

FasterCures
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Honest Brokers for Cures

How Venture Philanthropy Groups are
Changing Biomedical Research

Hope

Change

Collaborative

Urgency

Drive
Cure

Accelerate

Focused

Overview

NONPROFIT DISEASE RESEARCH FOUNDATIONS, often referred to as venture philanthropies, are fast becoming the engine behind innovation in biomedical research. These groups are moving away from the more conventional models of public charities and nonprofits and instead are adopting the tools and techniques of venture capital finance, and the strategies and tactics of high-technology business management. This transition promotes the realignment of incentives across academic, industry, and public interests around one goal, and one goal alone: accelerating the development of treatments and cures for some of the world's most challenging diseases. As a result, these organizations are changing the landscape of biomedical research, often well below the radar of the traditional medical research community.

Interest within industry and academia in engaging the nonprofit disease research foundation community, particularly those with a venture philanthropy focus, is at an all-time high, but awareness of the landscape of players and how to approach them is limited.

To better understand the unique potential of these organizations, and to identify their challenges and successes, *FasterCures* conducted a series of interviews in the fall of 2012 with senior leaders of 20 participating organizations of The Research Acceleration and Innovation Network (TRAIN). TRAIN was established by *FasterCures* to create opportunities for these innovators to discuss and tackle the challenges that cut across diseases. It is a group of 55 unique nonprofit foundations that fund and conduct medical research across a spectrum of diseases, from breast cancer to Parkinson's disease. In many cases, TRAIN foundations were created by patients and their families who are frustrated by the slow pace of change in the traditional medical research system. They are collaborative, mission-driven, strategic in their allocation of resources, and results-oriented. They are organizations with a singular focus on, and a significant stake in, getting promising therapies from the laboratory bench to the patient's bedside as rapidly as possible.



MONICA COENRAADS
Executive Director
Rett Syndrome Research Trust

“We decided to be focused on research. We are about knowledge and access to knowledge.”

Previously, no resource existed that cataloged the operational and partnering practices of these organizations. In the summer of 2012, *FasterCures* published an inventory of the TRAIN organizations as a free, public, Web-based resource (www.fastercures.org/traininventory). The inventory found that, combined, these groups provide more than half a billion dollars in medical research grants in a year, and are worth more than \$2.2 billion. One in three groups has supported at least one clinical trial. Nearly 9 out of 10 groups partner with biotechnology and pharmaceutical companies.

These interviews added greater texture to the inventory, as we asked leaders to tell us about their near- and long-term challenges, their perspectives on trends and emerging conditions, and their success stories. This publication summarizes the interviews but does not do justice to the depth and breadth of these organizations. We urge you to visit their Web sites to learn about the full span of their activities.

Many of these groups have been around for several years, even decades. Others are relatively new, as young as two or three years old. All of them, however, have been frustrated by the disconnect between the research opportunities in the therapeutic sciences and the responses of government, academic, and industrial actors in pursuing and resourcing these opportunities. As a result, they have been creative in building workarounds, honing a laser-like focus on treatment science.

While the private sector pursues many leads across many disease areas, and government funding agencies work to ensure that the money is spread broadly across many diseases, scientific disciplines, and institutions, venture philanthropies are solely focused on their disease, and nothing else. As such, failure is not an option.

Emergence of a New Business Model for Biomedical Research

EVEN FIVE YEARS AGO, some of these groups were following a more traditional method of dispersing funds. They waited for scientists to come to them with good ideas, awarded them grants, and waited to see if any flowers bloomed. Impatience with this slow pace and lack of control over the direction of research led to what Louis DeGennaro, Chief Mission Officer, Leukemia & Lymphoma Society, called an epiphany. “We realized that we needed to become active in the drug development space,” said DeGennaro. “If we were not on the lookout to advance good ideas out of the academic setting, then, maybe nobody was.” Like so many other groups in this environment, the Society knew that it would never have enough funds to invest in the full range of drug development; it had to rely on industry partnerships, and to do so, it had to de-risk the process for its industrial partners.

Scott Johnson, CEO and Founder, Myelin Repair Foundation, said that an increased focus on gathering scientific intelligence and fostering strategic discovery research is necessary because people do not realize how broken the current funding paradigm is. Impatience is a great motivator, especially for disease-focused organizations. Johnson said that the Myelin Repair Foundation’s strategic focus has allowed it to accomplish in 8 years what most people thought would take 30.

When the disease in question advances rapidly and dramatically, time is of the essence, which dictates a more targeted effort. Rett Syndrome is a disorder of the nervous system that leads to developmental reversals, especially in the areas of expressive language and hand use. For parents of these children, for example, Monica Coenraads, Executive Director, Rett Syndrome Research Trust, the sense of urgency is profound. The process of issuing a request for proposals, identifying reviewers, and managing the peer review process is too labor-intensive, slow, and expensive, said Coenraads. For every dollar raised, the Trust spends 96 cents on research.

Similarly, Steve Rose, Chief Research Officer, Foundation Fighting Blindness, said that his foundation also found the typical investigator-initiated approach to research inefficient. As a result, the Foundation now focuses entirely on directed research with milestones and deliverables that are well defined in advance.

Ramping Up Expertise

This new business model required organizations to ramp up their in-house and at-hand expertise. For example, the Leukemia & Lymphoma Society totally rebuilt its research program over the past five years. Today, its Therapy Acceleration Program involves partnerships with biotechnology and pharmaceutical companies and relies on business contracts rather than grants to achieve its research goals. DeGennaro said that in order to make this model work, the Society had to grow its own research staff so that it could bring its own intelligence and expertise to the table. This transition was not without controversy.



LOUIS DEGENNARO
Chief Mission Officer
Leukemia & Lymphoma Society

“We are not your grandmother’s charity. We survey the scientific and clinical landscape ourselves, develop an agenda to strategically deploy our dollars, and then work to ensure we are making the smartest use of our money.”



No longer are these philanthropies viewed as “well-intentioned old ladies in tennis shoes,” but rather as unique and powerful resources with the ability to leverage public and private investments.

Leadership debated whether this business model was consistent with the mission of a voluntary health agency. But, since the Society has changed its business model, DeGennaro said its ability to identify early-stage winners has been validated; specifically, five of its small biotechnology company partners have either been acquired, licensed, or had cash infusions from big pharmaceutical companies.

The Leukemia & Lymphoma Society’s story is familiar to many other groups. The Michael J. Fox Foundation for Parkinson’s Research has built a critical mass of in-house scientific expertise. Todd Sherer, CEO, said this has advanced the Foundation’s strategy to define high-priority research areas for Parkinson’s disease—therapeutic targets and approaches that are closest or most critical to practical relevance in patients’ daily lives. This in-house intelligence is then used to leverage donor-raised capital to push projects into trials, and ultimately the clinic. To date, the Foundation has supported 51 clinical trials.

The Alpha-1 Foundation began its operations trying to achieve a balanced portfolio of basic and clinical research. And while it still supports basic studies, it now issues requests for proposals in very targeted areas where there are gaps in knowledge. It also contracts research to develop tools that are essential to the field, for example, stem cell lines or a critical assay. John Walsh, Co-Founder and President, said, “If we don’t focus on directed, targeted research, and then contract out those studies, we will get left behind in our search for a cure. This is important to us even if it means we will fund less basic science.”

Numerous organizations rely on the equivalent of a tiger team, in which individuals are selected for their experience, energy, and imagination, to identify gaps in knowledge and opportunities for filling them. These groups identify the expertise they need, and then go after experts to try to persuade them to join the team. Because of this strategy, these small organizations are often *the* experts in their disease. This stature has increased the power of their position when negotiating or collaborating with public funding agencies or the private sector. No longer are these philanthropies viewed as “well-intentioned old ladies in tennis shoes,” but rather as unique and powerful resources with the ability to leverage public and private investments.

Even for those without an in-house scientific team, nearly all rely on a scientific advisory board that pulls experts from across the country and even the world, which helps them find the best science. In addition, a business advisory group composed of individuals from venture capital and industry typically helps them identify projects that are practical and actually have a chance for further funding.

Focusing Their Strategy

The Cystic Fibrosis Foundation has focused its strategy heavily on drug development activities. Tactically, this means forcing collaborations, said Robert Beall, President and CEO. It also means keeping patients aware of and involved in trials, for example,

through the Foundation's clinical trials alerts system. Today, there are nearly 30 cystic fibrosis (CF) drugs in development or already in use by patients—more than in the entire history of the disease. The Foundation is propelling each of these medicines forward. Its most recent success is an oral pill taken twice a day for the treatment of CF in people ages six and older with a specific mutation. The drug was developed by a pharmaceutical partner with significant scientific, clinical, and financial support from the Cystic Fibrosis Foundation, including a \$75 million investment.

In vast contrast to the traditional nonprofit role, several organizations have established their own nonprofit laboratories to conduct research, or to support investigators in academic laboratories around the country. Also, unlike some of their predecessors, these venture philanthropists often take ownership and control of the research they are funding.

Others seek scientists in academic and private settings who are willing to directly contract with them on targeted research projects. In those cases, the foundations control access to data and intellectual property to ensure that they are widely available. This top-down and directed approach contrasts with the way many academic scientists view their research roles. But that hasn't deterred the philanthropies. Most interviewees said that academic scientists *do* want to make a difference, and it is nearly impossible for them to turn down an opportunity to contribute, especially when these "honest brokers" provide such a compelling sense of urgency.

Many organizations have made a deliberate decision to focus only on research, leaving more patient-focused activities, such as education and support, to others. And, of those, some have narrowed their research portfolio to focus only on drug discovery. For example, the Alzheimer's Drug Discovery Foundation does not fund basic research; instead, it promotes innovation that could lead directly to drugs for novel targets. According to Howard Fillit, Executive Director and Chief Science Officer, the Foundation has funded 26 clinical trials, mostly Phase 2. To scan the environment for leads, the Foundation has three scientists on staff.

This new business model includes the establishment of milestones and benchmarking, and accountability auditing. For example, the Chordoma Foundation is measuring the effectiveness of its research networks through social network analysis. New negotiation models include milestone payments on royalties or march-in rights. Many foundations adhere to a "use it or lose it" intellectual property model. If they invest in a project and the innovator allows it to sit on the shelf, they retain the right to take back the discovery if there is promise in its development by some other entity.

Some foundations have not totally rejected the notion of trying to gather a return on their own investment. Their view is that they made the investment to jumpstart the field and if drugs came to market producing a revenue stream, they can seek some of those returns for reinvestment in research.



TODD SHERER
CEO
The Michael J. Fox Foundation for
Parkinson's Research

“We have a focused, longer view. We put patients front and center in our decision-making all the time, whereas government and private-sector funders cannot always do that. This informs our sense of urgency and our willingness to take greater risks. We have a different risk/benefit balance than do academics, regulators, or industry.”

Meeting Scientific Challenges

NO AMOUNT OF MONEY can cure a disease if basic understanding of its pathophysiology is lacking. Human biology is incredibly complex, and understanding how disease begins, progresses, and differs among members of the population creates exponentially complicated challenges. Often a lack of tools and technologies slows progress. Sometimes the considerable variability of human populations obscures causes and effects. In the case of rare disease, access to sufficient numbers of patients to make meaningful inferences can delay the testing of potential new therapeutics.

Like any other organization pursuing new treatments, venture philanthropies must confront the realities of human biology and the complexities of clinical research. Thus, they tackle the science where it needs the most effort and resources, from basic to clinical research, and everywhere in between.

Unraveling Complexity

Some organizations are contending with a multitude of heterogeneous diseases. For instance, the Leukemia & Lymphoma Society invested more than \$76 million in blood cancer research, including several forms of leukemia and lymphoma, myeloma, and myelodysplastic syndromes and myeloproliferative disease. Thus, the Society faces obstacles at all points along the continuum—from basic science to the marketplace. For example, scientific understanding of the basic pathophysiology of acute myeloid leukemia is lagging, and no new therapies have emerged in 30 years. It is a genetically complex disease, requiring a steady investment by the Society. On the other hand, although the pathways of chronic lymphocytic leukemia are well understood, industry is not interested in pursuing a market of only 20,000 patients a year. Philanthropies that target many diseases aim to achieve a balance in their portfolio that meets the scientific needs of each disease. This is no easy task.

Even when focused on a singular disease, the nature of some conditions makes the science incredibly convoluted. For example, alpha-1 antitrypsin deficiency is a hereditary condition that affects the lungs and/or the liver. Thus, clinical trials have to effectively assess, for example, the modifier genes that affect the liver and the lung, or evaluate outcomes that measure lung disease progression, liver disease progression, or both. Isolating the effects of one disease on many systems can be a challenge, said Walsh, a patient himself.

Likewise, Richard Insel, Chief Scientific Officer, Juvenile Diabetes Research Foundation, said that the heterogeneity of juvenile (Type 1) diabetes has clouded clear understanding about the fundamental aspects of the disease. While the causes



ROBERT BEALL
President and CEO
Cystic Fibrosis Foundation

“We don’t just give scientists money, they have to earn it.”

of Type 1 diabetes are not yet entirely understood, scientists believe that both genetic factors and environmental triggers are involved, which could explain why its onset and severity varies among affected children. Research in this field is further challenged by the fact that what works therapeutically in animal models does not invariably work in humans and what may work in adults does not necessarily work in children, which provides not only a scientific challenge but also a regulatory encumbrance.

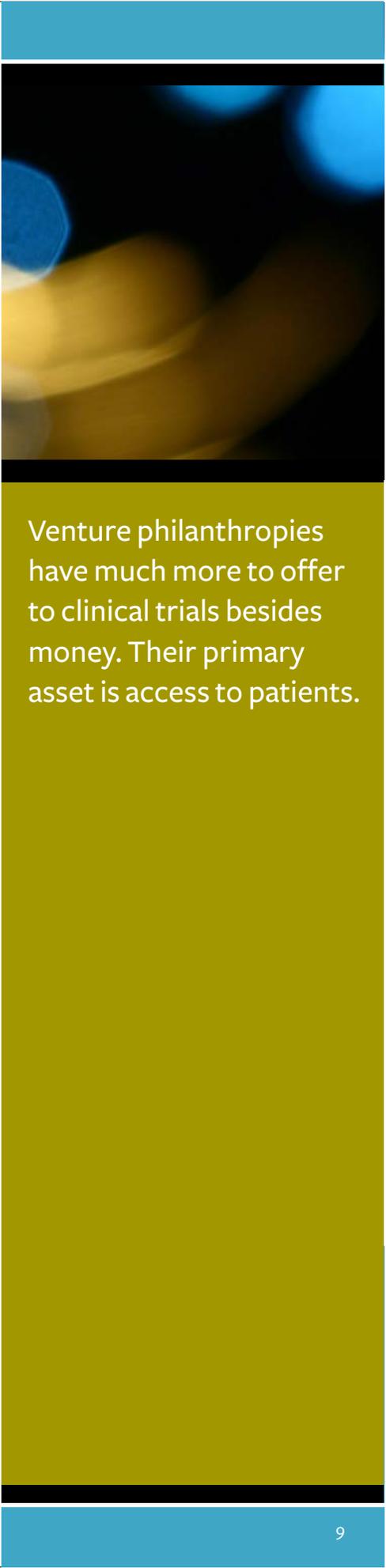
Some organizations have dealt with complexity by eliminating some of the noise. In the case of multiple sclerosis, understanding the multitude of pathways by which the disease might involve has been daunting. Convinced that myelin repair is the only current research area that has the potential to both restore lost function and halt the progress of multiple sclerosis, the Myelin Repair Foundation was founded as the only nonprofit medical research foundation solely focused on identifying myelin repair drug targets that will lead to treatments for multiple sclerosis. “We don’t want to be all things to all people with regard to multiple sclerosis,” said Johnson, also a patient. “We are just about myelin repair.”

Pioneering and Seeding Clinical Trials

Most groups interviewed are supporting or conducting at least one clinical trial. Those who are not yet there are looking forward to reaching that critical milestone. Few are able to fund a Phase 1 or 2 trial entirely, but they often provide the seed money that jumpstarts the process.

Venture philanthropies have much more to offer to clinical trials besides money. Their primary asset is access to patients. Because they are considered the honest brokers, these groups are able to “muster the troops” in clinical studies, and often are the trusted bankers of clinical data and biospecimens. These groups can bring the patients to the research, creating networks sometimes in the tens of thousands that can be mobilized for clinical trials. They also are often the experts in the room. Their accumulated experiences, knowledge, and networks can lead to ambitious, brave, and innovative study designs.

Some diseases require innovative approaches to clinical trials. For example, the heterogeneity of multiple myeloma is vast. The Multiple Myeloma Research Foundation is working to identify all of the disease subtypes so that the right drugs and combination therapies can be found for each subtype. According to Kathy Giusti, CEO, Founder, and a patient, coping with heterogeneity requires building a critical mass of patient data and tissue. The Foundation has launched its own trial of 1,000 patients. In this study,



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TIM COETZEE
Chief Research Officer
National Multiple Sclerosis Society

“We serve a critical role in therapeutic advances. Although we are focused on drug discovery, it is also important that we support efforts to understand the underlying biology of the disease. If we step up those efforts in a way that companies and FDA can see a precise understanding of how a drug might work in the disease process, we have made progress.”

untreated bone marrow is collected and patients are followed over time to understand the effects of different treatment approaches. This type of critical observatory study, which is not testing a new compound, is essential, said Giusti, and one unlikely to be funded by drug companies. Giusti hopes that by providing scientists with access to samples and data that include both naïve and sequential information, subtypes can be identified and genomic data can be elucidated to identify potential markers and targets for cures. Like many venture philanthropies, the Foundation has built a large clinical consortium to serve its mission, paying for Phase 1 and 2 studies to collect data at a rate faster than would be expected in industry.

Speed is part of the core makeup of some of these groups, especially those for whom every second counts. Progeria is a rare, fatal genetic condition characterized by an appearance of accelerated aging in children. The gene for progeria was identified in 2003. In 2012, The Progeria Research Foundation announced the results of the first-ever clinical drug trial for children, funded and coordinated by the Foundation. The drug—a farnesyl transferase inhibitor—was originally developed to treat cancer. Every child showed improvement in one or more of four ways: gaining additional weight, better hearing, improved bone structure, and/or, most importantly, increased flexibility of blood vessels.

Other groups have been fortunate to be in the right place at the right time. Since its founding in 2007, the Melanoma Research Alliance has become the largest private funder of melanoma science. It came onto the scene just as scientific opportunities were exploding. Wendy Selig, President and CEO, said that melanoma research had been stuck for a long time and, in 2007, the moment in science was just right for an infusion of funds and focus. The Alliance was well positioned to step in and move the field forward. Today, 14 clinical trials are testing promising new agents and there are two new drugs on the market for melanoma.

Interviewees noted that despite their sense of urgency and desire to push hard, they face the same types of challenges as other research groups, namely, the need for good clinical endpoints and an ability to validate them, and the frustration of extrapolating from animal models to the human.

Supporting Natural History Studies as First Step

Some organizations are facing a disease in which the natural history of its course is not well documented. Thus, they focus much of their resources on trying to understand the trajectory of the disease as a first critical step. This can be particularly challenging when there is no way to aggregate clinical data gathered from across many sites and when the disease is so rare that even finding patients to follow can be strategically difficult. Rett Syndrome is a prime example. Only recently was it identified as a single gene disorder. But because there was no diagnostic test, it had not been diagnosed in patients until

recently. In addition, it has not had the visibility of other diseases or the deep and longitudinal clinical datasets needed for mining clues. Such deficiencies not only slow the science but also make it harder to attract scientists to the field. Coenraads said that natural history studies of rare diseases such as Rett Syndrome are critical to understanding how this disease of deterioration evolves and building the Foundation on which more targeted research can proceed. When the science of the disease is still immature, venture philanthropies such as the Trust have to build networks of scientists to work through early findings and develop promising ideas for new experiments in clinical trials.

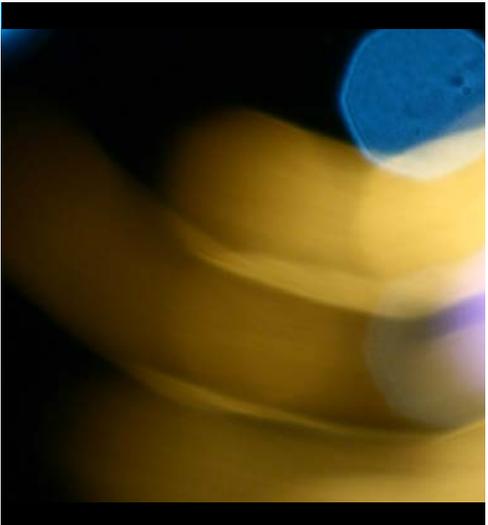
Similarly, Stargardt disease, the most common form of inherited juvenile macular degeneration, lacks natural history data. Steve Rose, Chief Research Officer, Foundation Fighting Blindness, said that the Foundation is about to launch a natural history study in this disease that will allow scientists to understand disease progression and identify midpoints and endpoints of disease progression that can be used in future clinical trials.

Building the Infrastructure, Tools, and Resources, Often from the Ground Up

Every segment of the research continuum—from the laboratory to the market—can face scientific and technical obstacles. Venture philanthropies think strategically along the entire continuum, identifying where the science or the technology is lagging behind because of one or many factors. This means they often fund more workmanlike projects, searching for targets, models, and tools that will push the science forward. And, although everyone wants to hit a home run, many believe it is equally important to focus on funding these types of incremental improvements that will move the field forward. This means they invest funds in tissue banks, databases, patient registries, research platforms, assays, and people.

Intellectual capital, in the form of trained investigators, is a critical resource supported by many organizations. Jonathan Simons, President and CEO, Prostate Cancer Foundation, said that in addition to championing research and building a global research enterprise—the Foundation has invested nearly \$10 billion in 1,500 research programs at 200 research centers in 12 countries—investing in human capital is a critical asset in the fight against prostate cancer. He said fulfilling this need is especially difficult given the current funding environment.

Some organizations are focused on diseases that are so rare that the infrastructure and resources needed to even begin studying them hardly exists. For example, the Chordoma Foundation realized early on that the research community lacked the basic reagents and materials needed to do their work. As a result, it focused on building repositories of cell lines, tissue banks, and animal models that can then be made freely available to the scientific community. According to Josh Sommer, Founder and Executive Director, who is affected by chordoma, building the field and creating a network of researchers was the first order of business. This is already paying off. Sommer said that chordoma research has been



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KATHY GIUSTI
CEO and Founder
Multiple Myeloma Research Foundation

“We are the trusted third party to write the strategic plan for our disease, identify partners, and work together with all parties to achieve the cure.”

advanced by the creation, validation, and banking of three chordoma cell lines that can be made available to 52 laboratories, including four drug companies. In addition to leveraging millions of dollars’ worth of research by distributing cell lines, the Foundation has proactively funded projects identified as strategic priorities by its scientific advisory board, such as sequencing the chordoma genome and *in vivo* drug screening.

Brain cancer is another disease with unique resource needs. Brain tissue is particularly difficult to obtain. Max Wallace, CEO, Accelerate Brain Cancer Cure, said that his organization knew a critical need had to be filled and worked with the Jackson Laboratory to create a mouse model that duplicates human brain tumors. This resource is then made available to anyone conducting brain cancer research.

Numerous organizations have created a one-stop shop for research into their disease. “We’ve got it all,” said Audrey Gordon, President and Executive Director, The Progeria Research Foundation. “Our comprehensive programs allow scientists working in this area to get cells, tissues, funding, and clinical information. And our International Registry is an important tool for clinical drug trials enrollment.”

Multiple organizations expressed a need for more intelligent and elegant biomarkers. Biomarkers play an important role in drug discovery and development and can serve as early measurements of drug safety and efficacy. The better they are, the more valuable they are to any group developing therapies. Thus, it is in the collective interest of research groups to collaborate on finding useful biomarkers for drug studies. Several venture philanthropies invest their funds in collaborative efforts to identify and validate biomarkers. For example, the Alpha-1 Foundation has teamed up with chronic obstructive pulmonary disease groups to form a consortium to search for biomarkers for lung disease in a large number of study subjects.

The New York Stem Cell Foundation is an outlier among these venture groups in that it focuses exclusively on one area of science that can be used in the service of nearly any disease, embryonic stem cell research. Its goal is to create the bridging technology and research in a field that has been stalled by politics and lack of funding. To advance the field of stem cell research, the Foundation supports 40 investigators who work for them as a nonprofit biotechnology company, as well as 60 investigators around the country. Susan Solomon, CEO, feels strongly that a critical role of a private philanthropy such as hers is to do the proof-of-concept work necessary to develop stem cell science as a resource for all diseases. In addition to supporting investigators nationwide, the Foundation operates its own laboratory.

Collaboration and Sharing

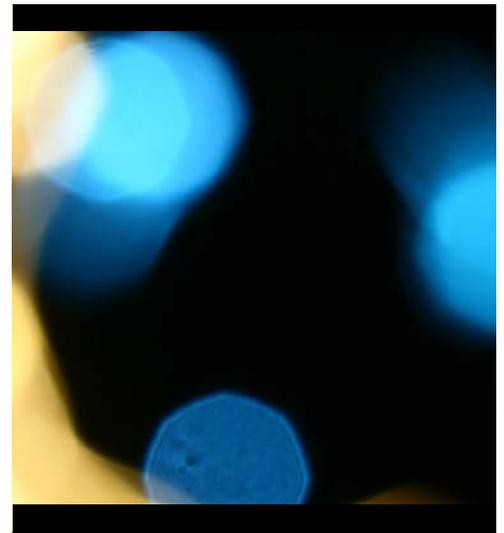
ONE TREND THAT NEARLY EVERY interviewee discussed was the increasing reliance on collaboration. Every organization engages in extensive collaborations with university and industrial scientists, and many are actively engaged with government agencies, such as the National Institutes of Health.

Gordon said that for the most part cooperation trumps competition for the simple reason that competition eats up time and resources. Several organizations cited their frustration with the culture of esoteric academic research, in which scientists compete for funds and publications, a climate that creates incentives that can be out of alignment with the search for cures. Furthermore, the siloed nature of academic medical research has fostered an environment in which the best minds in academic laboratories do not always play well together.

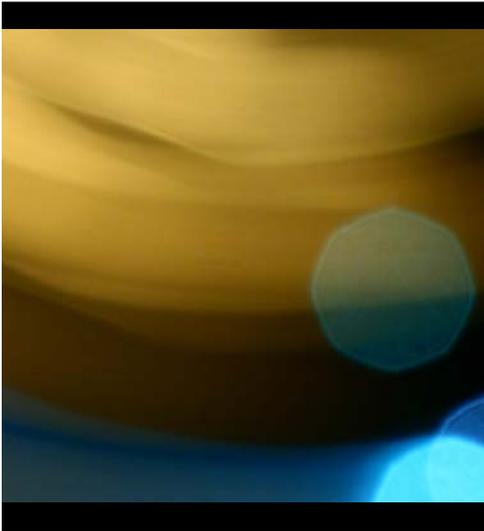
Wallace said that at his philanthropy's first major research conference on brain cancer, the academic experts sat in opposite corners of the room. That dynamic has gradually changed, although Wallace said that some academic scientists continue to protect their turf rather than partner. Undeterred, Wallace continues to believe that American universities are the "hatchery of innovation" and it is worth finding the best minds and encouraging them to cooperate. He has found it is possible to engage universities in collaborative efforts that he calls "high-throughput, low-ego" arrangements.

Most interviewees said that collaboration has grown out of necessity along with an awareness of how broken the current system is in crossing the so-called "Valley of Death" in translational research. The willingness of academic scientists to work collaboratively, and even in a top-down management environment, has paid off for most of these organizations. Many said that their patient groups, and even academic scientists, originally held an aversion to working with industry. For the patients, it was because of negative feelings about pricing practices; for academic scientists it was the perceived "taint" of private funds. While those feelings still linger for some, these organizations have made it clear to all parties that no one can go it alone in treatment science; thus, collaboration is essential.

Another emerging trend that has made it easier to collaborate is growing interest of some pharmaceutical companies in rare diseases. Traditionally, market sizes were too small to warrant major investments. But a handful of companies have begun to understand that a portfolio of rare diseases can help the bottom line. More importantly, the rare disease model can provide critical insight into related common diseases. For example, understanding the pathophysiology of progeria could provide important insights into the normal aging process and the diseases associated with it, such as Alzheimer's disease and Parkinson's disease.



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Several philanthropies make collaboration a centerpiece of their work. For example, the Addario Lung Cancer Medical Institute is an offshoot of the Bonnie J. Addario Lung Cancer Foundation. It is a contractual consortium of academic and community-based researchers structured to directly advance the understanding of disease biology and accelerate the development of significantly more effective lung cancer treatment options. It links researchers via shared infrastructures and prioritized research programs including standardized biorepositories, data systems, contracts, study protocols, and, as significantly, through ongoing collaboration discussions among the scientists.

Another example of collaboration is the Alzheimer's Disease Neuroimaging Initiative (ADNI), which aims to define the progression of Alzheimer's disease. A major goal of ADNI has been to collect and validate data such as MRI and PET images, cerebral spinal fluid, and blood biomarkers as predictors of the disease. Data from Alzheimer's disease patients, mild cognitive impairment subjects, and elderly controls are available to scientists through this resource. These types of pre-competitive consortia were far more difficult to form and manage even five years ago than they are now.

Another factor that drives collaboration is the need for common tools and resources. For example, one area attracting a lot of attention and resources with regard to collaboration is the search for biomarkers. Because it is so challenging to gather data on the extent to which therapies modify disease, biomarkers offer a parameter that can be used to measure the progress of disease or the effects of treatment. However, because biomarkers in and of themselves do not lead directly to products, no one entity is likely to invest scarce R&D dollars into something that would benefit competitors. Thus, many organizations work hard at building biomarker consortia, often with other nonprofit partners.

Despite the growing trend toward cooperation, frustrating to many of these groups is the traditional model of research that does not disseminate research results widely. Many reject the culture in which individual scientists or laboratories take ownership of their data and instead have aimed to build an alternative universe in which critical information is rapidly disseminated to the people that need it. A major goal of the Chordoma Foundation, for example, is to engage in more strategic sharing of information to break the logjam of academic publications and industry prohibitions.

Ongoing Challenges

Confronting and Coping with the Regulatory Environment

ORGANIZATIONS ARE AT DIFFERENT PLACES with regard to the regulatory environment; in fact, some are not even close to contending with that world. For those that have entered the world of clinical trials, several issues emerge.

Because many of these groups are focused on rare diseases, they are compelled to spend time educating regulatory agencies about the need to develop clinical trials with very small sample sizes. And while they want drugs to be safe, some groups also are frustrated by the benefit/risk assessment used by the U.S. Food and Drug Administration (FDA).

Some organizations work fast and furious in supporting clinical trials only to come to a roadblock with the FDA and its requirements that they collect more data over longer periods of time to better address safety issues and concerns. As personalized medicine becomes a reality, many organizations are concerned that the traditional regulatory approach is not ready to assess tailored therapy or combination therapy. Thus, these groups have had to be creative in their clinical trials design.

Particular frustration can grow in the area of devices, which some organizations are pursuing, and for which the regulatory environment can be daunting. Not only can this slow the introduction of devices to patients but also it can serve as an important deterrent to investment. Warren Lammert, Chairman and Co-founder, Epilepsy Therapy Project, said that epilepsy is especially amenable to therapeutic devices, for example, to detect and attenuate seizures. Lammert said that some devices have been approved for use in European markets but are stalled at the FDA.

Several organizations admit the problem is not always the FDA and the regulatory regime but rather the quality of the science being presented to the agency. Increasingly, they are learning the value of approaching the FDA early on in the process to identify the kinds of data that will be required to determine and satisfy safety and efficacy requirements. A few organizations have even helped draft guidance for the FDA in order to speed the process. Many have hired full-time regulatory staff just to anticipate and plan for the submission and approval process, and to work closely with the FDA on data needs and study design.

In fact, working closely with the FDA has become a survival skill for many venture philanthropies. For example, despite the vast knowledge about the pathophysiology of Duchenne muscular dystrophy, potential targets for therapy remain elusive, and identifying study designs that meet regulatory requirements with validated outcomes



SUSAN SOLOMON
CEO
New York Stem Cell Foundation

“A critical role of private philanthropy is to do the proof-of-concept work.”



Unlike some larger foundations, most of these groups do not sit on their cash. Funds are deployed as soon as a need emerges, and the goal is to maintain a certain level of cash at all times to keep the process rolling.

measures is an obstacle. Pat Furlong, Founder and CEO, Parent Project Muscular Dystrophy, and parent, has been urging her community to weigh in on new benefit/risk equations being considered by the FDA. Furlong is also trying to communicate the special features of Duchenne's to the FDA's neurology division so that they might consider quality-of-life and other mid-range measures when calculating risk and benefit. For example, Duchenne's causes boys to peak in function at age 7 to 10, and then lose function, "so that each loss, each small negative change should be viewed as a 'little death,' from the boy's perspective as well as the increasing burden in terms of required care." Furlong is working to keep the FDA focused on the fact that a degenerative disease is not at all the same as a chronic disease, and thus requires a different regulatory analysis.

It's Always About the Money

Venture philanthropy is always in fundraising mode. And as federal funding has decreased, funding by venture philanthropy has played a larger role. Rose said that the lack of venture capital poses real challenges because of the expectation that the nonprofit world can somehow fill the gap.

Unlike some larger foundations, most of these groups do not sit on their cash. Funds are deployed as soon as a need emerges, and the goal is to maintain a certain level of cash at all times to keep the process rolling. If a great idea comes along and they do not have the funds to support it, they go out and look for them. Most allocate more than 85 percent of their funds to research; so there is a constant need to replenish their base.

Like all nonprofits, venture philanthropies can find fundraising more difficult during economic downturns. In this environment, raising funds for earlier-stage, higher-risk studies is even more challenging. Some speculate that the Valley of Death, the space that lies between basic research and the clinic, is getting wider. Sherer said that he senses that the goal line is being pushed further back on both sides. That is, industry is not interested in taking on a project until it is further along in the pipeline, and public funding agencies are less willing to fund high-risk studies, playing it safe and protecting their portfolios.

Newer organizations, such as the Rett Syndrome Research Trust, are finding that they have to compete with older, more established, and more visible nonprofits—there is a lot of competition for a small pool of cash.

Some organizations find themselves victims of their own success, that is, responsible for an effective new therapy, which then diminishes the sense of urgency and the ability to raise more funds. Tim Coetzee, Chief Research Officer, National Multiple Sclerosis Society, is proud of the Society's role in the approval of two new therapies

and other potential drugs in the pipeline. The challenge now is sustaining momentum in industry for better therapies and possibly cures. “I worry that there will be an enthusiasm gap that will affect investments because there are so many effective new therapies available,” said Coetzee. “But we can do better and we need to.” Coetzee emphasized that groups like his cannot underwrite large clinical trials; they just do not have that type of capital. So their goal is to drive and create collaborations between academic and industrial scientists in such a way that risks are minimized for industry and they are willing to make the investment.

Managing Expectations

Disease-focused venture philanthropies must always contend with the difficult job of managing expectations. Although they have a unique advantage in that they have the pulse on the patient population and their trust, this is also a population that can be anxious, impatient, and even desperate for a cure. Venture philanthropy leaders say they must always walk a fine line between instilling the hope and optimism necessary to keep the research enterprise moving and avoiding hype or creating false expectations. Sherer said that Michael J. Fox urges his supporters to be “pragmatically optimistic.”

Coetzee noted that his constituents are highly connected and very well informed. “They follow the research, and they will call you out if you are hyping anything,” said Coetzee. “It’s a good process though—it reminds us who were working for.”



AUDREY GORDON
President and Executive Director
The Progeria Research Foundation

“Our sole purpose is to help children with progeria. We don’t care about profits, glory, or fame. We just want a cure.”

What Makes Venture Philanthropy Unique?

VENTURE PHILANTHROPIES are not just passively handing out funds—for many, their goal is not to be considered just a “funder” but rather as a strategic organization that coordinates all available resources around potential. It is not just about the research that they have paid for; it is also about how they have built something that is far greater than the sum of its parts.

Given their small share of the overall biomedical R&D investment, venture philanthropies are proving that they can be disproportionately successful, that is, they can do a lot with a little. And, if any given person starts to feel the fatigue of always trying to do so much with limited resources, there are legions of others willing to step in.

Importantly, these groups have an unending willingness to experiment and try new approaches. They focus on measurable results, and typically donors and grantees assess progress based on mutually determined benchmarks. They avoid getting entrenched—there is a readiness to shift funds among organizations and across goals based on tracking those measurable results.

In the end, the most central characteristic of these groups is their close connection to the disease they are pursuing. For most, it is personal—either they or a family member or close friend is or has been affected by the disease. This focus is both a burden and a great gift—it heightens and strengthens their capacity to align incentives to reach their goals. It spurs them to find the dollars to meet the challenges and change the trajectory of research. They are not afraid to do the heavy lifting when no one else will. They are changing how we do biomedical research.



MAX WALLACE
Chief Executive Officer
Accelerate Brain Cancer Cure

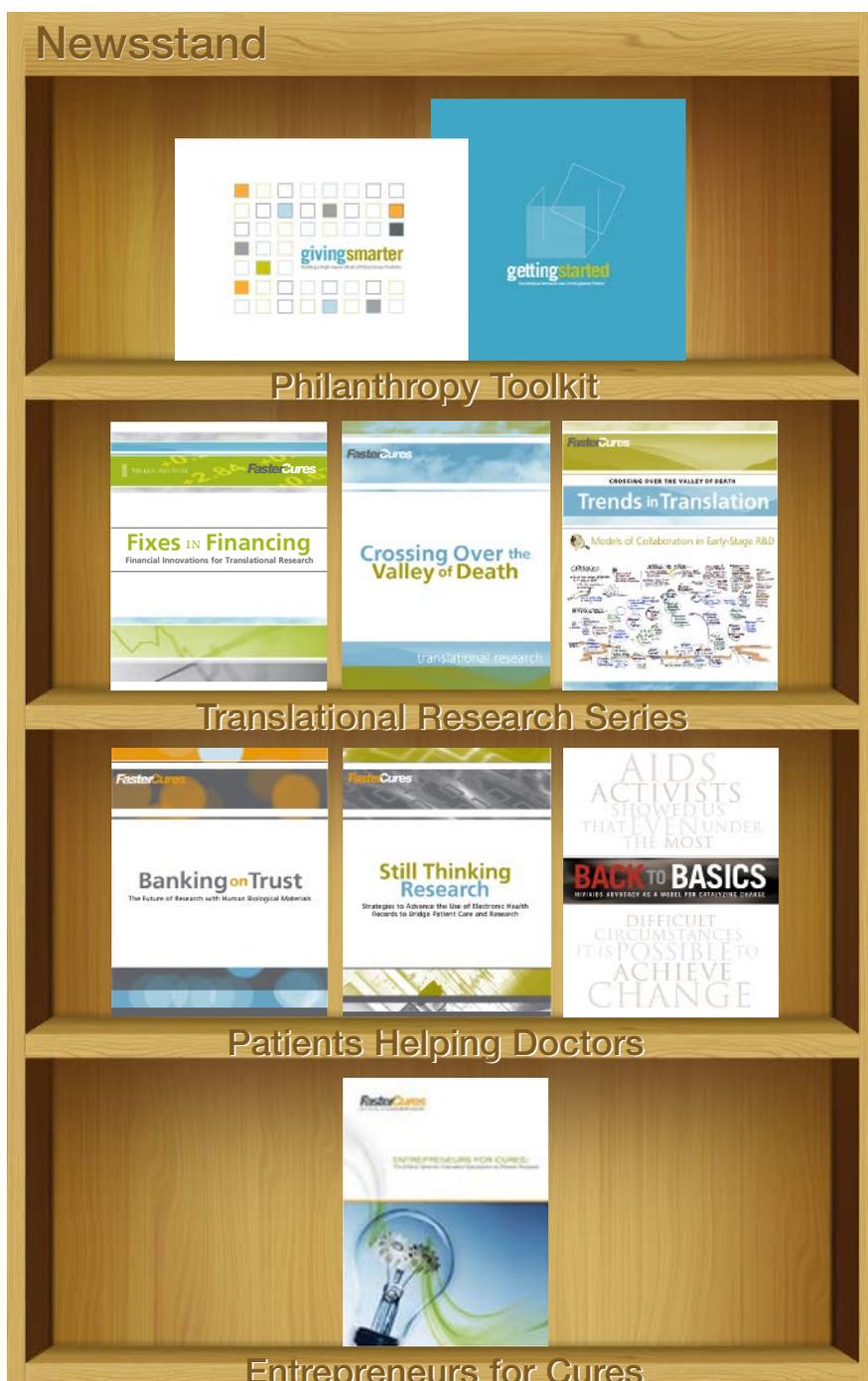
“We are guerrilla warriors—the equivalent of Special Forces. We will do what it takes... We will run around you and through you and over you in pursuit of a cure.”

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Check out these resources about venture philanthropies and medical research on *FasterCures'* Web site, www.fastercures.org, under “Publications.”



To help philanthropists looking to make an impact, and organizations trying to improve their effectiveness, *FasterCures* created **Getting Started: A Medical Research and Development Primer** and **Giving Smarter: Building a High-Impact Medical Philanthropy Portfolio**.

These publications—**Crossing Over the Valley of Death, Trends in Translation: Models of Collaboration in Early-Stage R&D**, and **Fixes in Financing: Financial Innovations for Translational Research**—focus on the type of science that translates a basic discovery into a chemical or biological compound that is ready to be tested in humans.

In fighting disease, patience is not a virtue—patients are. These publications—**Banking on Trust: The Future of Research with Human Biological Materials**, **Still Thinking Research: Strategies to Advance the Use of Electronic Health Records to Bridge Patient Care and Research**, and **Back to Basics: HIV/AIDS Advocacy as a Model for Catalyzing Change**—focus on building a culture of participation in research.

Entrepreneurs For Cures: The Critical Need for Innovative Approaches to Disease Research lays out the critical need for innovative approaches to disease research.



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