

## Crossing Over the Valley of Death

translational research

# Overview

## No time to waste.

**Sherif Ali:** There is the railway. And that is the desert. From here until we reach the other side, no water but what we carry with us. For the camels, no water at all. If the camels die, we die. And in twenty days they will start to die.

**T. E. Lawrence:** There's no time to waste, then, is there? *from Lawrence of Arabia*

Stem cells. Genes linked to Alzheimer's, autism, diabetes. Cancer drugs tailored to treat an individual tumor.

Every day we see stories in the media about the latest medical “breakthroughs” that could lead to cures for dreaded diseases.

And yet, over the years, many breakthroughs like these have yet to bear fruit for patients. Why? Perhaps the media over-hype early discoveries. After all, science is complex and unpredictable. We have to first fail – numerous times – before we succeed, but we tend not to hear about the failures. No one gets rewarded for failure.

The fact is that many basic discoveries barely get to start the journey down the therapeutic development pipeline. Fascinating observations and creative insights often get lost in translation because they lack funding, incentives, and technical expertise to advance any further. They get stuck in an ever-widening gap in funding and support for the kind of research that moves basic science down the path toward treatments. That gap has come to be called by many the “Valley of Death.”

According to the National Institutes of Health (NIH), 80 to 90 percent of research projects fail before they ever get tested in humans.<sup>1</sup> By industry’s reckoning the number may be even higher—for every 5,000 compounds tested, only five make it to clinical trials, and only one is ever approved by the Food and Drug Administration (FDA). Half of all experimental drugs in Phase III trials never become approved medicines.<sup>2</sup>

In a seminal paper published in *The Journal of the American*

*Medical Association* in 2003, members of the Institute of Medicine’s Clinical Research Roundtable wrote, “Without mechanisms and infrastructure to accomplish this translation in a systematic and coherent way, the sum of the data and information produced by the basic science enterprise will not result in tangible public benefit.”<sup>3</sup>

Everyone who cares about getting more and better treatments to patients sooner should be concerned about the lack of therapies that reach the stage of clinical testing and the even smaller number of therapies that ultimately are approved and made widely available.

Trends have conspired to make the translation gap wider rather than narrower. Limited and constrained budgets at the NIH, which has historically funded much of the basic scientific discovery at academic institutions, have made its grantmaking conservative. In industry, which generally takes such basic discoveries and turns them into products, skyrocketing research costs and declining approval of new treatments have caused companies and investors to become increasingly risk-averse.

In this paper, *FasterCures*, in collaboration with the Parkinson’s Action Network, reviews the drug development pipeline from the most basic research conducted at academic research centers and supported by the NIH to the large-scale Phase III clinical trials conducted by pharmaceutical companies. We highlight the importance of translational research in the therapeutic development process, identify some of the major challenges to its conduct, and point the way toward some possible solutions.

### Table of Contents

- 03 OVERVIEW
- 04 THE PRODUCTIVITY GAP
- 05 FROM MOLECULE TO MARKETPLACE
- 09 TRAVERSING THE VALLEY OF DEATH
- 12 CLOSING
- 13 ENDNOTES

# The Productivity Gap

The medical research enterprise is facing a serious productivity gap. The amount of money invested by all sources – government, industry, philanthropy – has been increasing while the number of new products approved is decreasing or stagnant. After years of rapid growth and record profits by the pharmaceutical industry, the era of blockbuster drugs seems to be coming to an end.

Fewer unique molecules are being discovered, and only a small percentage of these ever make it into clinical trials and through the regulatory process. For example, the number of new molecular entities (NMEs)\* approved by the FDA fell from 53 in 1996 to 19 in 2009, despite increases in federal, private, and nonprofit spending in biomedical research. It takes as long as 15 years to take an idea through development, testing, and regulatory approval.<sup>4</sup>

## NATIONAL INSTITUTES OF HEALTH

Between 1995 and 2005 the NIH budget doubled. Since then, it has flattened and even declined in real terms, as applications have increased. As a result, recent NIH funding success rates have declined.

The average age of an investigator receiving his or her first “Ro1-equivalent” award (a virtual prerequisite for professional advancement at many academic institutions) increased from 37 years old in 1980 to 42 years old in 2008. NIH is funding significantly more investigators over the age of 70 than under the age of 30.<sup>5</sup>

A recent NIH study of its peer review system for evaluating grant applications noted that “significant concern was raised that the current peer review system discourages creativity and innovation, while favoring incremental discoveries and tolerating repetition.”<sup>6</sup> NIH

\* New molecular entities (NMEs) are drugs that include an active ingredient that has not previously been approved for marketing in the United States in any form.

Director Francis Collins, in an interview, conceded, “It is true, especially in tight budgetary times, that peer review can tend in a conservative direction, of funding the things that are more surefire as opposed to the high-risk ones.”<sup>7</sup>

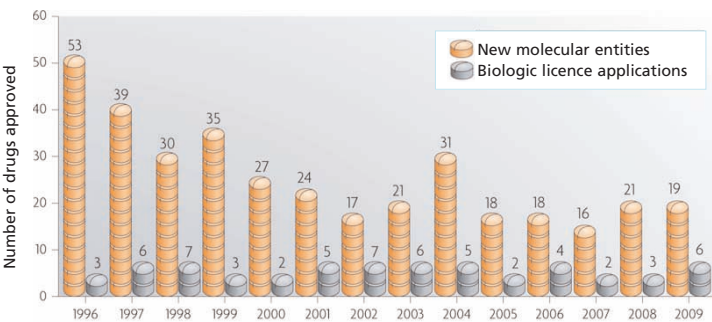
## BIOTECHNOLOGY AND PHARMACEUTICAL INDUSTRIES

On average today, companies spend an estimated \$1.2-1.3 billion on research and development for each approved drug or biologic (accounting for the cost of failures along the way), almost double what it cost 10 years ago.<sup>8</sup>

In this environment, pharmaceutical companies have become increasingly risk-averse, less likely to pursue truly innovative new products. In fact, only 17 percent of the new drugs approved in 2009 could be considered “first-in-class”.<sup>9</sup>

Venture investors are seeking to support products in the later stages of clinical development. According to Ernst & Young’s 2010 annual report on the state of the biotechnology industry, venture capitalists are more selective, less likely to invest outside their existing portfolios, looking for faster returns, and seeking “more mature, de-risked investments.”<sup>10</sup>

Figure 1:  
New Molecular Entities and Biologic Licence Applications

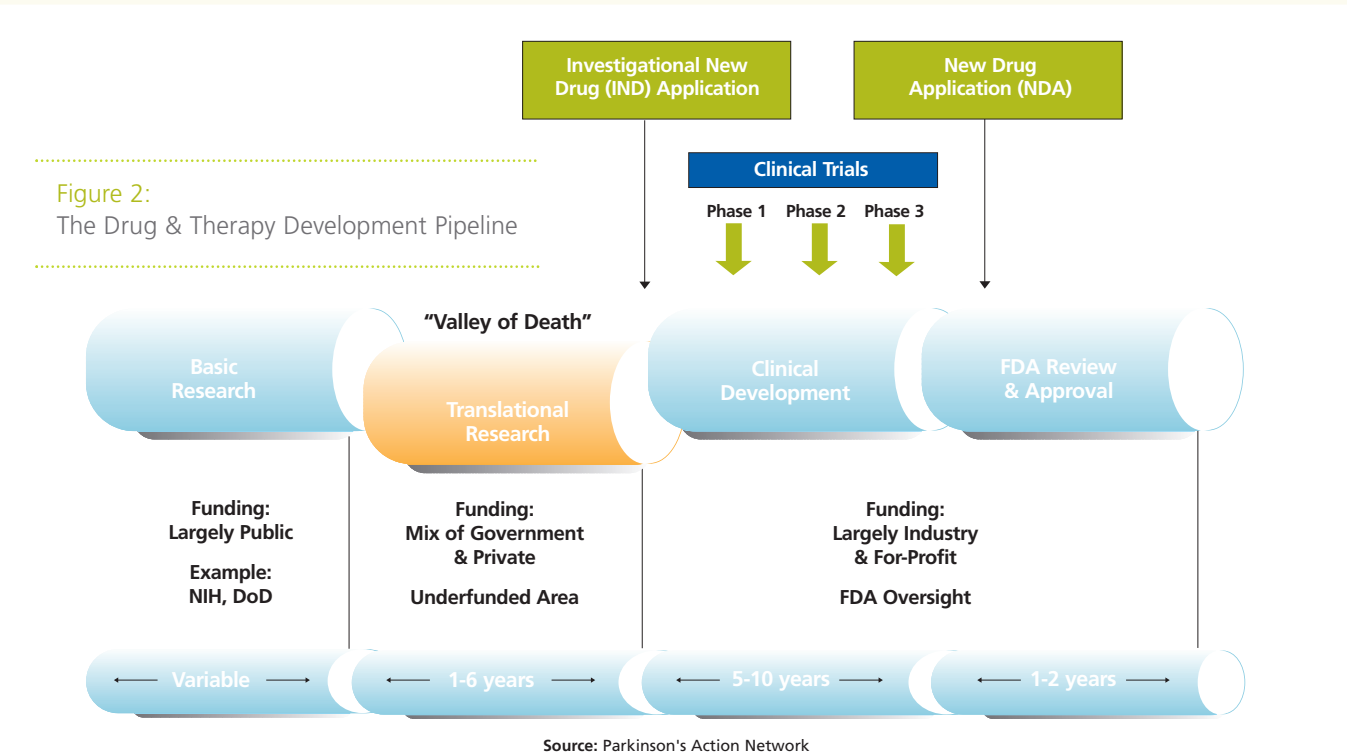


Source: Nature Reviews Drug Discovery 9, 89-92 (February 2010)  
[http://www.nature.com/nrd/journal/v9/n2/fig\\_tab/nrd3101\\_F1.html](http://www.nature.com/nrd/journal/v9/n2/fig_tab/nrd3101_F1.html)  
(Accessed November 30, 2010)

# From Molecule to Marketplace

In the simplest terms, there are three stages of medical research: **BASIC RESEARCH OR BASIC DISCOVERY** is the earliest stage of research, carried out for the advancement of knowledge, without necessarily any regard for its application to practical problems. **TRANSLATIONAL RESEARCH** is the process of applying ideas, insights, and discoveries generated through basic scientific inquiry to the treatment and prevention of human disease – the critical bridge between basic research and clinical research. It

includes intermediate steps such as identification of biomarkers, target and pathway validation, and development of and testing in animal models. **CLINICAL RESEARCH** is research in human subjects aiming toward approved treatments for patients. FIGURE 2 shows the many steps along the continuum of the development of a therapy, and where funding has historically come from for those steps.



Our current publicly-funded academic research infrastructure, as guided by the policies and practices of NIH – the single largest sponsor of biomedical research in the world – has focused primarily on unlocking the underlying questions of biology, that is, **basic research**. This has been a critical approach, leading to many advances in our understanding of human and disease biology, but it is not sufficient to develop a therapy for a patient. In most cases, this approach barely takes research to the point of identifying a target that a drug might act upon to change the course of a disease.

The biotechnology and pharmaceutical industries fund primarily clinical research – and as costs have grown and uncertainty increased, companies are in many cases investing later along the research continuum and becoming more conservative in their decisions about what to fund.

**Translational and clinical research**—which aim to apply fundamental knowledge to the human condition—are more difficult and expensive to conduct than basic research because they often involve complex organisms (i.e., animal models, humans) living in multifaceted environments. In general, costs increase while failure decreases as a project moves down the development pipeline. As ideas survive the steps in the process, they become relatively less risky, but the research involved in moving them forward becomes exponentially more expensive, especially in later-stage trials in humans.

Translating a basic discovery into a chemical or biological compound that is ready to be tested in humans is no simple matter. There are a number of complicated, time-consuming steps in between, and the academic scientists who make the discoveries are not always or even *often* well-suited to – or even interested in – translating them to the next step.

## 1 Case Study 1

Funding Gap Stalls Potential Breakthrough in Sickle Cell Disease<sup>2</sup>

**STEPHEN SEILER, CEO OF AESRX**, has a promising therapeutic, Aes-103, for sickle cell disease, a recessive disorder of the hemoglobin that can lead to a wide range of serious, sometimes life-threatening, conditions. More than 13 million individuals worldwide suffer from sickle cell disease, approximately 75,000 of them in the United States and 12 million in sub-Saharan Africa. Sickle cell is recognized in the United States as an orphan disease, which means that it is a rare disease that affects a small percentage of the population. Aes-103 has already been granted orphan drug status by the FDA, qualifying it for accelerated approval.

Aes-103 is attractive for several reasons: the proposed mechanism of action has already been validated in humans, it binds a relevant target, and there is a large body of safety data. It has already benefited from two NIH grants: a Small Business Innovation Research grant to further the pre-clinical development of the compound and a Rapid Access to Intervention Development grant that has funded cGMP manufacture of enough drug substance for Phase 1 trials. Seiler is working with a clinician at the National Heart, Lung, and Blood Institute’s (NHLBI) Intramural Research Program to conduct a series of Phase I trials at NIH’s state-of-the-art Clinical Center in Bethesda, Md. Once proof-of-concept in humans is established, several blue-chip venture funds have expressed interest in investing in AesRx to take the program forward.

Despite all this effort and support, Seiler was still teetering on the brink of the Valley of Death. AesRx needed to complete pre-clinical toxicology, formulate the API into a drug, compile and file an Investigational New Drug Application with the FDA, and complete certain bioanalytical work that had to be conducted outside NIH. His collaboration with NHLBI could not fund these expenditures and venture capital would not step in this early. He faced a funding gap of several million dollars, without which this potential breakthrough would never see the light of day.

Fortunately Aes-103 was rescued by a new program at NIH, Therapeutics for Rare and Neglected Diseases (TRND)<sup>13</sup>, which selected it as one of TRND’s pilot projects. This new initiative, funded initially at \$24 million, will help support promising discoveries in rare and neglected diseases through some of the translational steps necessary to develop them into drugs. But even if TRND’s funding were to increase dramatically, it could not help every worthy company or researcher. NIH’s heightened interest in further development of the products of basic research is welcome and necessary, but it cannot by itself be a solution to the systemic problem of the Valley of Death.

The steps include:

**TARGET VALIDATION:** demonstrating that a molecular target is involved in a disease process, and that impacting the target is likely to have a therapeutic effect;

**ASSAY DEVELOPMENT:** developing a relevant test to measure the activity of a compound;

**SCREENING AND HITS-TO-LEADS:** screening a library of compounds for activity against the target, or “hits”, and then further winnowing the field to higher-quality “leads”;

**LEAD OPTIMIZATION:** refining a lead compound to improve its drug characteristics and ultimately produce a drug candidate ready for testing in humans;

**PRE-CLINICAL DEVELOPMENT:** compiling existing data or undertaking new studies through animal testing showing that a compound is safe to administer to humans.”

These are very complex and iterative processes that can frequently be a significant bottleneck in drug development. Even after these steps have been successfully accomplished, many companies and investors are now primarily interested in investing in compounds that have an established “proof of concept,” which usually comes in late Phase I or even early Phase II clinical studies. Proof-of-concept is early confirmation of the validity of a hypothesis about a disease or its treatment, and without it, drug development cannot move forward.

### THE VALLEY OF DEATH

The Valley of Death is the place where many good ideas in the drug development pipeline drop off – the arid land between a promising discovery and the point at which a company is willing to pick it up and move its development forward. It is a substantial problem facing patients everywhere. Basic research continues to provide numerous avenues of promising ideas and knowledge for all diseases. But structural, intellectual, and funding barriers have made it difficult to translate basic research into clinical applications.

The challenges in moving research through the Valley of Death can be summarized as:

**Lack of funding.** Funding for translational research can be difficult to come by, especially as companies become increasingly risk-averse.

**Lack of technical expertise.** Most basic researchers simply do not have the skills or knowledge to move their discoveries through the pipeline. They need information and help to carry these forward.

The business of basic research and the business of therapy development require different support structures and different management. Translational and clinical research, like basic research, are dependent upon the tenacity and creativity of the principal investigator. But they also require expertise in regulatory, intellectual property, and privacy issues, among others; access to specialized technical infrastructure; and a level of oversight and management that is generally beyond the reach and experience of those conducting NIH-supported basic research. Tangible and accurate information about this expertise are quite limited.

Technology transfer offices at research universities – whose mission is primarily to out-license promising discoveries from their academic labs – cannot usually offer the kind of support needed to push an idea further down the pipeline and closer to a proof-of-concept.

**Lack of incentives.** Even if academic scientists had the skills necessary and the support available to move their discoveries forward, they have few professional incentives to do so. They are generally rewarded with tenure by their institutions for receiving NIH grants, publishing novel basic research in professional journals, and holding patents on their discoveries. If they are interested in collaborating with companies to move their discoveries forward toward therapies, they often open themselves up to charges of conflict of interest.

**High-risk of failure.** For every 5,000-10,000 compounds that enter the drug discovery pipeline only 250 will progress to pre-clinical development. Five will move forward to Phase I studies, and only one will survive to be an approved drug.<sup>14</sup> While failure is inevitable and even necessary in science, these are stiff odds and put enormous pressure on companies with regards to where they place their bets. New therapies must be tested for safety and efficacy in populations both small and large, a very drawn-out process that can take decades.





The goal has to be to take early discoveries from academia to the point of investment.

## 2 Case Study 2

Sequential De-Risking Needed to Move Products Forward<sup>15</sup>

**PETER LANSBURY** has been trying to decode the basic mechanisms of neurodegenerative diseases for decades at Harvard Medical School and Brigham & Women’s Hospital in Boston. He is a leader in the scientific understanding of protein misfolding and aggregation in neurodegeneration.

In the 1990s Lansbury became interested in Parkinson’s disease, and eventually focused his research on an enzyme that has been heavily studied in oncology. Lansbury was aware that many experimental drugs had been developed in pharmaceutical companies targeting this enzyme’s role in cancer. Might he be able to “reposition” (in the industry’s current lingo) one of these drugs to treat neurological diseases like Parkinson’s and Alzheimer’s? Such an approach would be a short-cut through the “Valley of Death,” taking a huge amount of time and risk out of the research process.

It proved to be difficult to accomplish this from inside academia. Most companies were reluctant to share their proprietary compounds, despite the fact that it was becoming clear that this class of drugs did not have efficacy in cancer. This reluctance was based on a culture in which proprietary compounds, and the patents that protect them, are sacred and cannot be shared under most circumstances. When he did find a company willing to work with him, he realized that there was no precedent (or funding) for bringing intellectual property into an academic institution to further

its development. “Universities are set up to out-license, not to in-license,” says Lansbury. “I had to leave academia. The only way to get the molecule was to deal with pharma on their terms, as a peer.”

Lansbury started a company called Link Medicine. To fund it he worked with a philanthropist who is also a Parkinson’s disease patient. Together, they were able to raise two years’ worth of critical funding from other angel investors, many of whom also had a personal experience with neurodegeneration. “Philanthropists in medicine are interested in outcomes, so angel investing in a company was not a tough sell for them.” After the first two years, Link Medicine had made significant progress and was able to complete a \$40 million round of venture capital funding.

Thanks to the initial support of “angel philanthropists,” Lansbury and Link Medicine appear to be on solid footing to pursue their promising research, and pharma is interested in their platform because it has relevance for treating a broad range of neurodegenerative diseases. But as a general matter, Lansbury says, “The other side of the Valley of Death is moving away from us. Pharma is much more risk-averse. They are protecting against negative results; academia is seeking a positive result. Everyone wants to go right for the big question. But this process of drug development is about sequential de-risking. The goal has to be to take early discoveries from academia to the point of investment.”

# Traversing the Valley of Death

“Why can’t we continue to answer the underlying questions in biology while also addressing those questions critical to specific diseases? Why can’t we do both?”<sup>16</sup>

**DAVID BALTIMORE, NOBEL LAUREATE, PROFESSOR OF BIOLOGY, CALIFORNIA INSTITUTE OF TECHNOLOGY**

The success of the translation from laboratory bench to patient bedside depends on the joint efforts of all funders, including NIH, academic institutions, nonprofit foundations, and the pharmaceutical and biotechnology industries. The Valley of Death is a very real and significant challenge, but there are some hopeful signs of movement to bridge the divide in a variety of places.

## NATIONAL INSTITUTES OF HEALTH

In recent years NIH has acknowledged the need to enhance its commitment to translational research so that Americans will see a better return on the enormous investment of their tax dollars in the form of improved health and cures for disease. The NIH Roadmap<sup>17</sup>, launched in September 2004, sets many of the right goals: fostering more collaborative research, linking existing clinical research networks, providing core services to aid those conducting translational research, and supporting the training and career development of physician-investigators.

NIH has made progress, within its existing structures and with limited funding, toward promoting translational research with some helpful trans-NIH initiatives. Examples of such efforts include:

**NATIONAL CHEMICAL GENOMICS CENTER:** Part of the Molecular Libraries Initiative, this state-of-the-art facility performs automated high-throughput screening (HTS) and chemistry optimization on confirmed hits to produce chemical probes for dissemination to the research community.

**THERAPEUTICS FOR RARE AND NEGLECTED DISEASES (TRND):** This new program, funded initially at \$24 million, will help support promising discoveries in rare and neglected diseases through some of the translational steps necessary to develop them into drugs.

**RAPID ACCESS TO INTERVENTIONAL DEVELOPMENT (RAID):** Provides core services needed by researchers encountering roadblocks in trying to translate a promising discovery to clinical testing – services such as the capacity to manufacture agents in sufficient quantity for testing, and logistical and regulatory expertise.

**CLINICAL AND TRANSLATIONAL SCIENCE AWARDS (CTSAs):** A national consortium of academic research institutions across the country, which NIH funds to build national clinical and translational research capability, provide training and improve the career development of clinical and translational scientists, enhance consortium-wide collaborations, and advance translational research.

**NIH-FDA JOINT LEADERSHIP COUNCIL:** This new body will work together to help ensure that regulatory considerations form an integral component of biomedical research planning and that the latest science is integrated into the regulatory review process.

**CLINICAL CENTER:** NIH has taken steps toward opening up this state-of-the-art research hospital on its campus in Bethesda, Md., to improve collaboration with researchers from outside the NIH’s Intramural Research Program.

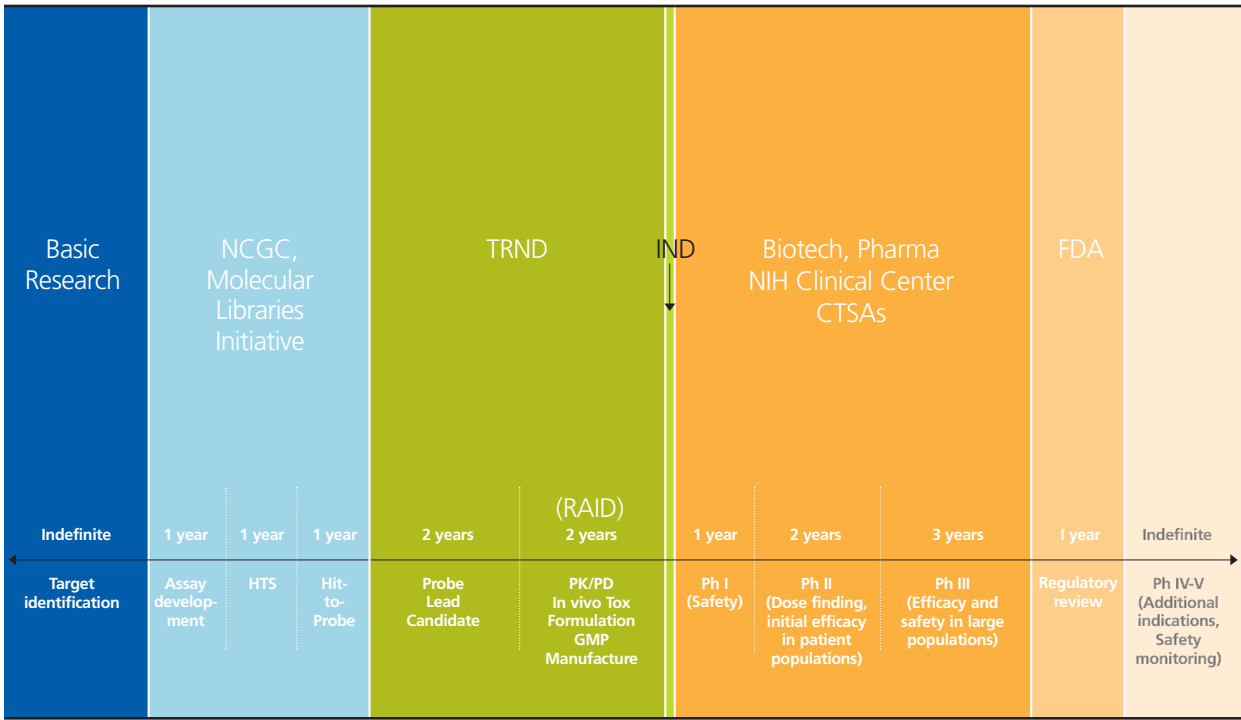
In addition, the 2010 healthcare reform law, the Patient Protection and Affordable Care Act, established a **Cures Acceleration Network** (CAN) at NIH that aims to move promising science through the Valley of Death. CAN, as authorized, seeks to cut the time between discovery and development of drugs and therapies through new grant-making mechanisms at NIH. It will establish CAN within the Office of the Director of NIH and authorize grants expected to move discoveries from the lab into the next generation of therapies. CAN will be overseen by a board of 24 diverse members from several fields, including research, FDA, a venture capital, and patient advocacy. In addition, CAN will work with the FDA to coordinate approval requirements with the goal of expediting the development and approval of products. CAN needs appropriated funding in order to link NIH-funded discoveries with development efforts in industry.

FIGURE 3 shows how NIH is thinking about how these efforts can help bridge gaps in the therapeutic development pipeline.

NONPROFITS

Forward-thinking philanthropic funders of disease research – foundations such as the **Michael J. Fox Foundation for Parkinson’s Research**, the **Cystic Fibrosis Foundation**, and a growing number of others – can play an absolutely critical role in stimulating research in under-resourced disease areas, and helping to bridge the Valley of Death.<sup>18</sup> Free of the pressures of publication and career advancement in academia and the bottom-line imperatives of the private sector, nonprofit foundations are ideally positioned to make relatively high-risk investments that could significantly move a field of research forward and increase the likelihood that other parties also will invest.

Figure 3: NIH Can Help Bridge Gaps in the Pipeline



Source: Christopher P. Austin, National Chemical and Genomics Center, NIH

Medical research foundations are already doing this by:

- developing pre-clinical tools that benefit everyone in a disease area;
- targeting research in areas that will help translate basic scientific discoveries into therapies – such as biomarkers, target and path way validation, animal models, and small pilot clinical trials;
- creating funding mechanisms that enable or even require academic researchers to work with industry partners;
- bringing focus, management, and accountability to academic research;
- providing access to a patient community and resources by creating patient registries, biorepositories, and networks of trained clinical trials sites;
- working with companies to explore new indications for existing drugs;
- employing high-throughput screening to help industry identify better investment opportunities;
- facilitating industry access to academic scientific experts and clinicians;
- advocating with the FDA for the approval of new treatments; and
- serving as a “Good Housekeeping Seal of Approval,” validating particular researchers, paths of inquiry, clinical trial designs, endpoints, or targets for follow-on industry investment.

BIOTECHNOLOGY AND PHARMACEUTICAL INDUSTRIES

Within the pharmaceutical industry, the realization is sinking in that the productivity gap is unsustainable and that the block-buster model of drug development can no longer be relied upon. It appears that many companies “have begun to substantially increase investments in the earlier stages of drug discovery; this is reflected by the number of candidates entering Phase I trials, which has increased significantly.”<sup>19</sup> Experts are advocating for a “quick win, fast fail” paradigm for drug development that would result in earlier proofs-of-concept and fewer therapeutic candidates advancing into Phases II and III.<sup>20</sup> Innovations like Eli Lilly’s CHORUS program have been successful at reducing attrition at these later stages.

Companies are also demonstrating themselves to be interested in new and more partnerships with other funders, including

universities and nonprofits – and even with other companies in pre-competitive areas of research such as biomarkers. Among the growing number of examples are:

- The **Asian Cancer Research Group**, announced in February 2010, is a collaboration among Eli Lilly, Merck, and Pfizer with the goal of creating a significant pharmacogenomic cancer data base, initially with data and tissue samples from lung and gastric cancer patients, which will be shared broadly with cancer researchers.
- **Enlight Biosciences** is a venture fund supported by six of the largest pharmaceutical companies, which invests in companies developing enabling technologies that have benefits for all companies’ R&D efforts, such as RNAi and gene microarrays.
- The **Alzheimer’s Disease Neuroimaging Initiative** is a government-mediated collaborative effort among the NIH, 20 companies, two nonprofits, and universities to define the rate of progress of mild cognitive impairment and Alzheimer’s disease, to develop improved methods for clinical trials in this area, and to provide a large database that will improve design of treatment trials.

# Closing

All of these efforts are steps in the right direction, but the whole has yet to add up to more than the sum of its parts.

While the media heralds the promise of the latest scientific discoveries, within the biomedical research establishment there is a developing consensus that the traditional model for turning those discoveries into new treatments is broken. With some strategic federal and philanthropic investment, the paradigm is beginning to shift. Primarily on the left side of the valley, NIH and some nonprofit collaborators are marching forward into the Valley of Death. But we are far from reaching the other side.

To get there we will need to grapple with difficult questions, such as:

- **CAN WE** change the model of medical research in ways that reduce the cost of innovation without jeopardizing patient safety?
- **CAN WE** recalibrate incentives within academia so that investigators interested in translation can be rewarded for it?
- **CAN WE** take a more nuanced approach to patents and licensing, and share pre-competitive information more freely?
- **CAN WE** create an infrastructure that supports collaboration among sectors while guarding against conflicts of interest?

There are successful models out there – within medical research and outside it – for us to learn from. We seem to be at an inflection point in the dialogue within the biomedical research establishment where action to address these challenges is possible. We need to take advantage of this moment, and we need to bring the public and policymakers into the conversation.

There’s no time to waste.

# Endnotes

<sup>1</sup> National Institutes of Health. 2009. “NIH Announces New Program to Develop Therapeutics for Rare and Neglected Diseases,” <http://www.nih.gov/news/health/may2009/nhgri-20.htm>, accessed September 29, 2010.

<sup>2</sup> Pharmaceutical Research and Manufacturers of America (PhRMA). 2008. *Profile 2008*. Washington, DC: PhRMA.

<sup>3</sup> Sung, Nancy S., William F. Crowley, Jr., Myron Genel, et.al., 2003. “Central Challenges Facing the National Clinical Research Enterprise,” *Journal of the American Medical Association*, 289(10)

<sup>4</sup> DiMasi, J.A. New drug development in the United States 1963-1999. *Clinical Pharmacology & Therapeutics*. 2001 May; 69(5):286-96

<sup>5</sup> National Institutes of Health. 2008. *2007-2008 Peer Review Self-Study*. Bethesda, MD: NIH..

<sup>6</sup> Ibid.

<sup>7</sup> Interview of Francis Collins by Ira Flatow, *Science Friday*, National Public Radio, September 11, 2009.

<sup>8</sup> Pharmaceutical Research and Manufacturers of America (PhRMA). 2009. *Profile 2009*. Washington, DC: PhRMA.

<sup>9</sup> Paul, Steven M., Daniel S. Mytelka, Christopher T. Dunwiddie, Charles C. Persinger, Bernard H. Munos, Stacy R. Lindborg, and Aaron L. Schact. 2010. “How to Improve R&D Productivity: The Pharmaceutical Industry’s Grand Challenge,” *Nature Reviews Drug Discovery*, 9(3).

<sup>10</sup> Ernst & Young. 2010. “Biotech Industry Showing Resilience Despite Challenging Conditions,” <http://www.ey.com/US/en/Newsroom/News-releases/Biotech-industry-showing-resilience-despite-challenging-conditions>, accessed September 29, 2010.

<sup>11</sup> Eckstein, Jens. ISOA/ARF Drug Development Tutorial, <http://www.alzforum.org/drg/tut/ISOATutorial.pdf>, accessed September 29, 2010.

<sup>12</sup> *FasterCures* communications with Dr. Stephen Seiler, 2010.

<sup>13</sup> See page 9 of this white paper.

<sup>14</sup> Pharmaceutical Research and Manufacturers of America (PhRMA). 2008. *Profile 2008*. Washington, DC: PhRMA

<sup>15</sup> *FasterCures* communications with Dr. Peter Lansbury, 2010.

<sup>16</sup> From Summit on Innovation in Disease Research, *FasterCures* Meeting Report, December 3, 2004, [http://www.fastercures.org/objects/pdfs/meetings/Innovation\\_Report.pdf](http://www.fastercures.org/objects/pdfs/meetings/Innovation_Report.pdf).

<sup>17</sup> National Institutes of Health.<http://nihroadmap.nih.gov/aboutroadmap.asp>, accessed September 29, 2010.

<sup>18</sup> *FasterCures* has extensively analyzed the role of nonprofits in the funding and conduct of medical research in its 2008 white paper “Entrepreneurs for Cures,” available at [http://www.fastercures.org/objects/pdfs/white\\_papers/FastercuresWP\\_Innovation\\_052808.pdf](http://www.fastercures.org/objects/pdfs/white_papers/FastercuresWP_Innovation_052808.pdf).

<sup>19</sup> Paul, Steven M., Daniel S. Mytelka, Christopher T. Dunwiddie, Charles C. Persinger, Bernard H. Munos, Stacy R. Lindborg, and Aaron L. Schact. 2010. “How to Improve R&D Productivity: The Pharmaceutical Industry’s Grand Challenge,” *Nature Reviews Drug Discovery*, 9(3).

<sup>20</sup> Ibid.



Fifteen Years.

That's how long it takes to develop new medical treatments.

But the thousands of people  
diagnosed with a deadly disease today  
cannot wait 15 years.

That's why *FasterCures* is working  
across sectors and diseases  
to accelerate the process of discovery  
and development of new medical solutions.

**To save lives, we must save time.**

***FasterCures***  
The Center for Accelerating Medical Solutions  
It's not just our name, it's our mission.

*FasterCures*/The Center for Accelerating Medical Solutions is a nonprofit think tank and catalyst for action that works across sectors and diseases to improve the effectiveness and efficiency of the medical research enterprise. *FasterCures*, a center of the Milken Institute, is nonpartisan and independent of interest groups.

*FasterCures'* mission is to accelerate the process of discovery and development of new medical solutions for deadly and debilitating diseases.





**Get Involved!**

**Learn More:** [www.fastercures.org](http://www.fastercures.org)

**Be in the Know:** *FasterCures SmartBrief*

**Read and Comment:** The *FasterCures* Blog

**Stay Connected:** [@fastercures](https://twitter.com/fastercures) [f FasterCures](https://www.facebook.com/FasterCures)

1101 New York Avenue, NW, Suite 620, Washington, DC 20005 / 202-336-8900 / [www.FasterCures.org](http://www.FasterCures.org)

*FasterCures, a center of the Milken Institute, is nonprofit, nonpartisan, and independent of interest groups.*