PATIENT CAPITAL 3.0



Confronting the Crisis and Achieving the Promise of Venture-Backed Medical Innovation

Patient Capital 3.0

Content compiled, researched and developed by
the National Venture Capital Association (NVCA) and the
Medical Innovation and Competitiveness (MedIC) Coalition.

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"We must protect and foster the business environment in which innovative medical startups form and grow."

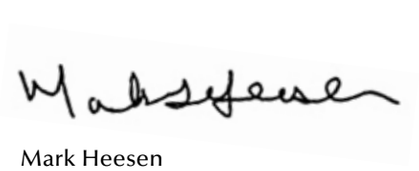
Introduction

Few human achievements capture our attention more readily than new medical treatments and cures for deadly diseases. These achievements amaze us with their ingenuity. They stoke our hopes for longer and healthier lives – for us and our loved ones. And they promise implicitly that they will be there for us should we ever need them.

While such innovations impress and reassure us, most people know very little about how scientific breakthroughs evolve into new drugs, devices and diagnostic tools. The reality is that each new discovery or idea must be translated into a viable, safe and effective product before it can benefit even a single patient. This process involves testing the new technology, developing it, manufacturing it and distributing it profitably. In many cases, it requires starting and growing a new company from scratch. Doing so is exceptionally difficult, and it very rarely takes place without private investment sources such as venture capital.

For this reason, we must protect and foster the business environment in which innovative medical startups form and grow. That includes the regulatory process, the process of selecting which medical innovations healthcare payors will cover, intellectual property laws, and the capital markets that provide long-term funding to these innovative companies. Conditions must be conducive to investing in and building companies to develop novel drugs, devices and diagnostics. If we fail to sustain a supportive business environment for entrepreneurial medical companies, we risk choking off the flow of innovative treatments and cures to patients in need – at a time when the number of such patients and the socioeconomic burden of disease continue to grow. We also risk destroying an innovation ecosystem that has generated high-quality jobs and growth for the U.S. economy for decades.

We have compiled this report because failure is not an option. In the following pages, we describe how medical innovation occurs in the U.S., the role that venture capital plays in driving it, and the benefits it delivers to all of our citizens. We also examine the critical challenges venture-backed innovation now faces, and the role that public policy can play in helping us overcome those challenges. By understanding the issues and working together, we are confident that we can ensure that America will continue to lead the world in producing medical innovations that cure diseases and improve the lives of millions of patients in the U.S. and worldwide.

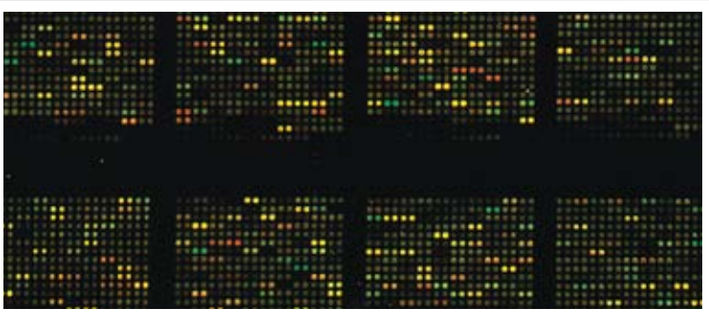


Mark Heesen

President, National Venture Capital Association

Venture capital drives U.S. medical innovation, but today that ecosystem is at risk.

Executive Summary



Venture capital plays a critical role in driving medical innovation in the United States. It spurred the creation and growth of our country's biopharmaceutical, medical device, and diagnostics industries, and it remains one of the few sources of funding for the startup companies that bring life-saving and life-changing medical treatments and technologies to the marketplace.

Venture-backed medical breakthroughs cure diseases, provide new treatment options, produce better health outcomes for patients, and raise our overall quality of life in the U.S. Such breakthroughs include new medicines for our most devastating diseases, as well as medical technologies, such as angioplasty and magnetic resonance imaging (MRI), that have transformed healthcare. In addition, venture-backed medical innovations help to decrease overall healthcare costs over time and serve as a crucial part of the research and development (R&D) pipeline for large corporations. Finally venture-backed medical startup companies spur U.S. economic growth through the jobs and revenues they generate.

Today, America's medical innovation ecosystem is at risk. Venture investment in biopharmaceutical, medical device, and diagnostics companies has declined at an alarming rate. The rapidly escalating time, cost and uncertainty now associated with medical innovation have prompted many limited-partner investors to pull their capital out of life sciences venture capital in favor of other asset classes. While there are many factors driving this trend, public policy – notably, the regulatory approval and the coverage and payment processes – plays a key role. In a recent survey of U.S. venture capitalists, more than 60 percent identified the cost and uncertainty of the review and approval process at the U.S. Food and Drug Administration (FDA) as having the highest impact on venture investment. Nearly 40 percent of respondents pointed to concerns over coverage and payment policy for innovative products, which is shaped in significant part by the Centers for Medicare and Medicaid Services (CMS). As a result, many of these venture capitalists have been decreasing their investments in biopharmaceutical, medical device, and diagnostics companies. They are also reducing their concentration in critical disease areas and shifting investment toward other industries. As a result, early-stage investment in promising new medical technologies is now difficult to find, particularly for the most innovative technologies.

While conditions in the U.S. market have grown more challenging for innovative medical startups, other developed countries have begun to emulate the U.S. venture model. They have increased their funding of basic R&D; they have made their regulatory processes more straightforward; and they have begun to offer lucrative financial incentives to entrepreneurs and venture investors to build companies there instead of here. If these efforts prove successful, the resulting shift will delay the availability of life-saving and life-sustaining treatments for Americans, decrease the number of jobs generated by this important sector, and threaten America's global leadership in medical innovation.

Despite these challenges, America's medical innovation ecosystem continues to offer tremendous promise. Thanks to breakthroughs in fields such as human genetics, molecular biology and nanotechnology, U.S. venture capitalists have opportunities to invest in some of the most groundbreaking medical innovations the world has ever seen. Venture-backed medical innovations also have the potential to increase our ability to control and reduce the costs of treating our most common chronic and deadly diseases. Such advances underscore the enormous benefits that venture-backed medical innovation delivers to patients and to our economy. And we must continue to fuel that innovation by promoting public policies that encourage and reward it – before it is too late.

A successful medical innovation requires:

- a patient who needs it
- a team that can turn it into a safe, effective product
- a company that can develop, manufacture and market it profitably
- investment capital to fund it
- a provider willing to use it
- an insurer willing to cover it

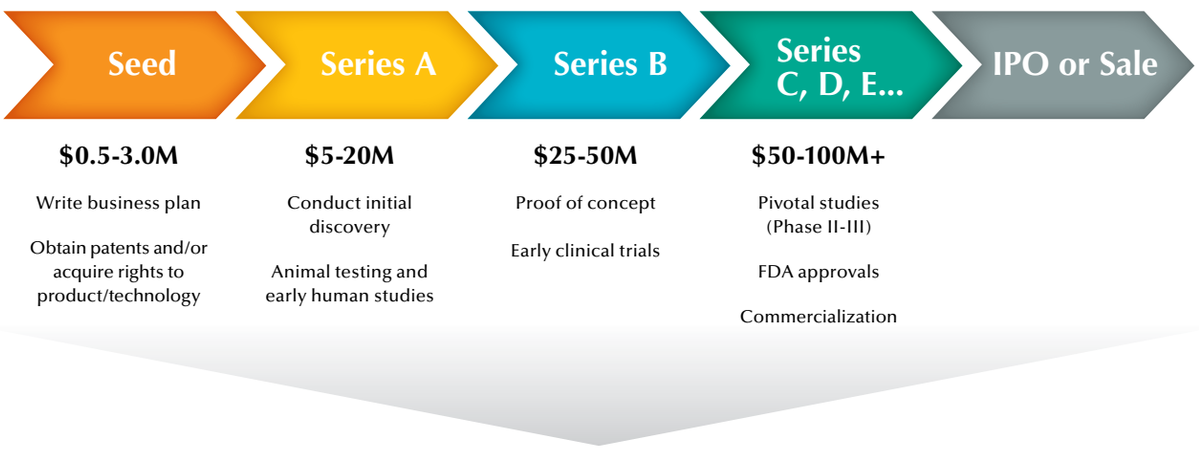
The Venture-Backed Medical Innovation Model:
How Does It Work?



Most medical innovations begin as breakthroughs and discoveries by scientists working in government and private labs, at corporations, and at academic medical research centers. However, this new knowledge cannot help patients in and of itself. Rather, it must be "applied" through the development of new drugs, devices and diagnostic tools. In turn, these must be approved by the FDA, selected for coverage and payment by CMS and private insurers, and then made available to physicians and patients via the healthcare marketplace. This process requires extraordinary amounts of time, money, expertise and risk. In many cases, it also requires building a brand new company from scratch.

Enter the venture capitalist (VC), who works with the scientific team in such cases to form a startup company and guide it through the process outlined above. Providing more than just funding, the VC counsels the company's management team regarding strategy, operations, development

Chart A: Venture Capital Investment Process & Timeline



and production, as well as makes connections to aid sales and marketing efforts. As part of this partnership, the venture capitalist also guides the startup through the process of obtaining the large amounts of capital required to support the company through many years of product development. Throughout this process, the company must meet certain milestones to receive additional funding, without which it will likely fail.

Making investments across the life cycle of a new medical company involves significant entrepreneurial risk. Developing truly novel technologies is a highly unpredictable process, requiring both prudence and patience. In addition, all new medical products are subject to review and approval by the FDA based on data generated by a series of clinical trials. Customarily funded by venture investment, a startup's clinical trials take many years and cost millions of dollars per trial. Trials can present even greater challenges and generate more uncertainty when a discovery is "first-in-class" because there is no historical roadmap for how to design a trial for a truly novel product.

After the trials conclude, the startup must submit the trial data and other extensive information to the FDA for review. This process itself can take many years during a time when the company is spending hundreds of thousands – or even millions – of dollars per month to stay in operation with no guarantee of FDA approval. If the clinical development and regulatory process takes significantly longer than expected, it can be difficult for companies to raise and sustain enough capital to stay in business until regulatory approval is obtained.

Once a product gains FDA approval, the company must convince government and private health insurance payors to provide coverage for the technology. Again, novelty can work against an innovative product due to the lack of similar products to which it can be compared. In addition, pioneering coverage and payment for a novel drug or device can be costly and time-consuming, at a time when a company may have little or no product sales.

In all, this process often takes 10 to 15 years, costing an average of $1.2 billion for a new drug[1] and $92 million for a novel medical device.[2] More companies fail than succeed. Most that do succeed follow one of two paths: They become public companies by selling shares through an initial public offering (IPO), or they are purchased by larger, established companies. In either case, the VC "exits" the investment at this point and distributes any shares of the proceeds from the transaction back to his or her investors. These are often public and private pension funds, university endowments, foundations, and individuals – all of whom become "limited partners" in the venture fund. All of these parties are willing to accept these risks as long as the returns generated by the handful of successful companies outweigh the losses incurred by the failures.

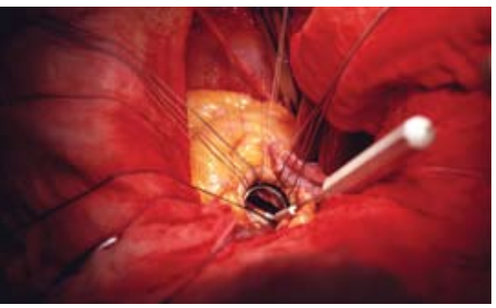
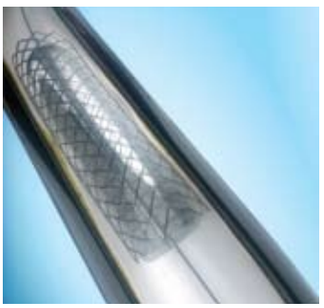
Unfortunately, the combination of high risk and long timeframes strongly discourages investment by government, banks and public markets, while the scale of investment almost always exceeds what individual investors can provide. That's why venture capital is typically one of the few viable sources of funding available for translating medical innovations from promising ideas into real products that physicians can use to cure diseases and treat patients with unmet needs.

These elements of venture capital – the patience, the optimism, the hands-on guidance, the willingness to risk failure, and the persistence to overcome it – make it unique as an asset class and as an engine for innovation, jobs and U.S. economic growth.

Learn more about how venture builds innovative startups from scratch at nvca.org

[1] DiMasi, J.A. and H.G. Grabowski. "The Cost of Biopharmaceutical R&D: Is Biotech Different?" Managerial and Decision Economics 2007; 28:469–479.
[2] Makower, Josh, et al., "FDA Impact on U.S. Technology Innovation," November, 2010

Section 1: Venture Investment Is a Key Driver of U.S. Medical Innovation

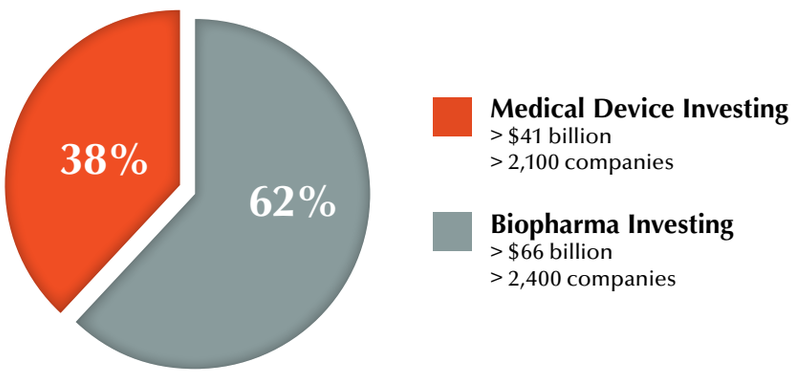




The U.S. Life Sciences Industry Was Built with Venture Capital

Venture capital plays a critical role in the life cycle of medical innovation in the United States. In fact, investment by venture firms and the corporate venture arms of established life sciences companies provides one of the few sources of funding for turning breakthrough research into life-saving and life-changing drugs, devices and diagnostics.

From 1980 to 2012, venture capitalists invested nearly $108 billion into an estimated 4,600 startup life sciences companies, constituting 19 percent of all venture investment in the U.S. for that time period. This historical investment has resulted directly in the creation and growth of our country's biopharmaceutical, medical device, and diagnostics industries, comprising thousands of companies dedicated to saving and improving the lives of patients worldwide.

Chart B: Venture Investment in Life Sciences: 1980-2012



Since 1980, venture capitalists have invested nearly $108 billion in 4,600 life sciences start ups.

Source: PwC/NVCA MoneyTree™ Report based on data from Thomson Reuters.

Venture-Backed Innovation Delivers Incalculable Benefits to Patients

Venture-backed medical breakthroughs cure diseases, provide new treatment options, produce better health outcomes for patients, and raise our overall quality of life in the U.S. Often, they also result in cost savings elsewhere in the healthcare system. Indeed, many of the most important medical breakthroughs of the past several decades have come from venture-backed companies. These include monoclonal antibodies, therapeutic proteins, novel vaccines, MRI, ultrasound and pulse oximetry. (See the graphic spread on Pages 16-17 for more innovations.) All have entirely changed how we think about disease and medical conditions – and how we attack them.

Select healthcare companies founded with venture capital:

- 23andMe
- Alexion
- Amgen
- BÂRRX
- Biogen IDEC
- Boston Scientific
- Cameron Health
- Genentech
- Gilead Sciences
- Human Genome Sciences
- Intuitive Surgical
- Lumina
- Millennium
- Onyx
- Vertex

Venture-Backed Innovation Creates Efficiencies and Cost Savings

Venture-backed medical innovations also help to decrease overall healthcare costs over time. For example, every one dollar invested in newer therapies saves nearly seven dollars in other costs, including hospitalizations, inability to work at full capacity, and inability to live independently.[3] Medical innovations also save nine times their estimated cost when the value of increased workforce participation is factored in.[4]

Specifically, disruptive technologies that deliver better care at lower costs are creating new efficiencies in treating some of our most prevalent diseases:

- Minimally invasive breast biopsies made possible by venture-backed technology can lower costs by 50 percent or more compared to open surgical biopsies.[5]
- Genetically targeted drug therapies and companion diagnostics enable physicians to choose and tailor treatments for specific patients and disease variations – increasing both the effectiveness and efficiency of treatments.
- Angioplasty and stents have changed the medical industry's approach to heart surgery, costing significantly less and requiring shorter hospital stays than open heart bypass surgery.
- Next-generation antibiotics shorten hospital stays through increased efficacy and by battling drug-resistant infections.
- MRI and ultrasound diagnostic imaging have eliminated exploratory surgery for countless conditions.
- Novel medicines, continuous glucose monitoring and insulin pumps are reducing long-term complications in insulin-dependent diabetics.
- Novel drugs are attacking a range of pediatric diseases earlier in patients' lives – leading to improved disease management, better quality of life and greater ability to control costs of care over the patient's lifetime.

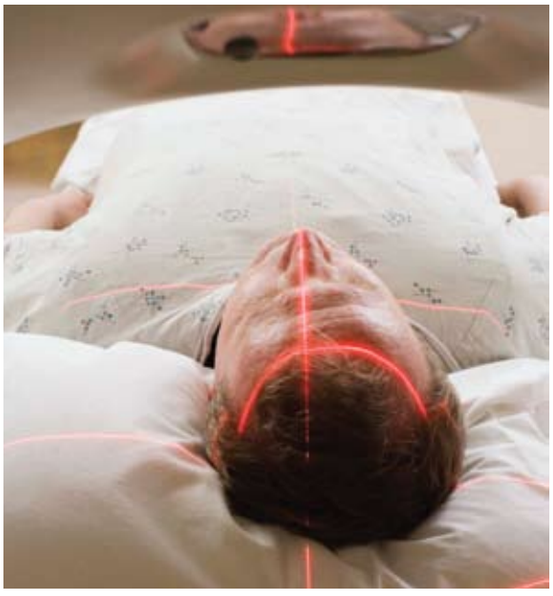
[3] Litchenberg, Frank. "Benefits and Costs of Newer Drugs: An Update." Managerial and Decision Economics, John Wiley & Sons, Ltd., vol. 28 (4-5), p. 485-490.

[4] Ibid

[5] Source: AdvaMed

Corporate venture investment in life sciences is growing

As the time and costs to bring medical innovations to market have grown, the corporate venture arms of established life sciences companies have begun to partner with private venture firms earlier and more frequently on new deals. In 2012, 29 percent of all corporate investment in the United States went to life sciences companies, and one of every six life sciences deals had corporate investment participation.[6]



Venture-Backed Life Sciences Companies Contribute to U.S. Economic Growth

Not only do venture-backed life sciences startups improve the lives of American patients, but they also spur U.S. economic growth through the jobs and revenues they generate. Since 1980, more than 700 venture-backed life sciences companies have gone public on a U.S. stock exchange,[7] where they have raised substantial capital for development and growth. In the process, they have created new, high-quality jobs for Americans both within their walls and at the new companies that spring up to provide products and services to them. Furthermore, history has shown that these public companies operate as training grounds for the next generation of innovators and entrepreneurs, who will often spin out and form their own startups focused on new breakthroughs.

Venture-Backed Life Sciences Companies Drive Economic Growth

Company	2012 Jobs	2012 Revenues
Amgen	18,000	$17.3 billion
Biogen IDEC	5,950	$5.5 billion
Gilead Sciences	5,000	$9.7 billion
Intuitive Surgical	2,362	$2.2 billion
Selectide	6,000	$5.5 billion
St. Jude Medical	15,000	$5.5 billion
Vertex	2,200	$1.5 billion

Source: IHS Global Insight, Venture Impact 7.0

Venture-Backed Companies Fuel the R&D Pipeline for Large Corporations

Venture-backed companies play a major role in the overall U.S. medical innovation ecosystem by making significant contributions to the R&D pipeline. Many of the technologies developed by venture-backed companies are often acquired by larger, more established companies that have the resources to develop the products further and deliver them to patients in need. Since 1980, more than 750 venture-backed life sciences startups have been purchased by established companies.[8]

Despite this robust legacy, venture investment in life sciences companies faces significant challenges that put the future of medical innovation in the U.S. at extreme risk.

[6] PwC/NVCA MoneyTree™ Report based on data from Thomson Reuters.
[7] Source: NVCA and Thomson Reuters
[8] Ibid

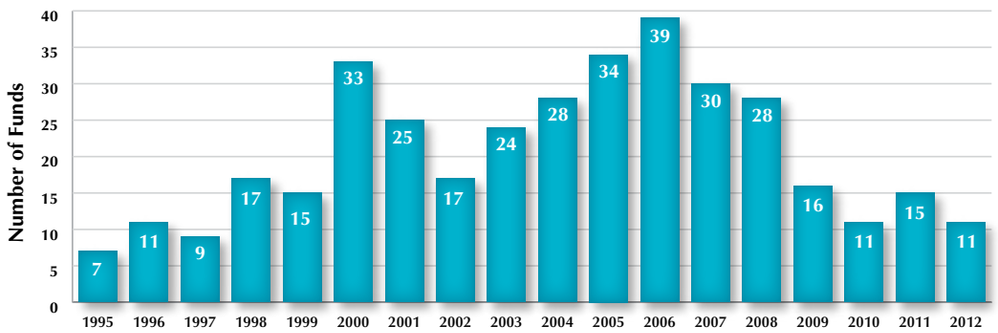
Section 2: Venture Investment in Medical Innovation Is at Risk



The U.S. medical innovation ecosystem has sustained itself for decades – thanks to the commitment of the entrepreneurs and investors who power it. Indeed, the business of saving and improving lives attracts dedicated people who are motivated to tolerate the uncertainty inherent in the development of new medical technologies, but even they have limits. Today's economic, regulatory, and coverage and payment environments are testing those limits.

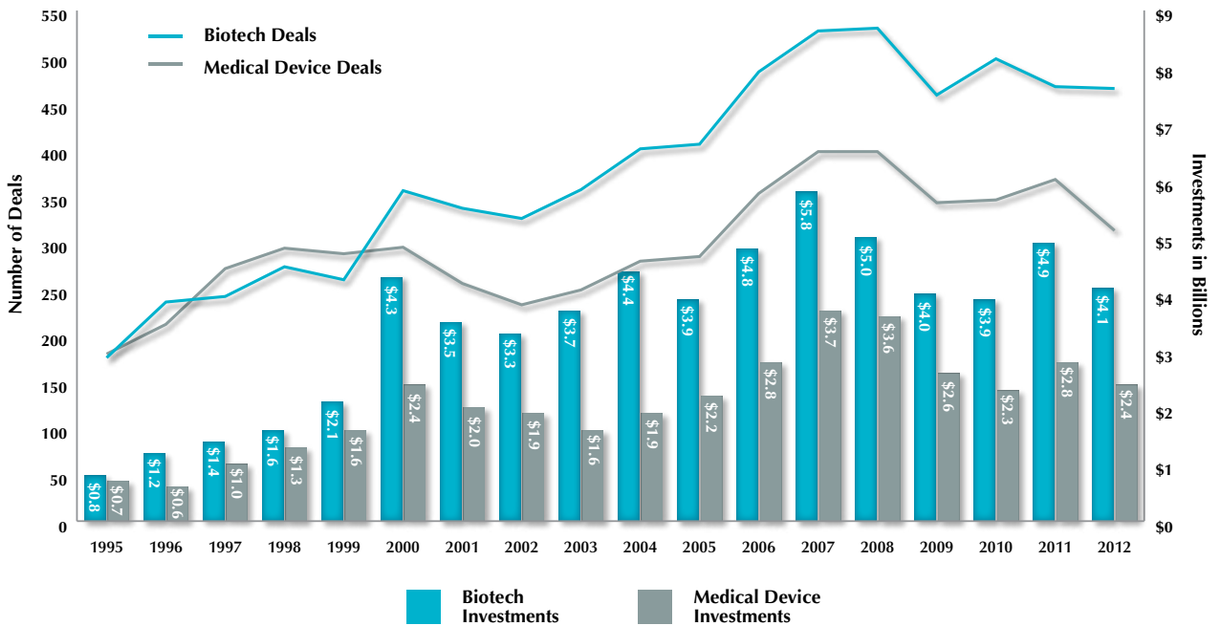
Over the last decade, the number of venture capital firms investing in life sciences companies has decreased, as shown in Chart C. As a result, venture investment in biopharmaceutical, medical device, and diagnostics companies has declined at an alarming rate (Chart D). Worse, this decline has been marked by a significant reduction in first-time fundings – a surrogate measure for startup activity – to the lowest levels in more than a decade (Chart E). As the flow of first-time investment slows, so, too, will the flow of innovation as breakthrough ideas for drugs, devices and diagnostic tools become stranded in the lab.

Chart C: The Number of Life Sciences Venture Funds Raised Is Declining



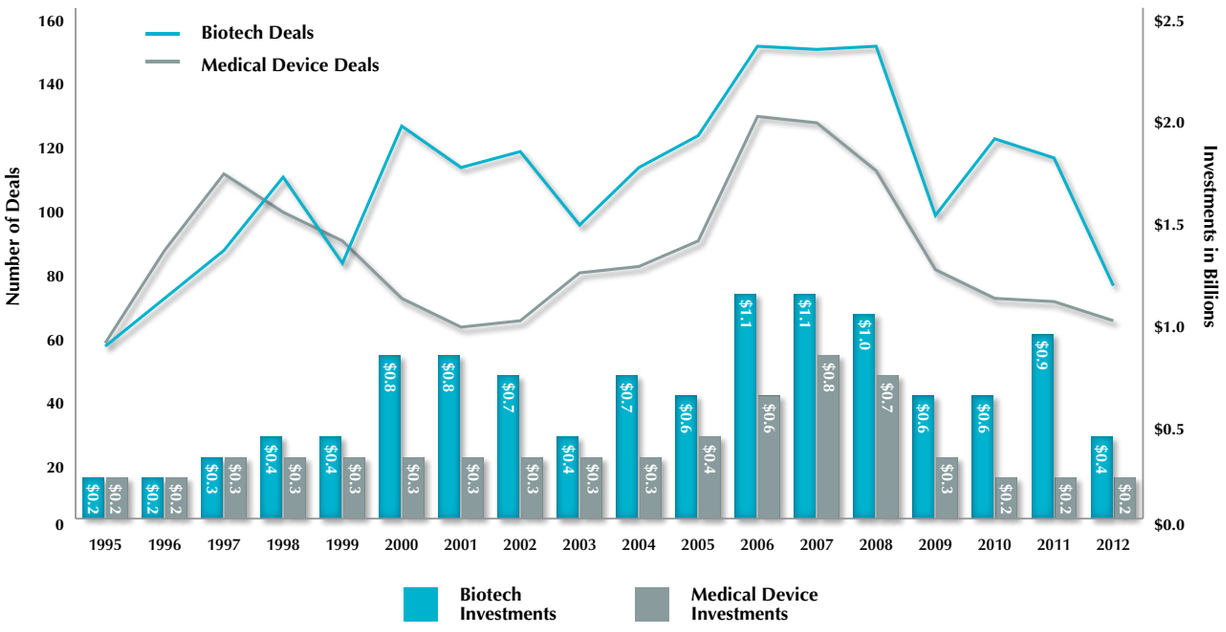
Source: NVCA and Thomson Reuters

Chart D: Total Venture Investment in Biopharma and Medical Devices Is Declining



Source: PwC/NVCA MoneyTree™ Report based on data from Thomson Reuters.

Chart E: First-Time Fundings for Biopharma and Medical Devices Are Declining



Source: PwC/NVCA MoneyTree™ Report based on data from Thomson Reuters.

Time, Cost and Uncertainty Discourage Investment

What has driven this decline in investment? The evidence is clear: The rapid escalation of cost and uncertainty associated with medical innovation, as indicated in Charts F and G, have significantly hurt venture capital returns over the last decade. This has prompted some limited partner investors to pull their capital out of life sciences venture capital in favor of other asset classes. As a result, many venture capitalists have been forced to invest in areas where there are more manageable risks and a better chance for a return in a more reasonable time frame – but without the potential to yield breakthrough treatments for serious diseases. Inevitably, less investment in medical innovation leads to fewer new diagnostics and therapies available to benefit patients, our healthcare system and our economy.

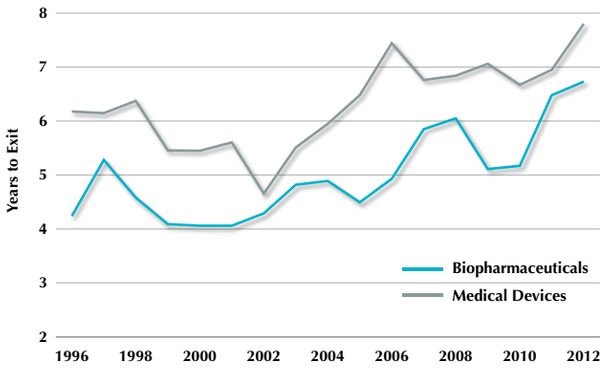
Investment challenges in the current environment abound, but two important drivers of time, cost and uncertainty are the regulatory and the coverage and payment processes in the United States. In 2011, a study conducted by NVCA and MedIC confirmed the impact of these trends on VC investment decisions. Named Vital Signs, the survey drew responses from more than 150 venture capitalists investing in life sciences in the U.S. Of these VCs, more than 60 percent identified the increasing cost and uncertainty in obtaining FDA approvals as having the highest impact on venture investment. Nearly 40 percent of respondents pointed to uncertainty and concerns over coverage and payment policies for new products, including the impact of decisions made by CMS, as indicated in Chart H. NVCA and MedIC have engaged the FDA, CMS and policy-makers on both sides of the aisle in very constructive dialogues about these issues, and great progress has been made in recent years.

According to the same study, U.S. venture capitalists are now decreasing their investments in biopharmaceutical, medical device, and diagnostics companies.

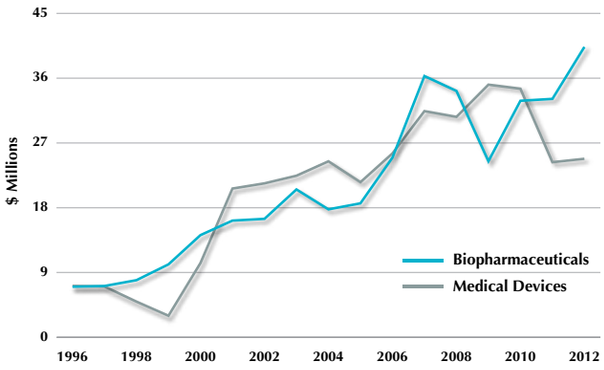
To read the entire Vital Signs survey report, visit http://medic.nvca.org/news-and-info.html

Charts F &G: Time and Cost of Funding Venture-Backed Life Sciences Companies Is Growing

Median time to acquisition of U.S. venture-backed healthcare companies by year of exit*



Median equity raised to acquisition by year of exit*

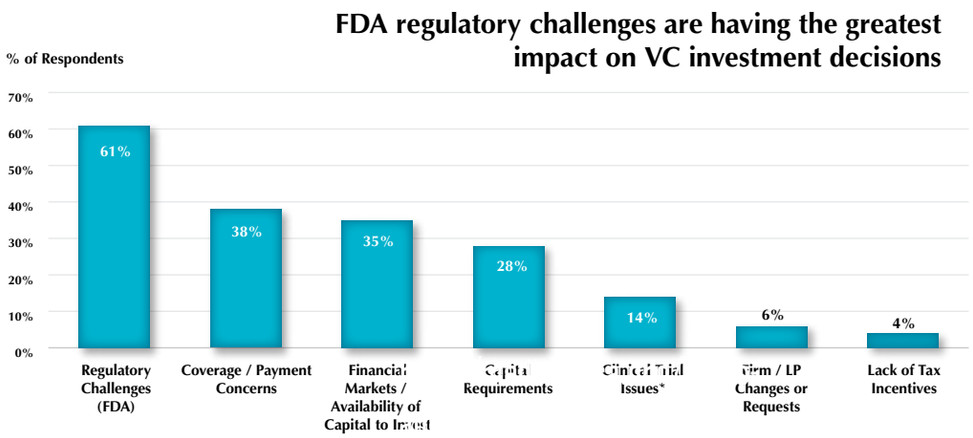


* Two year backwards rolling average

Source: Dow Jones VentureSource, January 2013

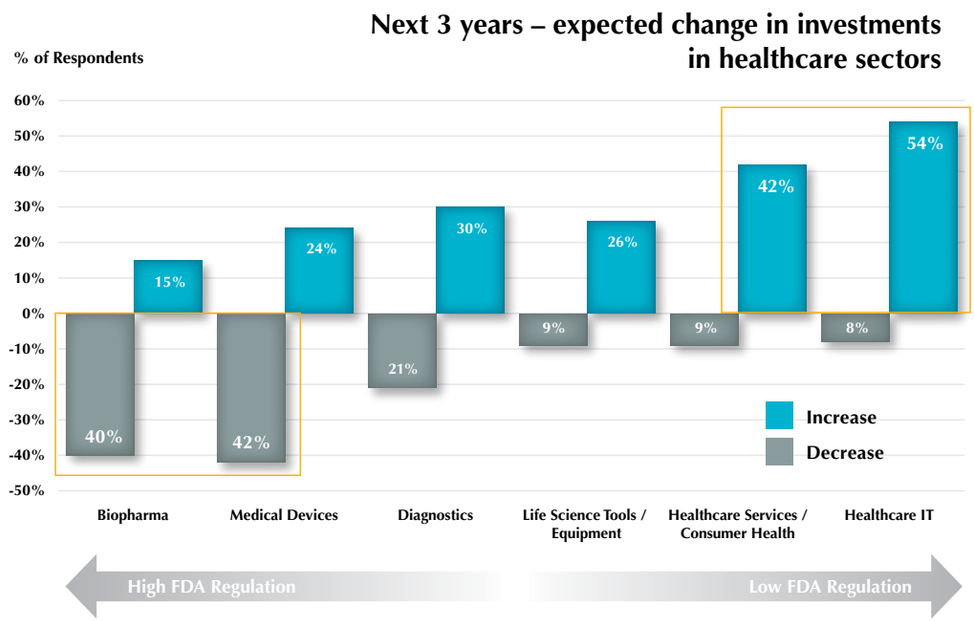
They are also reducing their concentration in prevalent disease areas and shifting investment towards other industries. Overall, 39 percent of respondent firms have decreased their investments in life sciences companies over the last three years. Worse, the same percentage expects to further decrease these investments over the next three years – some by more than 30 percent. These trends are demonstrated in Chart I.

Chart H: Factors Cited as Having the Highest Impact on VC Investment



*Unrelated to Regulatory Challenges
Source: NVCA MedIC Vital Signs Report, October 2011

Chart I: VC Investment in Biopharma & Medical Devices Is Expected to Continue to Decline

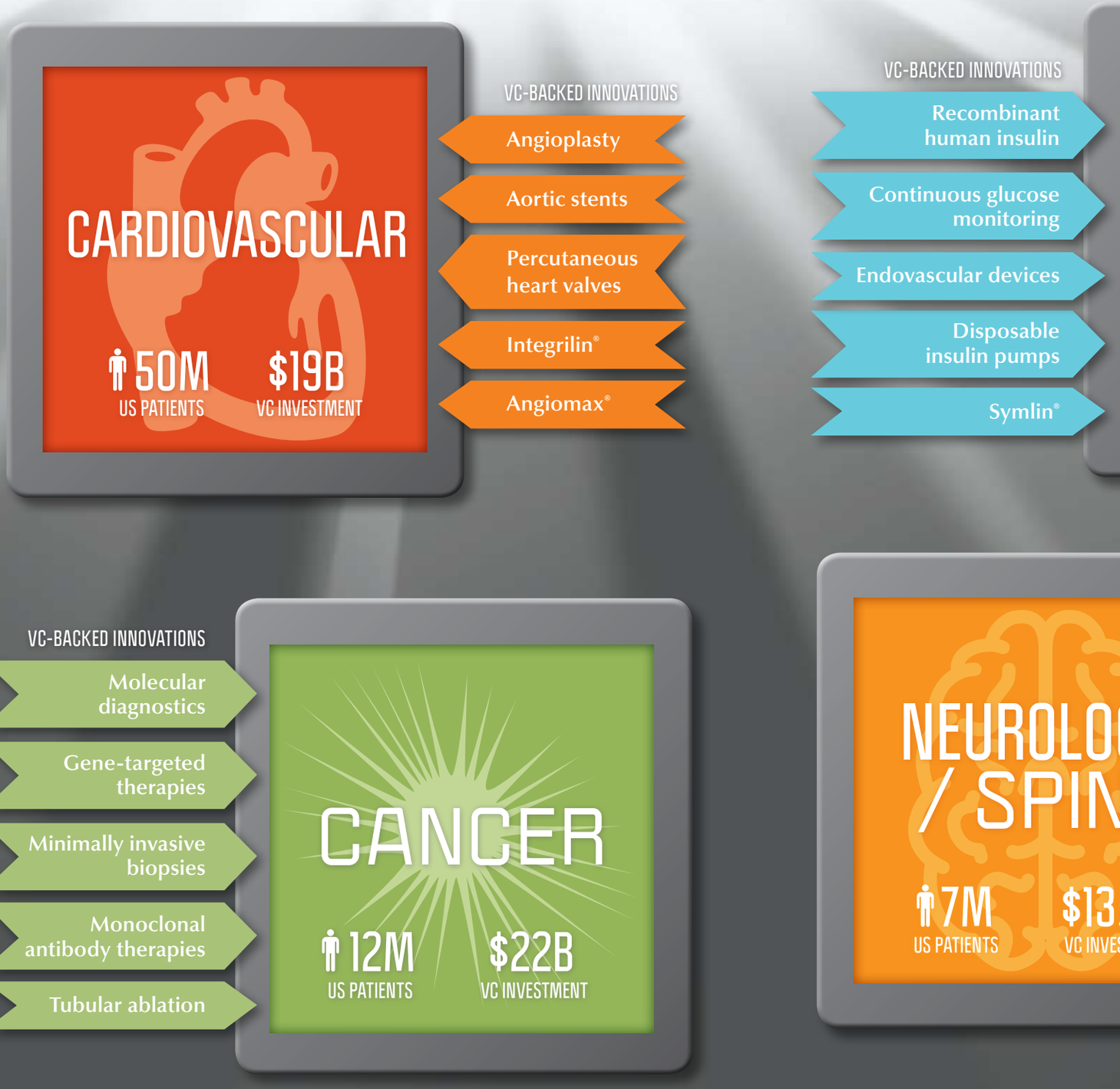


Source: NVCA MedIC Vital Signs Report, October 2011

Section 2 Continued on Page 18

Venture-Backed Innovations Fight Our Deadliest Diseases

For decades, venture capitalists have funded medical innovations aimed at diagnosing, treating and curing our most deadly and costly diseases. Since 1980, VCs have invested more than $108 billion in such drugs, devices and diagnostics. In turn, these have vastly improved patient outcomes, improved our quality of life and reduced long-term costs to our healthcare system.



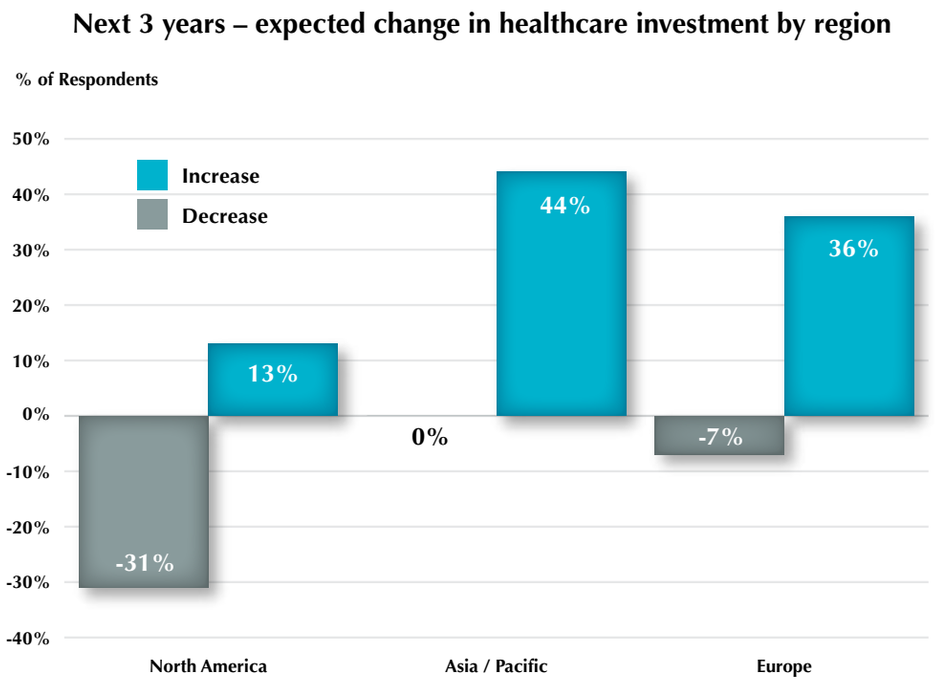
Investment data source: PwC/NVCA MoneyTree™ Report based on data from Thomson Reuters.
Patient data sources: NVCA MedIC Vital Signs Report, October 2011; American Diabetes Association
*Estimate

Global Competition and Innovation Migration Threaten U.S. Leadership

While conditions in the U.S. market have grown more challenging for innovative medical start-ups, other countries have begun to emulate the U.S. venture model. In addition to increasing their funding of basic R&D, many of our international competitors are clarifying their regulatory pathways and have begun to offer lucrative financial incentives to entrepreneurs and venture investors to build companies there instead of here.

This strategy appears to be working. According to the Vital Signs survey, 36 percent of VCs surveyed planned to increase investment in life sciences companies in Europe, while 44 percent planned to do the same in Asia. Only 13 percent planned to increase investment in life sciences companies in North America, as compared with 31 percent of firms that indicated plans to *decrease* such investments.

Chart J: VCs Expect to Shift Investment Away From North America



Source: NVCA MedIC Vital Signs Report, October 2011

In addition, a majority of the respondents indicated they would seek regulatory approval and commercialization of many products outside the U.S. first. This is a major shift, as the U.S. has long been the first market in which the majority of new medical innovations are introduced. This new trend will reduce the availability of life-saving and life-sustaining treatments for Americans, decrease the number of jobs generated by this important sector, and threaten America's global leadership in medical innovation.

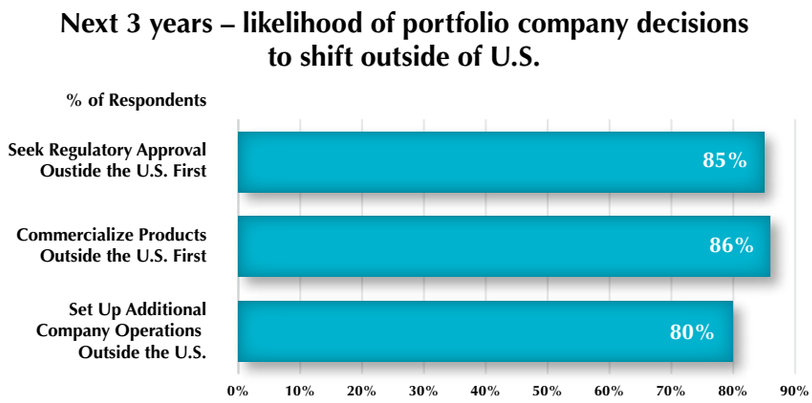
In another concerning trend, some U.S. entrepreneurs and venture capitalists are starting to base new medical technology companies outside the U.S., not only because of the lower cost of operation and lower regulatory hurdles to get a product to market, but also because tax policy in the U.S. has grown less favorable to medical innovation than in other countries. Historically we have seen more innovators from other countries move to the U.S. to build medical technology companies, as opposed to the other way around. While outflow hasn't yet overtaken inflow, we may see the flow of entrepreneurship reverse for the long run without significant improvements in the U.S. business environment.

The current state of venture capital investment in life sciences innovation is extremely troubling, but it is not irreversible. It is imperative that we address the issues and trends outlined above and continue the progress we have begun to make in improving our regulatory and our coverage and payment environments so that innovation can continue to prevail in the U.S.

Innovation incubation efforts abroad:

- Increased grants and funding for R&D
- Direct investments in innovative startups through national development banks and strategic business units
- Public/private investment funds focused on pre-seed, small- and medium-sized innovators
- Dedicated technology transfer and commercialization departments
- Tax credits and tax flow-through benefits

Chart K: VC-Backed Companies Expect to Seek Approvals, Commercialization Abroad Before in U.S.

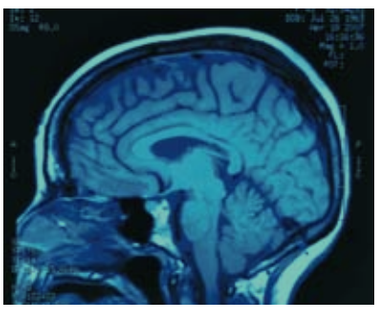


Source: NVCA MedIC Vital Signs Report, October 2011

Venture capitalists have opportunities to invest in some of the most groundbreaking medical innovations in history.

Section 3: Venture Investment Can Renew the Promise of American Medical Innovation



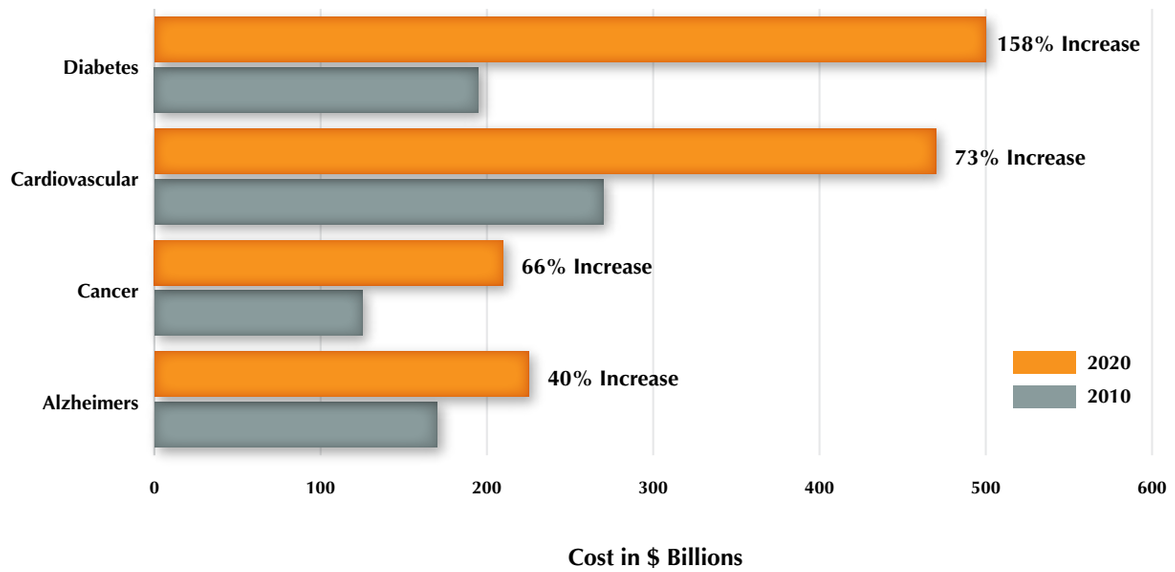


Despite the challenges it faces, America's medical innovation ecosystem continues to offer tremendous promise. Groundbreaking innovations are emerging from academic medical research centers, private companies and government labs at an unprecedented pace. The philosophical commitment and enthusiasm that has drawn entrepreneurs to the life sciences space persists, and venture investors remain passionate about investing in it. In short, medical innovation is still America's game to lose.

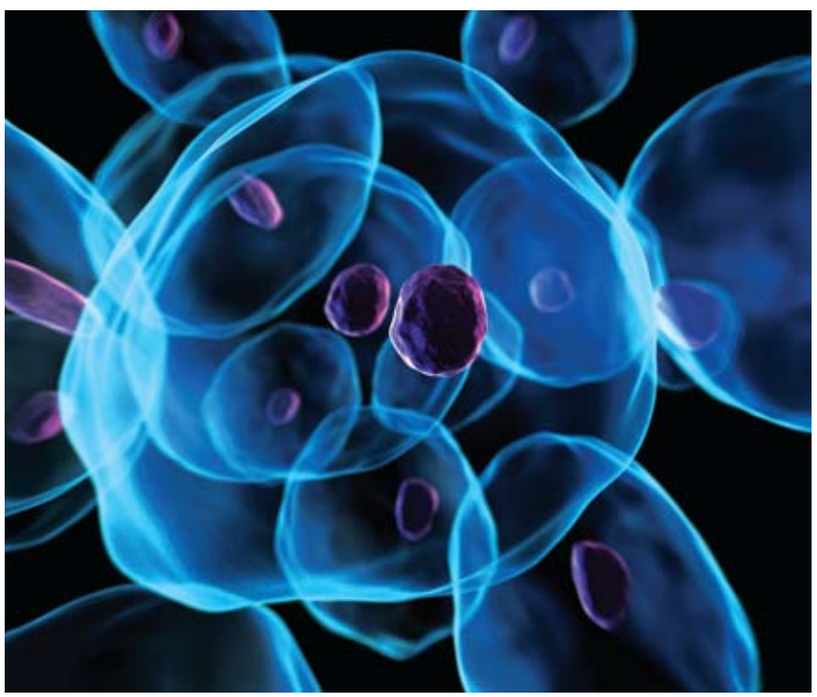
Needs and Costs Are Growing

America's need for ongoing medical innovation continues to escalate. We still lack cures for many major diseases, and the aggregate need for medical care on the part of the U.S. population is poised to increase significantly. Average life expectancy continues to rise – topping 78 years in 2010.[9] By 2030, nearly one out of every five Americans – approximately 72 million people – will be 65 years or older.[10] As the number of baby boomers entering the Medicare system grows, so will our need to control the rise of healthcare costs. Doing so won't be easy: Most experts expect the costs for treating some of our most common chronic diseases to increase significantly by 2020 (Chart L).

Chart L: Projected Costs of Treating Chronic Diseases in 2020



Source: BIO, compiled from projections by the National Cancer Institute, Alzheimer's Association, United HealthCare, American Heart Association.



Venture-Backed Medical Innovation Can Address These Most Pressing Issues

Venture capitalists today have opportunities to invest in some of the most groundbreaking medical innovations the world has ever seen. Breakthrough advances in areas such as human genetics, molecular biology and nanotechnology are revolutionizing how we look at health and attack disease. And the new startups emerging from these innovations offer tremendous promise for new treatments, cures and diagnostics.

[9] Source: World Bank

[10] Alliance for Aging Research

Venture-Backed Innovations in the Pipeline

Disease or Field	Innovations	Impact
Cancer	Molecular diagnostics; targeted therapies; immunotherapy	Improved survival and enhanced quality of life; early detection; reduced toxicity; shorter hospital stays
Heart disease/stroke	Novel anticoagulants; improved atrial fibrillation ablation; percutaneous heart valves; drugs and devices for congestive heart failure	Reduced risk of stroke, congestive heart failure, and arrhythmias; lower healthcare costs
Diabetes/obesity	Improved drug therapies for diabetes; improved glucose monitoring; improved insulin delivery; drugs and devices for obesity	Increased treatment efficacy, quality of life and work productivity for significant patient population
Infectious diseases	Anti-viral drugs; next-gen antibiotics to fight drug-resistant bacteria; novel vaccines	Enhanced cure rates; decreased infection; shorter hospital stays
Ophthalmology	Artificial retina technology; improved therapies for glaucoma and macular degeneration; improved drug delivery	Sight for blind patients; prevention and treatment of vision loss with aging

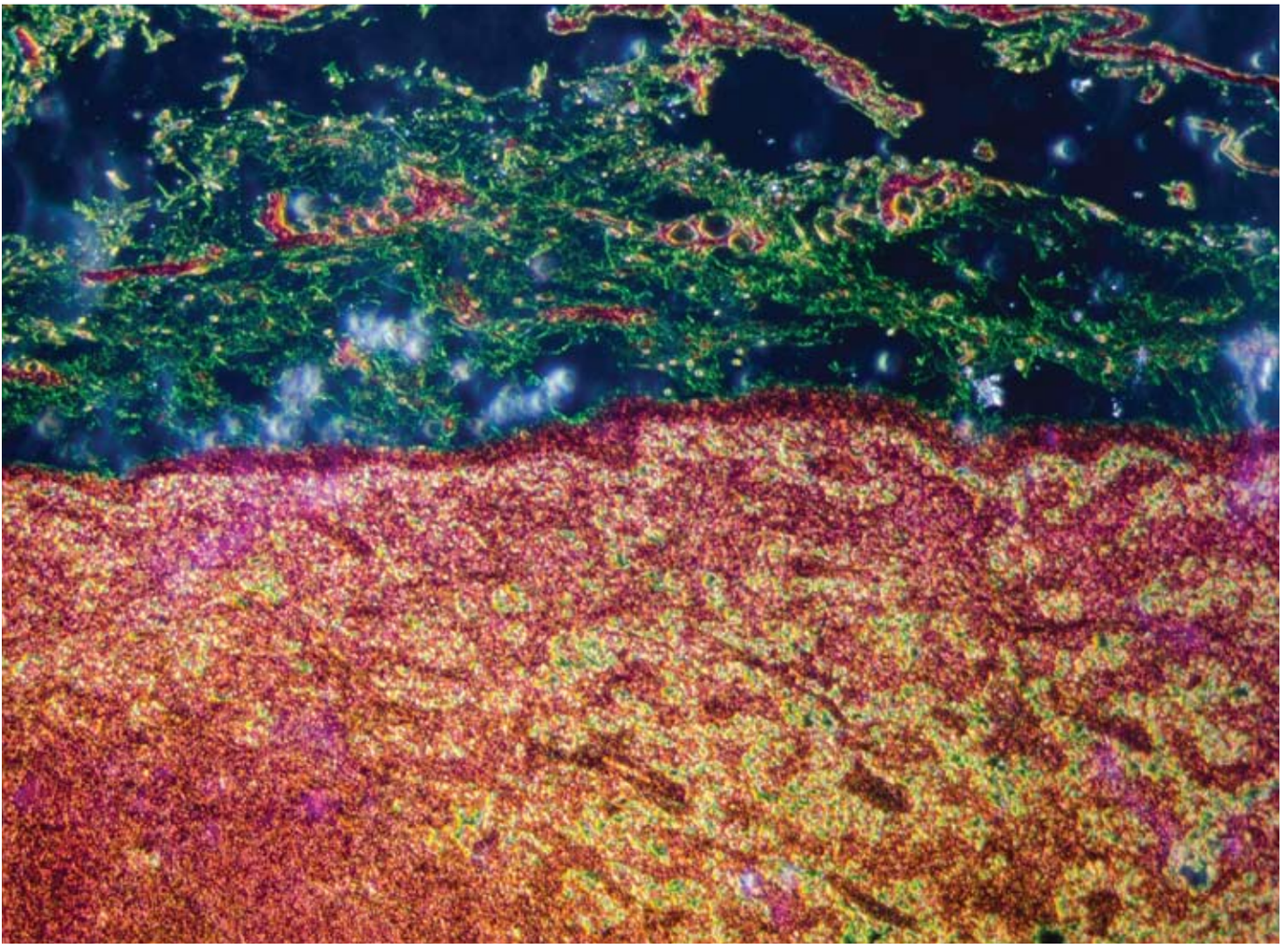
Venture-backed medical innovations also increase our ability to control and reduce the costs of treating our most common chronic and deadly diseases over the long term. In the fight against cancer, new diagnostic tools and technologies that profile the patient's tumor tissue at the molecular level can help doctors identify both the likelihood of chemotherapy effectiveness and the likelihood of future recurrence for particular sub-populations and disease types. For example, only four out of every 100 patients with early-stage, node-negative breast cancer benefit from chemotherapy.[11] In the past, physicians had no way of identifying which four. Today, they can, thanks to Oncotype DX, an innovative diagnostic test developed by California-based Genomic Health. Studies have estimated that the test results in an at least $1,160 savings per patient on direct costs alone (on the basis of a meta-analysis in the reduction of chemotherapy). Meanwhile, among patients whose test result indicated a high risk of recurrence, those who chose chemotherapy were estimated to receive a 20 percent to 30 percent reduction in the risk of breast cancer recurrence and associated mortality.[12] The company is now working on a similar diagnostic for prostate cancer. Many other technologies in the pipelines of venture-backed companies are poised to similarly transform treatment of other cancers and other diseases.

[11] Gelber, Richard D., Bernard F. Cole, Aron Goldhirsch, Carsten Rose, Bernard Fisher, C. Kent Osborne, Francesco Boccardo, Richard Gray, Nahida H. Gordon, Nils-Olof Bengtsson, Paul Sevelda. "Adjuvant chemotherapy plus tamoxifen compared with tamoxifen alone for postmenopausal breast cancer: meta-analysis of quality-adjusted survival." Lancet 1996 April 20; 347(9008):1066-71

[12] Hornberger, John, MD, MS; Rebecca Chien, BA; Katie Krebs, MHA; Louis Hochheiser, MD. "US Insurance Program's Experience with a Multi-Gene Assay for Early Stage Breast Cancer." Journal of Oncology Practice, Vol. 7, Issue 3S (2009).

Progress in the fight against obesity provides another example. Obesity affects nearly 35 percent of all Americans, and often accompanies or leads to other serious and costly health problems – including cardiovascular disease and diabetes.[13] Not surprisingly, it is estimated that obesity will cost the U.S. roughly $344 billion annually in medical-related expenses by 2018, accounting for approximately 21 percent of healthcare spending.[14] Fortunately, venture-backed companies are beginning to introduce next-generation therapies targeting the obesity epidemic. For example, two newly launched venture-backed drugs – Qsymia™ and Belviq® – could drastically reduce the costs associated with obesity while helping patients control their weight. In addition, a new and more patient-friendly form of gastric intervention technology, named EndoBarrier® and developed by Massachesetts-based GI Dynamics, can be implanted without surgery, enabling patients to go home as soon as 30 minutes after the procedure. Already approved for use in Europe and currently in clinical trials in the U.S., EndoBarrier drastically reduces surgical and hospital costs in the short run, while providing enormous potential savings in disease management for each patient in the long run.

Such advances underscore the enormous benefits that venture-backed medical innovation delivers to patients and to our economy. And we must continue to fuel that innovation by promoting public policies that encourage and reward it.

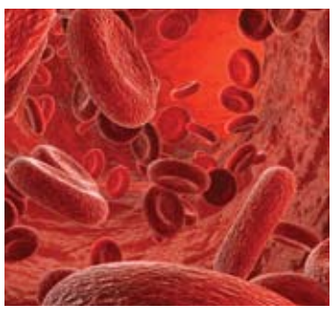
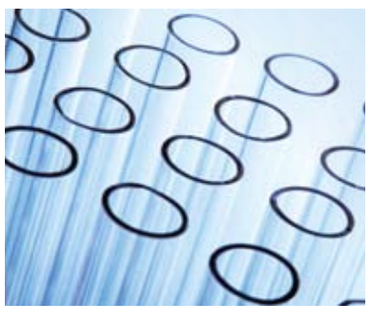


[13] America's Health Rankings, the 20th Annual Assessment of the Nation's Health. Special analysis on obesity by Kenneth Thorpe, Chairman of the Department of Health Policy Management at Emory University

[14] Ibid

"Without our venture investors, Seattle Genetics would not exist. They provided funding, as well as invaluable insights into how to build a business and move our technology into the clinic."

Seattle Genetics: Using Antibody-Drug Conjugates to Kill Cancer Cells While Sparing Healthy Cells

For decades, doctors have struggled with the same challenge when using drugs to fight cancer: How to kill cancer cells without destroying healthy, normal cells in the process. Oncologists knew that antibodies, one of the body's natural defense mechanisms, could lead them directly to cancerous cells, but most antibodies alone lack the potency to kill tumors and provide lasting remissions or cures. Thus, scientists began searching for a way to empower antibodies by attaching potent drugs that could be delivered directly and exclusively to certain cancer cells without harming healthy tissue.

In our market-based system, however, achieving a scientific breakthrough is only part of the challenge. Turning an innovation into a commercially viable drug and getting it to the marketplace requires an entirely different process. Once there, it must not only prove its efficacy, but outperform existing treatments.

During the mid-1990s, Dr. Clay Siegall, a researcher at Bristol Myers Squibb, and some of his colleagues began to make significant progress toward this goal. By 1998, Dr. Siegall and one of his colleagues believed they were close enough to a breakthrough to leave their jobs and risk their careers in order to found a new company, Seattle Genetics, through which they could continue their research. The new company's mission: develop new treatments, shepherd them through clinical trials to regulatory approval, and finally get these antitumor agents into the hands of clinicians.

Dr. Siegall had never built a company from scratch before, but he and his colleagues knew that it would take more capital and business expertise than they could bring to bear. So they turned to venture capital.

"Without our venture investors, Seattle Genetics would not exist," explains Dr. Siegall. "They provided funding, as well as invaluable insights into how to build a business and move our technology into the clinic."

Driven by a passion for improving patient outcomes, Seattle Genetics focused on forging a molecular link between synthetic cancer-killing drugs (called auristatins) and an antibody (resulting in an antibody-drug conjugate, or ADC) that could remain stable within the bloodstream long enough for the treatment to be effective. Early generation linkers lasted about a day – far shorter than the typical seven to 14 days that most antibodies reside in the bloodstream. But Dr. Siegall's team saw an opportunity to develop a stable linker, and was successful in doing so.

Working with its venture investors, Seattle Genetics continued pushing its ADC technology forward while growing its management team, readying its FDA engagement strategy and developing its product development capabilities. By 2001, the company had made enough progress across all of these fronts to go public – enabling it to raise more capital for clinical trials and continued innovative research.

After the IPO, product development continued apace, which allowed Seattle Genetics to dramatically expand the number of drugs in its pipeline and conduct clinical trials to test these products – critical aspects for a biotechnology startup. Many companies are unable to move products through the phases of development towards a commercial entity, for reasons ranging from lack of treatment efficacy to simply running out of money before the process is complete.

Seattle Genetics was confident in the science behind its lead ADC, which it named ADCETRIS®, but it still had to navigate the clinical trial phase and gain FDA approval before it could start benefitting patients. Fortunately, ADCETRIS performed exceptionally well in its clinical trials – enabling the FDA to grant the drug accelerated approval in August 2011 for the treatment of two types of lymphoma. In fact, ADCETRIS was the first ADC of its kind to earn FDA approval.

Today, the promise of Seattle Genetics' technology seems limitless. ADCETRIS has the potential to improve the lives of tens of thousands of patients, and that number will likely grow. The company has embarked on a broad clinical development program to evaluate its therapeutic potential for treating other types of lymphoma, other cancers with similar biological traits, and possibly a number of autoimmune disorders.

Meanwhile, Seattle Genetics continues to grow. It has expanded its workforce from an initial 14 employees to more than 550 today – not including the nearly 100 contractors it engages. A true next-generation leader and innovator in America's biotechnology field, the company is poised to improve patient outcomes for decades to come.

SeattleGenetics®

Insulet: Easing Burdens and Improving Care for Diabetes Patients

Ask a person on the street what deadly disease they dread most, and you probably won't hear "diabetes." That is, unless the person you ask is one of the 25.8 million[15] Americans affected by it. Diabetics know their disease can kill them if they don't manage it properly – every minute of every day.

It's a cruel burden – especially for kids, whose peers are often free to eat, run and play as they please. It can be hard to fit in when your friends cut holes in their clothes to look cool, while you cut yours to hide the tubes from your insulin pump. For one father, watching his adolescent son struggle with these issues convinced him of one thing: Diabetes technology had to get better.

As a founding venture capitalist at Prism Ventures, John Brooks was uniquely positioned to do something about it. Marshaling the experiences and contacts he acquired during his career in the life sciences field, John began recruiting the foremost diabetes experts and the best technologists he could find to the cause. In 2000, this group founded a new company, Insulet, with the simple mission of improving the traditional insulin pump.

Insulin pumps deliver numerous benefits over multiple daily injections (MDI) – including better glycemic control, fewer hypoglycemic events and reduced glycemic variability.[16] Despite these benefits, most people still choose MDI therapy largely due to the complexity, cost and inconvenience of conventional pump technology. For this reason, the Insulet team sought to develop a pump that was smaller, less intrusive and free of tubes, yet also more convenient and intuitive to use. They also wanted to give users the option to apply the pump at multiple sites on the body – as opposed to only a few locations, such as the abdomen, which scar from repeated trauma caused by traditional pumps.

Developing such a system would require overcoming a number of difficult technological challenges. First, they had to find a way to pack more functionality into a smaller package that could be unobtrusively used 24 hours a day. In addition, the actual pump mechanism would need to continuously deliver an accurate insulin dose – down to a fraction of a milliliter – every single time. Finally, the unit had to be cost effective.

The Insulet team tackled the size-functionality challenge by splitting the mechanism into two parts: 1) the actual pump mechanism (named the OmniPod®), which is worn on the body and attached directly to the skin, and 2) a PDA-like module (named the Personal Diabetes Manager, or PDM, which can be discreetly carried in a pocket or handbag) that enables touch-screen management and sends commands wirelessly to the pump. For added convenience, the PDM also features a built-in blood glucose monitor and an e-library of 3,000 foods and their carbohydrate counts. The development team also banished the formerly ubiquitous electric motor technology employed by traditional pumps by designing a novel pumping mechanism driven by a wire made of a unique shape-memory metal alloy that actually contracts – as opposed to expanding – when it heats. Adapted from stent technology, these characteristics enable this innovative pumping mechanism to deliver an accurate insulin dose – reliably and at low cost.

With a $1 million seed investment from Prism, Insulet was able file key patents and move its prototype pumping mechanisms along the developmental path. In turn, this progress enabled the company to raise the additional capital it needed to keep advancing the technology.

While Insulet's developers pushed the technology forward, the management team worked with its venture investors to build the company's marketing and manufacturing capabilities. The former required reaching out to influential diabetes experts and physicians, educating them on the new device's benefits over existing technology, and enlisting their support as both advocates and potential customers. "Early on, our VCs were instrumental in introducing us to leading physicians and helping us gain traction for our technology," recalls Duane DeSisto, Insulet's president and CEO. "Without their deep-rooted knowledge of the industry, it would have taken us forever to make the connections we needed to make to be successful."

By 2004, Insulet's developers believed the OmniPod was ready for clinical trials. The firm's VCs lent their expertise to help shepherd the company through clinical development, the FDA approval process and later through the process of securing reimbursement at CMS. They also helped Insulet optimize the efficiency of its manufacturing capabilities and build relationships with health insurance providers, whose willingness to cover their customers' use of the pumps would be critical to its success.

Insulet gained FDA approval to market the OmniPod in 2005. After a modest launch consisting of five users, the company has grown that number to more than 40,000. In the process, it has grown its revenues from $4 million in 2006 to $210 million in 2012[17] and its workforce to 660 worldwide. In between, Insulet became a publicly-traded company in 2007.

Today, Insulet continues to refine and improve its technology – although the company notes that the costs and timelines for doing so have increased significantly. Despite these challenges, the company won approval in December 2012 for its next-generation OmniPod, which is more than one-third smaller and one-quarter lighter than the original model. The new device epitomizes Insulet's commitment to providing superior treatment options and life-long health benefits for people with diabetes by breaking down the barriers to insulin pump therapy.

Insulet Corporation

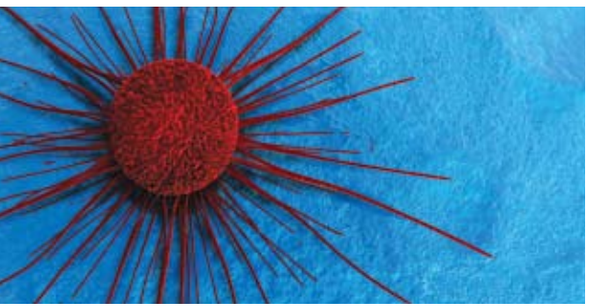
[15] American Diabetes Association

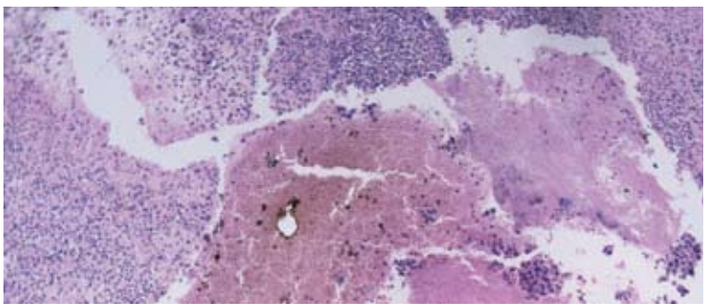
[16] Diabetes Control and Complications Trial Research Group. "The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus." New England Journal of Medicine.1993:329:977-986.

[17] Estimate as of November 8, 2012.

"The biggest breakthrough in melanoma treatment, ever."

Plexxikon: Fighting Cancer, Molecule by Molecule, with a Blend of Innovative Science and Business Savvy





Spend some time with prolific drug-inventor Dr. K. Peter Hirth, and you may hear him say, "New drugs don't grow on trees."

It sounds obvious, but Dr. Hirth's irony underscores just how lengthy, complex and often inefficient our process for drug discovery and development can be. Fortunately, these difficulties did not deter Dr. Hirth and his company, Plexxikon, from revolutionizing the very process by which new drugs are discovered and developed.

The Plexxikon team attacked the challenge with a key insight in drug discovery: While new drugs don't grow on trees, they can grow across families – protein families. Dr. Hirth believed that if researchers could mine previously unexplored areas of biochemistry using technology in different ways, they could create novel, yet relatively simple, safe and highly targeted molecules that could inhibit the aberrant protein production of diseased cells. Once a scaffold molecule was discovered to bind to the common site within a family of proteins, this scaffold could be optimized iteratively to selectively inhibit different targets within that family and create multiple drugs for different disease indications.

Similarly, Plexxikon saw a significant advantage for clinical development and regulatory approval in developing selective and targeted drugs – even for the treatment of cancer. By testing a targeted agent in the most appropriate patients (selected via a companion diagnostic test), the potential

effectiveness of such an agent could be seen even in a Phase 1 trial. Hence, the possibility of also accelerating the development of new drugs could become a reality. But would it?

"Very few people were interested in funding drug discovery companies in 2001," recalls Michael Carusi, of the venture firm Advanced Technology Ventures (ATV). "Even today, most investors want to see a return in three years," he explains, "but it was taking 12 to 15 years to develop just a single drug." Yet, Carusi and a handful of other VCs grasped the transformative potential of Plexxikon's approach. By mid-2006, ATV and other venture firms had put $67 million to work in Plexxikon.

Importantly, since the company was able to demonstrate early on its investigational new drug (IND) engine capability, Plexxikon was able to fund further pipeline investment through creative and non-dilutive deals with partners in the pharmaceutical industry, and has generated another $276 million to date, excluding royalties. These partnerships were crafted by Kathy Glaub, president of Plexxikon since 2001, to provide stable funding, profit from each partnered project with each upfront payment, and funding to generate subsequent IND candidates. Additionally, Plexxikon retained over 50 percent of the value of each partnered asset as well as strategic commercial rights, including the right to sell Plexxikon's first oncology product. Not only did this prevent further dilution of Plexxikon's investors, but it also positioned the company well for either an IPO or acquisition.

A key driver for the company's success was Plexxikon's breakthrough treatment for melanoma, PLX4032 (also known as vemurafenib, or Zelboraf®), which targeted tumor cells exhibiting a specific genetic mutation (known as mutant BRAF). By 2006, the company had rapidly developed this small molecule drug that selectively inhibited the mutant BRAF enzyme within the cancer cells that drove their runaway growth. Since the mutant gene was exclusive to the tumor and PLX4032 was highly selective for this mutation, the drug rapidly shrank tumors in otherwise terminally ill patients with breathtaking effectiveness and few side effects. One prominent oncologist called it "the biggest breakthrough in melanoma treatment, ever."[18]

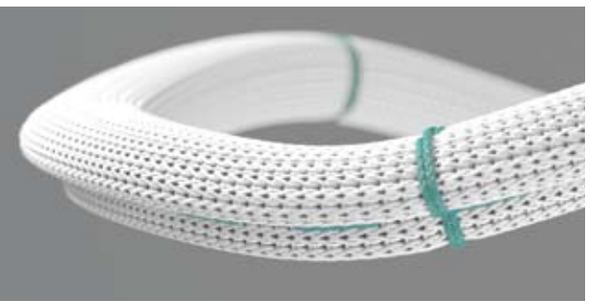
Ironically, Zelboraf was so novel, and so much more effective than prior treatments, that its pathway to regulatory approval became more complicated and less certain midway through its clinical trials. There was very little to compare it to for patients in the latest stages of the disease; up to this point, they were simply beyond treatment. Furthermore, its overwhelming efficacy, seen even in the initial Phase 1 trial, raised concerns about the appropriateness of denying patients in the control group access to the drug in development, particularly those who would likely only live a few more months without treatment. As the efficacy seen in Phase 1 was further confirmed by early results seen in the Phase 2 and 3 trials (which were conducted in parallel) and as public pressure grew, the FDA, together with Plexxikon and its partner Roche, worked collaboratively to modify the design of the Phase 3 trial in order to expedite the evaluation and decision about the drug's approval.

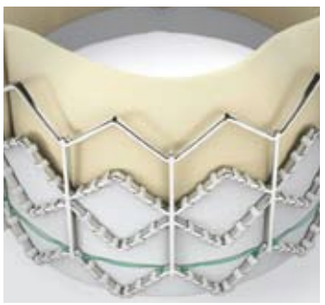
Zelboraf achieved marketing approval in the U.S. in 2011, in the remarkably short time of six years from initial discovery. Today, it is on the front lines in the fight against melanoma in over 40 countries. "A late-stage diagnosis of melanoma used to be a death sentence," says Dr. Hirth. "Now we can give patients months of additional, high-quality time with their families."

Plexxikon

[18] Szabo, Liz. 2010 'Breakthrough' melanoma drug shrinks tumors. http://usatoday30.usatoday.com/news/health/2010-08-26-1Amelanoma26_ST_N.htm [March 27, 2013]

Edwards Lifesciences:
Collaboration on the Cutting Edge of Heart Disease





Artificial heart valves have helped save countless lives since their invention more than 50 years ago. But during most of that time, and despite nearly constant improvements in technology, their promise came with one critical caveat: A patient had to be healthy enough to undergo the open heart surgery required to implant them.

Patients suffering from severe aortic stenosis (AS), a form of heart disease that slowly chokes the flow of blood through the aortic valves, often face this dilemma. More than half a million Americans have severe AS.[19] Once symptoms develop, patients typically die within two to five years[20] unless they receive a valve replacement. Until recently, however, there was no alternative for those too sick for surgery.

The fortunes of such patients changed dramatically in April 2002, thanks to an innovative venture-backed startup company named Percutaneous Valve Technologies, or PVT. Led by a small team of physicians and entrepreneurs in Israel, France and the U.S., PVT had been working relentlessly on a revolutionary valve that could be delivered to a patient's beating heart via a catheter and then expanded in place with a balloon – thus obviating the need for open heart surgery and removal of the native valve. During this time, venture capital played a critical role in funding both the technology development and the company's operations. "Our venture partners believed in us when no one else did," explains Stan Rowe, PVT's CEO at the time. "It took vision and courage to invest."

After years of development and successful animal trials, they found themselves with an opportunity to test their transcatheter aortic valve on a human patient. The risks for everyone were enormous – not least for the patient, who was exceptionally ill. The team at PVT believed their technology could save his life – but what if it didn't? Or what if the procedure worked, but the patient died anyway? What would happen to their nascent technology – and the countless other patients to whom it could offer new hope? "If we failed," says Rowe, "who would do the next one?" Despite the risks, PVT decided to perform the procedure. "I didn't really sleep that night," Rowe recalls.

Early complications seemed to confirm the PVT team's worst fears. The patient experienced cardiac arrest just prior to the valve's implantation. However, PVT's Prof. Alain Cribier was able to implant the valve while chest compressions were being performed on the patient. The replacement of the valve via balloon inflation restored the patient's heartbeat, and he pulled through. By that evening, the patient felt well enough to share a glass of champagne with the doctor. His life was saved.

Not surprisingly, PVT's successful transcatheter aortic valve replacement (TAVR) procedure attracted intense attention from the world's leading medical device manufacturers. One of these companies, Edwards Lifesciences, was already the leader in surgical heart valve replacements, and had been developing its own transcatheter valve technology on a track parallel to PVT's efforts. While the Edwards team estimated that PVT's technology was about a year ahead of its own, they were also convinced that by combining technologies and talents, the two companies could develop valves that could become the standard of care for inoperable AS patients. To make it happen, now it was Edwards's turn to take some big risks.

First, Edwards had to convince PVT that Edwards offered a better opportunity than larger potential suitors such as Johnson & Johnson, Boston Scientific and Medtronic – all of which already had seats on PVT's board. Here, PVT's venture investors helped the company evaluate its options within the context of what path would be best for their live-saving technology, while also rewarding the dedication and hard work of everyone who had brought it this far. After extensive analysis, PVT chose Edwards. "Our venture board members really helped us through the process," says Rowe, who is now Chief Scientific Officer at Edwards. "I could not have asked for better partners in this exciting journey to save the lives of these needy patients."

Next, Edwards would have to take PVT's promising but still immature technology and improve it to the point where it would be safe and effective enough for widespread clinical and commercial use. Then, Edwards needed to prove it had done so to the FDA through a grueling clinical trial process – even though the technology continued to evolve. Finally, Edwards would have to bridge the burgeoning rivalry between heart surgeons and interventional cardiologists in order to gain adoption of TAVR.

Edwards tackled these last two challenges by designing a groundbreaking clinical trial, aptly named The PARTNER Trial. The world's first randomized, controlled pivotal trial of a transcatheter aortic heart valve in the history of valve surgery, PARTNER brought together both heart surgeons and interventional cardiologists – encouraging them to work together so that patients could benefit from both sets of skills and expertise. The study determined that the procedure not only substantially decreased mortality and improved quality of life for patients in the inoperable cohort of the trial, but also proved cost effective for the benefit it provides. The official analysis of the results concluded that "[b]alloon-expandable TAVI should become the new standard of care" for AS patients who cannot have open heart surgery. On the strength of these results, the FDA approved the valve, which the company named the Edwards SAPIEN Transcatheter Aortic Heart Valve, for use in inoperable patients in November 2011, and for high-risk patients in October 2012.

Since the European approval of the SAPIEN Transcatheter Aortic Heart Valve in 2007, more than 45,000 patients around the world have benefitted from this groundbreaking technology. During this time, Edwards has continued to invest and innovate in the development of next-generation valves. In the process, the company has provided high-quality jobs and strong revenues to the U.S. economy, and hope to patients for whom there was none before.

Edwards

[19] Nkomo 2006, Iivanainen 1996, Aronow 1991, Bach 2007

[20] Ross and Braunwald. 1968. "Post Mortem Study." Circulation, 1068.

The Role of Policy in Medical Innovation

Public policy plays a pervasive role in the medical innovation ecosystem. Often, government-funded research lays the critical groundwork for scientific breakthroughs. As venture-backed companies form around these breakthroughs, they rely on the U.S. patent system to protect their intellectual property. The FDA oversees the processes by which breakthrough drugs, devices and diagnostics are tested for safety and efficacy and the requirements for marketing approval. In addition, public agencies such as CMS, and private entities like insurance companies, determine which drugs, devices and diagnostics they will cover and at what cost level. Other areas as seemingly unrelated as tax policy, securities regulation and immigration laws affect an investor's decision to commit to funding a medical breakthrough.

For these reasons, public policy can impact the medical innovation ecosystem in enormous ways. That's why NVCA and MedIC have issued a national call to action to preserve the U.S. medical innovation ecosystem. We must develop a national agenda that will harness the extraordinary promise of modern science and technology to deliver breakthrough medical products – products that can provide better treatments for patients, save lives, improve quality of life, and lower healthcare costs. As part of this effort, policy-makers and stakeholders together must address the following priorities:

1. Create a national advocacy strategy focused on preserving U.S. leadership in medical innovation.
2. Support continued government funding for basic R&D, which drives the discovery of breakthrough innovations with the potential to cure disease and treat unmet patient needs.
3. Ensure that the FDA has the resources and the mandate it needs to fulfill its dual missions of protecting patient safety and encouraging medical innovation.
4. Develop coverage and payment policies that reward investment in medical innovations that provide value both to patients and the healthcare system.
5. Foster and protect long-term investment in breakthrough products by providing meaningful intellectual property and exclusivity protections, e.g. maintaining 12 years of data protection for innovative biologic medicines.
6. Assure that other areas of policy – such as securities regulation, tax policy and immigration policy – all work to encourage both the private and public capital markets to continue to support U.S.-based companies pursuing medical breakthroughs.

Success in these initiatives will help to cement America's leadership in medical innovation and generate economic growth and high-quality jobs across the U.S. for decades to come.

NATIONAL VENTURE CAPITAL ASSOCIATION
Funding innovation. Empowering entrepreneurs.

Venture capitalists are committed to funding America's most innovative entrepreneurs, working closely with them to transform breakthrough ideas into emerging growth companies that drive U.S. job creation and economic growth. As the voice of the U.S. venture capital community, the **National Venture Capital Association (NVCA)** empowers its members and the entrepreneurs they fund by advocating for policies that encourage innovation and reward long-term investment. As the venture community's preeminent trade association, NVCA serves as the definitive resource for venture capital data and unites nearly 400 members through a full range of professional services. For more information about the NVCA, please visit www.nvca.org.

MedIC
Medical Innovation & Competitiveness Coalition

The MedIC Coalition educates policy-makers on the critical role America's medical innovation plays in the U.S. healthcare system and high quality job creation; where and how disruptive innovations are developed; and the challenges currently facing the medical innovation system. MedIC actively works with policy-makers, educates stakeholders, and supports legislation to address the threats facing America's medical innovation system. Founded in 2010 as a partnership between the National Venture Capital Association (NVCA), member venture capital firms and their early-stage portfolio companies, the coalition aims to preserve U.S. leadership in medical innovation and ensure that America remains the primary incubator for global innovation. MedIC is based in Washington, DC.