Nonprofit Disease Foundation Investments in Biotechnology Companies: An Evaluation of Venture Philanthropy

by

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Submitted to the Harvard-MIT Division of Health Sciences and Technology in partial fulfillment of the requirements for the degree of Master of Science in Health Sciences and Technology at the

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

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Abstract:

In the past decade, the practice of venture philanthropy, defined in this research as the provision of capital by a nonprofit entity to a for-profit company, has become an increasingly common asset allocation strategy for nonprofit disease-focused foundations. Both nonprofit organizations and biotechnology firms alike have praised these funding relationships as instruments that help enable, de-risk, and ultimately accelerate the development of new therapies. However, data on the composition and performance of these venture philanthropy investment portfolios remains scarce. While the field of venture philanthropy is too young to have robust outcome data as of yet, we attempted to understand the methodologies for venture philanthropy portfolio construction, the historical mix of projects funded, and the performance of these portfolios thus far. We hypothesized that our independent assessment of grant portfolio composition would be congruent with stated portfolio policy. Instead, we found that organizations did not have a predetermined asset allocation framework against which to compare their investments. We collected data on industry-funding portfolios from three major participants in venture philanthropy in three different disease areas: the Cystic Fibrosis Foundation (CFF), the Juvenile Diabetes Research Foundation (JDRF), and the Michael J. Fox Foundation for Parkinson’s Research (MJFF). Data was gathered from organization websites, annual reports, and financial filings. Interviews were conducted with grant program executives at each of the three organizations. While it was not possible to confirm or reject our hypothesis on the basis of portfolio congruence, we were able to show that in the absence of articulated portfolio policy, investment choices may not be aligning with stated program aims to fund earlier-stage, risky projects.

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Introduction:

There are nonprofit foundations representing nearly every disease that we have been able to name and characterize. For most of these organizations, their primary activity is to support disease research, in the hopes of developing new therapies for their patient stakeholders. In many instances, and certainly for the major diseases of our time, there are biotechnology companies working in parallel on therapeutic research and development in those same disease areas. However, for much of the history of biomedical research, these two entities have worked in independent silos, with nonprofit organizations funding academic laboratories, and biotechnology firms pursuing whichever program areas were profitable, or were the best fit for their company strategy. Venture philanthropy has begun to change this paradigm.

This thesis examines current trends in disease foundation venture philanthropy through an analysis of portfolio composition of three leading disease organizations: The Juvenile Diabetes Research Foundation (JDRF), The Cystic Fibrosis Foundation (CFF), and The Michael J. Fox Foundation for Parkinson’s Research (MJFF). First, we examine the history and landscape of venture philanthropy among disease-focused foundations. We then attempt to characterize the portfolios of the three organizations in our sample using interview data and descriptive statistics. We conclude by making recommendations for nonprofit managers, and for future areas of research in the field of nonprofit asset allocation.

While venture philanthropy in biomedical research will remain a more niche strategy, and does not represent a sea change in the spending patterns among most nonprofit disease organizations, it has become an integral part of the strategies of some of the largest, most influential organizations in the sector. Of the 24 largest U.S. not-for-profit health organizations by revenue, more than 20% now have venture philanthropy investment programs; this figure does not include large foundations, many of whom have venture philanthropy programs as well. The emergence of venture philanthropy practices in disease-focused organizations has been attributed, in part, to a growing impatience among patients and disease-focused foundations surrounding the dearth of new therapies reaching the clinic. This frustration is of
course shared by biotechnology firms and their investors, and the reality of the decrease in new drug approvals has been well characterized. There has been an exponential decline in R&D productivity (as defined by new molecular entities per billion dollars of R&D spend), and a slowing of clinical development timelines for even the successful drug candidates. From 2007 to 2009, average “new molecular entity” approval times increased by 6.4 months. Traditional investors are becoming more reluctant to invest the substantial time and capital required to surmount both scientific and regulatory hurdles, and are therefore less willing to bet on early stage biotechnology companies, leaving a gap for unconventional investors to take on the risk. From 2009 to 2010, though overall capital inflow to biotechnology firms increased, 83% of the funding went to the top 20% of companies, and funding for pre-commercial companies decreased by 21%. In the first quarter of 2011, there were fewer venture capital deals in biotechnology than in any quarter for nearly a decade. Though there have always been gaps in the funding of assets from discovery through clinical readiness, the growing hesitance of venture capitalists and pharmaceutical companies to make bets on earlier stage therapies is making the role of non-financially motivated investors even more critical. In trying to adjust to the current state of drug development, stakeholders across the biomedical research industry are beginning to rethink how they allocate their research and development dollars, and nonprofit organizations are no exception.

In this era of changing business models in biomedical research and development, nonprofit organizations have stepped into a new, more prominent role in the development of therapies by partnering with industry. Nonprofits have been driven by their own assessments of where the best science is, as well as how they can most effectively use donor dollars to fulfill their missions. Additionally, as traditional investors begin to reallocate their dollars to other parts of the development value chain, or to other industries altogether, there are new opportunities for these organizations to fill the gap. Venture philanthropy, which began in small orphan diseases that couldn’t get the attention of mainstream investors, and in diseases of developing economies, is becoming ever more common across a range of disease areas, including conditions with very large domestic markets where traditional investors are also active. It is
now being practiced by over 25 nonprofit organizations in the domestic disease space alone, according to a tally performed at the time of this research (See Figure A).

Figure A: Select Nonprofits Engaging in Venture Philanthropy:

<table>
<thead>
<tr>
<th>Organization</th>
<th>Total Revenue (2009)</th>
<th>Net assets (fiscal year end)</th>
<th>Investment Focus</th>
<th>Approximate start date of program</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukemia and Lymphoma Society</td>
<td>$246,744,046</td>
<td>$109,447,069</td>
<td>Blood cancers</td>
<td>2008</td>
</tr>
<tr>
<td>Juvenile Diabetes Research Foundation</td>
<td>$198,388,186</td>
<td>$31,554,115</td>
<td>Type 1 diabetes and its complications</td>
<td>2004</td>
</tr>
<tr>
<td>Muscular Dystrophy Association</td>
<td>$179,394,809</td>
<td>$74,500,992</td>
<td>Muscular Dystrophy</td>
<td></td>
</tr>
<tr>
<td>Cystic Fibrosis Foundation</td>
<td>$101,136,919</td>
<td>$0</td>
<td>Cystic Fibrosis</td>
<td>1998</td>
</tr>
<tr>
<td>Fast Forward (National Multiple Sclerosis Society)</td>
<td>$91,383,906</td>
<td>$15,080,669</td>
<td>Multiple Sclerosis</td>
<td>2007</td>
</tr>
<tr>
<td>Michael J. Fox Foundation</td>
<td>$51,388,940</td>
<td>$24,028,001</td>
<td>Parkinson's and dyskinesia</td>
<td>2005</td>
</tr>
<tr>
<td>Goldhirsh Foundation</td>
<td>$34,559,848</td>
<td>$114,688,464</td>
<td>Brain cancer</td>
<td>2006</td>
</tr>
<tr>
<td>Prostate Cancer Foundation</td>
<td>$33,363,098</td>
<td>$22,547,661</td>
<td>Prostate Cancer</td>
<td></td>
</tr>
<tr>
<td>Foundation Fighting Blindness</td>
<td>$30,712,330</td>
<td>$22,420,196</td>
<td>Spectrum of retinal degenerative diseases</td>
<td></td>
</tr>
<tr>
<td>Multiple Myeloma Research Foundation</td>
<td>$20,730,000</td>
<td>$9,086,898</td>
<td>Multiple Myeloma</td>
<td>2006</td>
</tr>
<tr>
<td>CHDI Foundation</td>
<td>$18,055,454</td>
<td>$21,770,444</td>
<td>Huntington's disease</td>
<td></td>
</tr>
<tr>
<td>Cancer research institute</td>
<td>$13,685,488</td>
<td>$21,847,056</td>
<td>Cancer immunotherapies</td>
<td>2010</td>
</tr>
<tr>
<td>Christopher and Dana Reeve Foundation</td>
<td>$13,372,322</td>
<td>$6,202,015</td>
<td>Spinal cord injury and paralysis</td>
<td></td>
</tr>
<tr>
<td>Myelin Repair Foundation</td>
<td>$12,381,441</td>
<td>$15,944,466</td>
<td>Multiple Sclerosis</td>
<td>2003</td>
</tr>
<tr>
<td>ALS Therapy Development Institute</td>
<td>$8,913,050</td>
<td>$4,267,657</td>
<td>ALS</td>
<td>1999</td>
</tr>
<tr>
<td>Iacocca Foundation</td>
<td>$4,303,268</td>
<td>$37,751,862</td>
<td>Type 1 diabetes</td>
<td>2008</td>
</tr>
<tr>
<td>Blanchette Rockefeller Neurosciences Institute</td>
<td>$4,038,662</td>
<td>$28,783,894</td>
<td>Alzheimer's disease and other neurological disorders</td>
<td></td>
</tr>
<tr>
<td>Friedreich's Ataxia Research Alliance</td>
<td>$3,264,591</td>
<td>$3,215,258</td>
<td>Friedreich's ataxia (FA)</td>
<td>2005</td>
</tr>
<tr>
<td>Alzheimer's Drug Discovery Foundation</td>
<td>$2,460,993</td>
<td>$1,413,408</td>
<td>Alzheimer's Disease</td>
<td>1999</td>
</tr>
<tr>
<td>Epilepsy Therapy Project</td>
<td>$1,478,321</td>
<td>$551,751</td>
<td>Epilepsy</td>
<td>2004</td>
</tr>
<tr>
<td>Accelerate Brain Cancer Cure</td>
<td>$1,285,211</td>
<td>$1,459,472</td>
<td>Brain Cancer</td>
<td>2001</td>
</tr>
<tr>
<td>Melanoma Therapeutics Foundation</td>
<td>$275,824</td>
<td>$80,388</td>
<td>Melanoma</td>
<td></td>
</tr>
<tr>
<td>Stanley Medical Research Institute</td>
<td>-$10,682,922</td>
<td>$204,509,852</td>
<td>Schizophrenia and Bipolar Disorder</td>
<td></td>
</tr>
</tbody>
</table>

Source: Organization 990s (Guidestar); HBS Case “Vertex Pharmaceuticals and the Cystic Fibrosis Foundation: Venture Philanthropy Funding for Biotech”; Chang (2010), Organization Interviews
As philanthropic players, nonprofits may have greater risk-tolerance, more patience, and different incentives than traditional actors who seek a financial return over a specified time period. Nonprofits are thus positioned to be able to fill gaps and invest in companies and technologies that other investors might overlook. But, even as external market circumstances in R&D put more emphasis on the role of nonprofit actors, and organizations themselves get galvanized by the idea of helping to drive translational therapies forward to commercialization, analysis of the landscape of venture philanthropy remains scarce. Here we attempt to examine the current state of venture philanthropy, in order to ascertain, as best as possible, how it is performing thus far. While there are tremendous potential benefits to funding for-profit entities that have more expertise in translating research and reducing it to practice, there’s an opportunity cost as well, and this underscores the importance of gathering more data on existing venture philanthropy programs. Funds for research are limited and for every grant made to a for-profit entity, there are fewer dollars available for researchers in academic settings. Dr. Robin Goland, Co-Director of the Naomi Berrie Diabetes Center, described this tradeoff in the diabetes research field, saying that despite patients’ eagerness for a cure, we don’t know enough about the basic science, and our animal models to test new therapies aren’t adequate. While there is value in funding promising science, regardless of the sponsoring entity, academic centers are responsible for training new scientists, and for performing critical basic and translational research. By opting to fund commercialization, there is the potential to create an anemic pipeline of research candidates and researchers in the next generation. There is also the risk more generally, as some critics of venture philanthropy have cited, that for-profit companies are not appropriate recipients of non-dilutive nonprofit capital.

Those involved in both running and supporting nonprofit disease foundations have begun to recognize that independent analysis of the industry’s activities is overtly lacking. As philanthropist Larry Flax put it, “I run a public company. I look at how we compete for investment dollars. There is a whole group of people out there, they call them analysts. And all they do is try to tell everybody how I’m doing. We’re competing for the investor dollar. I think what’s needed in philanthropy is this layer of analysts.” This thesis endeavors to take an
analytic approach to evaluate the emerging practice of disease-focused venture philanthropy. The field of venture philanthropy is still too young to have robust outcome data from investments. Ideally, one would be able to look at such variables as, the speed between clinical stages, and overall approval rates for assets in the nonprofit portfolio, and compare these to industry averages. As the data is too scant to make such comparisons, instead, we focused on characterizing the portfolios of three large disease-focused not-for-profits, MJFF, CFF, and JDRF. We looked at existing methodologies for constructing and managing these venture philanthropy portfolios, and the make-up of these portfolios with respect to company size, stage and financing.

We hypothesized that our characterization of the three portfolios would reveal a portfolio composition that was congruent with the stated program aims and portfolio goals described by the organizations. This research provides an independent, external assessment of disease foundation venture philanthropy, and of the strategy that underlies it. The results may be useful to the organizations themselves in understanding how they differ from their peer organizations, with respect to portfolio policy, portfolio makeup and portfolio measurement. The data generated may also help organizations improve their accountability, addressing philanthropists’ concerns around not having adequate resources to evaluate giving options or nonprofit organization performance. The research may also provide a fresh perspective on existing portfolios, with the potential to inform future portfolio management.

**Background:**

*Philanthropy in Biomedical Research*

Of the $139B dollars of estimated health research spending in 2009, pharmaceutical, biotechnology, and medical device companies spent $73B, the Federal government spent $47B (this includes the entire NIH budget, plus contributions from other agencies), and philanthropic foundations, voluntary health organizations and research institutes spent $3.7B, contributing about 3% of total R&D dollars. Though this represents a much smaller contribution toward
R&D in the United States, nonprofit money plays an entirely different role than either industry or government money.

Unlike U.S. government entities or major corporations that have a duty to be responsive to the public or to shareholders, and are subject to many protective layers of bureaucracy, nonprofits can make a funding decision with the approval of a quorum of board members, and can do so almost immediately. Additionally, in contrast to venture capital investors who are constrained by external market circumstances, expected returns and payout timelines, nonprofits can fund projects that are financially risky, counter-cyclical, or of longer duration. Nonprofits have the ability to fund research that is not only time-sensitive, but also politically controversial, higher-risk, or even unproven. This unique role for nonprofit organizations was manifest in the early 1990s in AIDS research, and more recently in the field of stem cell research. The Aaron Diamond Foundation’s AIDS research center, founded in 1991, began heavily investing in AIDS research at a time when the U.S. government was slow to get involved, and the foundation’s lab is credited with the discovery of protease inhibitors that now form the basis of the AIDS treatment cocktail. In the field of stem cell research, when government funding was restricted in 2001 by President Bush, disease-focused nonprofit organizations came forward to fund stem cell labs at a time when even industry players were hesitant to fund the risky research. Nonprofits can help bear the burden of scientific risk by providing researchers with funds to generate the proof-of-concept data for newer ideas that government and industry may not be willing to fund. The capacity for rapid, nimble funding is epitomized by the Michael J. Fox Foundation’s Rapid Response Innovation Award program, which is dedicated to funding high-risk ideas with very little available data. These grant applications are accepted on a rolling basis; funding is announced within 6 weeks of application submission, and is disbursed within 12 weeks of submission. This is in stark contrast to NIH’s grant mechanisms with narrow request for application topics, fixed submission dates, and award timelines of approximately 18 months. Though SBIR and STTR award timelines are more condensed (approximately 8 months from submission), these grant mechanisms carry restrictions as well, such as eligibility requirements based on existing financing and ownership structure.
It is important to distinguish between the two main types of nonprofit organizations, or voluntary health organizations, these are: public charities and private foundations. Public charities have to raise their budgets every year, whereas foundations are private, endowed institutions. Private foundations have to meet a minimum distribution threshold equal to 5% of the average fair market value of their assets every year; public charities face no such spending requirements. In the biomedical research sector, examples of public charities include, the American Heart Association, the American Cancer Society, and the three foundations profiled in this research, JDRF, CFF, and MJFF. Major private foundations include, the Howard Hughes Medical Institute, and the Bill and Melinda Gates Foundation. Public charities are often the recipients of funds from these private foundations. Additionally, because public charities have to raise their budgets every year, they have to be more aware of how their activities are perceived by their donor base. It is for this reason, in part, that we have selected three organizations that rely on donor support for our case study, so that potential interactions between investment strategy and donor accountability can be assessed. In this paper, we refer to nonprofit disease foundations, which is inclusive of both types of nonprofit organization.

Traditionally, nonprofit organizations have funded earlier stage academic lab research, and the majority of philanthropic dollars continue to flow into this early-stage work in research laboratories. Even within this stage of research funding, there is a wide range of potential areas to focus financial support. Organizations will often choose to invest in a particular segment of the funding continuum, such as basic research, translational research, post-doctoral research fellowships, senior investigator grants, etc. Later-stage research—from preclinical large animal work to all stages of human clinical trials—has been funded for the most part by venture capital, angel investors, and large corporations, and this continues to be the case.

A History of Venture Philanthropy

Though there are instances where nonprofits have funded the commercialization of new therapeutics that date back to the early 20th century, such as the National Foundation for
Infantile Paralysis’ funding of the polio vaccine, the most frequently cited first articulation of venture philanthropy theory in the literature is Letts et al.’s 1997 piece, “Virtuous Capital: What Foundations Can Learn from Venture Capitalists.” Letts (1997) lamented the lack of management and capacity-building undertaken by grant-making organizations, and described the potential for foundations to act more like venture capitalists. This breed of philanthropy involved greater managerial oversight, more performance milestones and metrics, longer-term relationships, and a goal of achieving sustainability of the investment. Stemming from these initial theories of venture philanthropy, a number of nonprofits began to experiment with venture philanthropy strategies, and the term venture philanthropy now encompasses almost any nonprofit funding activities that could be construed as having been borrowed from the for-profit sector. For the purposes of this research, however, we define venture philanthropy quite narrowly, as the investment of capital by a nonprofit disease-focused organization in a for-profit biotechnology or pharmaceutical firm. The disease organizations represented here also use milestone structures for their grants, along with sophisticated evaluation processes and oversight, consistent with broader definitions of venture philanthropy, but they would define their venture philanthropy activities according to the same parameter of for-profit partnership that we use here.

For the most part, early experiments in venture philanthropy among disease-focused foundations occurred in orphan diseases and the global health arena, markets which struggled to gain momentum with traditional capital alone. For-profit investors typically couldn’t rationalize the upfront development costs and risks for a drug that would serve a very small market, or a patient population with a low ability to pay. Robert Beall, CEO of The Cystic Fibrosis Foundation, is credited with one of the first major venture philanthropy deals. In 1998, the organization struck a $47 million dollar research funding agreement with Aurora Biosciences. In describing the impetus for the grant, Beall explained, “No company was ever going to invest this kind of money in cystic fibrosis.” On the global health stage, The Gates Foundation and the International AIDS Vaccine Initiative, among others, have also been engaging in venture philanthropy for years. But organizations representing much larger disease
populations in domestic markets have followed suit, and now venture philanthropy is a key part of the research funding strategy for disease organizations in cancer, diabetes, multiple sclerosis, Parkinson’s, Alzheimer’s, and other disease areas where for-profit companies have shown consistent activity, but simply haven’t delivered.

U.S. disease foundation venture philanthropy is increasing, both in terms of the number of organizations disbursing capital to for-profit companies, and the amount of money spent on industry partnerships. Between 2000 and 2007, annual venture philanthropy investments in biotechnology and pharmaceutical firms increased more than ten fold, to $75 million dollars.\textsuperscript{26}

Deal values keep growing. In 2011, the Cystic Fibrosis Foundation announced a 5-year funding agreement with Vertex Pharmaceuticals, valued at up to $75 million dollars, marking the largest venture philanthropy collaboration to date.\textsuperscript{27} While the total annual dollar value of the investments is relatively small when compared to the sum of for-profit investor activity or even nonprofit grant-making overall, the investments are intended to fill timely strategic gaps, and to serve an unmet need in moving translational research toward the clinic. Additionally, the very existence of this funding mechanism is causing nonprofit organizations to reassess their entire grant-making process, with due-diligence practices, milestone and reporting requirements being put in place for traditional grants to nonprofit entities and academic laboratories as well.

On the opposing side of the table, the opportunity to ally with a major nonprofit and to receive potentially non-dilutive funding, has for-profit biotech firms considering entirely new options for early stages of financing. These venture philanthropy financings, it could be argued, are having a ripple effect on the entire biomedical research funding landscape.

\textit{The Spectrum of Venture Philanthropy Activities}

Since the state of scientific understanding, the patient population, and the competitive market dynamics vary from one disease to the next, we would expect that venture philanthropy strategies would vary accordingly. And indeed, organizations’ strategies do depend on these external market circumstances, but they also differ based on the entirely internal opinions of board members and the management team. For example, in an analysis of disease foundation
investment activities, Chang (2010) found that disease foundations vary considerably in where they are willing to invest along the continuum of therapeutic development. JDRF, CFF and the Alzheimer’s Drug Discovery Foundation invested in projects through Phase 3 of clinical development, whereas MJFF, the Multiple Myeloma Research Foundation, and the Foundation Fighting Blindness were only investing in projects up through Phase 2. The Christopher and Dana Reeve Foundation as well as the Prostate Cancer Foundation were only investing in development through Phase 1 safety trials. As was mentioned previously, given the varied nature of each disease space, it would be impossible to have a venture philanthropy program framework that was suitable to all these organizations. However, it is equally difficult to ascertain whether these actors are playing in particular parts of the development chain because of external factors (the science, the market, their budgets), or the internal strategies and the risk-tolerance level of the organization. Given the diversity within and across categories, it seems likely that the latter plays a role to some extent. Figure B below was created by the Alzheimer’s Drug Discovery Foundation to visualize the role venture philanthropy plays in filling a gap in drug development.

Figure B: Biomedical Venture Philanthropy and the Financing Gap in Drug Development

![Figure B: Biomedical Venture Philanthropy and the Financing Gap in Drug Development](image)

Source: Alzheimer’s Drug Discovery Foundation
In the case of investment mechanism, it also seems to be the case that internal decisions, not necessarily driven by external market factors unique to the disease area, account for a portion of the strategy. Disease foundation venture investments have taken the form of grants, equity, warrants, and convertible notes. But not every foundation employs that same variety of financial instruments in their deal structures. To contrast two of the organizations in our current sample, JDRF has both equity and grant investments in their portfolio, while MJFF has restricted its funding to grants only. Former MJFF CEO Katie Hood described this decision as having come from the organization’s Board of Directors; they felt that any attempt to make an equity investment in a for-profit company would take longer than giving a grant, and would thus go counter to the organization’s efforts to accelerate the pace of development. JDRF has one equity investment in Tolerx; the rest of their investments are milestone-based grants. When asked about the decision to take an unprecedented equity position instead of providing a grant, Peter Lomedico, who manages strategic alliances for JDRF, explained that Tolerx had approached them and said that an equity investment would be most helpful to their fundraising efforts at that time. It is precisely these sorts of strategic decisions in venture portfolio construction that warrant external analysis, and this thesis will attempt to shed light on the key differences between the strategies and portfolio policy of these principle industry actors. There is, however, one critical difference in the accounting of grant vs. equity funding from a nonprofit entity that may have bearing on organizations’ choices in this matter. For private foundations, equity investments do not count toward the required 5% annual spend, and might therefore require dipping into the endowment’s corpus. Additionally, all nonprofit organizations, according to nonprofit GAAP, must report the amount of their annual giving that represents programmatic spend, in other words, the amount that goes toward activities in service of their mission. For a public charity, an equity investment is kept on their books as an asset, and does not count toward programmatic spending. Unfortunately, external nonprofit rating agencies such as Guidestar and Charity Navigator place undue emphasis on this percentage of crudely determined program spend intended for accounting purposes. This system makes the decision to make an equity investment additionally complicated for nonprofit organizations.
Deal Sourcing, Structure, and the Portfolio Entity

Deal sourcing is relatively consistent across disease foundation venture philanthropy programs. Most organizations report deals emanating from a variety of sources, including senior management, Board of Directors, requests for applications, for-profit companies, and academic investigators. Additionally, organization leaders have noticed that as their venture philanthropy programs become more mature, more companies begin to approach the foundations, and the balance of sourcing shifts toward company initiation. Deal selection is also fairly similar across groups, with most organizations having both a scientific and a business team involved in the selection of projects. With respect to deal structure, the majority of investments are in the form of grants with milestone payment structures for relevant scientific or clinical goals achieved. Both CFF and JDRF require matching funds, whereas MJFF does not. Most agreements also include royalty payments either in the form of a multiple of the original investment made, or a traditional percentage of net sales. Organizations also usually include an additional kick-back provision should the therapy hit a certain unexpected level of commercial success. These royalties are not meant to result in windfalls for the nonprofits, but rather allow them to recoup their investments, and earn a modest return that they can then re-invest in other promising projects.

According to the current body of knowledge in the field of venture philanthropy, it is known that organizations have varying approaches to creating, measuring, and rebalancing their portfolios of industry projects. While each individual deal may bear some structural similarity across organizations (many of the organizations use the same law firm that specializes in venture philanthropy agreements), the portfolio as an entity is not assessed in the same way at any of the organizations. These organizations have not relied on traditional venture capital metrics, such as return on investment, and as a result have developed other ways to evaluate their portfolios. However, the extent to which these groups are articulating a portfolio policy, and measuring themselves against it, is unclear. The CFF measures increases in median life expectancy for the disease, and has its own point system to track the progress of their pipeline. MJFF and JDRF both track the progress in their pipeline, and are beginning to look at follow-on
funding and acquisitions of companies they have funded.\textsuperscript{39,40,41} While these measures, such as progress through the pipeline, can be useful for quickly communicating progress at a high level to a potential donor, they are not indicators for investment strategy and portfolio management.

As is evidenced by the examples above, some measures of performance exist for this field, but they vary by organization, and these metrics alone do not communicate the intended portfolio composition, or the strategic changes that take place from year to year. This is in contrast to other institutional investors, who are accustomed to articulating an asset allocation policy. For example, The Harvard Management Company, which manages Harvard University’s endowment, publishes a Policy Portfolio every year. The Policy Portfolio describes how their portfolio is theoretically allocated among asset classes. This policy is used as a yardstick against which actual investment allocation and performance can be measured.\textsuperscript{42} The nonprofits in this research are undoubtedly facing a different set of strategic challenges than an endowed institution, but these existing Policy Portfolios set a standard for disclosure and accountability. Even though nonprofit disease organizations share their program aims and strategies at a high level, and have metrics in place to evaluate themselves, unless clearly stated asset allocation goals are established a priori, it is more difficult to demonstrate the intention behind their investments.

Neither industry rating groups, such as Charity Navigator, nor the majority of the nonprofit donor base, have demanded a mechanism to assess venture philanthropy portfolios. There is also no precedent in the industry for benchmarking or portfolio reporting. Without external pressure to develop these measures, there has been no incentive to standardize, and organizations have developed their own measurement practices. Though this can provide some data to donors and the organizations themselves, it leaves a wealth of comparator and accountability data on the table. FasterCures, a nonprofit organization dedicated to accelerating translational research and therapeutic development across the entire biomedical industry, has served as a convener and data clearinghouse for organizations involved in venture philanthropy. They also run a Philanthropy Advisory Service that has begun to measure and
benchmark organization performance. But, much research remains to be done on the current state of venture philanthropy investment, and potential standard measures for venture philanthropy portfolios. In order to better characterize the performance of venture philanthropy overall, the industry requires external probing to determine what portfolio policies are in place currently, and whether existing portfolios are doing precisely what they are ostensibly intending. Though in the present research, we analyze only three of the groups involved in venture philanthropy, we hope that this analysis can serve as a framework and starting point for additional portfolio and performance research in the field.

Other Types of Industry Partnerships

It bears mentioning that financial investments in for-profit companies are not the only way in which organizations have begun to work more closely with industry to accelerate the development of therapeutics. Some partnerships take the form of collaborative grant-making, such as JDRF’s agreement with Johnson & Johnson where both groups have agreed to fund a particular area of diabetes research. Organizations have also become active in the clinical trial management space, creating patient networks to help with recruitment, funding clinical trial centers, and providing clinical trial design assistance and contracting templates to ensure that clinical development proceeds both expediently and as effectively as possible. Research consortiums have emerged, such as the Cancer Research Institute’s Cancer Vaccine Collaborative, and the Multiple Myeloma Research Foundation’s Multiple Myeloma Research Consortium that aggregate critical clinical research elements, such as patient samples, intellectual property, and chemical compounds.43

Beyond the clinical development stage, nonprofits have funded research activities that have contributed to successful reimbursement of new commercial products for their patients. When continuous glucose monitors were not being reimbursed by payers because of sparse evidence of their clinical effectiveness, JDRF assembled a team to address the problem. They spoke to payers to understand the outcome data they would require before agreeing to cover the devices, reached out to the three medical device manufacturers with continuous glucose
monitors, and proceeded to fund a multi-center trial that resulted in a New England Journal of Medicine paper, and reimbursement for the devices.\textsuperscript{44,45} These activities are also a vital piece of nonprofit strategies to accelerate the development of new therapies. In this research, however, we will focus only on the provision of capital directly to a company.

\textit{Nonprofit Assets}

There are several key contributions that a nonprofit can make to a for-profit biotech’s drug development program. The first, and most obvious, is the value of the grant or investment itself, and the associated brand name of the investor. For the most part, nonprofits provide non-dilutive financing, which can ease traditional tensions between founders and investors in the process of raising capital. Less dilution and fewer for-profit investors also means that companies may be able to negotiate an acquisition and an exit more easily.\textsuperscript{46} Biotechnology firms also report being able to raise additional funds after receiving the seal of approval from a nonprofit investor. Kineta Bio’s Chief Financial Officer Ken North said that after receiving a grant from the Iacocca Foundation, they were able to leverage the nonprofit’s brand with other potential funders.\textsuperscript{47}

An extension of the financial benefits, the strategic nature of nonprofit funding also confers an advantage upon biotech partners. Nonprofits are able to invest without the same concern over financial return or short-term payout timelines, resulting in patient capital with potentially high risk-tolerance. They are less restricted by the potential market opportunity, the projected duration of the research, and by their own fund vintage than a venture capital firm or angel investor. Because they are focused primarily on moving work forward, instead of profitability, nonprofits can fund companies or projects that financially motivated investors may not want to fund, and can pay for the development of unprofitable tools and assays that might make the difference between a successful or a failed clinical trial. An interesting parallel could be drawn between nonprofit investors and corporate venture capital groups. Similar to the nonprofit investor, corporate venture capital is considered to be a more strategic, rather than financially motivated, investment mechanism.\textsuperscript{48} A comparison between strategic corporate investors, and
strategic nonprofit investors is worthy of further research, however we assert that key
differences already exist. Corporate venture capital arms represent the strategic interests of
their parent company. As a result, they don’t possess the same level of neutrality as a nonprofit
organization. Additionally, because they represent company interests, and not the interests of a
patient population, their portfolio strategy might fluctuate dramatically with shifts in parent
company strategy, causing them to abandon investment in a disease area.

Most companies who have received nonprofit monies would likely say that other components
of the relationship are even more important than the financial capital, notably, access to
“intellectual capital”. Nonprofits often have scientific advisory boards comprised of leaders in
a particular field. Not to mention that the organizations themselves invest tremendous
resources into surveying the entire landscape of research and investment in their disease area.
By allying with the nonprofit, biotech partners position themselves at the frontier of high
quality scientific and competitive analysis in their disease area.

The other key asset relates to the patient population and patient advocacy. Nonprofit
relationships with patients are invaluable, especially in orphan or rare diseases. Nonprofits can
facilitate trial design and trial speed by giving partner companies access to their patient
registries and samples. Nonprofits can help with patient recruitment, and can also use their
clout to advocate on regulatory decisions with the FDA.

The Need for Venture Philanthropy

Pisano (2006) identified three key flaws in the current structure of the biotechnology industry,
as it relates to its profitability and productivity. The first, that the management of risk and
reward by biotech investors is incongruent with long R&D timelines necessary to commercialize
new therapies; the second, that the fragmentation of the industry creates pockets of expertise
that resist critical integration; and third, that the system of intellectual property, while allowing
groups to invest heavily in a technology, permits only one group to work on that invention at a
time. Given these industry circumstances, there exist myriad promising scientific programs
that are simply not financially attractive to for-profit investors, and where nonprofits can step in. These projects might be too risky, or the timelines too long. As Bill Gates has said, “Some of the projects we fund will fail. We not only accept that, we expect it—because we think an essential role of philanthropy is to make bets on promising solutions that governments and businesses can’t afford to make.” In addition to being able to make potentially unattractive bets, nonprofits can serve as neutral aggregators of data, of patient material, of research, and of intellectual capital, thereby surmounting some of the problems that stem from the fractured, siloed industry Pisano describes.

In addition to problems on the commercial side of therapy development, there are flaws in the structure of academic science as well. Academic research incentives do not always align with bringing new therapies out of the laboratory. Many principal investigators are on tenure tracks, where publication is the primary goal, and reducing a discovery to practice is of little interest, or a much lower priority. The publication circuit causes a secondary issue, which is the lack of publication of negative results, causing a dearth of publicly available data on what has failed. This results in, at the very least, some duplicative research, and at the very worst, large-scale clinical trial failures that could have been better informed by having more information from previous failures that went unpublished. To make matters worse, in recent years, institutional restrictions for clinical research and faculty involvement with industry have become even tighter, potentially stymieing company formation and product commercialization. Since these new regulations restrict researcher activity based on the quantity of involvement, they are especially onerous for the most prolific researchers who have more industry relationships.

**Benefits Conferred upon the Nonprofit Organization**

Not only is there a well-established need for venture philanthropy, and an ideal alignment between the structure of nonprofit organizations and the riskiness of R&D, but nonprofit organizations and their constituents stand to benefit as well. According to practicing organizations, and our own analysis, the following are the major reasons why venture philanthropy can be a beneficial strategy for the nonprofit entity. First and foremost, there is
the best-case scenario where the investment brings a new therapy to clinical practice. More broadly, however, it is a way to ensure that nonprofits are fulfilling their mission of funding the best science in search of new therapies. Katie Hood, former CEO of MJ Fox emphasized, that “it’s not just a nice thing to do, it’s a required thing to do.”54 She further explained that by funding both academic labs and the commercialization of therapies, MJFF can ensure that “the failures are purely scientific in nature.”55 Margaret Lawrence, Executive Director of the Iacocca Foundation explained that it doesn’t make sense to restrict the organization’s investments to nonprofit entities, and that investing in players in different parts of research and development acts as a portfolio diversification technique for the Iacocca Foundation.

Further, venture philanthropy can serve to sustain the organizations themselves. For investments that have been successful, organizations, such as CFF, are already seeing royalty payouts that can support the organization and its future research investments.56 Even beyond this most rare of cases, if the company achieves a successful exit, the nonprofit’s investment achieves a level of sustainability that is unheard of in traditional philanthropy. A recent example includes Merck’s buyout of the preclinical stage insulin company SmartCells, in which JDRF had invested $1.5M.57 Merck’s infusion of over $500M to the company, not to mention their management resources, will lend momentum to the research, while JDRF can go on to fund other projects. Even the venture grants to companies that are ongoing or unsuccessful serve a marketing and communications function; they generate press for the organization, potentially spurring additional contributions. Many donors like the entrepreneurial and commercially-focused nature of the strategy, and have contributed more money to the organizations than they did previously. Some organizations have even engineered new ways in which donors can participate, on an individual basis, in the returns from a company partnership. Though donors to the nonprofit cannot receive financial returns from their donations, the Alzheimer’s Drug Discovery Foundation came up with an innovative program whereby donors could receive a return from a successful venture, and could then decide to reinvest it in ADDF, or in another nonprofit of their choosing.58
Still, there are risks to a venture philanthropy strategy. As Robin Elliot, Executive Director of the Parkinson’s Disease Foundation articulated, in some cases “We don’t have the most reliable scientific foundation to launch these trials. If you don’t have the underlying science, your failure rate is going to be much higher.” The Parkinson’s Disease Foundation, while enthusiastic about the concept of venture philanthropy investments, chooses to fund earlier stage academic research, and given their annual budget of approximately $6M, Elliot said a venture philanthropy strategy doesn’t make sense for them. There is a potential opportunity cost to funding fewer for-profit entities at a high level, rather than many academic labs doing more basic research, and training the next generation of researchers.

Despite the defined need and purported benefits of venture philanthropy strategies, there is still much around the practice that remains unclear. In order to answer questions such as, what percentage of nonprofit resources should be allocated to venture philanthropy, we need more analysis of the state of the field. While there will invariably be different needs and appropriate strategies for each disease area, existing venture philanthropy portfolios are a rich, and largely untapped dataset for evaluating the practice.

**Methods:**

**Research Goals**

Disease foundation stakeholders, including, executives, donors, patients, families, and research partners, rely on disease foundation funding strategies. As nonprofit groups continue to pioneer new efforts to accelerate research through strategic financing of for-profit companies, this paper attempts to provide a snapshot of the state of venture philanthropy by examining the portfolios of three leaders in the field. While there is transparency around which companies have been funded, more detail is needed on how these investment decisions are made, how portfolios are constructed, and the current mix of projects in these portfolios. This research endeavors to identify some of the present trends in venture philanthropy portfolios for all the aforementioned industry stakeholders.
Literature Review

A thorough review of existing literature was performed using Harvard and MIT library databases, bibliographies of seminal papers in the field, consulting and market research reports, and nonprofit organization websites. The literature review included articles on the history of health care nonprofit activities, venture philanthropy, biomedical research funding, asset allocation, and the current state of research and development productivity. These works provided background and context for this research, and also served to inform interviews and discussions with program executives at the nonprofit organizations.

Organization Selection and Interviews

The three organizations whose portfolios are profiled here were selected for this research because of the following commonalities: they are all disease-focused nonprofit public charities; they are the largest public charities not only in their own disease area, but are among the largest nonprofit health organizations in the U.S.; they have all been identified in the literature and the press as leaders in the field of venture philanthropy; and each organization has maintained an active venture philanthropy program for at least five years. Additionally, there were known differences between the organizations that also contributed their inclusion in the dataset, providing a more diverse sampling of venture philanthropy strategies. These included variations in patient population, market, and scientific understanding in each disease area, as well as different approaches to funding agreements, including use of financial instruments, intellectual property ownership, and success metrics.

In order to test our hypothesis that nonprofit organization portfolio composition is congruent with stated funding objectives, as well as to better understand the breakdown of these industry partnership portfolios, interviews were performed with program heads from each of the three organizations. These individuals were selected for their ability to speak to the portfolio strategy, management, evaluation, and success of their organization’s for-profit research partnership program. The goal of these interviews was to understand each organization’s program from a qualitative perspective, to gain access to historical investment data, and to shed light on
current and future trends in venture philanthropy. We were not attempting to achieve statistically significant results from interview data.

In most instances, after approaching each nonprofit organization with a copy of the baseline interview guide, the nonprofit made the final determination as to which executives would be best suited to participate in the research. The interviews were conducted between April 2011 and August 2011 and ranged from 30-75 minutes in length. Interviews with representatives who were involved in managing the for-profit investment portfolios closely followed the interview guide below. In addition to these discussions with nonprofit venture philanthropy program leaders, we sought out other thought leaders in the field who could speak to research funding allocation, or venture philanthropy more broadly: A director of a disease-focused clinical research center, a health care industry consultant with experience on venture philanthropy projects, directors of other nonprofit disease foundations in the same disease areas, directors at a philanthropic advisory service and medical research think tank, and a finance executive from a biotech that has received non-dilutive nonprofit funding.

In total, 13 interviews were performed, 6 of which were with representatives from JDRF, CFF, and MJFF:

1. Robin Goland, Co-Director, Naomi Berrie Diabetes Center
2. Marie Schiller, Partner, Health Advances
3. Robin Elliot, Executive Director, Parkinson’s Disease Foundation
4. Margaret Laurence, Executive Director, Iacocca Foundation
5. Ken North, Senior Vice President of Finance, Kineta
6. Melissa Stevens, Director of Strategic Initiatives, FasterCures
7. Kristin Schneeman, Program Director, FasterCures
8. Katie Hood, former CEO, Michael J. Fox Foundation
9. Sohini Chowdhury, Vice President of Research Partnerships, Michael J. Fox Foundation
10. Peter Lomedico, Strategic Alliances and Industry Partnerships, Juvenile Diabetes Research Foundation
11. Bob Beall, President and CEO, Cystic Fibrosis Foundation
12. Diana Wetmore, Former VP of Alliance Management, Cystic Fibrosis Foundation
13. Chris Penland, Director of Research, Cystic Fibrosis Foundation

Baseline Interview Guide:

1. What is your role at the foundation?
2. When did the organization begin engaging in venture philanthropy?
3. What problem(s) is the organization trying to solve by giving money to for-profit companies? Where do you think the “gaps” or market failures are? Why do you think there are market failures? Where do you believe your limited $ gets the most “bang for the buck”?
4. How do you attempt to construct your portfolio of investees (are certain percentages of funds allocated to different strategic buckets? Academic labs vs. companies, new high risk projects that traditional investors won’t fund vs. supplementary funding) Do you have priority allocations between different types of investments?
5. How do you track/monitor progress? How frequently do you communicate with your investees? In what form? How good is the information you get back? How confident are you that the progress data you get is good/accurate/adequate?
6. How do you evaluate the success of your investments and the portfolio as a whole?
7. Do you benchmark yourself against other disease-focused nonprofits who are also engaging in venture philanthropy? What about against traditional investors?
8. Do you anticipate investing more/less/the same in for-profit companies in future years? If there may be a potential change in the future, why?
9. Would you be willing to share historical information about your organization’s portfolio, or dashboards representing your portfolio makeup or success indices?
Portfolio Data

Per the interview guide, organization representatives were asked whether they would be willing to share information about the list of companies funded from the start of the venture philanthropy program to the present, including, company name, investment date, dollar value of investment, type of investment (grant, equity), phase of program at date of investment, current phase of program, funding at the time of investment (with an understanding that information would only be reported in aggregate). Though all organizations were willing to share deal data, content was variable and had to be filled in with additional research. Historical deal databases were received from CFF and JDRF, but not from MJFF. Nonprofit websites, company websites, historical press releases, and clinicaltrials.gov were all used to compile information about research funded and clinical program status to the extent possible. MJFF maintains an entire database of their funded grants online, while JDRF and CFF list only their current industry funding partnerships. No information about existing investors, follow-on funding, venture capital money or public company status was received from the nonprofit organizations. This information was subsequently sourced from ThomsonOne, company websites, and other media sources.

Industry Databases

In order to assess performance of the nonprofit portfolios, this thesis initially endeavored to compare the subset of projects within a nonprofit disease organization’s portfolio to all the ongoing clinical programs in the entire disease area. We wanted to compare the two datasets on a number of metrics, including riskiness of the assets, time between clinical phases, and success rates of programs. We were unable to achieve meaningful results from this component of the research for two reasons. The first is that of the three industry references examined, PharmaProjects, VentureXpert, and BioScan, PharmaProjects proved to be the most comprehensive, but was still missing much of the data on the smaller companies in the nonprofit portfolios, biasing the industry-wide data toward more mature companies and projects. The second problem is that on any given metric of clinical program evaluation, the number of companies in the nonprofit portfolios was simply too small to provide meaningful
results. Additionally, in speaking with the disease foundation program representatives, it became clear that nonprofit involvement with clinical programs extended to companies that they hadn’t directly invested in, thereby blurring the line between the nonprofit grant portfolio, and the larger universe of projects. Notably, according to the Director of Research at the Cystic Fibrosis Foundation, their clinical trial network conducts almost all of the trials for cystic fibrosis drugs in the US, so even if they haven’t supported a compound through a grant to a company, they have facilitated the trial with other financial support and resources.

*Portfolio Analysis*

Responses from nonprofit interviews were compiled in order to summarize the organization’s stated industry funding strategy and goals. Many of the funding strategies focused on pursuing specific scientific areas, and this research does not examine whether scientific criteria were met. Instead, we focus on the financial and business metrics. Portfolios were evaluated on the following measures:

- Descriptive statistics: Number of projects funded, dollars spent
- Level of scientific risk in the portfolio: Clinical stage used as a proxy for riskiness of asset
- Other existing funding: Did the company have venture capital money at the time of the investment, and how much had it raised? Was the company public at the time of the investment, and what is its market capitalization?
- Changes in portfolio composition over time

In an effort to understand the amount of scientific risk in each disease organization’s portfolio, we examined clinical stage, and used this measure as a proxy for risk. We tallied the number of projects across stages of development for each organization. We analyzed both the makeup of the portfolio at investment, as well as changes in portfolio composition over time (if the organization made a clear distinction between their current portfolio and their historical portfolio). In order to assess the level of business risk, or the likelihood that a company will remain a going concern, we examined the funding received by the companies prior to the
investment made by the nonprofit. The goal was to ascertain whether the nonprofit organizations were funding companies that traditional investors were too risk-averse to fund, or whether they were funding companies that were well-capitalized. For both the scientific and the financing aspects of the portfolio, we attempted to compare the results of our analysis to the program aims described by the nonprofits.

Results:

Interview Summary

Background of Interviewees:

The majority of program directors interviewed had advanced scientific degrees, and had also spent time working in large for-profit drug development companies before transitioning into roles within the nonprofit organizations. All interviewees had worked for their respective organizations for at least a few years (some since the venture philanthropy program’s inception), and all had significant exposure to and involvement in negotiating venture philanthropy deals and managing industry partnerships.

Trends in Venture Philanthropy:

When asked whether they anticipated spending more or less on company partnerships in the future, 2/3 of the interviewees predicted that their organizations would spend more on venture philanthropy going forward, and 1/3 thought that spending would at the very least continue apace, with the understanding that if foundation revenues increased, more money could be dedicated to industry funding. There was evidence of a need to balance growing spending on drug development partnerships with other important obligations to academic research, training and education. As Sohini Chowdhury of MJFF put it, “Academic research will always remain important, to find new targets, to develop animal models and biomarkers. Initial leads come out of academic labs.”

61
All program executives noticed a shift in the sourcing of industry deals over time. Initially, when an organization’s venture philanthropy practice was just starting out, the nonprofit organization took the initiative to approach companies in the hopes of forging a partnership, in some cases having to construct a case demonstrating the potential value of the opportunity to the company partner. Diana Wetmore, former VP of Strategic Alliances at CFF, now working in Business Development at a biotech company, said that in the early 2000s, the Cystic Fibrosis Foundation did an extensive market analysis demonstrating the potential value of a cystic fibrosis therapy and would use this analysis to convince for-profit companies to work with them.62 However, as venture philanthropy achieved some successes, became more common, and more biotech companies caught on to the appeal of working with a nonprofit partner, nonprofits received many more unsolicited investment requests from companies. As Peter Lomedico of JDRF described the phenomenon, “There’s more recognition now from the biotech community. More and more people are coming to us, simply because there’s visibility. In the early days, it was 50% outreach vs. 50% companies coming to us, now a lot more companies come to us.”63

The growing enthusiasm for strategic alliances between companies and nonprofits, has spurred a new tension, a supply and demand problem. On the supply side, while nonprofit organization representatives have said that they would like to dedicate more resources to venture philanthropy, their revenues are not increasing commensurately (see Figure C). Additionally, some of the projects they have funded are moving forward through clinical trials, but have not yet been partnered by a large pharmaceutical company. The end result is that in some cases, nonprofits are funding expensive later-stage programs to a greater degree than they may have anticipated.64 Since one of the primary strategic goals is to enable a therapy to reach patients, if a larger investor has not assumed complete responsibility for a promising project, the nonprofit will likely continue to invest in it. CFF’s partnership with Vertex is one such example. CFF recently agreed to fund Vertex’s cystic fibrosis program for an additional $75M dollars, depending on whether agreed upon milestones are met. Bob Beall, CEO of CFF explained, “Maybe if we had been patient, some other drug companies would have come along. I am
spending $75M with Vertex for something that they would maybe develop in 3 to 4 years, but my $75M will accelerate it by 2 to 3 years. If we really want to drive our destiny, we can’t take the chance that someone else might not pick up a project.”

Diana Wetmore further explained that the high capital demands of the Vertex partnership inevitably means that there is less available capital for other industry partnerships. And at the same time, demand for non-dilutive funding is increasing. According to Wetmore, “Over the last ten years there has been a shift in small companies automatically looking for opportunities to bring in non-dilutive funding. The success that the foundations have had has had a not-so-positive side effect that people will make the case, even if it’s not there.” Demand is also increasing because of difficulty securing venture capital funding, and as Wetmore put it, “some VCs have forgotten what the V part stands for.”

If supply of venture philanthropy money stays relatively constant, and demand for non-dilutive capital from biotech companies continues to increase, this only underscores the importance of having strong frameworks in place for nonprofits to evaluate their current portfolios and future investment decisions.

Figure C: CFF, MJFF, JDRF Revenues

<table>
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<th>2006</th>
<th>2007</th>
<th>2008</th>
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<td>$42,077,867</td>
<td>$51,259,577</td>
</tr>
</tbody>
</table>

Source: Organization 990s (Guidestar)

Portfolio Management:

All three organizations reported managing the investments with teams of both PhDs and business strategists. These teams received quarterly or semi-annual updates from the
companies. Larger investments were often assigned a customized steering committee, tasked with advising on the project, troubleshooting and auditing milestone achievements. Nonprofits did not view themselves as arms-length investors, but instead as partners in helping to influence the direction of the research and move it forward. In the words of MJFF’s Sohini Chowdhury, the nonprofit-industry relationship, “is not like a bank, but a partnership.”

Though having representatives from a diversity of backgrounds was determined to be the best approach for good oversight of the investment, managing these groups was sometimes challenging. Diana Wetmore of CFF explained that it takes a fair amount of work to get the steering committees to operate smoothly: to get all parties to understand the restrictions on IP, the confidentiality, and most importantly, the end goal of the research. Suggestions for research direction were often colored by an individual’s background. As Wetmore put it, “Academics would often have suggestions that weren’t practical. They eventually had to accept a result that was good enough to tell you what direction to take, even when they didn’t understand all of it. They had to leave it be.”

Despite some small hiccups in the process of overseeing investments, all representatives were very involved with the companies their organizations had funded, and were satisfied with the level of interaction and quality of reporting from their industry partners.

Risk:

Representatives from all of the organizations said that not only do they not consider the level of risk in their portfolio at any given time, they do not consider risk or return in evaluating an investment. Though representatives from CFF alluded to implicitly taking into account the riskiness of a project during the evaluation process, CEO Bob Beall emphasized that, “the biggest risk is not to take the risk.” Further, Diana Wetmore said that they never considered the potential value of their portfolio as a whole based on size of the opportunities they had invested in, and probabilities of achieving success, as one might in a for-profit portfolio. Overall, each organization felt that their goals and priorities as strategic investors were so different from those of traditional investors that entertaining the concept of risk, or adopting traditional portfolio policy, metrics and management techniques would not be useful.
Benchmarking:

There was unanimous agreement across all interviewed parties that the organizations did not benchmark themselves against one another, neither performance benchmarking, nor asset allocation benchmarking. They instead reported frequently sharing best practices and exchanging information with one another. The prevailing sentiment was that the individual disease areas and the state of the science were so different as to make benchmarking irrelevant. One interviewee articulated that benchmarking against other virtual drug development companies might be more appropriate, but this was not common practice across the organization. Despite the lack of formal benchmarking, organizations were highly aware of their peer venture philanthropy organizations, and referenced one another extensively. The collaborative nature of these groups manifested recently in a deal between JDRF, Fast Forward (MS Society) and Axxam Spa. While there have been companies, such as Bayhill Therapeutics, and Tolerx, where a few nonprofit players have invested in the same company at different junctures, the Axxam Spa deal marks the first time that two nonprofits joined forces to fund a company together in a collaborative agreement.70

Portfolio and Program Overview

In order to better understand the external context for each organization’s portfolio, it is worthwhile to note some of the key differences that exist in disease prevalence, and in the drug development landscape in each disease area. In the United States, about 30,000 people are currently diagnosed with Cystic Fibrosis, and according to PharmaProjects data, there are 139 compounds in development (or that were recently in development) for a cystic fibrosis indication.71 Since Cystic Fibrosis affects fewer than 200,000 people in the United States, it qualifies as an orphan disease under the Orphan Drug Act.72 500,000 people suffer from Parkinson’s Disease, and correspondingly, there are 441 drug assets listed by PharmaProjects for a Parkinson’s indication (again, this includes compounds for which development has ceased).73 Approximately 940,000 individuals have been diagnosed with Type 1 diabetes, and
there are 1842 compounds listed for a diabetes indication in PharmaProjects (183 focused on Type 1 diabetes).\textsuperscript{74,75}

Fundamental differences in these markets have had some impact on the venture philanthropy strategies of the three organizations. When asked why the organization was engaging in venture philanthropy, CFF representatives explained that the initial goal of their venture philanthropy investments was to address the dearth of traditional investor interest in an orphan disease. However, now that investor interest in cystic fibrosis has heightened, their funding strategy has evolved to more closely resemble the "de-risking" that other nonprofits are attempting. Sohini Chowdhury of MJFF, an organization addressing a much bigger patient population, is focused on the funding gap that exists for mid to late stage preclinical projects. According to Chowdhury, "Venture capital has dried up for that space. If they're looking for an exit in the 5-7 year time frame, then they are often looking for later clinical stage...Medicinal chemistry, early efficacy, PK, PD, toxicology, there's a lot of opportunity for foundations there because other funders have moved to later stages."\textsuperscript{76} Peter Lomedico of JDRF also noted a difference between his organization and CFF; he says that with the smaller patient population, CFF initially struggled to get company buy-in for projects in their disease area, and consequently had to take on a greater funding burden for certain projects, whereas JDRF funds only a portion of their projects. None of the organizations had a policy portfolio that could be used to compare organizations to one another or to assess congruence of their actual investments to their stated portfolio strategy.

\textit{Portfolio Data}

\textbf{JDRF portfolio:}

JDRF began engaging in venture philanthropy in 2004. The organization described the goal of their industry partnership program as follows:

"JDRF's industry partnership structure can support programs or entire companies, public or private, that are aligned with our core research and strategic therapeutic objectives ... JDRF particularly encourages partnerships: (a) to translate early-stage academic and industry
research discoveries with the goal of identifying more advanced therapeutic candidates, (b) to conduct testing of therapeutic candidates in relevant animal models or in people, and (c) to work closely with private and public capital allocators to leverage funds and source opportunities in our strategic areas.”

**Portfolio construction:** There was no pre-determined funding allocation between academic labs and companies, these come from the same budget. No consideration of the level of risk in the portfolio. Evaluations are made on a case by case basis, based on how well a project fits with JDRF’s research objectives.

**Success metrics:** Achievement of milestones, advancement of a therapeutic from one development stage to the next, program uptake by pharma, delivery of a disease-modifying therapeutic to the marketplace. No financial metric.

**Figure D: JDRF Portfolio Data**

<table>
<thead>
<tr>
<th>Overview</th>
<th># Partnerships</th>
<th># Funded projects in dataset (historical portfolio)</th>
<th># companies in dataset (historical portfolio)</th>
<th># projects (current portfolio)</th>
<th>Total $ awarded</th>
<th>Deal Value Range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>40</td>
<td>33</td>
<td>31</td>
<td>18</td>
<td>$75M</td>
<td>$150,000-$8.01M</td>
</tr>
<tr>
<td>Clinical Stages</td>
<td>67%</td>
<td>33%</td>
<td>11</td>
<td>4</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Financial</td>
<td>87%</td>
<td>Mean: $1.5M; Median: $0.5M</td>
<td>94%</td>
<td>45%</td>
<td>Mean: $36.2B; Median: $18.8B</td>
<td>1</td>
</tr>
</tbody>
</table>

Source: JDRF website, Company Information, Interviews, Clinicaltrials.gov, ThomsonOne Banker

**Scientific Breakdown:**

Over the life of the industry-funding portfolio, JDRF has funded 33 projects in 31 companies. 67% of these projects historically have been discovery or preclinical phase investments, and 33% were in clinical phases at investment. At present, 4 projects have advanced from preclinical to clinical stages, or to a subsequent clinical stage, and 11 projects have advanced from
discovery to a preclinical categorization. In the organization's current portfolio of projects, which is determined by the organization, there are 18 projects, 50% of which are in clinical stages.

**Financing:**
27 of 31 companies, or 87% of all company investments made to date have had venture capital funding in advance of an investment from JDRF. Mean amount of venture capital raised prior to the JDRF investment was $51.5M, with a median of $50M. We were not able to obtain financing data for all companies in the portfolio, which means that these descriptive statistics may skew slightly higher, since larger companies were more likely to be listed in the ThomsonOne database. In the current portfolio, an even greater proportion had venture capital funding prior to the JDRF investment, 94% of companies. Current total financing data was not available/disclosed for enough companies in the portfolio to be reported. 14 of the 31 companies funded were public at the time of the investment (45%), with mean current market capitalization of $38.2B, and median $18.8B. Only 1 out of 33 investments was an equity investment, or 3% of all investments. Many deal values are not disclosed, but disclosed investments ranged from $150,000 to $8.01M.

**MJFF portfolio:**
MJFF began its venture philanthropy program in 2005. The organization described the goal of their industry partnership program as follows:

“Our goal is straightforward: speed the results of good work toward clinical testing and patients in need... Consider approaching us when you: seek an injection of non-dilutive capital to improve robustness of pre-clinical Parkinson’s data or add features to a clinical trial; need access to predictive tools to inform critical decisions in starting or expanding a Parkinson’s program; have an idea for a targeted partnership at a specific stage of the Parkinson’s drug development pipeline; or need the insight of a strategic consultant for the PD field.”

**Portfolio construction:** The portfolio is made up of investigator-initiated projects and grants that fit with pre-determined priority focus areas. Three broad strategic buckets exist:
biomarkers, disease-altering therapies, and symptoms/side effects. No consideration of the level of risk in the portfolio.

Success metrics: Code every grant as a clear positive or clear negative outcome (considered a success either way), or as an inconclusive outcome, which is not considered a success. Measure progress of therapeutic candidates in the pipeline.

Figure E: MJFF Portfolio Data

<table>
<thead>
<tr>
<th>Overview</th>
<th># Partnerships</th>
<th># Funded projects in dataset (historical portfolio)</th>
<th># companies in dataset (historical portfolio)</th>
<th>Total $ awarded</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical Stages</td>
<td>% discovery/preclinical (historical portfolio)</td>
<td>% clinical stage (historical portfolio)</td>
<td># projects advanced from discovery to preclinical</td>
<td># projects advanced to next clinical stage</td>
</tr>
<tr>
<td></td>
<td>92%</td>
<td>8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Financial</td>
<td>% companies with VC funding at time of investment (historical portfolio)</td>
<td>$ raised prior to investment</td>
<td>% Companies public at investment</td>
<td>Current Market Capitalization</td>
</tr>
<tr>
<td></td>
<td>83%</td>
<td>Mean: $35.1M; Median: $22.7M</td>
<td>34%</td>
<td>Mean: $15.3B; Median: $220M</td>
</tr>
</tbody>
</table>

Source: MJFF website, Company information, Interviews, Clinicaltrials.gov, ThomsonOne Banker

Scientific Breakdown:
The MJFF portfolio is comprised of predominantly discovery and preclinical stage assets. 92% of the portfolio is dedicated to this earlier stage translational work, and 8% is clinical stage projects, when measured at the time of the investments.

Financing:
Of the companies for which we were able to gather venture-financing data, 59 of 71, or 83%, had venture capital backing prior to the MJFF grant. The mean level of investment prior to the nonprofit’s grant was $35.1M, and the median level $22.7M. 30 of the portfolio companies
were public at the time of investment, or 34%. Mean current market cap of companies in the portfolio is $15.3B, with a median market cap of $226M. The MJFF portfolio is exclusively grants and contains no equity investments. Grant amounts were not available, but are on average smaller than the other two organizations, given the higher number of programs funded and the lower amount committed to venture philanthropy overall.

**CFF portfolio:**
The Cystic Fibrosis Foundation made its first venture philanthropy investment in 1998, and the Cystic Fibrosis Foundation Therapeutics arm was established in 2000. CFFT describes its program as follows:

“To bridge the gap between what has been learned in the laboratory and the evolution of new therapies, the Therapeutics Development Program was created. This model initiative has the infrastructure in place to support a virtual “pipeline” of CF therapeutics development from the discovery phase through several stages of clinical evaluation. . . . the Therapeutics Development Program provides companies and academia with a powerful new opportunity to have investment capital during the early phases of drug research.”

**Portfolio construction:** No predetermined allocation of funding to academic labs vs. funding to companies. Funding is evaluated on a case by case basis and dependent upon the projects coming in.

**Success metrics:** Achievement of milestones, progress of therapeutic candidates in the pipeline.
Scientific Breakdown:
The historical portfolio of investments is made up of 70% discovery and preclinical stage investments, and 30% clinical stage investments. 15 investments have led to clinical stage development, and 2 to commercial products.

Financing:
24 of 32 companies that we were able to characterize had venture capital funding at the time of investment. Of the venture-funded companies that disclosed funding amounts, the mean amount of capital in the company prior to a CFF investment was $31.4M, the median was $15.5M. 10 of 32 companies were public at the time of investment, or 31%, with mean current market cap of companies in the portfolio at $14.9B (median is $146M). Amount disbursed to grantees ranges from $32,100 to $42.7M, however, total investment commitments are much higher, up to $75M for certain projects.
Discussion:

We had initially hypothesized that our independent analysis of nonprofit portfolio composition would be congruent with the asset allocation strategies and portfolio policies that emerged from discussions with venture philanthropy program executives. Instead, organizations for the most part, do not have an explicitly stated portfolio allocation strategy (except along the scientific dimension), making it impossible to support or reject our hypothesis. Investment decisions are made on a case by case basis, and are explicitly judged for fit with scientific priorities, but not explicitly evaluated for other potential dimensions of portfolio composition, such as the risk that the entity will remain a going concern, or the level of existing financing.

Though organizations were able to communicate their investment successes and de-risking activities through individual anecdotes, the lack of a pre-articulated strategy made it difficult to determine whether their overall investment portfolio was aligning with the aims of the venture philanthropy program. The three nonprofit organizations we profiled highlight their ability to fund riskier projects that would otherwise be overlooked by traditional investors, which we interpreted to mean earlier stage projects with less existing financing. In our portfolio analysis, the majority of investments across all three organizations were made in companies that traditional investors were also willing to fund. Between 75-87% of companies funded by the organizations had pre-existing venture capital money, with mean venture capital financing prior to investment ranging from $31.4M to $51.5M for the three organizations. Every organization had forged partnerships with public companies, and these public company investments represented approximately one third of the projects across the three portfolios.

Of course, the level of capitalization in a company does not necessarily indicate that the nonprofit is acting as a supplementary funder to traditional capital, as opposed to a risk-taking agent. Nonprofits could be initiating new therapeutic programs for their disease area within a larger company, or they could be funding less profitable elements of therapeutic programs, such as biomarkers or tools that are critical to the drug development process. Nevertheless, a substantial amount of this nonprofit capital seems to be serving as a supplement to traditional
capital, instead of serving a more risk-taking role by enabling new companies that are thinly
capitalized. Additionally, even in cases where the nonprofit is funding a mission-critical cost
center activity within a larger company, just as with traditional grants to academic labs, it can be challenging to audit the time and effort dedicated to the agreed-upon grant activities.

Nonprofits have been careful in their deal negotiations to specify where funds are to be spent, and to maintain control over research priorities. Nevertheless, there is an inherent risk in funding a larger company. The organizations might not be leveraging their funds at the same level that they would in a smaller company, and this cannot be entirely mitigated by contract provisions.

More important than the actual financial circumstances of portfolio companies and the interpretation thereof, is that the target percentage of funds used to supplement traditional capital, or to fund risky ventures, is not determined a priori. Organizations are able to demonstrate a pre-articulated scientific strategy, but are not explicitly characterizing the other types of risk in their portfolio. Though these organizations are ostensibly risk-embracing, they do in fact have to consider various types of commercial risks in their investments, and it would serve them to explicitly address these risks. The value of their venture philanthropy investment work would be strengthened if they publicly articulated a policy portfolio with a projected distribution of assets across non-scientific strategic categories, and benchmarked themselves against it. By making their investment thesis less intuitive, and more explicit, they could potentially demonstrate that they are funding the exact strategic gaps they identified, and are putting donor money to work most effectively. This strategy is not meant to be prescriptive. There is an expectation of inevitable divergence from the policy. But, with a standard in place, the organization can better show when they are on plan, where they diverged, and why they diverged. They would also have standard asset allocation measures in order to compare themselves to other organizations. While this comparison may be of questionable value in the near term, as the practice of venture philanthropy becomes more common, it is likely that relevant comparators will emerge.
**Scientific Agenda**

All the nonprofits we spoke with had a very clear and well-developed scientific agenda. They had performed a careful gap analysis across the research and development space in their disease area. They had expert cross-disciplinary teams of scientists and business strategists that helped determine which priority areas they should be funding. This led to the segmentation of funding into different strategic areas, and the organizations would ensure that they were funding an appropriate number of projects in each area, adjusting the balance over time if need be. The scientific content of all proposals was carefully vetted through a rigorous process. The degree to which each organization achieves their scientific agenda is outside the scope of this research. Instead, we attempted to assess the level of scientific risk in the portfolio using clinical stage as a proxy. Clinical stage is not a perfect representation of scientific risk, as some compounds may be new entities, others may be repurposed compounds with existing safety and efficacy profiles in other indications. However, we propose that the percentage of clinical stage assets in a portfolio gives some indication of the level of risk that an organization is taking on.

Through interviews with nonprofit venture philanthropy executives, organizations indicated a tremendous willingness to fund risky projects, a desire to de-risk therapeutic candidates, an expectation of failure, and a desire to fund gaps in early drug development that traditional investors wouldn’t fund. These executive comments were echoed in the program mission statements on organization websites. Organizations did not, however, have an articulated strategy or a quantitative assessment of how much scientific risk they wanted in their portfolios at the time of investment, or thereafter. Given the program emphasis on absorbing risk, we expected the portfolios to carry a high degree of scientific risk, as defined by the percentage of the portfolio programs in discovery and preclinical stages. The level of scientific risk varied significantly across disease organizations. JDRF’s historical portfolio was considered to be the lowest risk, with 67% discovery and preclinical stage entities at the time of investment, shifting to 50% discovery and preclinical in the current portfolio. MJFF’s was the highest risk with 92% discovery and preclinical stage entities at the time of investment.
The level of scientific risk in the organization’s portfolio might be influenced by the opportunities in a particular disease area, and the success of investments thus far. However, without an articulated allocation, it is difficult to tell how the portfolio took shape. There is an interesting tension between the clinical and scientific success of programs, and the level of risk that an organization carries in that portfolio. As a program moves through clinical stages, it generally requires more capital. And while movement through the pipeline is undoubtedly the ultimate goal, there is a trade-off. Nonprofit funding for industry partnerships is limited by annual revenues. If the portfolio is comprised of more expensive later-stage assets, then there might be a set of riskier, new innovations that are not getting funded. As mentioned previously, venture philanthropy managers are indeed seeing the concentration of funds into some clinical investments more so than they may have anticipated. It could be useful in these instances to have a target level of scientific risk that the organization would like to maintain at any given time even if a promising later-stage opportunity causes them to move away from the target. This target would represent a balance between sustaining existing projects, and funding the risky, earlier innovations that other investors won’t fund, and that might replenish the pipeline. If the organization diverged from their target, they would be doing so while maintaining transparency and accountability with respect to pre-existing funding aims.

Business and Commercial Agenda

While organizations had tremendous clarity around the scientific areas that they wanted to fund, their strategies around how to measure business risk when financial return was not the priority were less well-developed. Just as organizations did not have a predetermined goal for the amount of scientific risk they took on in their investments, they also did not measure the amount of commercial or business risk they assumed with each investee. Organizations were averse to the idea of financial risk or return, and as a result, did not quantify the risk of company sustainability that they were implicitly taking into account in their investments. Though the predominant sentiment was that risk was not a factor in their investment decisions, when probed further, it emerged that there is some implicit consideration of risk, even though it is not clearly characterized. Peter Lomedico of JDRF acknowledged that in fact, funding earlier
stage companies still remains a struggle for them, “We’re selecting for companies that already have funding and are financially healthy, which works to our advantage. We can select more mature companies with better investors and a better financial base. But it’s also created a gap...Our inability to go in and fund start-ups, provide seed funding, and invest in earlier stage opportunities is still a challenge and we haven’t figured that out yet.” Diana Wetmore of CFF confirmed that they also had difficulty determining the extent to which they should fund earlier stage, riskier companies that might not be as sustainable as more mature, well-capitalized firms, “There were some investments, especially in the early days, in companies that didn’t have venture funding . . . that became less and less the case. In our experience, if the company couldn’t support itself, then the project would come back to us through an interruption clause.”81 It seems as though nonprofits are so averse to being investors with a financial return motive, that they are reticent to explicitly consider other types of highly relevant risk, such as probability of company failure, and project sustainability. However, these other types of risk are clearly factoring into their decision-making process.

Despite a desire to take on risk that traditional investors cannot, a majority of projects in nonprofit portfolios are taking place in well-capitalized, venture-funded or even public companies. Though it is quite reasonable that nonprofits would require matching funding from the company, and would want them to have “skin in the game” as Peter Lomedico described it, the mean level of financing prior to nonprofit investment was over $31M for all three organizations, higher than the upper range of most of the nonprofit foundation investments. The level of capitalization, again, is not necessarily indicative of whether a company is an appropriate recipient for nonprofit funds. However, our portfolio analysis, and our evaluation of qualitative remarks from foundation interviewees, seem to indicate that nonprofit investors are also seeking commercial success, and might not be as open to failure as they describe. Either way, an articulated portfolio policy describing asset allocation goals would make the interpretation of the portfolio investments far more clear. Peter Lomedico aptly described the tension JDRF faces in speaking about the organization’s willingness to take risks. According to Lomedico, “We [JDRF] have invested in tons and tons of projects that haven’t returned anything.
We’re comfortable with technical failure, it’s all driven by our strategic need to advance project candidates”. Herein lies one of the core issues that may be in part responsible for differences between portfolio make-up and our assessment of funding goals; technical failure does not simply represent the loss of a financial return, it also represents the loss of a potential product candidate. If these organizations are measuring themselves against the progress of their pipeline, and their ability to produce therapies for patients, then there is a strong need to balance scientific risk and business, or commercial risk. Opting to fund companies that have a higher likelihood of advancing product candidates continues to leave a gap for small companies that have less data, and are riskier investments from a commercial standpoint. Investing in more well-capitalized companies may be beneficial for the nonprofit portfolio, but this strategy should be more clearly articulated, and the tradeoffs acknowledged.

The strength of the scientific agenda interacts substantially with the commercial goals in the portfolio. In fact, we assert that the strength and the clarity of the scientific portfolio strategy may perhaps outweigh, and at times overshadow, other portfolio composition considerations that are also of importance. This is especially true in the absence of explicit allocations for the level of business risk or commercial risk. It is possible that promising science will get funded, without enough consideration for the amount of commercial risk in the project. In other words, the impulse to fund scientifically promising candidates, without a target level of scientific risk to maintain, combined with the desire to fund companies that will achieve commercial success, pushes even the return-indifferent investor in the direction of less risky companies. Not only does this leave some scientific candidates in riskier companies high and dry, but it places nonprofit investors in a more overlapping position with traditional investors, which is exactly where they don’t necessarily want to be. Nonprofits may, as a result, be providing supplementary money to scientifically and commercially exciting companies that can already secure funding from other sources. Because the priority is to leverage their strengths and capabilities as non-traditional investors, and to make efficient use of donor capital, this underscores the need for portfolio policy to serve as a benchmark for investment choices.
Furthermore, in the current investor climate, with an increasing unwillingness on the part of VCs to take risks on protracted therapeutic development, it seems reasonable to expect the pattern of companies seeking nonprofit funding to continue trending upward. This will not only create a more competitive evaluation process, but may put additional pressure on organizations to consider funding firms that are more thinly capitalized. This increasing need for funding calls for additional forethought with respect to risk tolerance. Here we characterized the existing capitalization of investee firms, and found that a majority had attracted significant traditional funding before receiving a nonprofit investment. However, this breakdown does not enable us to categorize the business risk of these investments, it only suggests a need for additional analysis and disclosure to come from the nonprofit organizations themselves.

**Portfolio Measurement**

Organizations struggled with how to measure the success of their investments and portfolios. Many of the metrics that were used to measure success, such as the number of candidates that reached patients, or progress through the therapeutic pipeline represent the ultimate goals of the organization, but do not offer much feedback in the nearer term. These metrics also don’t serve to guide investment strategy. Each of the three organizations here can point to compounds they have supported that are progressing toward the clinic. They can also cite research programs, and even entire disease areas, where they were responsible for sparking interest from larger pharmaceutical firms. But while these anecdotal measures of success are promising and praiseworthy, they don’t provide the breadth or level of detailed information that should be available to venture philanthropy program managers, or to donors. While pipeline metrics are needed to represent the large goals, current and future investors (donors) want to know how their dollars have been allocated, and that they have been distributed according to a clearly articulated strategy.

Given the unprecedented and pioneering nature of these investment groups, there is very little data for them to draw on from comparable companies in order to generate portfolio policy. However, as the field of venture of philanthropy grows and become more mature, it will be
essential for these leading organizations to set a precedent for measuring the portfolio. The following are some suggested measures that could serve as part of a venture philanthropy asset allocation strategy:

- % of total foundation funds allocated for venture philanthropy vs. academic research
- % of active portfolio (by project and by dollars spent) in preclinical/discovery stages
- % of active portfolio categorized as high scientific risk (early stage or novel)
- % of active portfolio (by project and by dollars spent) categorized as high market risk
- % of active portfolio (by project and by dollars spent) with existing venture capital or corporate funding
- % of active portfolio with public investors

Conclusion:

The field of venture philanthropy is still young. Even in its first decade, we have witnessed a shift in strategy as executives learn from early outcomes and take new paths. The data here indicate a pattern of nonprofit investment that is worth exploring further. The pattern is two-fold: Investments occur on a case-by-case basis and don’t follow a fixed allocation strategy; investments are made in primarily well-funded companies. We show that in trying to accelerate research in their respective disease areas, organizations have opted to make bets on companies that for the most part, already have substantial funding from traditional investors. They may be initiating funding for riskier programs within these companies, but without an articulated investment strategy, it is difficult for external parties to interpret the allocation of funds.

Nonprofits, while eternally patient when it comes to return on investment, are actually quite impatient investors with respect to getting new therapies to their patient stakeholders. This pressure, while it can make them excellent catalysts, might drive them to make unforeseen and unplanned tradeoffs in their funding decisions. There is a potential convergence between the commercial incentives of traditional investors, and the patient health incentives of the nonprofit investors. Nonprofits should be cautious to leverage this overlap, while maintaining their distinct role as investors. There is tremendous potential value in the partnerships these
organizations are forging with industry, and nonprofits could strengthen their programs even further by articulating specific asset allocation targets each year, and then demonstrating whether these were met. Measurement enables these groups to be clear about their goals, to be accountable to their own investors, to have a pulse on how their tactics are faring in the near term, and ultimately to guide the foundation’s portfolio in the appropriate strategic direction. Organizations should be continually re-evaluating these policies, but should be explicit and fully cognizant of their portfolio choices as they relate to the program strategy and ultimately the fulfillment of their mission.

Future Directions for Research:

The current research had several limitations that may influence the interpretation of results. The first is that our sample size was limited to only three organizations, and these organizations were not selected at random. There are many more nonprofit disease-focused organizations engaging in venture philanthropy, and as we have discovered here, portfolio composition can differ significantly between organizations. Another potential limitation stems from our use of proxy measures for scientific and commercial risk that may not have been accurate representations of the true level of risk in organization portfolios. A third limitation of our data is the sourcing of investee company information from databases that were more likely to have thorough profiles for larger companies, potentially biasing our descriptive statistics on financing.

If venture philanthropy continues to grow in popularity, as many of our nonprofit experts predict, then there will be an even greater need to continue this line of inquiry into nonprofit venture philanthropy portfolios. The current research could be extended by including more organizations, and incorporating more outcome data as it becomes available over time. With additional performance data, and more investments to consider, this might enable a fruitful comparison between nonprofit portfolios and the overall performance of therapeutic development in each disease area using for-profit industry databases that we weren’t able to use productively here.
There are also additional interesting variables that were outside the scope of this research, but should be considered in the evaluation of venture philanthropy practices, including, the full range of funding opportunities for the investees, detailed data on follow-on funding (after the nonprofit investment is made), and patterns of licensing and company acquisitions. Here we looked at money in the company at the time of the investment, and focused on venture capital funding, but NIH funding, SBIR grants, and angel investors all play a role in the development of new companies and therapies, and serve as both alternative sources of capital, and sources for matching funds. In order to best assess the nature of nonprofit investments, all capital flows, both pre and post-investment into the portfolio companies should be explored.

In order to better evaluate portfolio congruence with the current program funding aims, this would require a more detailed articulation of funding strategy from several program executives at each organization. Additionally, since the portfolio objectives are made up of both scientific and business priorities, an independent assessment of the science could be performed by a qualified group of external scientists to audit the organization’s ability to meet its scientific goals, in addition to its business goals. This would allow for a more thorough assessment of portfolio congruence.

Since the interviews performed here suggest that nonprofit organizations find little value in benchmarking against their peers, and struggle to find useful metrics and relevant comparators from their for-profit counterparts, there is an opportunity for additional research to shed light on this portfolio policy problem. A survey of independent venture capital firms as well as corporate venture capital firms could not only provide for an interesting comparison on measures such as riskiness of assets in the portfolio, it could also yield insights into potential portfolio allocation targets that would be useful to implement in a nonprofit portfolio. A portfolio framework would also provide a benchmark and potential guideline for other organizations that are developing new venture philanthropy programs.
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