Improving the Incentives of the FDA Voucher Program for Neglected Tropical Diseases

Cameron Graham Arnold
Master's Student
London School of Hygiene and Tropical Medicine

Thomas Pogge
Director of Global Justice Program
Yale University

The largest Ebola outbreak to date—first detected in December 2013 and still ongoing as of April 2015—has cast new light on the shortfalls of international public health systems.[1] As in previous health crises, scrutiny has reemerged over the pharmaceutical industry's ability and willingness to innovate new medicines for underserved disease areas. The public debate has intensified following revelations that promising drug candidates to treat Ebola had gone undeveloped despite compelling preclinical results.[2] This lack of development is especially troubling because it occurred after a recently implemented U.S. incentive scheme—the Food and Drug Administration's (FDA) tropical disease priority review voucher program—designed to counteract exactly this problem.

224

Cameron Graham Arnold is currently completing a Masters of Science in Public Health at the London School of Hygiene and Tropical Medicine with a focus in health economics. He has nearly five years of experience working in various analytical roles within the biopharmaceutical industries in Denmark and the United Kingdom. Arnold is the recipient of two Richard U. Light Fellowships and holds a Bachelor of Arts from Yale University, where he majored in East Asian literature and Mandarin Chinese. He will matriculate to medical school in fall 2015.

Thomas Pogge is Leitner Professor of Philosophy and International Affairs and founding Director of the Global Justice Program at Yale University. He holds part-time positions at King's College London and the Universities of Oslo and Central Lancashire. Pogge is a member of the Norwegian Academy of Science, as well as President of Academics Stand Against Poverty (ASAP) and of Incentives for Global Health. Pogge's recent publications include *Politics as Usual* (Polity 2010); *World Poverty and Human Rights* (Polity 2008); and *Freedom from Poverty as a Human Right* (Oxford & UNESCO 2007).

Taking Ebola as a case in point, it is useful to examine the short history and ongoing refinement of this voucher program, since it represents one of the most significant legislative efforts to systematically address the relative absence of commercial rewards for drugs targeting tropical diseases. This analysis evaluates the voucher program's effectiveness for both stimulating private sector innovation and achieving positive health impacts among populations most severely burdened by tropical diseases. It then proposes specific recommendations for how lawmakers can improve the program's legislation to better achieve these objectives.

Background

Investment by private pharmaceutical companies into the research and development (R&D) of novel medicines targeting neglected tropical diseases (NTDs) has historically been limited by poor prospects for adequate financial returns. NTDs remain significant causes of morbidity and mortality globally, and developing countries and poor populations bear nearly all of this burden.[3] Under the rules of the Trade Related Aspects of Intellectual Properties Rights (TRIPS) agreement, administered by the World Trade Organization (WTO), patients and governments with scant financial resources do not constitute attractive markets for a profit-driven industry because they can rarely pay the high markups on patented therapies. Since commercial gain is the core consideration driving private sector investment, NTD pharmaceutical research often fails to progress into the high-cost clinical phases of development. The overall rate of new drug authorizations for NTDs, measured by the number of FDA approvals in the past 50 years, has languished in comparison to those for more lucrative disease areas such as chronic illnesses (e.g., diabetes or rheumatoid arthritis) that afflict affluent, increasingly senescent populations.[4] The pharmaceutical industry's persistent reluctance to address the enormous unmet medical needs associated with NTDs is therefore justifiably considered a critical market failure.

Pharmaceutical research for neglected tropical diseases often fails to progress into the high-cost clinical phases of development.

Public frustration with this failure has stimulated various solutions aimed at directing innovation and commercialization efforts to areas where they have previously been lacking. In 1983, the U.S. Congress passed the Orphan Drug Act (ODA) to make it more economically viable for pharmaceutical companies to pursue R&D for drugs targeting rare, or orphan, diseases. This class of diseases

included any disease affecting fewer than 200,000 Americans or, alternatively, a disease affecting a number of Americans above that threshold but for which the costs of drug development and marketing could not reasonably be expected to be recovered from U.S. sales.[5] The legislation coordinated several incentives, including federal tax credits for up to half of clinical testing costs, faster FDA regulatory review, and an extension of market exclusivity from five to seven years.[6] The first two incentives are push mechanisms, subsidizing the inputs of research, while the third acts as a pull mechanism, using a reward to entice companies to bring to market drugs previously thought to be unprofitable. Thirty years later, the FDA considers the ODA to have succeeded in increasing the rate of pharmaceutical innovation against rare, predominately genetic diseases that affect Americans.[7] This success can be partially attributed to the surprising profitability of breakthrough drugs where there had previously been few, if any, treatment options. This profitability, in turn, was driven by a strong disposition among healthcare purchasers in high-income countries to pay for these drugs at high prices.

The ODA's legacy for NTDs, on the other hand, is considerably less impressive. Its incentives have not been sufficient to increase the rate of FDA–approved drugs for NTDs to the same degree that they appear to have done for rare diseases affecting affluent populations. Evidently, such subsidies, generous as they are, are not enough when prospective gains from commercialization are poor. To address this deficit, a wholly new type of reward—an FDA priority review voucher—was adopted with the passage of the FDA Amendments Act of 2007.[8] Compared to the ODA, which significantly subsidizes the inputs of innovation ("push"), the priority review voucher program rewards only the successful outputs of the pharmaceutical R&D process. The vouchers, therefore, serve exclusively as a pull mechanism to stimulate the development of drugs that might not otherwise be brought to market due to insufficient sales potential.

Under the voucher system, any drug approved by the FDA for preventing or treating certain listed NTDs will earn its pharmaceutical owner a priority review voucher. The recipient company can then use the voucher to substantially accelerate FDA review for any other drug candidate in its pipeline. The voucher achieves this by changing the status of the new drug application from standard to priority review, wherein the FDA aims to process the application within six months rather than 10. While review times vary from year to year for both review designations, priority review designation lengthens the time that a drug can be sold with a patent-protected markup by roughly four months, since earlier market entry does not affect patent expiry.[9] Vouchers are therefore

likely to be used where they would generate the most revenue: on prospective blockbuster drugs with enormous sales potential. Also critical to the value of a voucher is that it can be sold by one company to another. David Ridley et al., who originally proposed the idea of the voucher mechanism in a *Health Affairs* paper in March 2006, estimated that a priority review voucher used to extend the effective patent life of a high grossing drug might be worth more than $300 million.[10] The voucher program quickly attracted attention on the world stage after it was signed into law. At the 2008 World Economic Forum, Bill Gates used the voucher program as an example of "the highest-leverage work that governments can do…to set policy to create market incentives for business activity that improves the lives of the poor."[11]

Whether or not the FDA voucher program is considered successful depends on its ability to increase the rate of pharmaceutical innovation for NTDs and improve health outcomes in endemic regions. Due to the slow pace of drug development, it is still too early in the program's history to assess its impact. Nonetheless, looking back over the seven years since the voucher mechanism was adopted, there are signs that it may not be functioning as intended. Therefore, it is worth considering how effective the criteria of the program—that is, the specific reward and use requirements associated with the vouchers—have been thus far in facilitating pharmaceutical innovation and health gains.

Reviewing the FDA Priority Review Voucher Program: 2007–2014

To date, four tropical disease priority review vouchers have been awarded. Most recently, in March 2014, the FDA approved miltefosine for the treatment of leishmaniasis, one of the 16 tropical diseases eligible for reward under the program. Knight Therapeutics, which acquired certain marketing rights to miltefosine from Paladin Therapeutics following a spin-off transaction in early 2014, picked up a priority review voucher for the drug's successful U.S. registration.[12] Controversy followed. Notably, while miltefosine had never been legally authorized in the United States, it had been used abroad for over a decade. At the time of its FDA approval, miltefosine was registered for use in treating the cutaneous and visceral forms of leishmaniasis in over a dozen countries.[13] The burden of disease was, and continues to be, greatest in most of these countries located either in the Indian subcontinent or Latin America. Additionally, according to Médecins Sans Frontières (MSF), clinical testing of the compound in the 1990s and early 2000s had been conducted predominately by the WHO/TDR program with public and private funding.[14] It thus seemed problematic that, long after milt-

efosine had been developed by others, a company was rewarded with a voucher for securing its approval in the United States, where the drug's use was likely to be very limited. It also seemed problematic that a voucher could be awarded to a drug already in use in endemic regions. But there was no mistake: awarding the priority review voucher for miltefosine's FDA approval was appropriate under the program's legislation. After incurring an estimated $10 million in costs related to the FDA regulatory filing of miltefosine, Knight sold the voucher to Gilead Sciences on 19 November 2014 for $125 million.[15] The case is an important example of the extent to which loopholes in the legislative details of the voucher program can severely undermine its intended functionality.

As the vouchers awarded to Knight Therapeutics and Novartis illustrate, a company can collect a voucher without contributing any new innovation.

Similar controversy surrounded the issuance of the first voucher under this program in 2009, which Novartis received upon FDA approval of the drug artemether-lumefantrine (AL) for the treatment of malaria.[16] As was the case with miltefosine, the AL combination had already been included for several years on WHO's Model List of Essential Medicines before being registered in the United States. Furthermore, AL had had a long history of authorized use in countries where malaria is a major threat to public health.[17] Before the voucher scheme, there was little reason for pharmaceutical companies to incur the costs associated with FDA review for drugs targeted at tropical diseases not endemic in the United States. The introduction of the voucher scheme created a powerful incentive for companies to register drugs in the United States that had been developed and used abroad before the scheme was adopted. As the vouchers awarded to Knight Therapeutics and Novartis illustrate, a company can collect a voucher without contributing any new innovation. This possibility defeats a core purpose of the scheme and represents a critical oversight in the original legislation. To close this loophole, the U.S. Congress must approve additional criteria for voucher eligibility to ensure that R&D conducted prior to the voucher scheme is ineligible for reward.

There are also indications that the priority review vouchers, as currently designed, do not induce pharmaceutical companies to provide access to winning drugs. At present, there are no provisions linking the award of a voucher to any requirements that the winning drug be affordably priced for its manufacture, registration in endemic countries, or technology transfer of any kind. To receive

a voucher for its new drug, a company must only win approval for it in the United States; it is not required to make any efforts to facilitate access to this drug for those who need it.

After AL, bedaquiline (BDQ) earned the second priority review voucher following its FDA approval in December 2012 for the combination treatment of multidrug-resistant tuberculosis (MDR-TB).[18] As the first drug to be approved for pulmonary MDR-TB in more than 40 years, BDQ clearly represented the kind of novel, breakthrough therapy that the voucher scheme was intended to reward. The company responsible for BDQ's commercialization, Janssen Pharmaceuticals, subsequently initiated regulatory filings in countries with significant prevalence of MDR-TB including Russia, India, China, Colombia, Peru, Thailand, and Vietnam.[19] Janssen has additionally announced the donation of 30,000 courses of treatment and supported a pilot study of BDQ for the Health Impact Fund, a novel incentive scheme also seeking to spur pharmaceutical innovation in NTDs. Despite these efforts, MSF's Access Campaign has criticized Janssen because reportedly very few MDR-TB patients have been treated with BDQ in the two years since its approval in the United States.[20] Civil society and advocacy NGOs like MSF have also identified the drug's tiered pricing for a six-month course—$30,000, $3,000, and $900 respectively for high-, middle-, and low-income payers—as insufficient to facilitate sustainable access in low- and middle-income countries. They have coordinated efforts to request that Janssen either lower the price of BDQ for poor patients to approximate the drug's cost of production or grant non-exclusive voluntary licenses when appropriate.[21] Similar requests have been made of Knight Therapeutics for miltefosine, which has presented similar access issues for healthcare providers in endemic countries.[22] Thus far, these requests have not been heeded.

NGO criticism of the FDA voucher program has targeted two deficiencies of the program in particular: 1) that it rewards the registration of old drugs in the United States even if they are not needed there and 2) that it rewards the mere approval of drugs without requiring that they be made accessible to patients who need them. However, the ongoing Ebola epidemic in West Africa has drawn attention to another flaw: the absence of Ebola and the filovirus family from the original list of 16 NTDs eligible for reward under the voucher program.

This omission presumably occurred because, when drawing up its list in 2006–07, the FDA consulted WHO's Department of Control of Neglected Tropical Diseases—which does not recognize Ebola or the filovirus family due to the historically low mortality and morbidity they had caused as compared to other NTDs prevalent in developing countries.[23] Before the current outbreak,

Ebola had been responsible for approximately 1,500 deaths since its original classification in 1976.[24] Almost any infectious disease standard would therefore assess the cumulative mortality from Ebola to be small. As a point of comparison, tuberculosis and malaria respectively account for about 1.5 and 0.6 million annual deaths worldwide.[25] Ideally, had Ebola been included in the original list of eligible NTDs, promising drug candidates that target the disease might have attracted investment and entered clinical trials. Instead, auspicious early research stalled due to a lack of interest from the private sector. VSV-ZEBOV, a vaccine candidate originally discovered by a group of Canadian scientists in Winnipeg, faced this very scenario. Results from a preclinical trial in macaque monkeys, published in *Nature* in June 2005, looked promising: the compound demonstrated good safety and was completely effective in protecting all of the treated monkeys against Ebola.[26] The researchers were thus optimistic that the compound would soon be licensed to a pharmaceutical partner and proceed to human testing. But given poor profit prospects, it was not until five years later that a willing collaborator, Newlink Genetics, emerged. Furthermore, it was not until four years after that, in October 2014, that VSV-ZEBOV began its first Phase I trial in humans—after 14,000 people in West Africa had been infected in the Ebola outbreak.[27]

Unfortunately, even if Ebola had been on the list of voucher-eligible disease targets, it is likely that VSV-ZEBOV and other Ebola vaccine candidates still would not have seemed sufficiently rewarding for industry to take on the costs of clinical trials. Pharmaceutical development today necessitates participation from at least one private company partner to help shoulder the high clinical trial costs involved in bringing a drug to market. Strategic decisions about R&D investment are thus made in a climate of opportunity costs, where scarce resources are necessarily allocated to ventures that offer the most attractive risk-reward profile from the perspective of shareholders. Before the most recent outbreak, Ebola's impact was confined to small regions in rural West Africa and did not figure prominently on major national and international public health agendas. A priority review voucher would have existed as the lone commercial reward for any effective Ebola vaccine. Considering the costs of modern vaccine development, often estimated at upward of $1 billion, a voucher valued in the

Even if Ebola had been on the list of voucher-eligible disease targets, it is likely that it still would not have seemed sufficiently rewarding for industry to take on the costs of clinical trials.

low $100 million range is not large enough to stimulate the needed investment on its own.[28] This is not to imply that the voucher mechanism is destined to be ineffective, but that it is important to recognize that additional incentives may be needed to draw private pharmaceutical investment into NTD research.

Political visibility can play an important role here. Following the Global Health Security Agenda Summit on 26 September 2014, where Ebola featured prominently, both the United States and European Union committed significant funds to address the crisis. The Innovative Medicines Initiative, a European public–private pharmaceutical partnership, announced the Ebola+ program, which commits approximately $350 million to vaccine and diagnostic R&D.[29] Risk sharing with the public sector, a form of input subsidy, will continue to be crucial to generating interest from industry in otherwise unprofitable areas of research.

Suggestions for Amending the FDA Priority Review Voucher Program

The U.S. Congress revised the FDA priority review voucher program on 16 December 2014, choosing to incorporate three changes. First, Ebola and the filovirus family were formally included on the list of tropical diseases eligible for reward.[30] The second change permitted vouchers to be sold between companies any number of times. The third reduced the advance notice required to use a voucher from one year to 90 days. These are positive amendments to the program, since they enhance the value of priority review vouchers and will thereby encourage greater interest in NTD drug candidates within the industry.

However, these amendments fall short by failing to correct the voucher mechanism's two most critical problems: 1) that it pointlessly rewards old innovation and 2) that it fails to set reasonable expectations for access to rewarded drugs. To address the former, the program's rules must be changed to ensure that drugs approved in other jurisdictions before a certain cut-off date—for example, the program's legal enactment on 27 September 2007—are ineligible for a voucher in the event of FDA approval. This is a better solution than categorically disqualifying drugs previously registered abroad because it does not discourage companies from seeking regulatory approval in endemic regions first and foremost.

To confront the issue of access, the program must incorporate new rules that make explicit demands of companies that seek or win a voucher. First, any company trying to win a voucher should first be required to demonstrate that certain reasonable efforts are being made to facilitate access to its new drug in

endemic regions. This would include, at a minimum, that companies already have formally applied for regulatory approval in affected countries. The approvals themselves would not be necessary prerequisites for receiving a voucher because the duration and outcome of this process are beyond any company's control. But as a condition of receiving a voucher, companies should be required to show that they have competently sought such marketing approval. Requiring this step prior to awarding a voucher would ensure that a winning drug is receiving solid support toward being made available to patients in affected regions.

In addition, any company receiving a priority review voucher should be contractually obligated to make the drug genuinely accessible to those who need it. This could be accomplished in a number of ways. The company could itself manufacture and market the drug to poor patients at an affordable price, potentially as low as the cost of manufacturing. Alternatively, the company could give cost-free, voluntary licenses to reliable generic producers to facilitate the same outcome. The Health Impact Fund has proposed both methods as potential solutions to a similar problem concerning drug access in developing countries.[31] Full voluntary licensing would entail the innovator company granting other pharmaceutical companies the right to produce, import, and distribute their drug in certain regions.[32] These licenses could either be extended on an exclusive or non-exclusive basis, depending on the context. In regions with a competitive generics industry, non-exclusive licenses have been found to work well, driving down drug prices by encouraging competition among manufacturers. It would also be instructive to examine the experience of the Medicines Patent Pool (MPP), a venture initially developed to improve access of HIV/AIDS medicines to patients in developing countries.[33]

One way to make exclusive licensing attractive in markets without a competitive generics industry is to use a request for tenders to award the exclusive license to the firm that commits to ensuring a reliable supply at the lowest sales price. The tendering process would encourage companies competing for the exclusive license to bid the drug price down in order to win the opportunity to supply the entire market. China and New Zealand are examples of markets in which tendering systems have been effective in facilitating low drug prices for patients.[34]

There is an additional reason in favor of exclusive licensing when drug resistance is an issue. If only one company were responsible for marketing the drug in a given region, it would be strongly incentivized to avert drug resistance emerging in the population. The reason is simply that the company would exclusively bear any future losses resulting from lower sales volume. With non-

exclusive licensing, by contrast, each licensee would suffer only a fraction of the future losses (while still collecting the full gain) resulting from its lax distribution practices. Therefore, the incentive to invest in averting drug resistance would be much weaker in that scenario.

It should also be permissible for pharmaceutical companies receiving a voucher to provide a more limited type of license, which would grant another company the right to manufacture the drug but not to market it. This applies equally to the non-exclusive and exclusive licensing scenarios described previously. One of the key advantages of limited licensing over full voluntary licensing is that generic manufacturers do not need to obtain regulatory approval for the production of the drug—that responsibility falls on the innovator pharmaceutical company. This condition is beneficial because approval only needs to be achieved by one company as opposed to many. All of these distribution methods should be acceptable under the voucher scheme to provide the rewarded company with a range of options for how to provide effective access to the drug in endemic regions. A company failing to make any of these kinds of efforts toward securing effective access for its rewarded medicine would be subject to a financial penalty. A daily fine, levied for every day in breach of contract, would be an effective way of incentivizing companies to fulfill their added drug access obligations under the voucher program.

Conclusion

Amending the FDA priority review voucher program for neglected tropical diseases is absolutely critical if the program is to function effectively. Loopholes in the current legislation undermine the mechanism's ability to promote pharmaceutical innovation in NTDs and to ensure that winning drugs have a strong chance of reaching the patients that need them most. The Ebola outbreak in West Africa is a powerful reminder of the downstream effects that health crises originating in the developing world can have on geopolitical stability and the global economy. To successfully address future challenges, governments must not only bring public resources to bear but also use legislation to galvanize the efforts of industry. In particular, governments should try harder to more effectively align the economic incentives guiding private pharmaceutical investment with the broader interests of public health.

The short history of the voucher scheme has demonstrated that pharmaceutical companies can be rewarded without achieving improvements in innovation or health. To ensure that the law functions as intended, three changes must be

made. First, drugs approved in other countries before the original legislation was enacted should not be eligible for the reward. Second, a company must demonstrate that it has sought approval for its drug in endemic countries as a precondition for receiving a voucher. Third, contractual access requirements must be included to compel a company either to manufacture and distribute the drug itself, or to pursue licensing agreements to facilitate access in collaboration with commercial partners. Once these loopholes are closed, there is reason to be optimistic about the reward's ability to motivate more effective private sector involvement in the fight against NTDs. WA

Notes

1. WHO Global Alert and Response, "Ground zero in Guinea: the outbreak smoulders—undetected—for more than 3 months," World Health Organization.

2. Denise Grady, "Ebola Vaccine, Ready for Test, Sat on the Shelf," *New York Times*, October 23, 2014.

3. World Health Organization, *Investing to Overcome the Global Impact of Neglected Tropical Diseases: Third WHO Report on Neglected Tropical Diseases* (Geneva: World Health Organization, 2015).

4. U.S. Food and Drug Administration, *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations* (Silver Spring, MD: U.S. Food and Drug Adminstration, 1984).

5. "Developing Products for Rare Diseases & Conditions," U.S. Food and Drug Administration, February 26, 2015.

6. Aaron S. Kesselheim, "Innovation and the Orphan Drug Act, 1983–2009: Regulatory and Clinical Characteristics of Approved Orphan Drugs," in *Rare Diseases and Orphan Products: Accelerating Research and Development*, ed. Thomas F. Boat and Marilyn J. Field (Washington, DC: National Academies Press, 2010).

7. Matthew T. Thomas, "The Orphan Drug Act and the Development of Products for Rare Diseases," Office of Rare Disease Research at the FDA, September 13, 2012.

8. "Food and Drug Administration Amendments Act (FDAAA) of 2007," U.S. Food and Drug Administration, December 2, 2011.

9. U.S. Government Accountability Office (GAO), "Prescription Drugs: FDA Has Met Most Performance Goals for Reviewing Applications," GAO, March 2012.

10. David B. Ridley, Henry G. Grabowski, and Jeffrey L. Moe, "Developing Drugs for Developing Countries," *Health Affairs* 25, no. 2 (2006): 313–24.

11. Bill Gates, "A New Approach to Capitalism in the 21st Century," World Economic Forum 2008, January 24, 2008.

12. Knight Therapeutics, "Knight Therapeutics Inc. to begin trading on March 3, 2014," *Knight Therapeutics*, February 28, 2014; Knight Therapeutics, "Knight Therapeutics Inc. Announces FDA Approval for Impavido® (Miltefosine) for the Treatment of Visceral, Mucosal and Cutaneous Leishmaniasis—Awarded Priority Review Voucher," Knight Therapeutics, March 19, 2014.

13. "Application for Inclusion of MILTEFOSINE on WHO List of Essential Medicines," World Health Organization, November 2010.

14. "Patient Access to Miltefosine in Developing Countries Not Secure Despite Award of US FDA Priority Review Voucher Sold for USD 125 Million," Drugs for Neglected Diseases Initiative, November 25, 2014.

15. "Knight Sells Priority Review Voucher to Gilead," Knight Therapeutics, November 19, 2014.

16. "FDA Approves Coartem Tablets to Treat Malaria," U.S. Food and Drug Administration, April 8, 2009.

17. "Review of Application for Inclusion of a Drug in the WHO Essential Drugs List," World Health Organization, March 18, 2012.

18. Janssen Research & Development, LLC, "U.S. FDA Grants Priority Review to Bedaquiline (TMC207) for Multi-Drug Resistant Tuberculosis Treatment," PR Newswire, September 5, 2012.

19. "SIRTURO® (bedaquiline) Receives Conditional Approval in the European Union for the Treatment of Multi-Drug Resistant Tuberculosis," Johnson & Johnson, March 6, 2014.

20. "MSF response to Janssen's bedaquiline donation announcement," MSF Access Campaign, December 12, 2014.

21. AIDS-Free World et al., "Open letter: Reducing the price of bedaquiline," AIDS-Free World, September 10, 2014.

22. MSF Access Campaign, "Patient Access to Miltefosine in Developing Countries Not Secure Despite Award of US FDA Priority Review Voucher Sold for USD 125 Million," Drugs for Neglected Diseases Initiative, November 25, 2014.

23. "Neglected Tropical Diseases," World Health Organization, December 12, 2014,

24. "Ebola Virus Disease Distribution Map," *Centers for Disease Control and Prevention*, January 23, 2015.

25. World Health Organization, "Executive Summary" in *Global Tuberculosis Report 2014* (Geneva, World Health Organization, 2014); World Health Organization, *World Malaria Report 2014* (Geneva, World Health Organization, 2014), x.

26. Steven M. Jones et al., "Live attenuated recombinant vaccine protects nonhuman primates against Ebola and Marburg viruses," *Nature Medicine* 11, no. 7 (2005): 786.

27. "Safety and Immunogenicity of Prime-Boost VSV Ebola Vaccine in Healthy Adults," ClinicalTrials.gov, October 29, 2014.

28. Arianna Waye et al., "Vaccine Development Costs: A Review," *Expert Review of Vaccines* 12, no. 12 (2013): 1495–1501.

29. Innovative Medicines Initiative, "Innovative Medicines Initiative Launches Ebola+ Programme," *Innovative Medicines Initiative*, November 6, 2014.

30. "S.2917—Adding Ebola to the FDA Priority Review Voucher Program Act," 113th Congress, Library of Congress, December 16, 2014.

31. "A Summary Overview," The Health Impact Fund.

32. "Cost-Containment Mechanisms for Essential Medicines, Including Antiretrovirals, in China—Health Economics and Drugs Series No. 013," World Health Organization, 2003.

33. Krista L. Cox, "The Medicines Patent Pool: Promoting Access and Innovation for Life-Saving Medicines Through Voluntary Licenses," *Hastings Science & Technology Law Journal* 4, no. 2 (2012): 293–326.

34. Mariko Watanabe and Shi Luwen, "Institution on Pricing," in *Pharmaceutical Industry in China: Intellectual Property Protection, Pricing and Innovation*, ed. Chen Xiaohong and Mariko Watanabe (Tokyo: Institute of Developing Economies Japan External Trade Organization, 2007), 24–9; Steve Morgan et al., "Influencing Drug Prices Through Formulary-Based Policies: Lessons from New Zealand," *Healthcare Policy* 3, no. 1 (2007): 121–40.