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## Finding a Cure: Incentivizing Partnerships Between Disease Advocacy Groups and Academic Commercial Researchers

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# FINDING A CURE: INCENTIVIZING PARTNERSHIPS BETWEEN DISEASE ADVOCACY GROUPS AND ACADEMIC AND COMMERCIAL RESEARCHERS

ANNE M. READEL, PH.D.\*

I.	INTRODUCTION .....	286
II.	PARTNERSHIPS BETWEEN DISEASE ADVOCACY GROUPS AND ACADEMIC AND COMMERCIAL RESEARCHERS: THE RISE OF VENTURE PHILANTHROPY .....	288
	A. <i>Disease Advocacy Group Funding for “De Novo” and “Repurposed” Drug Research</i> .....	288
	B. <i>The Shift from the Charitable Granting to Venture Philanthropy</i> .....	290
	C. <i>Benefits of the New Model: Removing Risk and Closing Funding Gaps</i> .....	291
III.	LEGAL AND SOCIAL ISSUES SURROUNDING THE VENTURE PHILANTHROPY MODEL .....	293
	A. <i>Structuring the Partnership</i> .....	293
	B. <i>Legal Issue: Seat on the Board of Directors</i> .....	293
	C. <i>Social Issue: Should Nonprofits be Making such Risky Investments?</i> .....	296
	D. <i>Despite these Concerns, Venture Philanthropy has Proven Its Value in Advancing Disease Research</i> .....	297
IV.	INCENTIVIZING PUBLIC-PRIVATE PARTNERSHIPS FOR DISEASE RESEARCH .....	298
	A. <i>Patent Law</i> .....	299
	3. A Proposal for Broader Experimental Use and Safe Harbor Exceptions for Orphan Drug Development .....	302
	B. <i>Priority Review Vouchers</i> .....	304
V.	WHEN A NEW DRUG IS DISCOVERED, SHOULD DISEASE ADVOCACY GROUPS CONTROL PRICING AND ACCESS? .....	308

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A.	<i>Orphan Drugs can be Expensive and May Not be Accessible to Everyone Affected by the Disease.....</i>	308
B.	<i>Public-private Partnership Contracts for Tiered Pricing Systems are a Good Mechanism to Control Orphan Drug Prices .....</i>	310
VI.	CONCLUSION .....	313

*Collaborations between for-profit drug companies and not-for-profit disease advocacy groups have risen in recent years in an effort to find cures for orphan diseases. These unique and beneficial collaborations are a result of disease advocacy groups assuming a more active role in drug development through the use of “venture philanthropy,” which employs concepts and techniques from venture capitalism and applies them to achieving philanthropic goals. While these collaborations have found remarkable success, such as the discovery of the first known cure for cystic fibrosis in 2012, venture philanthropy for drug discovery presents numerous legal and social challenges. This Article examines the challenges presented by these novel partnerships and suggests ways that changes in the law or regulations can promote these partnerships without undue harm to the overall goal of advancing research toward cures for patients. The Article further addresses the issue of when a new product is discovered, if and how disease advocacy groups should control drug pricing and patient access to the new drug.*

#### I. INTRODUCTION

*“The unique and mutually beneficial partnership that led to the approval of Kalydeco serves as a great model for what companies and patient groups can achieve if they collaborate on drug development.”<sup>1</sup>*

In January 2012, the FDA approved a new breakthrough drug for cystic fibrosis: Kalydeco (ivacaftor), the first available drug that treats the cause and not just the symptoms of cystic fibrosis.<sup>2</sup> Cystic fibrosis is the most common fatal genetic disease among Caucasians, affecting approximately 30,000 people in the United States.<sup>3</sup> The average life expectancy for people with the disease is thirty-eight years.<sup>4</sup>

<sup>1</sup> Press Release, U.S. Food and Drug Admin., FDA approves Kalydeco to treat rare form of cystic fibrosis (Jan. 31, 2012), <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm289633.htm>.

<sup>2</sup> *Id.* Cystic fibrosis causes abnormally thick mucus in the lungs and digestive tract. *Id.* The drug Kalydeco (ivacaftor) is for the treatment of a rare form of cystic fibrosis in patients ages 6 years and older who have the specific G551D mutation in the Cystic Fibrosis Transmembrane Regulator (CFTR) gene. *Id.* Of the approximately 30,000 people affected with the disease in the United States, roughly 1,200 people (4%) are believed to carry the G551D mutation. *Id.* While Kalydeco only treats a relatively rare form of cystic fibrosis, it may lead to additional drugs that treat people impacted by other forms of cystic fibrosis. *FDA Approves Kalydeco (VX-770) — First Drug That Targets the Underlying Cause of Cystic Fibrosis*, CYSTIC FIBROSIS FOUND. (Jan. 31, 2012), <http://www.cff.org/aboutCFFoundation/NewsEvents/2012NewsArchive/1-31-FDA-Approves-Kalydeco.cfm>.

<sup>3</sup> See Press Release, *supra* note 1.

While the gene that causes cystic fibrosis was discovered in 1989,<sup>5</sup> it has taken over two decades and a unique collaboration to find a cure.<sup>6</sup>

The collaboration that gave rise to this drug discovery involved a partnership between a for-profit bioscience company, Vertex Pharmaceuticals, and a national nonprofit organization, the Cystic Fibrosis Foundation.<sup>7</sup> The impetus for this collaboration was simple: “the disease is prevalent enough to cause widespread pain, but too small for profit-minded bioscience companies to risk massive resources in pursuit of a cure.”<sup>8</sup> Thus, the Foundation invested over \$45 million into Vertex in 2000 for research and development of a drug for the disease.<sup>9</sup> This was “the largest grant of its kind by a nonprofit disease group.”<sup>10</sup> By 2012, the Foundation had awarded Vertex over \$75 million in funding<sup>11</sup> and has invested \$260 million in drug development since the mid-1990s.<sup>12</sup>

When the Cystic Fibrosis Foundation made its initial investment, such “venture philanthropy” was uncommon.<sup>13</sup> As the chief executive, Robert Beall, told one reporter, it was “the biggest gamble I ever made.”<sup>14</sup> Today, however, such partnerships are becoming more common.<sup>15</sup> In 2008, U.S. disease foundations

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<sup>4</sup> Bruce C. Marshall & Leslie Hazle, PATIENT REGISTRY ANNUAL DATA REPORT 4 (2010), [www.cff.org/UploadedFiles/LivingWithCF/CareCenterNetwork/PatientRegistry/2010-Patient-Registry-Report.pdf](http://www.cff.org/UploadedFiles/LivingWithCF/CareCenterNetwork/PatientRegistry/2010-Patient-Registry-Report.pdf).

<sup>5</sup> Melissa A. Ashlock & Eric R. Olson, *Therapeutics Development for Cystic Fibrosis: A Successful Model for a Multisystem Genetic Disease*, 62 ANNU. REV. MED. 108-09 (2011).

<sup>6</sup> *Id.* at 107-25.

<sup>7</sup> *Id.*; see also Brian McGrory, *Driven by Loss, Father Inspires Tireless Pursuit of a Cure*, BOS. GLOBE, Feb. 9, 2012, [http://www.boston.com/news/local/massachusetts/articles/2012/02/09/joeyes\\_long\\_legacy/](http://www.boston.com/news/local/massachusetts/articles/2012/02/09/joeyes_long_legacy/).

<sup>8</sup> See McGrory, *supra* note 7.

<sup>9</sup> Matthew Perrone, *Kalydeco, Drug That Treats Root Cause of Cystic Fibrosis, Approved by FDA*, HUFFINGTON POST (Jan. 31, 2012), [http://www.huffingtonpost.com/2012/01/31/kalydeco-cystic-fibrosis-cause-drug\\_n\\_1244218.html](http://www.huffingtonpost.com/2012/01/31/kalydeco-cystic-fibrosis-cause-drug_n_1244218.html).

<sup>10</sup> *Id.*

<sup>11</sup> *Id.*

<sup>12</sup> Richard Haugh, *Disease Foundations Prime the Drug Pump*, HOSP. & HEALTH NETWORKS MAG. (Feb. 2012), [http://www.hhnmag.com/hhnmag/jsp/articledisplay.jsp?dcrpath=HHNMAG/Article/data/02FEB2010/1002HHN\\_Inbox\\_pharmaceutical&domain=HHNMAG](http://www.hhnmag.com/hhnmag/jsp/articledisplay.jsp?dcrpath=HHNMAG/Article/data/02FEB2010/1002HHN_Inbox_pharmaceutical&domain=HHNMAG).

<sup>13</sup> See Ashlock & Olson, *supra* note 5, at 116 (stating that the collaboration between Vertex Pharmaceuticals and the Cystic Fibrosis Foundation “pioneered” the venture philanthropy business model).

<sup>14</sup> See McGrory, *supra* note 7.

<sup>15</sup> Sarah Hanson, Lori Nadig & Bruce Altevogt, VENTURE PHILANTHROPY STRATEGIES TO SUPPORT TRANSLATIONAL RESEARCH 2 (2009), [www.nap.edu/openbook.php?record\\_id=12558&p=2](http://www.nap.edu/openbook.php?record_id=12558&p=2).

invested approximately \$90 million into for-profit companies for drug development.<sup>16</sup> This was thirteen times more than was invested in 2000.<sup>17</sup>

The objective of this Article is to examine the benefits and challenges of these novel partnerships and suggest ways that changes in the laws or regulations can promote these partnerships without undue harm to the goal of advancing research for cures for patients. To achieve this objective, Part I describes how partnerships between disease advocacy groups and for-profit companies have evolved and the benefits of the new venture philanthropy business model. Part II examines the legal and social issues of the venture philanthropy model. Part III then proposes various changes to laws and regulations that could help incentivize these partnerships. Finally, Part IV addresses the issue of when a new product is discovered, if and how disease advocacy groups should control drug pricing and patient access to the new drug.

## II. PARTNERSHIPS BETWEEN DISEASE ADVOCACY GROUPS AND ACADEMIC AND COMMERCIAL RESEARCHERS: THE RISE OF VENTURE PHILANTHROPY

*"I've seen all the elements of drug development from NIH to industry to academia to being a patient myself. . . nobody has bad intent, it's just an old and broken system that really needs to be updated."*<sup>18</sup>

### A. Disease Advocacy Group Funding for "De Novo" and "Repurposed" Drug Research

Voluntary health organizations, including disease advocacy groups,<sup>19</sup> have a "long-standing history of providing support to those suffering from disease."<sup>20</sup> The support provided includes offering care, educational resources, participant recruitment for clinical studies, and funding disease research to develop cures and novel therapies for particular diseases.<sup>21</sup> In terms of novel therapies, these groups

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<sup>16</sup> *U.S. Disease Foundation Investment in Biopharmaceutical Industry up 20% in 2008*, CTR.WATCH NEWS ONLINE (Sept. 5, 2008), <http://www.centerwatch.com/news-online/article/166/us-disease-foundation-investment-in-biopharmaceutical-industry-up-20-in-2008>.

<sup>17</sup> *Id.*

<sup>18</sup> *Venture Philanthropy on the Rise*, 14:8 CENTERWATCH 7 (2007), <http://www.themmr.org/assets/about-the-mmr/powerful-news/venture-philanthropy-on-the.pdf>.

<sup>19</sup> Voluntary health organizations include nonprofit charitable organizations, disease advocacy groups, and foundations. See Hanson, *supra* note 15, at 1.

<sup>20</sup> See Hanson, *supra* note 15, at 1.

<sup>21</sup> See Hanson, *supra* note 15, at 1; see Sharon F. Terry et al., *Advocacy Groups as Research Organizations: the PXE International Example*, 8 NATURE REVIEWS GENETICS 157, 164 (2007); David C. Landy et al., *How Disease Advocacy Organizations Participate in Clinical Research: A Survey of Genetic Organizations*, 14 GENETICS IN MED. 223, 227 (2012). A review of journal articles published in 2004 and 2005 reporting on clinical research on genetic diseases found that 33% of all articles that included a statement regarding research support acknowledged disease-advocacy group funding. Richard R. Sharp & David C. Landy, *The Financing of Clinical Genetics Research by Disease Advocacy Organizations: A Review of Funding Disclosures in Biomedical Journals*, 152A AM. J. MED. GENETICS PART A 3051, 3051 (2010).

have been concerned both with the discovery of new drugs, like Kalydeco,<sup>22</sup> as well as finding new uses for old drugs (known as “repurposing”).<sup>23</sup>

“De novo” drug development is expensive and time consuming.<sup>24</sup> Prior to being marketed in the United States, each drug must undergo a detailed U.S. Food and Drug Administration (FDA) review process.<sup>25</sup> The drug discovery process involves the following steps: 1) basic research to identify the underlying causes or genetic mechanism; 2) screening for compounds that show activity with the disease; 3) optimization of compounds to determine whether a drug candidate might be safe and effective if taken by humans; 4) identification of the best drug candidate and filing an IND application with the FDA; 5) clinical trials; and 6) post-marketing studies to monitor product safety.<sup>26</sup> With this process, a new drug takes ten to fifteen years to develop and \$1 billion to \$4 billion to bring the drug to the market.<sup>27</sup> For every 5,000-10,000 compounds that enter the drug discovery process, only one will be approved.<sup>28</sup>

In contrast, developing repurposed drugs can cost half that of “de novo” drugs because clinical research has already determined the toxicology, safety, dosage, and side effects of the drugs.<sup>29</sup> The federal government also provides incentives for companies to focus on drug repositioning, especially in the context of rare or neglected diseases.<sup>30</sup> For example, the FDA, through the Orphan Drug Act, provides some market exclusivity to companies that invest in repurposing drugs for the treatment for rare diseases, even if the patent term on the drug has expired.<sup>31</sup> The National Chemical Genome Center is also developing a library of approved drugs to in order for them to be more easily screened for additional uses.<sup>32</sup> These incentives have caused many biotechnology companies to increase their efforts in drug

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<sup>22</sup> See Press Release, *supra* note 1.

<sup>23</sup> Ramaiah Muthyala, *Orphan/rare Drug Discovery Through Drug Repositioning*, 8 DRUG DISCOVERY TODAY: THERAPEUTIC STRATEGIES 71, 71 (2011).

<sup>24</sup> See Garret A. FitzGerald, *Re-engineering Drug Discovery and Development*, 17 LEONARD DAVIS INST. OF HEALTH ECON. 1, 1 (2011).

<sup>25</sup> The U.S. Food and Drug Administration is the federal agency responsible for protecting and promoting public health through the regulation and supervision of food and drug safety. *About FDA*, U.S. FOOD & DRUG ADMIN. (Feb. 2012), <http://www.fda.gov/AboutFDA/Transparency/Basics/ucm192695.htm>. All drugs are required to receive FDA approval before being placed on the market. 21 U.S.C. §355(a) (2011).

<sup>26</sup> Paul T. Nyffeler, *The Safe Harbor of 35 U.S.C. §271(e)(1): The End of Enforceable Biotechnology Patents in Drug Discovery*, 41 U. RICH. L.REV. 1025, 1041-44 (2007).

<sup>27</sup> See FitzGerald, *supra* note 24, at 1.

<sup>28</sup> See FitzGerald, *supra* note 24, at 1.

<sup>29</sup> Marilyn J. Field & Thomas F. Boat, RARE DISEASES AND ORPHAN PRODUCTS 172 (2011), [http://www.nap.edu/openbook.php?record\\_id=12953](http://www.nap.edu/openbook.php?record_id=12953); Muthyala, *supra* note 23, at 71-76.

<sup>30</sup> See FIELD & BOAT, *supra* note 29, at 172; Muthyala, *supra* note 23, at 71-76.

<sup>31</sup> See FIELD & BOAT, *supra* note 29, at 172.

<sup>32</sup> See FIELD & BOAT, *supra* note 29, at 172.

repositioning, especially when business partnerships are available to create market value in the compounds.<sup>33</sup>

*B. The Shift from the Charitable Granting to Venture Philanthropy*

Traditionally, disease advocacy groups provided research funding in the form of charitable grants to academic or nonprofit researchers to support basic research on a disease.<sup>34</sup> However, many disease advocacy groups began feeling as though the standard grant approach was not yielding sufficient results.<sup>35</sup> Thus, in the late 1990's, disease advocacy groups began assuming a more active role in drug development through the use of venture philanthropy.<sup>36</sup>

In its most basic form, venture philanthropy employs concepts and techniques from venture capitalism and applies them to achieving philanthropic goals.<sup>37</sup> Venture capitalism is a mechanism for which money from various third-party sources are invested into typically high-risk areas.<sup>38</sup> As part of their investment strategy, venture capitalists utilize various techniques, including adopting performance measures, investing larger amounts of money in chosen organizations, partnering closely with the organizations to provide assistance and produce results, and developing an exit strategy.<sup>39</sup> Unlike traditional *charitable grants*, the venture philanthropy model treats funding like an *investment*, with its corresponding expectations of return, operating efficiencies, and management oversight.<sup>40</sup>

Drug advocacy groups are using venture philanthropy to accelerate drug discovery research for new therapies and cures for diseases.<sup>41</sup> Under the venture philanthropy model, disease advocacy groups are funding not only basic research in academia, but also *translational research* and early stages of drug development.<sup>42</sup>

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<sup>33</sup> See Muthyala, *supra* note 23, at 71-76.

<sup>34</sup> See FIELD & BOAT, *supra* note 29, at 168 (“advocacy groups have traditionally provided support for basic discovery research”).

<sup>35</sup> See FIELD & BOAT, *supra* note 29, at 168.

<sup>36</sup> Jessica Potts, *Venture Philanthropy: A Case Study of Three Nonprofit Organizations* (Oct. 1, 2011) (unpublished Masters thesis, Kennesaw State University) (on file with Kennesaw State University Library).

<sup>37</sup> *Venture Philanthropy*, WIKIPEDIA (Feb. 2012), [http://en.wikipedia.org/wiki/Venture\\_philanthropy](http://en.wikipedia.org/wiki/Venture_philanthropy).

<sup>38</sup> Christine W. Letts et al., *Virtuous Capital: What Foundations Can Learn from Venture Capitalists*, 75 HARV. BUS. REV. 36, 3 (1997), [http://www.wheatridge.org/wp-content/uploads/2012/03/Virtuous\\_Capital\\_HB.pdf](http://www.wheatridge.org/wp-content/uploads/2012/03/Virtuous_Capital_HB.pdf).

<sup>39</sup> *Id.*

<sup>40</sup> Bruce Sievers, *IF PIGS HAD WINGS: THE APPEALS AND LIMITS OF VENTURE PHILANTHROPY* 2 (2001), [http://cpnl.georgetown.edu/doc\\_pool/Nielsen0103Sievers.pdf](http://cpnl.georgetown.edu/doc_pool/Nielsen0103Sievers.pdf).

<sup>41</sup> *About Us*, ALZHEIMER'S DRUG DISCOVERY FOUND. (Feb. 2012), <http://www.alzdiscovery.org/index.php/about/learn-about-venture-philanthropy-faqs>.

<sup>42</sup> See HANSON, *supra* note 15.

This has led them to partner with *private sector* bioscience companies.<sup>43</sup> While venture philanthropy business models vary among disease advocacy groups,<sup>44</sup> most models have the following key characteristics: fast and flexible grant-making, long-term funding of “high risk, high reward” projects that complement NIH funding, high levels of disclosure and accountability with transparent performance metrics, interactive approach to connecting donors with beneficiaries, applying good governance and management practices, and taking an active, rather than passive facilitator role.<sup>45</sup> The Cystic Fibrosis Foundation is an excellent example of how one company came to adopt the venture philanthropy business model.<sup>46</sup>

*C. Benefits of the New Model: Removing Risk and Closing Funding Gaps*

Venture philanthropy is used to fill funding gaps that arise from drug development’s economic risks. As described above, drug development entails considerable time and expense.<sup>47</sup> Additionally, of approved drugs, only three of every ten compounds earn a profit, irrespective of therapeutic area, and only one of ten becomes a “blockbuster” drug that earns enough profits to fund further

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<sup>43</sup> *Id.* (The drug advocacy groups’ goal is to use “funding and strategic leadership to help draw discoveries out of the academic sector and into the hands of parties with the ability to commercialize new therapies.”).

<sup>44</sup> See Gambrill, *supra* note 18, at 9-14 (generally describing the different venture philanthropy models employed by the Cystic Fibrosis Foundation, Multiple Myeloma Research Foundation, Muscular Dystrophy Association, Juvenile Diabetes Research Foundation, and Michael J. Fox Foundation for Parkinson’s Research).

<sup>45</sup> JOANNE CHANG, BEST PRACTICES FOR VENTURE PHILANTHROPY COLLABORATIONS BETWEEN DISEASE-FOCUSED FOUNDATIONS AND FOR-PROFIT LIFE SCIENCES COMPANIES 10-12 (2010) (unpublished M.S. thesis, Massachusetts Institute of Technology) (on file with Massachusetts Institute of Technology Library).

<sup>46</sup> The Cystic Fibrosis Foundation is considered a pioneer in developing a successful venture philanthropy business model as a way to drive drug development for rare diseases. *Media FAQs*, CYSTIC FIBROSIS FOUND (Feb. 2012), <http://www.cff.org/aboutCFFoundation/PressRoom/MediaFAQs/>; see also Ashlock & Olson, *supra* note 5, at 116. Prior to 2000, the Foundation focused its drug discovery efforts by awarding small grants to academic researchers. “*Cystic Fibrosis Foundation*,” ANSWERS.COM (Feb. 2012), [www.answers.com/topic/cystic-fibrosis-foundation](http://www.answers.com/topic/cystic-fibrosis-foundation). This support led to the discovery of the cystic fibrosis gene in 1989, which could be used to identify the cause and treatment of the disease. *Id.* By 1997, the FDA had approved two drugs for treating the symptoms of cystic fibrosis; however, the progress was not as great as the foundation had hoped. *Id.* Around the same time, the Foundation also experienced a successful partnership with the for-profit bioscience company, PathoGenesis, which resulted in a top-selling drug product. *Id.* These experiences led the Foundation to adopt a new business model that encouraged *private companies* to conduct cystic fibrosis drug discovery research. *Id.* By 2001, the Foundation had given money to eleven for-profit companies. *Id.* By 2003, there were around two dozen cystic fibrosis therapies in development. *Id.*

<sup>47</sup> *Venture Philanthropy*, WIKIPEDIA (Feb. 2012), [http://en.wikipedia.org/wiki/Venture\\_philanthropy](http://en.wikipedia.org/wiki/Venture_philanthropy).

research.<sup>48</sup> Thus, to help “de-risk” drug development and fill funding gaps, disease advocacy groups direct money to bioscience companies and translational research.<sup>49</sup>

First, disease advocacy groups often fund bioscience companies. Traditionally, bioscience companies have relied on funding from venture capital firms.<sup>50</sup> From 1995 to 2005, venture capital investments in the U.S. biotechnology industry increased from \$830 million to almost \$4 billion and from 10 to 17 percent of all U.S. venture capital investments.<sup>51</sup> However, a study conducted by the National Venture Capital Association in 2011 suggests that venture capital is becoming increasingly unavailable for U.S. bioscience companies.<sup>52</sup> The survey found that 39% of U.S. venture capital firms decreased investments in life science companies between 2008 and 2011.<sup>53</sup> A similar number of firms expected to further decrease investments by as much as 30% over the next three years.<sup>54</sup> The primary reason cited for the decline was the increased risk from perceived unpredictability of the FDA process.<sup>55</sup>

Second, disease advocacy groups also fund *translational* research. “Translational research is a broad term used to describe the process of translating the basic biology of a disease into [actual] therapeutics.”<sup>56</sup> This journey from academia to clinical trials has been coined the “‘Valley of Death,’ because many therapeutic strategies start the journey but few finish.”<sup>57</sup>

Because of the risk, bioscience companies looking for programs to support are generally not interested in funding risky early-stage drug candidates.<sup>58</sup> When bioscience companies, and their venture capitalist backers, are willing to invest in early-stage research, they are more likely to focus on potential “blockbuster” drugs, at the expense of smaller more challenging diseases.<sup>59</sup> Thus, without public funding or investment to help minimize the risk, biotechnology companies generally do not

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<sup>48</sup> *Drug Discovery Process*, ALZHEIMER’S DRUG DISCOVERY FOUND. (Feb 2012), <http://www.alzdiscovery.org/index.php/alzheimers-disease/hope-through-drugs/drug-discovery-process>.

<sup>49</sup> Press Release, Nat’l Venture Capital Ass’n, U.S. Medical Innovation at Risk: Fewer New Companies and Therapies Receiving Funding, Says Report (Oct. 6, 2011), <http://sg.finance.yahoo.com/news/U-S-Medical-Innovation-Risk-iw-1103747796.html>.

<sup>50</sup> *Id.*

<sup>51</sup> Ke Chen et al., *How Much Does History Matter? An Analysis of the Geographic Distribution of Venture Capital Investment in the U.S. Biotechnology Industry*, 6 INDUS. GEOGRAPHER 31, 33 (2009).

<sup>52</sup> Press Release, Nat’l Venture Capital Ass’n, *supra* note 49.

<sup>53</sup> Press Release, Nat’l Venture Capital Ass’n, *supra* note 49.

<sup>54</sup> Press Release, Nat’l Venture Capital Ass’n, *supra* note 49.

<sup>55</sup> Press Release, Nat’l Venture Capital Ass’n, *supra* note 49.

<sup>56</sup> Hanson, *supra* note 15, at 4.

<sup>57</sup> Steven Finkbeiner, *Bridging the Valley of Death of Therapeutics for Neurodegeneration*, 16 NATURE MED. 1227, 1228 (2010).

<sup>58</sup> Nuala Moran, *Public Sector Seeks to Bridge ‘Valley of Death’*, 25 NATURE BIOTECH. 266, 266 (2007).

<sup>59</sup> *See* Hanson, *supra* note 15, at 3.

undertake translational research, especially for rare diseases.<sup>60</sup> Voluntary health organizations are one of the only organizations willing and able to fill these funding gaps.<sup>61</sup>

### III. LEGAL AND SOCIAL ISSUES SURROUNDING THE VENTURE PHILANTHROPY MODEL

*“Historically, investigators would apply for a grant from a foundation or another funding organization and they’d get the grant, and there would be no oversight, no accountability for what happened with that money. All of that is changing.”<sup>62</sup>*

While disease advocacy groups are willing to help bioscience companies and academic researchers balance the risks of drug discovery, their support does not come without expectations.<sup>63</sup> While venture philanthropy models vary among disease advocacy groups,<sup>64</sup> they all utilize at least some venture capitalist tools to structure the partnerships. This section describes some of the tools used to structure the partnerships, examines the legal issues involved with one of these tools, discusses one social issue with venture philanthropy, and then concludes that despite these issues, the benefits of the model outweigh the negative issues.

#### A. Structuring the Partnership

Venture philanthropy techniques can help disease advocacy groups achieve three objectives: *control*, *return on investment*, and *information sharing*. To maintain *control* of the research they fund, groups can contractually set milestones and termination rights, create price restrictions and distribution agreements, and negotiate for seats on a company’s boards of directors.<sup>65</sup> To secure *return on investment* in order to fund future research, groups can contract for royalties, purchase direct equity in a company, or purchase debt in a company.<sup>66</sup> Finally, to ensure *information sharing* in order to remove some of research impediments, groups can require assignment of patent rights, research tool sharing and patent pooling, and even provide access to disease advocacy group-controlled patient databases and bio-banks.<sup>67</sup>

#### B. Legal Issue: Seat on the Board of Directors

While these techniques can help groups meet objectives, they are not without legal issues. This section will explore the issues presented by placing members of a

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<sup>60</sup> Hanson, *supra* note 15 at 3; Gambrill, *supra* note 18, at 1.

<sup>61</sup> Hanson, *supra* note 15, at 40; Gambrill, *supra* note 18, at 1. The National Institute of Health also provides considerable funding for disease research. Chang, *supra* note 45, at 14.

<sup>62</sup> Quote by Linda Van Eldik, Professor in the Department of Cell and Molecular Biology at Northwestern University Feinberg School of Medicine. See Hanson, *supra* note 15, at 25.

<sup>63</sup> Gambrill, *supra* note 18, at 7.

<sup>64</sup> Gambrill, *supra* note 18, at 9-14.

<sup>65</sup> See Hanson, *supra* note at 15, at 27-35; Sievers, *supra* note 40, at 4; Letts, *supra* note 38.

<sup>66</sup> See Hanson, *supra* note 15, at 27-35.

<sup>67</sup> Hanson, *supra* note 15, at 27-35.

disease advocacy group on a for-profit company's board of directors. While legal issues can also arise with contracting for returns on investment,<sup>68</sup> contracting with researchers to secure patent rights,<sup>69</sup> and sharing patient databases or biobanks,<sup>70</sup> an analysis of these issues is beyond the scope of this paper.

In venture capitalism, investors typically assume an ownership role by becoming actively engaged in the management of the company.<sup>71</sup> This often entails taking seats on the company's board of directors to help shape strategy, secure other investors, and steer policy.<sup>72</sup> This control helps venture capitalists enhance the growth and sustainability of the investee company.<sup>73</sup>

"Based on this model, venture philanthropists are encouraged to become 'highly engaged' in the organizations to which they allocate their funds . . ."<sup>74</sup> As one scholar pointed out, this "raises sensitive issues of power and control."<sup>75</sup> This paper explores a director's fiduciary duty of loyalty to a company and potential conflicts of interest that may arise when a member of a disease advocacy group takes a director position in a for-profit company.

Directors of corporations owe fiduciary duties to the corporation and its shareholders.<sup>76</sup> One such fiduciary duty is the duty of loyalty, which requires

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<sup>68</sup> Hanson, *supra* note at 15, at 29. Foundations often believe they should receive a return on their investments. Hanson, *supra* note at 15, at 29. However, it can be difficult to determine what portion of the proceeds a particular organization should receive. Hanson, *supra* note 15, at 29. The time period between funding translational research and commercializing a drug may be years. Hanson, *supra* note 15, at 29. During that time, other investors or grantors may have contributed to the drug's development. Hanson, *supra* note 15, at 29. Determining the proportion a particular organization should receive can be complex. Hanson, *supra* note 15, at 29. According to Kenneth Schaner, a private practice attorney with extensive experience in venture philanthropy, the complexities of the issue often lead to many organizations forgoing attempts to recapture revenue. Hanson, *supra* note 15, at 29.

<sup>69</sup> See *Stanford v. Roche*, 131 S. Ct. 2188 (2011).

<sup>70</sup> See Hanson, *supra* note 15, at 42-44. The act of opening up patient databases and biobanks can raise issues about confidentiality, privacy, consent, and whether the researchers should share individual research results with tissue donors. Hanson, *supra* note at 15, at 42-44. Confidentiality is an issue because the identity of individuals can be identified from pooled genomic data. Hanson, *supra* note at 15, at 42-44. Legal and ethical questions can arise regarding whether patient consent was needed and obtained. Hanson, *supra* note at 15, at 42-44. Finally, patients that provide samples are often concerned with receiving their individual results, however, there are generally no agreements between parties for doing so. Hanson, *supra* note at 15, at 42-44..

<sup>71</sup> See Sievers, *supra* note 40, at 4.

<sup>72</sup> Sievers, *supra* note 40, at 4.

<sup>73</sup> See Letts, *supra* note 38.

<sup>74</sup> See Sievers, *supra* note 40, at 4.

<sup>75</sup> See Sievers, *supra* note 40, at 4 (focusing on the issues surrounding the inordinate influence of large donors on nonprofit organizational independence and the challenges that presents in a civil society).

<sup>76</sup> See, e.g., *Revlon v. MacAndrews & Forbes Holdings, Inc.*, 506 A.2d 173, 179 (Del. 1986).

directors to refrain from self-dealing.<sup>77</sup> This includes “refrain[ing] from doing anything that would work injury to the corporation, or to *deprive it of profit . . .*”<sup>78</sup> Thus, directors may have an obligation to avoid conflicts of interests,<sup>79</sup> and maximize shareholder returns on investments.<sup>80</sup>

Conflicts of interest can arise when a director has another interest that suggests divided loyalty between the corporation and another constituent.<sup>81</sup> Generally, directors do not owe fiduciary duties to other constituencies whose rights are purely contractual.<sup>82</sup> While many states have adopted “other constituencies” statutes that permit directors to consider the interests of non-shareholder constituencies in making corporate decisions, these statutes are only permissive, vary in the constituencies that are included, and are often vague as to how directors should weigh varying interests.<sup>83</sup> These statutes do not seem to impact litigation outcomes<sup>84</sup> and directors who favor another constituency over its shareholders can still violate their duty of loyalty.<sup>85</sup>

Conflicts of interest, and violations of the duty of loyalty, can arise when venture capital managers serve as directors of companies because of divided loyalty between the venture capital firm and the investee company.<sup>86</sup> Despite the fact that both parties typically want to maximize returns on investments,<sup>87</sup> they nonetheless may face conflicting interests when, for example, decisions must be made on the terms and conditions to sell or merge the company.<sup>88</sup>

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<sup>77</sup> Guth v. Loft, Inc., 5 A.2d 503, 510 (Del. 1939).

<sup>78</sup> *Id.* (emphasis added).

<sup>79</sup> See Stone v. Ritter, 911 A.2d 362, 370 (Del. 2006).

<sup>80</sup> Shun Wilson Leung, *The Inadequacy of Shareholder Primacy: a Proposed Corporate Regime that Recognizes Non-Shareholder Interests*, 30 COLUM. J.L. & SOC. PROBS. 587, 591 (1997).

<sup>81</sup> See Michael W. Peregrine & Robert A. Schreck, Jr., *Managing Constituent Interests in Healthcare Joint Ventures*, AHLA CONNECTIONS, Mar. 2012, at 1, [http://www.mwe.com/files/Publication/7ff5a67f-dac2-4494-b525-14842f7ed2fa/Presentation/PublicationAttachment/6269d2de-b529-421c-86d7-18a781c02716/Analysis2\\_March20121.pdf](http://www.mwe.com/files/Publication/7ff5a67f-dac2-4494-b525-14842f7ed2fa/Presentation/PublicationAttachment/6269d2de-b529-421c-86d7-18a781c02716/Analysis2_March20121.pdf).

<sup>82</sup> See, e.g., Katz v. Oak Indus., 508 A.2d 873, 879 (Del. 1986).

<sup>83</sup> Brett H. McDonnell, *Corporate Constituency Statutes and Employee Governance*, 30 WM. MITCHELL L. REV. 1227, 1230-41 (2004) (describing state constituency statutes).

<sup>84</sup> *Id.*

<sup>85</sup> Revlon v. MacAndrews & Forbes Holdings, Inc., 506 A.2d 173, 173 (Del. 1986) (holding that the Board of Directors breached their duty of loyalty due impermissibly considering noteholders’ interests at the expense of the shareholders).

<sup>86</sup> Jin-Kyu Koh & Theresa G. Carroll, *Venture Capital Directors—The Heightened Risk of Serving More Than One Master*, 28 MICH. BUS. L.J. 30, 31 (2008) (discussing potential conflict of interest situations for venture capital designated directors).

<sup>87</sup> John Dobson, *Is Shareholder Wealth Maximization Immoral?*, 55 FIN. ANALYST J. 69, 69 (1999).

<sup>88</sup> Marc Weingarten & Neil P. Horne, *Be Careful What You Wish For —Considerations When Obtaining Board Representation*, ACTIVIST INVESTING DEV., Spring 2006, at 3, <http://www.srz.com/files/News/e5ecb0c3-7c98-40cc-baa9-febbd5e04eb6/Presentation/News>

This Article argues that the risk of such conflicts of interest is heightened when a member of a disease advocacy group is placed on a for-profit company's board of directors. While the board may have an obligation to maximize profits for the company and its shareholders,<sup>89</sup> disease advocacy group members may want to pursue broader social values, such as maximizing drug distribution at minimized cost. If conflicts arise, directors can be personally liable for the loss suffered by the corporation.<sup>90</sup> Due to the inherent conflicts of interest and increased risk of liability, disease advocacy groups may want to forgo requests for board seats.

While relinquishing board seats may be advisable, disease advocacy groups do not have to relinquish all influence over a board. For example, disease advocacy groups may still request board observation rights.<sup>91</sup> Board observation rights provide individuals the right to attend and participate in board meetings, but not vote.<sup>92</sup>

*C. Social Issue: Should Nonprofits be Making such Risky Investments?*

In addition to potential legal issues, the venture philanthropy business model also faces numerous social criticisms. One criticism is whether nonprofit organizations should want to emulate the poor success rates of venture capitalism.<sup>93</sup> As one skeptic points out,

venture capitalists themselves are fond of saying that of every 10 investments, there will be 4 abject failures, 4 walking wounded, and maybe, if you are lucky, 1 or 2 real hits. Of course, in the financial world, the big hits make up for the dogs by returning huge profits, but we must ask whether this success rate is what we wish to emulate.<sup>94</sup>

The risk assumed by organizations adopting the venture philanthropy model can be understood by again examining the Cystic Fibrosis Foundation. While the Foundation was recently successful with the development of Kalydeco, they have experienced their share of failure from the high risks of such investment ventures. For example, in 2004-2005 alone, three relatively promising projects were terminated: Boehringer Ingelheim's anti-inflammatory drug and Targeted Genetics' aerosol gene treatment were pulled from Phase II trials; and Amelubant, a rheumatoid arthritis drug also failed in trials.<sup>95</sup> Additionally, in 2010, two

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<sup>89</sup> See *Guth v. Loft, Inc.* 5 A.2d 503, 510 (Del. 1939); Leung, *supra* note 80.

<sup>90</sup> See Koh & Carrol, *supra* note 86, at 30. Although state statutes can allow corporations to indemnify their board members for personal liability of a director for a breach of the director's duty of loyalty to the corporation. See, e.g., DEL. CODE ANN. tit. 8, § 102(b)(7) (2012).

<sup>91</sup> Koh & Carrol, *supra* note 86, at 32.

<sup>92</sup> Koh & Carrol, *supra* note 86, at 32.

<sup>93</sup> See Sievers, *supra* note 40, at 2.

<sup>94</sup> See Sievers, *supra* note 40, at 2.

<sup>95</sup> Becky Jungbauer & Bridget Silverman, *A Breath of Fresh Air for Cystic Fibrosis Drug Pipeline*, 12 PHARM. APPROVAL MONTHLY 12 (Dec. 2007).

pharmaceutical companies that were partnering with the Foundation had insufficient capital to finish their projects, leading the Foundation to terminate the partnerships and establish new partnerships with other companies to continue the project.<sup>96</sup> Such business decisions can cost companies support by investors and may have contributed to the Foundation's Charity Navigator Rating to be decreased from a 4-star to a 3-star rating in 2011.<sup>97</sup>

*D. Despite these Concerns, Venture Philanthropy has Proven Its Value in Advancing Disease Research*

The venture philanthropy model's ability to "de-risk" investments in order to spur private investment is precisely why the model was adopted by many disease advocacy groups in the first place. As Richard Insel, executive vice president of research at the Juvenile Diabetes Research Foundation (JDRF), has stated: "[i]f we don't take on risk as a foundation . . . nobody else is going to take it on . . . the obligation is on us to take on risk."<sup>98</sup> Many biotechnology companies have admitted that without the incentive of the venture philanthropy funding, their companies would never have invested in particular drug development research.<sup>99</sup>

Because of this need, numerous large disease advocacy groups, including the Juvenile Diabetes Research Foundation, the Michael J. Fox Foundation for Parkinson's Research, the Prostate Cancer Foundation, and the Alzheimer's Drug Discovery Foundation have adopted venture philanthropy business models in order to identify and fill gaps in particular disease research funding.<sup>100</sup> Like the Cystic Fibrosis Foundation and Kalydeco, many of these organizations have experience drug development success.<sup>101</sup> The Juvenile Diabetes Research Foundation has drug therapies that have completed the entire cycle from laboratory research to the patient market,<sup>102</sup> and all of the groups have numerous therapeutic drugs in the pipeline.<sup>103</sup>

Additionally, money is not the only value that these organizations provide to their venture partners. According to Robert Gallotto, vice president of Altus Pharmaceuticals, "[c]apital is only one part of the equation. It's much more the intellectual capital that was important for us."<sup>104</sup> Even if the public-private

<sup>96</sup> See Potts, *supra* note 36, at 8-9.

<sup>97</sup> See Potts, *supra* note 36, at 9.

<sup>98</sup> See Hanson, *supra* note 15, at 14.

<sup>99</sup> Hanson, *supra* note 15, at 14.

<sup>100</sup> See Potts, *supra* note 36, at 18.

<sup>101</sup> Potts, *supra* note 36, at 18.

<sup>102</sup> See Potts, *supra* note 36, at 19.

<sup>103</sup> Richard A. Insel et al., *Juvenile Diabetes Research Foundation: Mission, Strategy, and Priorities*, 21 PROSPECTIVES IN DIABETES 30, 30 (2012); CYSTIC FIBROSIS FOUND., <http://www.cff.org/research/DrugDevelopmentPipeline/> (last visited Mar. 29, 2013); MICHAEL J. FOX FOUND. FOR PARKINSON'S RESEARCH, [http://www.michaeljfox.org/research\\_fundingOpportunities.cfm](http://www.michaeljfox.org/research_fundingOpportunities.cfm) (last visited Mar. 29, 2013); PROSTATE CANCER FOUND., [http://www.pcf.org/site/c.leJRIROrEpH/b.7626255/k.A439/July\\_2011\\_Advances.htm](http://www.pcf.org/site/c.leJRIROrEpH/b.7626255/k.A439/July_2011_Advances.htm) (last visited Mar. 29, 2013); ALZHEIMER'S DRUG DISCOVERY FOUND., ISOA/ADDF PIPELINE PROJECT REPORT 3 (2008), [www.alzdiscovery.org/pdf/Pipeline\\_Report.pdf](http://www.alzdiscovery.org/pdf/Pipeline_Report.pdf).

<sup>104</sup> Gambrill, *supra* note 18, at 8.

partnership does not result in the discovery of the targeted drug, the knowledge and research likely provides transparency to the public and investors on drug discovery.<sup>105</sup>

#### IV. INCENTIVIZING PUBLIC-PRIVATE PARTNERSHIPS FOR DISEASE RESEARCH

*"Culture does not change because we desire to change it. Culture changes when the organization is transformed; the culture reflects the realities of people working together every day."<sup>106</sup>*

For all of the reasons stated above, partnerships between disease advocacy groups and commercial and academic researchers are worth incentivizing. This section proposes that changes to patent law could help reduce barriers to research on orphan drugs and incentivize many of these partnerships. This section then explores the use of priority review vouchers and concludes that such incentive mechanisms should not be employed for public policy reasons. Other ways to incentivize these partnerships could include funding research coalitions for disease research, creating an NIH task force to provide guidelines on the sharing of patient databases and biospecimen banks,<sup>107</sup> reducing fees under the Prescription Drug User Fee Act and Orphan Drug Act, and changing the tax code to make it easier for disease advocacy groups to make riskier investments.<sup>108</sup> But, these potential incentives are beyond the scope of this paper.

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<sup>105</sup> For example, the Alzheimer's Drug Discovery Foundation measures its impacts by identifying how many of its funded drug discovery programs advanced key stages in the drug development process, how many new intellectual property and licenses were secured, the ratio of time of progressive forward movement through the drug discovery stages to each dollar invested, the number of peer-reviewed articles published by funded investigators, and the monetary amount of "follow-on funding" that funded programs have attracted from government grants and initial public offerings. ALZHEIMER'S DRUG DISCOVERY FOUND., ISOA/ADDF PIPELINE PROJECT REPORT 3 (2008), [www.alzdiscovery.org/pdf/Pipeline\\_Report.pdf](http://www.alzdiscovery.org/pdf/Pipeline_Report.pdf).

<sup>106</sup> Frances Hesselbein, *The Key to Cultural Transformation*, LEADER TO LEADER (Spring 1999), <http://www.hesselbeininstitute.org/knowledgecenter/journal.aspx?ArticleID=52>.

<sup>107</sup> To facilitate partnerships, disease advocacy groups sometimes create research registries and biological repositories to enable research studies on particular diseases. As described in the footnotes above, many issues with privacy and confidentiality can arise with these databases. The Secretary of Health and Human Services assists these organizations by creating a federal task force to create guidelines on the sharing of patient and biospecimen databases. The task force would bring together a network of stakeholders from various government agencies including universities, voluntary health organizations, private biotechnology and pharmaceutical, and venture capital firms. Peter Lee, *Contracting to Preserve Open Science: The Privatization of Public Policy in Patent Law*, 58 EMORY L.J. 889, 889 (2009).

<sup>108</sup> For example, the Tax Reform Act of 1969 put in place the private foundation excise taxes of Chapter 42 to curb perceived abusive behavior by foundations. One of the most important Chapter 42 excise taxes is aimed at limiting a foundation's speculative investments and prohibits against the making of "jeopardizing investments" as set forth in IRC Section 4944. Excise taxes are imposed under this section not only on the private foundations but also potentially against foundation managers. Tax penalties can be severe. I.R.C. § 4944 (LEXIS 2013).

*A. Patent Law*

*“In today’s research environment, it is virtually impossible for researchers to identify a drug candidate without using some patented invention they do not own.”*<sup>109</sup>

Under federal law, a patent owner has the right to sue anyone who utilizes her patented invention without permission.<sup>110</sup> While patents may provide incentives for developing new technologies, they constrain access to those technologies, which can inhibit research and the development of needed therapies.<sup>111</sup> Two statutory and common law exceptions do exist that shield researchers from patent liability in narrow instances: the safe harbor provision under 35 USC §271(e)(1) and the common law research exception.<sup>112</sup> Unfortunately, judicial limitations to these provisions have created restrictions and ambiguity regarding their applicability to research funded by disease advocacy groups in conjunction with for-profit bioscience companies.

In order to get around these ambiguities, some groups are contractually creating “biomedical research commons,” where patented inventions are available to noncommercial researchers.<sup>113</sup> However, private ordering does not go far enough; as described above, many “noncommercial” researchers are often now affiliated with commercial bioscience companies. This section examines the current state of the patent law and proposes Congressional amendments to remove impediments to research on rare or orphan diseases, which would help encourage partnerships between disease advocacy groups and the private sector.

#### 1. Common Law Experimental Research Exception

Under the common law, the use of a patented invention for research purposes, and using research tools in drug delivery, was not considered infringement.<sup>114</sup> Whether the research exception could be used as a defense to patent infringement, however, depended on whether the person had an intention of gaining financially from the endeavor or if there was some commercial benefit.<sup>115</sup> If the person gained financially or commercially, then the exception generally did not apply.<sup>116</sup> Thus, the research exception was not available to pharmaceutical companies, even when they were seeking FDA approval for generic drugs.<sup>117</sup>

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<sup>109</sup> Nyffeler, *supra* note 26, at 1046-47.

<sup>110</sup> 35 U.S.C. §271 (West 2012).

<sup>111</sup> *See Lee, supra* note 107, at 889.

<sup>112</sup> Kelli Brensdal, *Rough Waters Ahead: The Status of the Safe Harbor Provision After Proveris Scientific Corp. v. Innovasystems, Inc.*, 8 J. Telecomm. & High Tech. L. 523, 525-30 (2010).

<sup>113</sup> *See Lee, supra* note 111.

<sup>114</sup> *See Brensdal, supra* note 112, at 525.

<sup>115</sup> Brensdal, *supra* note 112, at 527.

<sup>116</sup> Brensdal, *supra* note 112, at 527.

<sup>117</sup> Brensdal, *supra* note 112, at 527-28.

Until 2002, universities and other nonprofits were believed to be immune from patent infringement liability under the experimental use defense.<sup>118</sup> The Federal Circuit in *Madey v. Duke University* disagreed.<sup>119</sup> In *Madey*, the court held that research conducted at major research universities, such as Duke University, did not fall under the experimental use exception.<sup>120</sup> They explained that the exception only narrowly covers research performed “for amusement . . . idle curiosity, or for strictly philosophical inquiry.”<sup>121</sup> Thus, the exception is not limited to endeavors for commercial gain, but also extends to research that furthers the alleged infringer’s legitimate business.<sup>122</sup> While major universities fund many research projects with no commercial application, the research nonetheless furthers the institution’s legitimate business objectives, including education, increasing institutional status, and attracting research grants, students, and faculty.<sup>123</sup> The fact that universities may be non-profit institutions “is not determinative.”<sup>124</sup>

In effect, *Madey* disqualified all research universities and nonprofit research institutions from the experimental use defense.<sup>125</sup> Thus, it is highly unlikely that most drug development ventures between disease advocacy groups and for-profit bioscience companies could invoke the common law research exception if they infringed on a patented invention in the course of drug discovery. Under the new venture philanthropy model, these non-profits have become more commercial in nature. Additionally, funding disease research furthers their legitimate business objectives of finding cures for diseases, which can attract additional donors and federal grants. While disease advocacy groups are still funding basic research, that research is often directed at academic researchers,<sup>126</sup> who are similarly not covered under the exception. Finally, while some disease advocacy groups have contracted to provide drugs to patients in certain geographic or socio-economic spheres at no profit, some of the drugs are still sold to the public for profit.<sup>127</sup>

Denying the experimental research defense to universities and nonprofit institutions could have a chilling effect on basic research.<sup>128</sup> In theory, research will cost more and potentially even be slowed as institutions will have to devote more resources to costly patent searches, negotiate for patent licenses, and pay more due to royalty stacking of downstream discoveries through reach-through licenses.<sup>129</sup> While

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<sup>118</sup> See Michelle Cai, *Madey v. Duke University: Shattering the Myth of Universities’ Experimental Use Defense*, 19 BERKLEY TECH. L.J. 175, 178 (2004).

<sup>119</sup> *Madey v. Duke University*, 307 F.3d 1351, 1360-64 (2002).

<sup>120</sup> *Id.* at 1362.

<sup>121</sup> *Id.*

<sup>122</sup> *Id.*

<sup>123</sup> *Id.*

<sup>124</sup> *Id.*

<sup>125</sup> See Cai, *supra* note 109, at 183-84.

<sup>126</sup> See Hanson, *supra* note at 15, at 38.

<sup>127</sup> See Part IV.B, *infra*.

<sup>128</sup> See Cai, *supra* note 109, at 185.

<sup>129</sup> See Cai, *supra* note 109, at 185.

one scholar questions whether commercial patent holders will actively exert their patent rights against universities,<sup>130</sup> the new partnerships structured under the venture philanthropy model may be more targeted due to their commercial objectives.

## 2. Statutory Safe Harbor Provision

In 1984, Congress passed 35 USC §271(e)(1), often referred to as the safe harbor provision, to allow an exception to infringement if the research was “reasonably related to the development and submission of information” to the FDA.<sup>131</sup> The original intent of this law was to shield drug makers from patent infringement claims during generic drug development, since they did not fall under the common law research use exception, while having minimal impacts on patent law.<sup>132</sup> However, the language of the statute does not limit it to generic drugs.<sup>133</sup> Thus, the Supreme Court has interpreted the safe harbor exemption broadly<sup>134</sup>

In particular, in 2005 in *Merck v. Integra*, the Court held that the statute covered not only generic pharmaceutical drugs for which an IND was submitted, but “all uses of patented inventions that are reasonably related to the development and submission of any information under the FDCA.”<sup>135</sup> Thus, *Merck* extended the exception to pre-clinical research where a

drugmaker has a reasonable basis for believing that a patented compound may work, through a particular biological process, to produce a particular physiological effect, and uses the compound in research that if successful, would be appropriate to include in a submission to the FDA, that use is ‘reasonably related’ to the development and submission of information under . . . Federal law.<sup>136</sup>

However, the Court instructed that the safe harbor exception does not apply to

[b]asic scientific research on a particular compound, performed without the intent to develop a particular drug *or* a reasonable belief that the compound will cause the sort of physiological effect the researcher intends to induce . . . [be it would not be] ‘reasonably related to the development and submission of information’ to the FDA.<sup>137</sup>

Thus, the safe harbor exception should at least begin at the drug optimization stage, when a drug maker would have both the intent to make a drug and a

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<sup>130</sup> See Cai, *supra* note 109, at 185-86.

<sup>131</sup> 35 U.S.C. §271(e)(1). (West 2012).

<sup>132</sup> See Nyffeler, *supra* note 26, at 1026; see Brensdal, *supra* note 112, at 525.

<sup>133</sup> See Nyffeler, *supra* note 26, at 1026.

<sup>134</sup> For a review of the case law, see Nyffeler, *supra* note 26, at 1026; Brensdal, *supra* note 112, at 525.

<sup>135</sup> *Merck v. Integra*, 545 U.S. 193, 202 (2005).

<sup>136</sup> *Id.* at 207.

<sup>137</sup> *Id.* at 205-206.

reasonable belief that the compound analyzed would act in the desired manner.<sup>138</sup> However, it is more uncertain whether the safe harbor exception would apply if one, but not both, exceptions were met.<sup>139</sup> For example, it is uncertain whether the exception would apply to the screening stage of drug development where a researcher has the “intent to develop a particular drug” for FDA approval but may lack a “reasonable belief” that the compounds she is testing will cause the “physiological effect the research intends to induce.”<sup>140</sup> If screening were included under this exception, then the safe harbor exception would encompass virtually all of the drug discovery process.<sup>141</sup>

As one author eloquently stated “the failure of the legislature and judiciary to adequately define significant terms regarding the §271(e)(1) safe harbor exemption has resulted in a governmentally fashioned state of confusion. Within the arena of drug discovery and biotechnology there is no precise determination of where infringement stops and exemption begins.”<sup>142</sup> Neither the Supreme Court nor the Federal Circuit has clarified this issue.<sup>143</sup> This is problematic, as uncertainty in this area could have a chilling effect on drug development, especially due to the threat of treble damages for findings of willful infringement.<sup>144</sup>

### 3. A Proposal for Broader Experimental Use and Safe Harbor Exceptions for Orphan Drug Development

Scholars and judges have advocated for both broader experimental use exceptions and clarification of safe harbor exceptions.<sup>145</sup> One scholar suggested that allowing the experimental use exception may be justified in areas where patent exclusion causes socially harmful results; however, where and who draws the line between exempted and non-exempted research?<sup>146</sup> While funding agencies, such as the National Institute of Health (NIH), could be used to draw such a line, they might not be in any better position than the courts.<sup>147</sup> Others have proposed bright-line or

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<sup>138</sup> See Nyffeler, *supra* note 26, at 1049-50.

<sup>139</sup> See Nyffeler, *supra* note 26, at 1049.

<sup>140</sup> *Merck*, 545 U.S. at 202.

<sup>141</sup> *Id.* at 1052-53.

<sup>142</sup> See Nyffeler, *supra* note 26, at 1059-60.

<sup>143</sup> The federal circuit has recently narrowed the safe harbor provision generally by holding that the provision only applies to those inventions that were required to seek FDA approval before being placed on the market. *Proveris Scientific Corp. v. Innovasystems, Inc.*, 536 F.3d 1256, 1265 (Fed. Cir. 2008). “The statute does not apply to information that may be routinely reported to the FDA, long after marketing approval has been obtained.” *Classen Immunotherapies v. Biogen IDEC*, 659 F.3d 1057, 1070 (Fed. Cir. 2010). The statute does apply to non-routine “submissions that are required to maintain FDA approval,” *Momenta Pharmaceuticals, Inc. v. Amphastar Pharmaceuticals, Inc.*, 686 F.3d 1348, 1358 (2012).

<sup>144</sup> See Nyffeler, *supra* note 26, at n. 209.

<sup>145</sup> This Article will discuss only the proposals most relevant to the solutions proposed in this paper. For a review of the different proposals, See Nyffeler, *supra* note 26, at 1056; Cai, *supra* note 109, at 185.

<sup>146</sup> Cai, *supra* note 109, at 189.

<sup>147</sup> Cai, *supra* note 109, at 191.

categorical rules such as eliminating the experimental use defense for universities entirely,<sup>148</sup> or amending §271(e)(1) to state that the safe harbor exemption does not apply to research tools,<sup>149</sup> or is limited to the development of generic drugs.<sup>150</sup>

This paper combines both of these ideas into the following proposal: *Congress should statutorily extend the experimental use and safe harbor exceptions to orphan drug research.* Thus, basic research on orphan diseases undertaken by academic and nonprofit organizations would once again be shielded from patent infringement liability. Perhaps more importantly, it would help reduce the economic risk of early translational research, which may or may not be covered under the Court's interpretation of the safe harbor provision in *Merck*. This proposal would be both easy to implement while providing the proper balance between encouraging orphan drug research and upholding strong patent rights in commercial drug development.

First, this proposal would be relatively easy to implement. It creates a clear categorical exception since "orphan disease" is statutorily defined under the Orphan Drug Act as "a disease or condition that affects fewer than 200,000 people in the United States."<sup>151</sup> In close cases, organizations could potentially submit documentation that the proposed target population being researched involves fewer than 200,000 people in the United States to a review agency, such as the FDA, to receive designation status.<sup>152</sup> The FDA could maintain a public database of all diseases that have received orphan disease status.<sup>153</sup>

It would also be easy to identify the individuals conducting orphan disease research. In order to gain funding, scientists must typically claim some practical implications for their research, such as finding a cure for a particular disease.<sup>154</sup> Since many disease advocacy groups encourage or contractually require public dissemination of research findings supported by their funding,<sup>155</sup> individual scientists or organizations engaged in research on a particular disease may be identifiable. Also most orphan diseases have a genetic component,<sup>156</sup> which may make it possible to determine exactly what disease or variant is being researched if issues arise.

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<sup>148</sup> Cai, *supra* note 109, at 191.

<sup>149</sup> *Integra Lifesciences I, Ltd. v. Merck*, 331 F.3d 860, 877-78 (Fed. Cir. 2003); *See Brensda*, *supra* note 112, at 546.

<sup>150</sup> *See Nyffeler*, *supra* note 26, at 1060.

<sup>151</sup> 21 U.S.C. § 360bb (West 2013).

<sup>152</sup> This process is similar to that currently undertaken by the FDA for orphan drug designations. *See FIELD & BOAT*, *supra* note 29. Whether or not most diseases would qualify for orphan status should be relatively easy to identify. For example, "the National Institutes of Health lists approximately 6000 rare diseases . . . about 83% of these disorders affect fewer than 6000 patients." Craig L. Kephart, *Orphan Drugs: Small Markets, Big Opportunity*, *SPECIALTY PHARMACY TIMES* (Feb. 20, 2012), <http://www.specialtypharmacytimes.com/publications/specialty-pharmacy-times/2012/February-2012/Orphan-Drugs-Small-Markets-Big-Opportunity>.

<sup>153</sup> This could be similar to the Rare Disease Repurposing Database that was established by the FDA.

<sup>154</sup> *See Cai*, *supra* note 109, at 190.

<sup>155</sup> *See Hanson*, *supra* note at 15, at 41-44.

<sup>156</sup> *See FIELD & BOAT*, *supra* note 29, at 1 ("Many of the estimated 5,000 to 8,000 rare

Second, this proposal strikes the proper balance between encouraging orphan drug research and upholding strong patent rights in commercial drug development. The proposal would be consistent with government policy for encouraging orphan drug research. For example, over the last 30 years, Congress has enacted numerous statutes, including the Orphan Drug Act<sup>157</sup> and the Rare Disease Act of 2002<sup>158</sup> in an effort to reduce the barriers to such research. Even agencies have sought novel solutions, such as NIH's Office of Rare Disease Research,<sup>159</sup> and the FDA's recent launch of its Rare Disease Repurposing Database, which is meant to encourage venture investing into orphan drugs.<sup>160</sup>

The benefits derived from such a narrow amendment to patent law would outweigh any negative impacts. Opponents of expanding experimental use or safe harbor exemptions express concern that drug researchers would no longer receive compensation for the patented research tools that they invented.<sup>161</sup> Additionally, if patent protection in drug development was eroded, it could lead to a decrease in venture capital investments in biotechnology companies because many of the intellectual property assets generated would essentially be worthless.<sup>162</sup> This would in turn reduce the development of new research tools, which would hurt the overall pharmaceutical industry.<sup>163</sup> However, the narrowness of this proposal should help alleviate most of those concerns; in most cases, with the exception of orphan drug research, patent protection would remain unchanged. Thus, orphan drug research could progress without some intellectual property impediments, but patent holders would still derive monetary benefit from most bioscience industry research.<sup>164</sup>

#### B. Priority Review Vouchers

Priority review vouchers appear popular with Congress for the issue of rare and neglected diseases. This section describes the Priority Review Voucher program and argues that the program should not be expanded for public policy reasons.

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conditions are genetic or have a genetic component.”).

<sup>157</sup> 21 U.S.C. § 360aa et seq (West 2012).

<sup>158</sup> The Rare Disease Act of 2002, Pub. L. No. 107-84 (codified as amended in scattered sections of 42 U.S.C.).

<sup>159</sup> The office was established in 1993 and coordinates and supports rare diseases research, responds to research opportunities for rare diseases, and provides information on rare diseases. The Rare Disease Act of 2002, Public Law 107-280, established the ORDR by statute. Office of Rare Disease Research, <http://rarediseases.info.nih.gov/AboutUs.aspx> (last visited Mar. 9, 2013).

<sup>160</sup> Amy Dockser Marcus, *FDA Database Aims to Spark Orphan-Disease Drug Development*, WALL ST. J., June 18, 2010, <http://blogs.wsj.com/health/2010/06/18/fda-database-aims-to-spark-orphan-disease-drug-development/>.

<sup>161</sup> See Nyffeler, *supra* note 26, at 1062.

<sup>162</sup> See Nyffeler, *supra* note 26, at 1061-62.

<sup>163</sup> See Nyffeler, *supra* note 26, at 1062.

<sup>164</sup> See Kephart, *supra* note 152.

On September 27, 2007, the Food and Drug Administration Amendments Act of 2007 (FDAAA) was signed into law.<sup>165</sup> The Act included Section 1102, which added new section 524 to the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360n).<sup>166</sup> Section 524 authorizes the FDA to award a priority review voucher (“PRV”) to sponsors of drugs or vaccines for certain tropical diseases upon approval of the tropical disease product application.<sup>167</sup> A PRV entitles the holder to obtain priority review for any new future drug application that would not otherwise qualify for priority review.<sup>168</sup> A PRV can be used by the sponsor who obtains it or may be transferred or sold to another party.<sup>169</sup> By enacting Section 524, Congress sought to “stimulate new drug development by offering additional incentives for obtaining FDA approval of certain tropical disease drug products.”<sup>170</sup>

Proponents for PVRs argue that they are “a powerful new incentive” for companies to invest in the treatment of tropical diseases.<sup>171</sup> A voucher could be worth \$50-500 million,<sup>172</sup> and the benefits derived could include reducing FDA review by four to 12 months and allowing for earlier market entry, which could give a company greater advantage over competition.<sup>173</sup>

Enamored by the possibilities of these new vouchers, in March 2011, four senators cosponsored a bipartisan bill, the Creating Hope Act of 2011, which would amend the FDC Act § 524 to expand the priority review voucher program to include rare pediatric diseases.<sup>174</sup> The bill was designed to “encourage the development of

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<sup>165</sup> Press Release, White House, President Bush Signs H.R. 2669 and H.R. 3580 into Law (Sept. 27, 2007), <http://georgewbush-whitehouse.archives.gov/news/releases/2007/09/20070927-5.html>.

<sup>166</sup> Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, 121 Stat. 972 (codified at 21 U.S.C. § 360n); *see also* U.S. DEP’T. OF HEALTH & HUMAN SERV. GUIDANCE FOR INDUSTRY: TROPICAL DISEASE PRIORITY REVIEW VOUCHERS 1 (2008), <http://www.fda.gov/OHRMS/DOCKETS/98fr/FDA-2008-D-0530-gdl.pdf>.

<sup>167</sup> U.S. DEP’T. OF HEALTH & HUMAN SERV., *supra* note 166, at 1. *See also* Fee for Using a Priority Review Voucher in Fiscal Year 2011, 75 Fed. Reg. 55589 (Sept. 13, 2010).

<sup>168</sup> *See* Food and Drug Administration Amendments Act of 2007 Pub. L. No. 110-85, 121 Stat 823 (codified as amended in scattered sections of 21 U.S.C.).

<sup>169</sup> *See* U.S. DEP’T. OF HEALTH & HUMAN SERV., *supra* note 166, at 5 (stating that, while FDC Act § 524 allows for only a single actual transfer of a PRV from the original recipient to another sponsor, “contractual arrangements such as the use of an option or transfer of the right to designate the voucher’s recipient could comply with the terms of the statute”).

<sup>170</sup> *See* U.S. DEP’T. OF HEALTH & HUMAN SERV., *supra* note 166, at 2.

<sup>171</sup> BIO VENTURES FOR GLOBAL HEALTH, [www.bvgh.org/What-We-Do/Incentives/Priority-Review-Vouchers.aspx](http://www.bvgh.org/What-We-Do/Incentives/Priority-Review-Vouchers.aspx) (Last visited Mar. 9, 2013).

<sup>172</sup> *Id.*

<sup>173</sup> *Id.*

<sup>174</sup> Press Release, Senator Robert P. Casey, Jr., Casey Introduces Bipartisan Bill to Help Develop Treatments for Rare Diseases (Mar. 17, 2011), [http://www.casey.senate.gov/newsroom/press/release/?id=a8deb1ac-6ffd-424b-84b9-c166b4d6ff73;Creating Hope Act of 2011, S. 606, 112th Cong. \(2011\).](http://www.casey.senate.gov/newsroom/press/release/?id=a8deb1ac-6ffd-424b-84b9-c166b4d6ff73;Creating Hope Act of 2011, S. 606, 112th Cong. (2011).)

treatments for children with serious rare diseases.”<sup>175</sup> In September 2011, the House introduced a companion bill.<sup>176</sup> The President signed the Creating Hope Act of 2011 into law on July 9, 2012.<sup>177</sup>

In theory, it would be possible to expand PVRs to encompass all orphan diseases. However, this Article argues that while PVRs have much appeal, they present numerous public policy issues that outweigh their value. First, while the vouchers have received much attention and support for helping to spur research and innovation, at writing, the FDA has only issued a single PRV since the program began in 2007,<sup>178</sup> begging the question of whether they are in fact incentivizing research.

Second, the program invokes many concerns such as: whether the vouchers could slow the review of other drugs;<sup>179</sup> whether such drugs will ever reach the intended affected population since the program does not require sponsors to have secured a manufacturer willing to produce them;<sup>180</sup> and whether a drug subjected to priority review could pose greater safety risks due to faster reviews.<sup>181</sup> This Article will explore the first issue.<sup>182</sup> In particular, Congress needs to consider whether we want to prioritize drugs that should never have priority in the first place, especially when it may slow down priority review for other much needed drugs. An FDA priority

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<sup>175</sup> See Press Release, Senator Robert P. Casey, *supra* note 174; Creating Hope Act of 2011, S. 606, 112th Cong. (2011).

<sup>176</sup> H.R. 3059, 112<sup>th</sup> Cong. (2011). The Creating Hope Act 2011 was unanimously passed by the House Energy and Commerce Committee on May 10, 2012. Press Release, Representative Michael McCaul, House Committee Passes McCaul-Butterfield 'Creating Hope Act' Incentivizes Drug Companies to Develop New Treatments for Children with Rare Pediatric Diseases (May 10, 2012), <http://mccaul.house.gov/press-releases/house-committee-passes-mccaulbutterfield-creating-hope-act-incentivizes-drug-companies-to-develop-new-treatments-for-children-with-rare-pediatric-diseases/>.

<sup>177</sup> Press Release, Cong. Childhood Cancer Caucus, President Signs McCaul-Butterfield 'Creating Hope Act' (July 9, 2012), <http://childhoodcancer-mccaul.house.gov/press-release/mccaul-butterfield-myrick-van-hollen-introduce-creating-hope-act-2011>.

<sup>178</sup> See Waseem Noor, *Placing Value on FDA's Priority Review Vouchers*, 27 IN VIVO 1, 2 (2009). On April 7, 2009, the FDA issued a priority review voucher to Novartis Pharmaceuticals Corp. following approval of their anti-malarial drug, Coartem. *Id.* In February 2011, the company used the voucher to accelerate review for an arthritis drug. *Id.* The FDA recommended against approval of the drug. *Id.*

<sup>179</sup> HENRY G. GRABOWSKI ET AL., ENCOURAGING INNOVATIVE TREATMENT OF NEGLECTED DISEASE THROUGH PRIORITY REVIEW VOUCHERS 8 (Karen Eggleston ed. 2009), <https://faculty.fuqua.duke.edu/~dbr1/research/priority.pdf>.

<sup>180</sup> Nicola Dimitri, *The Economics of Priority Review Vouchers*, 15 DRUG DISCOVERY TODAY 887, 888 (2010).

<sup>181</sup> See Grabowski, *supra* note 179, at 8.

<sup>182</sup> See generally Jeffrey Moe et al., *FDA Review Vouchers*, 360 N. ENGL. J. MED. 837, 837–38 (2008); Aaron S. Kesselheim, *Drug Development for Neglected Diseases- The Trouble With Priority Review Vouchers*, 359 N. ENGL. J. MED. 1981, 1981–83 (2008) (“Drug Development”), Aaron S. Kesselheim, *Priority Review Vouchers: An Inefficient and Dangerous Way to Promote Neglected Disease Drug Development*, 85 CLIN. PHARM. THER. 573, 573–75 (2009); Jorn Sonderholm, *In Defense of Priority Review Vouchers*, 23 BIOETHICS 413, 413–20 (2009) (describing some of the early debates on the benefits and costs of the PRV program).

review designation “was meant to shorten the review time of products that represent major advances in treatment or that treat conditions for which no adequate therapy exists, such as certain types of cancer and infection with the human immunodeficiency virus (HIV).”<sup>183</sup> For such treatments, priority review is reasonable.<sup>184</sup> However, under the voucher program, drugs “for which there is little or no clinical urgency [may] be subject to accelerated deadlines . . . .”<sup>185</sup> In order to analyze those drugs more quickly, the FDA must employ additional resources.<sup>186</sup>

Proponents of the program have argued that the costs of those additional resources are recovered through the special user fee that must be paid by the company that uses the PRV for one of its products.<sup>187</sup> With the user fee, proponents argue that it should not be necessary for the FDA to slow other drugs awaiting approval.<sup>188</sup> While this argument appears convincing, its proponents fail to consider the realities of government appropriations and the risk that system presents.

Under the PRV program, the special user fees collected each year are deposited and credited as offsetting collections to the account providing appropriations to the Food and Drug Administration.<sup>189</sup> Offsetting collections are authorized to be credited to the account from which they will be spent at the program or account level, and remain there until expended.<sup>190</sup> However, offsetting collections can encourage appropriations committees to reduce spending.<sup>191</sup> This is because “[u]nder current scorekeeping rules, a committee that cuts spending in a program gets credit for the savings (and an increase in offsetting collections is treated as a decrease in spending).”<sup>192</sup> Thus, large influxes of money from the PRV special user fees could result in additional cuts to FDA appropriations. This is problematic. The 2012 State of the FDA identified agency funding as the greatest threat to the FDA’s future.<sup>193</sup> In

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<sup>183</sup> See Kesselheim, *supra* note 182.

<sup>184</sup> See Kesselheim, *supra* note 182.

<sup>185</sup> See Kesselheim, *supra* note 182.

<sup>186</sup> See David B. Ridley & Henry G. Grabowski et al., *Developing Drugs for Developing Countries*, 25 HEALTH AFFAIRS 313, 315 (2010).

<sup>187</sup> *Id.* at 318; see Sonderholm, *supra* note 182, at 415; see also Grabowski, *supra* note 179. For 2012, the special user fee is \$5,280,000, which represents the estimated cost incurred by the Agency for priority review of a drug. Fee for Using a Priority Review Voucher in Fiscal Year 2012 Notice, 76 Fed. Reg. 53910 (Aug. 30, 2011).

<sup>188</sup> See Ridley & Grabowski, *supra* note 186, 319-20; see Sonderholm, *supra* note 182, at 415; See Grabowski, *supra* note 179, at 7.

<sup>189</sup> 21 U.S.C. § 360n (West 2013).

<sup>190</sup> *The Federal Budget: A Primer*, TRUTH ABOUT POLITICS, <http://www.truthandpolitics.org/budget-basics.php> (Last visited March 9, 2013).

<sup>191</sup> Pearl Richardson, *The Growth of Federal User Fee Charges*, U.S. CONG. BUDGET OFFICE (1993) at 34.

<sup>192</sup> *Id.*

<sup>193</sup> Steve Grossman, *FDA Progress “At Risk:” An Update on Funding and a Call to Action*, FDA MATTERS, THE GROSSMAN FDA REPORT (March 25th, 2012), <http://www.fdamatters.com/?cat=11>.

FY 12, the agency received only a small increase in appropriated funding, and FDA faces potential cuts in FY 13.<sup>194</sup>

Additionally, Congressional mandates and amendments to the user fee reauthorization legislation will impose new unfunded requirements on the agency beyond what will be paid for by user fees.<sup>195</sup> Thus, FDA employees will already be overextended; a large influx of PRVs would only compound this problem, even if sponsors must pay a special user fee. This could result in slower priority review times and delay in getting life-saving drugs into the market.

V. WHEN A NEW DRUG IS DISCOVERED, SHOULD DISEASE ADVOCACY GROUPS CONTROL PRICING AND ACCESS?

*“The intention of orphan drug legislation . . . is to make the development of drugs for orphan diseases profitable. The unintended consequence is exploitation of the rules for profit. Like tax avoidance, this is legal, but not necessarily desirable.”*<sup>196</sup>

As discussed above, the new drugs developed through public-private partnerships could significantly improve the lives of many people.<sup>197</sup> However, there is concern that the drugs will be unaffordable and inaccessible to many people suffering from diseases.<sup>198</sup> This section explores that issue and suggests that disease advocacy groups partnering with for-profit bioscience companies should try to contract for patient drug access using a tiered pricing system.

A. *Orphan Drugs can be Expensive and May Not be Accessible to Everyone Affected by the Disease*

Orphan drugs are some of the most expensive drugs in the world, costing as much as \$400,000 per year per individual.<sup>199</sup> Many of the costs of developing a new drug are incurred regardless of the target population size.<sup>200</sup> Thus, companies argue that they must set high prices to recover drug development costs and make a profit.<sup>201</sup> Due to the market exclusivity provisions of the Orphan Drug Act, there may be only one drug on the market to treat the disease;<sup>202</sup> however, people are often

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<sup>194</sup> *Id.*

<sup>195</sup> *Id.*

<sup>196</sup> Robin E. Ferner & Dyfrig A. Hughes, *The Problem of Orphan Drugs*, 341 *BMJ* 1059 (2010).

<sup>197</sup> *See* Part II. D, *supra*.

<sup>198</sup> Keating B. & Côté A, *What is Wrong with Orphan Drug Policies*, 15 *VALUE HEALTH* 8 (2012).

<sup>199</sup> FIELD & BOAT, *supra* note 29, at 10.

<sup>200</sup> FIELD & BOAT, *supra* note 29, at 10.

<sup>201</sup> FIELD & BOAT, *supra* note 29, at 9.

<sup>202</sup> FIELD & BOAT, *supra* note 29, at 4. The Orphan Drug Act provides manufacturers with an exclusive right to market the orphan drug for seven years from the date of marketing approval. FIELD & BOAT, *supra* note 29, at 4. Thus, market exclusivity protects the drug from generic competition during that time period. FIELD & BOAT, *supra* note 29, at 4.

willing to pay high prices, and insurance companies lack leverage to negotiate lower prices.<sup>203</sup>

Even after patent and market exclusivity ends, orphan drugs face less price competition than nonorphan drugs.<sup>204</sup> For nonorphan drugs, generic drug competition will often drive down drug prices within six to twelve months of generic market entry.<sup>205</sup> However, fewer generic drugs are available for orphan diseases, in part, due to the small market potential.<sup>206</sup> Even when a generic is developed, it may only charge a slightly lower price (e.g. 15% less) than the brand-name drug.<sup>207</sup> Substantial price drops for nonorphan drugs typically only occur once additional generic competitors enter the market.<sup>208</sup> However, the development of multiple generic drugs for orphan diseases is less likely, resulting in overall limited price competition.<sup>209</sup> For these reasons, orphan drugs have monopolistic power, leading to their high prices.<sup>210</sup> Thus, despite small markets, orphan drugs can be very profitable,<sup>211</sup> and even result in “blockbuster orphans.”<sup>212</sup>

In one sense, the intention of the Orphan Drug Act has worked; financial incentives now exist for companies to develop treatments for rare disorders,<sup>213</sup> companies are able to make profits on orphan drugs, and there have been over 350 orphan drugs approved by the FDA since the Act was enacted in 1983.<sup>214</sup> Unfortunately, companies seemed to have exploited the system,<sup>215</sup> and the rationales commonly cited for high prices may not apply to all drugs. For example, although companies often cite high research and development costs as a motivating factor in the high pricing of orphan drugs, the argument does not apply to all orphan drugs.

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<sup>203</sup> FIELD & BOAT, *supra* note 29, at 10.

<sup>204</sup> FIELD & BOAT, *supra* note 29, at 181.

<sup>205</sup> FIELD & BOAT, *supra* note 29, at 181.

<sup>206</sup> FIELD & BOAT, *supra* note 29, at 181.

<sup>207</sup> FIELD & BOAT, *supra* note 29, at 181.

<sup>208</sup> FIELD & BOAT, *supra* note 29, at 181.

<sup>209</sup> FIELD & BOAT, *supra* note 29, at 181.

<sup>210</sup> Steven Simoens, *Pricing and Reimbursement of Orphan Drugs: The Need for More Transparency*, 6 ORPHANET J. RARE DISEASES 42, 6 (2011).

<sup>211</sup> In 2006, U.S. orphan drug revenues reached \$32.5 billion and were expected to reach \$47.8 billion by 2011. Aarti Sharma et al. *Orphan Drug: Development Trends and Strategies*, 2(4) J. PHARM. BIOALLIED SCI. 290, 290-99 (2010).

<sup>212</sup> One example of a blockbuster orphan drug is Cerezyme, which is manufactured by Genzyme Corp. for the treatment of Gaucher. Aaron Smith, *From Orphan to Blockbuster?*, CNN MONEY, JULY 8, 2005, <http://money.cnn.com/2005/07/08/news/midcaps/orphan/>. Gaucher is an inherited disease that causes the harmful buildup of fat in the spleen, liver, lungs, bone marrow and brain. *Id.* Genzyme charges up to \$200,000 a year for Cerezyme treatment. *Id.* In 2004, the Cerezyme was used to treat 4,500 people and generated \$839 million in sales. *Id.*

<sup>213</sup> See Simoens, *supra* note 210.

<sup>214</sup> FIELD & BOAT, *supra* note 29.

<sup>215</sup> See Ferner & Hughes, *supra* note 196.

As described above, many orphan drugs are repurposed drugs that had already received FDA approval for another use. In these instances, the research and development costs are substantially less.<sup>216</sup>

Additionally, marketing costs for orphan diseases should be substantially lower than non-orphan drugs, since target populations are small.<sup>217</sup> Furthermore, disease advocacy groups are generally active in informing those afflicted by the disease of new treatments, which can decrease marketing costs.<sup>218</sup>

The high prices of many orphan drugs have very real consequences: the drugs may be unaffordable, and thus unavailable, for many people afflicted by rare diseases.<sup>219</sup> Many individuals lack health insurance coverage and would be unable to afford such high costs on their own.<sup>220</sup> Individuals that seek coverage after being diagnosed with a disease have historically found it difficult to obtain insurance at all, let alone affordable insurance.<sup>221</sup> Finally, even if an individual has health insurance, many plans may cover the drugs but require substantial patient cost sharing.<sup>222</sup> These same people may then be without coverage when treatment costs exceed their plan's lifetime cap or drive premiums unaffordably high.<sup>223</sup>

*B. Public-private Partnership Contracts for Tiered Pricing Systems are a Good Mechanism to Control Orphan Drug Prices*

The issue of affordability and orphan drugs has attracted considerable attention.<sup>224</sup> Aside from federal price controls, numerous arguments have been made

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<sup>216</sup> See Simeons, *supra* note 210, at 3.

<sup>217</sup> FIELD & BOAT, *supra* note 29.

<sup>218</sup> FIELD & BOAT, *supra* note 29, at 371.

<sup>219</sup> OXFAM INT'L, ENDING THE R&D CRISIS IN PUBLIC HEALTH: PROMOTING PRO-POOR MEDICAL INNOVATION 17 (2008), available at <http://www.oxfam.org/sites/www.oxfam.org/files/bp122-rannd-crisis-public-health.pdf>.

<sup>220</sup> See Max G. Bronstein, *US Orphan Drug Policy: Effectiveness Analysis & Policy Recommendations*, 3 CONTEXT J. (2010), <http://dept.contextjournal.org/index.php?journal=context&page=article&op=viewArticle&path%5B%5D=23&path%5B%5D=72>.

<sup>221</sup> FIELD & BOAT, *supra* note 29.

<sup>222</sup> FIELD & BOAT, *supra* note 29.

<sup>223</sup> Thomas Maeder, *The Orphan Drug Backlash*, 288 SCI AM. 5, 87 (2003).

<sup>224</sup> Many scholars have argued for government intervention to reduce incentives under the Orphan Drug Act and control pricing. See Simeons, *supra* note 210, at 5. Some European countries have already adopted such government measures to control the prices of orphan drugs. See Simeons, *supra* note 210, at 2, 7. However, one study found that in high-income countries, extensive price controls have been found to lower the probability of rapid market entry. Jean O. Lanjouw, PATENTS, PRICE CONTROLS AND ACCESS TO NEW DRUGS: HOW POLICY AFFECTS GLOBAL MARKET ENTRY 36 (2005), [http://www.nber.org/papers/w11321.pdf?new\\_window=1](http://www.nber.org/papers/w11321.pdf?new_window=1). Another study found that a U.S. price control policy would lead to a decline in R&D investment of between 36.1 – 47.5%. John A. Vernon, *Drug Research and Price Controls*, REGULATION, at 24, Winter 2002-2003, <http://www.cato.org/sites/cato.org/files/serials/files/regulation/2002/12/v25n4-7.pdf>. The author concluded that “new price regulation in the United States could impose a very high cost in terms of foregone medical innovation. *Id.*”

that the drug industry should at least be encouraged to make drugs for rare diseases reflect value based pricing.<sup>225</sup> At least one scholar has suggested that public-private partnerships could be one mechanism for making drugs more affordable.<sup>226</sup> This Article expands on that idea and proposes that drug advocacy groups, when partnering with commercial and academic researchers, should attempt to contract for tiered-pricing structures that could allow public companies to make a profit while also making drugs available to people unable to pay.<sup>227</sup> In the context of drug products, tiered pricing is a mechanism that adapts a product's price to the purchasing power of consumers in different geographical or socio-economic segments.<sup>228</sup>

There are at least three recent examples of how public entities have controlled the prices of therapies developed in conjunction with private sector companies, two of which have used tiered pricing mechanisms in an attempt to provide affordable therapies for patients. The first partnership involves the state of California. In 2005, the state of California established the California Institute for Regenerative Medicine (CIRM) through a state-wide ballot measure.<sup>229</sup> The measure provided over \$3 billion for stem cell research and allowed CIRM to allocate the money through grants and loans.<sup>230</sup> These grants and loans are governed by numerous regulations, some of which helped to ensure that Californians pay a fair price for drugs they helped create.<sup>231</sup> For example, CIRM requires that for-profit grantees must submit a plan on how uninsured Californians would access a drug produced wholly or partly from CIRM-funded research.<sup>232</sup> Furthermore, the drug must be sold at a price

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<sup>225</sup> See Simeons, *supra* note 210, at 7.

<sup>226</sup> See generally Dan Phair, *Orphan Drug Programs, Public-Private Partnerships and Current Efforts to Develop Treatments for Diseases of Poverty*, 4 J. HEALTH & BIOMEDICAL L. 193,193-225 (2008).

<sup>227</sup> "While there is widespread consensus in support of differential pricing between the richest and poorest nations." PATRICIA M. DANZON & ERIC KEUFFEL, REGULATION OF THE PHARMACEUTICAL INDUSTRY 7 (2013), <http://www.nber.org/chapters/c12572.pdf>. I have not found any articles proposing its use by disease advocacy groups for making domestic orphan drugs more affordable.

<sup>228</sup> Prashant Yadav, DIFFERENTIAL PRICING FOR PHARMACEUTICALS 8 (2010), [http://www.accessmedicineindex.org/sites/www.accessmedicineindex.org/files/yadav\\_differential\\_pricing\\_for\\_pharmaceuticals.pdf](http://www.accessmedicineindex.org/sites/www.accessmedicineindex.org/files/yadav_differential_pricing_for_pharmaceuticals.pdf).

<sup>229</sup> CAL. INST. FOR REGENERATIVE MED., <http://www.cirm.ca.gov/about-cirm> (last visited Mar. 8, 2013).

<sup>230</sup> CAL. INST. FOR REGENERATIVE MED., <http://www.cirm.ca.gov/about-cirm/our-history> (last visited Mar. 8, 2013).

<sup>231</sup> CAL. INST. FOR REGENERATIVE MED., [http://www.cirm.ca.gov/IP\\_FAQ](http://www.cirm.ca.gov/IP_FAQ) (last visited Mar. 8, 2013).

<sup>232</sup> See CAL. CODE REGS. Tit.17 § 100407(a). Intellectual Property and Revenue Sharing Requirements, for For-Profit Organizations. CAL. INST. FOR REGENERATIVE MED., <http://www.cirm.ca.gov/our-funding/intellectual-property-faq> (last visited Mar. 29, 2013).

provided for under the California Discount Prescription Drug Program.<sup>233</sup> The need for tiered pricing formulas has also been examined.<sup>234</sup>

The second example involves a partnership between the Drugs for Neglected Diseases Initiative, a non-profit research and development organization, and the world's third largest pharmaceutical company, Sanofi-Aventis.<sup>235</sup> In 2004, the partnership was formed in order to develop a fixed-dose anti-malarial drug.<sup>236</sup> As part of the agreement, Sanofi-Aventis agreed not to seek patent protection on the drug and to sell it at cost to public health organizations.<sup>237</sup> In early 2007, the partnership launched its first anti-malarial drug.<sup>238</sup> As of 2010, over 80 million treatments had been purchased and the drug was registered in 30 sub-Saharan African countries and in India.<sup>239</sup> The wide success and availability of the drug is due, in part, to a tiered-pricing policy.<sup>240</sup> The tiered pricing policy allows for "no profit-no loss" pricing for the drug in the public sectors, including governments and non-profit NGOs.<sup>241</sup> The same drug is then also sold in the private sector under a different brand name at market prices to allow for profit margins.<sup>242</sup> Thus, the public sector pays less than \$1 for adults and \$0.50 for children per day, while the brand name drug is sold for \$2-3 to wholesalers that supply the private market.<sup>243</sup>

The third example involves the partnership between the Cystic Fibrosis Foundation and Vertex Pharmaceuticals, which produced the drug Kalydeco, described above. While a year's supply of the drug will cost \$294,000, Vertex has agreed to provide the medicine for free to people with no insurance and with household incomes of \$150,000 or less.<sup>244</sup> Furthermore, the company will cover 30 percent of co-pay costs for select patients who have insurance.<sup>245</sup>

As demonstrated above, tiered pricing systems have been successful, at least in some cases, in lessening at least one of the barriers to drug access—drug pricing.<sup>246</sup>

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<sup>233</sup> See CAL. CODE REGS. Tit.17 § 100407(b).

<sup>234</sup> See generally BRENT D. FULTON ET AL., COVERAGE, COST-CONTROL MECHANISMS, AND FIN. RISK-SHARING ALTS. OF HIGH-COST HEALTH CARE TECHS., (2009).

<sup>235</sup> See generally Press Release, Drugs for Neglected Diseases initiative, An agreement between the DNDI Foundation and Sanofi-Aventis (April 8, 2005), <http://www.dndi.org/media-centre/press-releases/archives.html>; See also Francois Bompert et al., *Innovative Public-private Partnerships to Maximize the Delivery of Anti-malarial Medicines: Lessons Learned from the ASAQ Winthrop Experience*, 10 MALARIA J. 143 (2011).

<sup>236</sup> See Bompert, *supra* note 235.

<sup>237</sup> See Press Release, Drugs for Neglected Diseases initiative, *supra* note 235.

<sup>238</sup> See Bompert, *supra* note 235.

<sup>239</sup> See Bompert, *supra* note 235.

<sup>240</sup> See Bompert, *supra* note 235.

<sup>241</sup> See Bompert, *supra* note 235.

<sup>242</sup> See Bompert, *supra* note 235.

<sup>243</sup> See Bompert, *supra* note 235.

<sup>244</sup> See Perrone, *supra* note 9.

<sup>245</sup> See Perrone, *supra* note 9.

<sup>246</sup> See Perrone, *supra* note 9; Bompert, *supra* note 235.

Thus, disease advocacy groups should consider the use of price control mechanisms when forming partnerships with commercial and academic researchers. However, the ability of disease advocacy groups to secure such contractual price controls may depend on their ability to derisk the venture, which may depend on the amount of initial funding, likelihood of future funding, their ability to provide access to patients for clinical trials, their ability to reduce marketing and advertising costs through access to patient registries, the potential market size for the drug, and the availability of orphan drug tax credits and market exclusivity.

#### VI. CONCLUSION

In conclusion, partnerships between disease advocacy groups and commercial and academic researchers present exciting new possibilities for drug development, including the development of orphan drugs. This paper advocates for Congress to support these new partnerships by amending the patent law to create a federally sanctioned “biomedical patent commons” for orphan disease research. Congress should not continue to expand the Priority Review Voucher program due to the negative impacts that it could have on the priority review process and overall agency funding. Finally, when disease advocacy groups do partner with bioscience companies, tiered pricing systems appear to be a good way to ensure that people unable to pay for therapies can nonetheless gain access to them.

