

ADVANCES IN DRUG DEVELOPMENT

Current Developments in Oncology Drug Research

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The Societal Benefit of Nonprofit Biotechnology Companies

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H&O What is the unmet need to which nonprofit biotechnology companies could respond?

RC Biotechnology investments are risky due to significant scientific and regulatory uncertainty. The high failure rate of oncology drug development has concentrated investor enthusiasm toward later stages of development in biotechnology, even as venture capital investment in the industry overall remains high. Uncertain regulatory enforcement, increasing political scrutiny of the prices of novel treatments and company profits, and the recent economic downturn appear to be operative in the stagnation of venture capital investment in biotechnology. Taken together, these forces push biotechnology research and development into areas meeting specific investment criteria. By necessity, for-profit biotechnology firms that are primarily financed by external funds require the expected profit associated with innovative product development to be large enough to cover research and development (R&D) expenses and the opportunity costs of capital investment, both in a timely way. Consequently, for-profit firms tend to focus efforts on the development of drugs or small molecules where the protection of intellectual property is clearly defined and legally defensible, the target population is large enough to potentially benefit from treatment and willing and able to pay for treatment innovation, and scientific uncertainty is minimized to the extent possible.

Taking scientific uncertainty in any R&D endeavor as a given, it is believed these incentives result in a variety of challenges: 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; the protection of intellectual property rights, particularly in the developing world; the size of the target population; and the nature of insurance coverage and reimbursement policy.

H&O How would nonprofit biotechnology companies be organized?

RC In essence, the nonprofit model is an integrated market-based approach to address the market failures engendered by current financing incentives through the efficient integration of financing with drug development. The non-profit biotechnology model capitalizes on existing tax-code structures—the 501(c)(3) charitable organization model—successfully used by all private academic institutions in the United States, existing nonprofit biotechnology firms, and nonprofit venture capital firms. The charitable 501(c)(3) organization model is also widely used in the healthcare market to deliver services. The nonprofit biotechnology model requires a leadership team with substantial expertise in clinical pharmacology and therapeutics, the design and implementation of clinical trials, and fundraising and regulatory affairs. Deep relationships with the for-profit industry and academia are critical in identifying middle- and late-stage products in development that may be donated or licensed to the firm. Finally, a commitment to furthering the social good and passion for pursuing the values of the firm through product development and approval are critical for success.

H&O Does the nonprofit model suit either the developed or the developing world better?

RC Current financing incentives appear to adversely affect R&D for technologies that would have significant societal benefit in the developed world but little opportunity for a high return on investment: treatments for pediatric patients with little adult analog, diagnostics to better guide use of existing medications, and therapies that are available generically or over-the-counter applied to alternative illnesses or populations. There has been a tendency to rely upon 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. The Best Pharmaceuticals for Children Act

and the Orphan Drug Act are prominent examples. The 2007 US Food and Drug Administration (FDA) priority voucher policy provides a direct financial incentive for the development of therapies for tropical diseases primarily affecting the developing world, with a strong emphasis on early-stage investment. To what degree this incentive spurs significant investment in R&D, translating into novel product development and approval, is uncertain at this time. Importantly, this incentive does not address financing problems in the developed world.

Nonprofit ventures are increasingly being established to address these concerns. Prominent example focus on the financing and/or development of global health products, such as the nonprofit biotechnology firm the Institute for One World Health (iOWH; www.oneworldhealth.org) and the nonprofit financing firm BIOVentures for Global Health. Both have been generously supported by the Gates Foundation, the biotechnology industry itself, and private individuals. Given the market failures in the developed world, there is no a priori reason why the nonprofit biotechnology firm model in use for the developing world would not also work in the developed world. We already see a number of firms aiming to complete product development for neglected developed-world populations.

H&O What current examples demonstrate the nonprofit model's success?

RC There are numerous firms that focus on coordinated financing and development of single agents, but it is believed firms with a portfolio strategy based on neglected diseases, populations, or technologies are the future. For example, the iOWH is perhaps the most successful example of a nonprofit pharmaceutical company devoted to the development of anti-infectives for the developing world. The company started with a low-risk project, resuscitating a drug that had gone off patent and was no longer available. Paromyocin for the treatment of visceral leishmaniasis was approved by the Drug Controller General of India last year. iOWH has been extremely successful at raising money to support its efforts; the Gates Foundation granted the organization \$42.5M in 2002. Already, iOWH is acting as an alternative funder for external ventures: Berkeley-based Amyris Biotechnology received \$12M last year for the development of an antimalarial product when it could not raise private financing. The Alfred E. Mann Foundation for Biomedical Engineering (www.aemf.org), founded in 1986, 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. The Institute for Pediatric Innovation (IPI; www.pediatricinnovation.org) is a new venture dedicated to the development and reformulation of drug-based treatments and devices for children, particularly the neonatal intensive care unit and

pediatric cardiology. IPI shows much promise, given its leadership team, partnerships with the leading children's hospitals in the United States, and focus on clinical areas where product development means literally the difference between life and death for children. For these companies, a focus on a set of neglected diseases, populations, and technological strategies allows for coordinated efforts to fundraise and identify, prioritize, and invest in complementary scientific efforts dedicated to maximizing social value.

H&O What are the next steps for the community at large toward more broadly adopting the nonprofit model?

RC It is believed the establishment of more nonprofit biotechnology 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. The establishment of more nonprofit biotechnology firms would provide alternative partners for academic researchers focused on translational treatment development in consonance with the FDA's Critical Path Initiative, while removing increasing public concerns about improper influence associated with profit motive. There are 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 the development of cancer therapeutics. However, translational cancer therapy is arguably the most expensive and scientifically uncertain area of R&D.

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 diagnostic 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, it is believed the development and use of these tests may have significant social value from cost savings through the reduction of misused or overused treatments. Still, there has been little investment by for-profit firms in pharmacogenomic diagnostics to date, possibly explained by the fact that diagnostics have traditionally been difficult to legally protect against competition because their intellectual property protection is based on use patents and insurance reimbursement for them has traditionally been low relative to therapeutics. Furthermore, pharmacogenomic

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diagnostics are ordered only once in a person's lifetime but may have implications for the treatment of other cancers and medical illnesses. The willingness to pay for these tests by any individual insurance company may not reflect their aggregate social value across all health benefits or any potential cost savings, given the fractured coverage system of the United States. Like iOWH, a firm could enter the pharmacogenomic diagnostic development process at the point at which for-profit firms find it unprofitable to continue R&D or when academic researchers have found no willing government or for-profit firm to partner with for further investment.

Scientific and business leadership 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. Almost one sixth of health philanthropy in the United States is devoted to cancer research; consequently funding for a cancer-based nonprofit biotechnology firm maybe relatively easy to raise.

In sum, a nonprofit oncology biotechnology firm

would allow for the leveraging of existing investment in the early stages of R&D by for-profit companies and academia, provide an infrastructure for technology transfer for these partners, and provide private donors the unique opportunity to commit directly to translational R&D (in contrast to existing cancer charities), with the goal of serving the public's interest. Ultimately, this focus would establish proof of principle for the establishment of nonprofit biopharmaceutical firms focused on other socially important, but neglected, areas for investment by for-profit firms in the future.

Suggested Readings

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