of medical innovation. The industry has mushroomed since 1992, with US healthcare biotech revenues increasing from $8 billion in 1992 to $50.7 billion in 2005[1] Further development promises treatment for patients suffering from illnesses for which there is currently little effective treatment as well as more targeted use of existing therapies. In 2006, more than 400 biotech products were in clinical trials.[1]

Biotechnology investments are risky as a result of significant scientific and regulatory uncertainty. The average cost of developing a drug approved by the US Food and Drug Administration (FDA) is more than $1 billion, including failure costs.[2] Recent evidence suggests that biotechnology companies are significantly more likely to experience a phase III clinical trial failure than the traditional pharmaceutical industry—74% compared with 5%.[3] This failure rate has concentrated investor enthusiasm toward later stages of

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CONFLICT OF INTEREST

Dr. Conti and Dr. Meltzer declared no conflict of interest. Dr. Ratain receives royalties related to pharmacogenetic testing before the prescribing of irinotecan. In addition, he is a co-inventor on several pending pharmacogenetic patents and a director of AspenBio Pharma, a public biotechnology company.

development in biotechnology, even as venture capital investment in the industry overall remains high.[4] Uncertain regulatory enforcement, increasing political scrutiny of the prices of novel treatments and company profits, and the recent economic downturn seem to be important factors in the recent stagnation of venture capital investment.[4–6]

Taken together, these forces push biotechnology research and development (R&D) into areas that meet specific investment criteria. By necessity, firms require the expected profit associated with innovative product development to be large enough to cover, in a timely way, R&D expenses and the opportunity costs of capital investment. Consequently, firms tend to focus efforts on the development of drugs or small molecules for which the protection of intellectual property is clearly defined and legally defensible, the target population is large enough to potentially benefit from treatment and is willing and able to pay for treatment innovation, and scientific uncertainty is minimized. The treatment of prevalent, chronic conditions primarily affecting the US population, particularly the care of middle-age and older adults with insurance coverage, is an ideal target from this standpoint —forces that help shaped the blockbuster-drug era and the proliferation of “me-too” therapies. However, targeted therapies for smaller patient groups may be commercially viable if payers—primarily insurance companies—are willing to reimburse high list prices. The 2001 introduction of imatinib for the treatment of chronic myelogenous leukemia is an important example.[6]

The missing markets for current investment in R&D

Attention has been focused on the lack of development of therapies for diseases that primarily affect the developing world, yet there are also important missed opportunities in the developed world. In the former, there are three areas of failure: the ability of individuals and/or governments to pay for new therapies at a rate that rewards the risks taken in producing them, the distribution system for getting therapies to needy individuals, and the protection of intellectual-property rights.[7] In the latter, the uncertainty associated with scientific opportunity, the size of the target population, the nature of insurance coverage and reimbursement policy, and the protection of intellectual property seem to be critical determinants of investment.[6] Specifically, current financing incentives appear to adversely affect R&D for technologies with the potential for significant societal benefit in the developed world but little opportunity for a high return on investment, for example, treatments for pediatric patients that have limited analogy to adults, diagnostics to better guide use of existing medications, and therapies that are available generically or over the counter applied to alternative illnesses or populations.

Responses to missing markets and the focus on nonprofit biomedical companies

There has been a tendency to rely on public policy to help guide the for-profit industry to undertake socially valuable R&D that does not meet investment criteria, but assessments have found them to be mixed in effectiveness and associated with unintended consequences. Recent work indicates that the “pediatric exclusivity” clause of the Food and Drug Administration Modernization Act has produced additional investment in clinical trials to

better target existing adult therapeutics for the pediatric population but not in the development of novel therapies for children.[6] The Orphan Drug Act seems to have improved incentives for the development of some novel therapies for targeted patient populations.[8] However, these therapies often target relatively large populations within the orphan definition (100,000–200,000 patients per year) or sets of patients that result from a dubious splitting of the market for existing therapies into smaller populations. The 2007 FDA priority voucher policy provides a direct financial incentive for the development of therapies for small patient populations with diseases that primarily affect the developing world. To what degree this incentive spurs significant investment in R&D, in turn translating into novel product development and approval, is uncertain. This incentive does not address financing problems for products targeting the developed world.

Innovative nonprofit ventures are increasingly being established to address these concerns. Table 1 lists leading nonprofit biomedical firms that integrate financing with direct medical product development and testing, drawn from the Initiative on Public–Private Partnerships for Health (http://www.globalforumhealth.org; search for “IPPPH”) and GuideStar (http://www.guidestar.org), the leading source of information on the nonprofit sector in the United States, and augmented by individual website searches and a review of the Internal Revenue Service’s information on 501(c)(3), the tax-law provision for tax-exempt status (http://www.irs.gov/charities/charitable/index.html). For these companies, a focus on a set of neglected diseases or population allows for coordinated efforts to raise funds and to identify, prioritize, and invest in complementary scientific efforts dedicated to maximizing social value. The Institute for OneWorld Health (iOWH) is the most prominent nonprofit pharmaceutical company devoted to the development of anti-infectives. [7] The company started with a low-risk project, resuscitating a drug for the treatment of visceral leishmaniasis that had gone off patent and was no longer available. The drug, paromomycin, was approved by the Drug Controller General of India in 2006. The Alfred Mann Foundation (AMF) is perhaps the most successful nonprofit focused on the development of innovative technical solutions for persons suffering from debilitating medical impairments, largely in the developed world. Founded in 1985, the foundation is responsible for the development of the Clarion Cochlear Implant, approved by the FDA in 1996 for implantation in patients with severe to profound hearing loss, among their successful products.

The Institute for Pediatric Innovation (IPI) is a new (established in June 2007) venture dedicated to the development and reformulation of drug-based treatments and devices for children, with emphasis on the pediatric neonatal intensive care unit and pediatric cardiology. We believe that this organization has much promise given its leadership team, partnerships with the leading children’s hospitals in the United States, and focus on clinical areas in which product development for this population literally means the difference between life and death. There are other firms that primarily act as “virtual” nonprofit biomedical companies, financing and coordinating development efforts in partnership with academic and for-profit firms. Prominent examples focus on global health concerns and include the Malaria Vaccine Initiative (http://www.malariavaccine.org) and the Global Alliance for TB Drug Development (http://www.tballiance.org).

The case for more nonprofit biomedical companies for the developed-world market

We believe the establishment of more nonprofit biomedical firms focused on the development of diagnostics and therapeutics for illnesses that primarily affect the developed world is an idea worth further testing in the marketplace. In essence, it is an integrated market-based approach to addressing the market failures engendered by current financing incentives by efficiently integrating financing with product development. The idea capitalizes on existing tax-code structures, the 501(c)(3) charitable-organization model. The establishment of more nonprofit biotechnology firms would provide alternative partners for academic researchers concentrating on translational research and development in consonance with the FDA's Critical Path Initiative, while removing the increasing public concerns about improper influence associated with profit motive. Critical to success would be the identification of priority diagnostics and therapeutics. In the experience of existing firms, novel agent candidates have been identified primarily from academic technology transfer offices and from for-profit pharmaceutical firms, with compounds either donated in exchange for tax benefits or licensed.

As the final column of Table 1 illustrates, the funding required for the establishment of new nonprofit biotechnological firms is available. As with existing nonprofits, potential initial funding sources include foundations, individuals, and corporations. The focus may also open other sources; for example, contributions could be sought from corporations with high health-care costs, since one goal of firms may be to reduce or stabilize the cost of medical care. Payers could also contribute in return for access to novel agents developed at substantially lower costs, similar to the arrangement deCODE has established with the Icelandic government. The ultimate goal would be for firms to be financially self-sustaining, at least in part through revenues from product sales.

The road ahead

There are good reasons to believe that cancer may be a good area for the future establishment of nonprofit biotechnology firms focused on promising but neglected R&D. In recent years there has been substantial for-profit investment in cancer treatment development. However, translational cancer therapy is arguably the most expensive and scientifically uncertain area of R&D, posing significant threats to for-profit investment.[2,5,6,9]

We believe that the development of pharmacogenomic diagnostics for personalized oncology treatment may be a critical focus of a new nonprofit biotechnology firm. There are a handful of approved diagnostics on the market and promising pharmacogenomic candidates in the middle and later stages of development in academic medical centers and for-profit firms. It is clear that the potential health benefits and cost savings derived from the validation and use of these tests in oncology practice may be substantial. In addition to the potential morbidity and mortality gains accrued from their application to guide oncology treatments for individual patients, we believe that they may have significant social value. Their application may produce cost savings through the reduction of misused or overused treatments. Nevertheless, there has been little investment by for-profit firms in

pharmacogenomic diagnostics to date, for a variety of reasons. Diagnostics have traditionally been difficult to legally protect against competition, because their intellectual property protection is based on use patents and insurance reimbursement is low relative to therapeutics. Furthermore, pharmacogenomic diagnostics are ordered only once in a person's lifetime but may have implications for the treatment of other illnesses over time. The willingness to pay for these tests by any individual payer may not reflect their aggregate social value (all net health benefits and cost savings) given the fractured US insurance system. Like iOWH and the AMF, the company could enter the development process at the point where for-profit firms find it unprofitable to continue R&D or where academic researchers have found no willing private partner. We propose that this new company would retain control of the manufacturing and distribution of its oncology products, although the actual production could be contracted out to for-profit companies. We envision the firm acting as a bricks-and-mortar enterprise, capturing returns to scale and expertise as the other firms listed in Table 1. However, the firm could also function in part as a "virtual" venture in partnership with academic institutions and for-profit companies, similar to iOWH's relationship with the California Institute of Quantitative Biomedical Research, Amyris Pharmaceuticals, and Sanofi-Aventis in its antimalaria project.

We believe that there is already potential scientific and business leadership that could be marshaled toward this purpose. There are many individuals in the for-profit industry and academia with significant expertise in clinical therapeutics and pharmacology, and a commitment to translational oncology product development. The public is rich with individuals with a deep personal commitment to finding effective cancer therapies. Finally, almost one-sixth of health philanthropy in the United States is devoted to cancer research;[10] consequently, funding for a cancer-based nonprofit biotechnology firm may be relatively easy to raise. In contrast to existing cancer charities, an oncology nonprofit would provide private donors the unique opportunity to commit directly to translational R&D.

The establishment of more nonprofit biotechnology firms serving the public's interest has substantial advantages in the current scientific and financing environment. Cancer diagnostics may be a priority focus given the state of financing and translational science, just on the cusp of transforming clinical practice. A nonprofit oncology biotechnology firm would be able to leverage existing investment in R&D by for-profit companies and academia, provide an infrastructure for technology transfer for these partners, and provide private donors with the unique opportunity to commit directly to product development. This focus would establish further proof of principle for more nonprofit biomedical firms focused on socially important R&D in scientifically ripe areas.

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Table 1

Survey of portfolio-based nonprofit biomedical firms, 2008

Name	Primary purpose	Primary population focus	Primary disease focus	Products in clinical trials/ approved	Year of formation	Annual budget	Major grants
Institute for Applied Biomedicine (http://www.appliedbiomed.org)	Financing, development, preclinical testing	Global health	Immune system–based treatments for HIV, autoimmune disorders	Immudel-gp120	1996	$31,236	
Global Solutions for Infectious Diseases (http://www.gsid.org)	Financing, development, and testing	Global health	HIV vaccine, pediatric dengue vaccine		2004	$1,019,073	Gates Foundation, $7.9 million (2006, HIV)
Institute for OneWorld Health (http://www.iowh.org)	Financing, development, and testing	Global health	Anti-infectives	Artemisinic acid/ paromomycin i.m. injection	1998	$23,391,795	Gates Foundation, $42.5 million (2004, artemisin); Gates Foundation, $10 million (2005, paromomycin); Gates Foundation, $46 million (2006, antidiarrhea program)
International Partnership for Microbicides (http://www.ipm-microbicides.org)	Financing, coordination, development, delivery	Women, global health	HIV transmission prevention	Dapivirine, L’644	2002	$18,775,834	
Alfred Mann Foundation (http://www.aemf.org)	Financing, development, and testing	Developed world	Physical medical impairments	Glucose sensor, cochlear implant, implantable microstimulator	1985	$20,735,358	
Institute for Pediatric Innovation (http://www.pediatricinnovation.org)	Financing, development, and testing	Children, developed world	Pediatric NICU, pediatric cardiology		2006	$43,260	

Primary sources: Initiative for Public-Private Partnerships for Health (http://www.globalforumhealth.org) and GuideStar (http://www.guidestar.org); secondary sources: IRS 501(c)(3) records (http://www.irs.gov) and searches of individual companies’ websites. NICU, neonatal intensive care unit.