STRENGTHENING BIOPHARMACEUTICAL INNOVATION:

THE GROWING ROLE OF CORPORATE VENTURE CAPITAL

OCTOBER 2018

Prepared for:

PhRMA
RESEARCH • PROGRESS • HOPE

Prepared by:

TECONOMY PARTNERS LLC

TABLE OF CONTENTS

EXECUTIVE SUMMARY

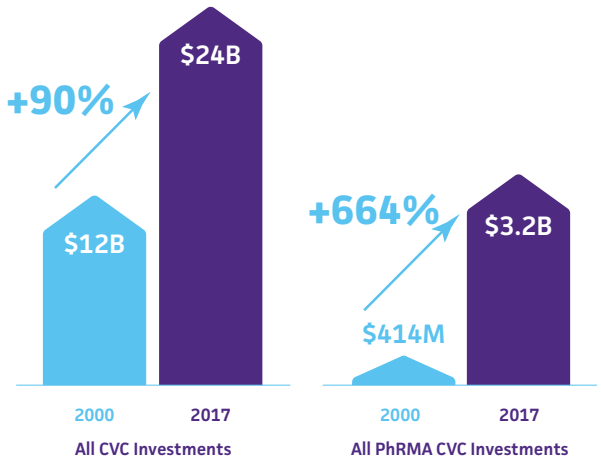
Innovative biopharmaceutical companies sit at the heart of a dynamic research & development (R&D) ecosystem advancing medical innovation in the United States. Significant advances in medical innovation have been brought forward in recent years, including the use of immunotherapy to treat cancers, ground-breaking gene and cell-based therapies and advancements in gene editing.

These are just some of the exciting developments that offer the promise of addressing unmet medical needs for today's patients. While innovative biopharmaceutical companies conduct the majority of research that translates basic science into new medicines, successful drug development also benefits from the contributions of a variety of public and private stakeholders found throughout the ecosystem.

One important facet of the U.S. biopharmaceutical innovation ecosystem is its robust venture capital industry of private investors practiced in the art of making equity investments in new and emerging biopharmaceutical companies. In recent years, venture capital investment in biotech startups has been reaching new heights. This includes significant contributions that existing biopharmaceutical companies are making through their Corporate Venture Capital (CVC) affiliates to support biotech startups. CVC activity is a subset of venture capital investment and occurs when corporations invest in an affiliated unit to make equity investments in promising start-up companies, usually related to the company's own industry.

This report was commissioned by the Pharmaceutical Research and Manufacturers of America (PhRMA) and examines the key ways in which PhRMA-member CVCs are contributing to the growth of biotech startups, through both financial and non-financial support. Through a detailed analysis of the extensive PitchBook database on venture capital investments, supplemented by interviews with representatives of CVCs and a review of existing studies, this report offers a unique view into how the

ES-1. Growth in PhRMA CVC Investments Outpace Overall CVC Investments from 2000 to 2017



CVC activity of innovation-based biopharmaceutical companies is unfolding and contributing to the medical innovation ecosystem.

This report brings to light important aspect of PhRMA-member CVCs, including the following:

- **PhRMA-member CVCs are growing faster than CVCs across all industries.** Venture investments in deals involving CVCs of 15 PhRMA-member companies grew faster than for all CVCs, rising from $414 million in 2000 to $3.2 billion in 2017, a gain of over 660%. By comparison, the value of deals that all CVCs have invested in rose 90% from $12.8 billion in 2000 to $24.3 billion in 2017 (Figure ES-1).

- **A significant share of the overall activity in biopharmaceutical investment is supported by PhRMA-member CVCs.** Investment deals involving PhRMA-member CVCs active in 2017 accounted for 20% of all biopharma VC investments that year and were responsible for over 30% of the increase in biopharmaceutical VC investment from 2016-2017.

- **PhRMA-member CVCs are doubling down on innovation in strategic areas of focus to their parent companies**, with a focus on many of the most complex diseases, many with no known cures, including many cancers, neurodegenerative diseases, autoimmune diseases, infectious diseases, and metabolic disorders and diabetes.

- **Active in early stage investments, PhRMA-member CVCs are helping to reverse a troubling trend away from such investments in biotech startups in recent years.** In the last two years, 74 percent of the investments in deals involving PhRMA-member CVCs were in early stage investments compared to 59 percent for deals involving only traditional venture capital firms.

- **PhRMA-member CVCs are encouraging strong partnerships with other investors.** PhRMA-member CVCs in more than 9 out of 10 investment deals co-invest with other venture capital investors, in what is known as “syndicated” deals. Since 2000, the deals involving PhRMA-member CVCs have included over 1,200 other venture investors.

- **Healthcare-related startups beyond biopharmaceutical development, are being supported by PhRMA-member CVCs.** Since 2013, investments in health technology and digital health have been growing rapidly, and PhRMA-member CVCs are part of that driving force to identify and advance patient-centered, value-based healthcare solutions derived from new technologies.

- **PhRMA-member CVCs are having measurable impacts by advancing innovation through support of biotech startups.** PhRMA-member CVCs provide expertise and advice to help biotech startups navigate drug development and regulatory issues that go beyond what a traditional venture capitalist can offer, resulting in a higher share of initial public offerings (IPOs) generated by biotech startups backed by PhRMA-member CVCs

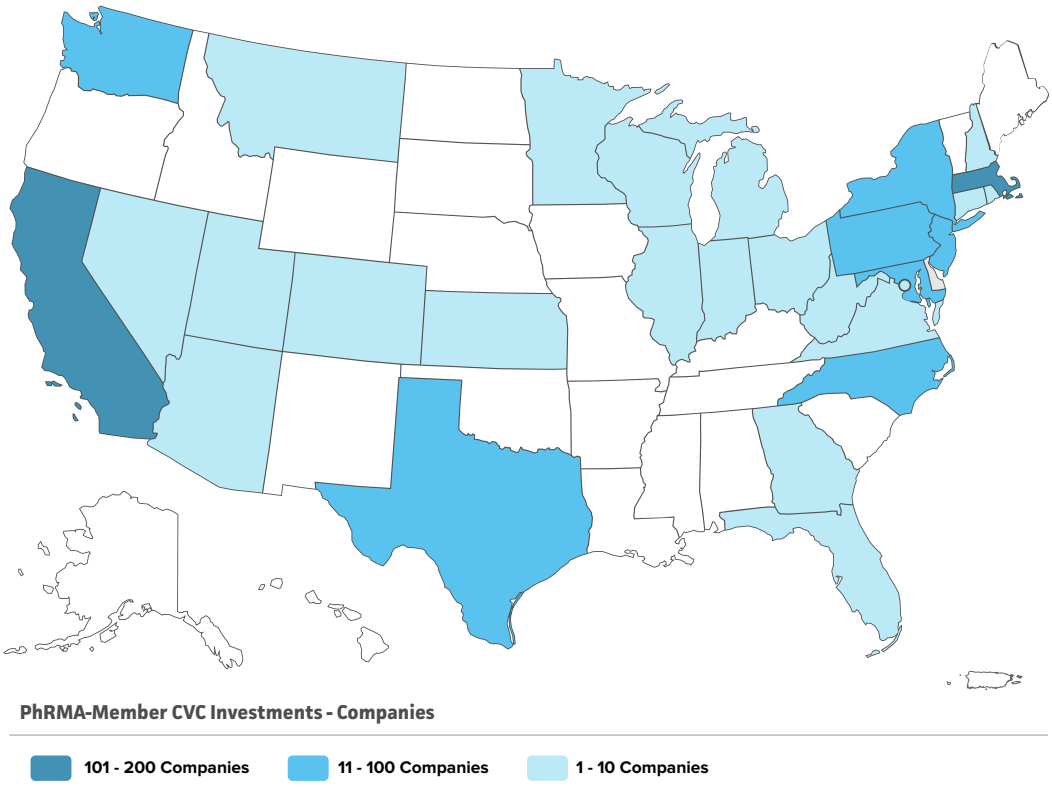
There is also a wide geographic distribution across the nation to the PhRMA-member CVC investments. In total, these CVC investments in 507 companies occurred in 29 states across the U.S. (Figure ES-2).

Looking forward, like other investors in startup biotech companies, biopharmaceutical CVCs face a high level of risk and uncertainty associated with lengthy and costly research and development timelines and increasing regulatory requirements that increase the costs and complexity of clinical trials. Moreover, biopharmaceutical research and development involves promising yet complex science with great uncertainty of success.

Public policies can play a role in shaping those risks. Close attention must be placed on ensuring a regulatory and policy environment that encourages rather than discourages investment in advancing medical innovations to address today's most challenging diseases and meeting the needs of patients.

PhRMA-member CVCs invested in **14% of all biopharmaceutical startups,** those startups represent **40% of all biopharmaceutical startups** that went public over the 2000 to 2017 period.

Figure ES-2. Distribution of PhRMA-member CVC U.S. Investments, 2000-2017: Companies



Source: TEConomy Partners analysis of PitchBook Venture Investment database.

INTRODUCTION: CORPORATE VENTURE CAPITAL COMES OF AGE

Innovative biopharmaceutical companies sit at the heart of a dynamic research & development (R&D) ecosystem advancing medical innovation in the United States. While biopharmaceutical companies conduct the majority of research that translates basic science into new medicines, successful drug development also benefits from the contributions of a variety of public and private stakeholders found throughout the ecosystem.

This report examines the critical role of one specific player in the drug development ecosystem: corporate venture capital (CVC) funds of biopharmaceutical companies. This report was commissioned by the Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA represents the country's leading innovative biopharmaceutical research companies, which are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives.[1] Since 2000, PhRMA member companies have invested more than $600 billion in the search for new treatments and cures, including an estimated $71.4 billion in 2017 alone. This report explores how America's innovation-based biopharmaceutical companies are catalyzing the development of startup companies across the spectrum of medical innovation through the establishment of CVC funds. These CVC funds act as an important complement to the critical R&D investments and activities occurring in-house.

The Rise and Transformation of Corporate Venture Capital

Venture capital is a form of financing provided by private investors (venture capitalists) or specialized financial institutions (development finance houses or venture capital firms) to startup companies and small businesses with long-term growth

Defining the Main Sources of Equity Investment

Traditional venture capital (VC) raises funds from a set of limited partners (e.g., institutional investors such as pension funds and universities) and seeks to provide a return through selective investments into a portfolio of young, innovative companies over a fixed period (usually 10 years). Typically, venture capital firms invest after a new venture has already achieved a key milestone and continue to invest in later rounds as the venture scales and enters the market. The fixed time horizons for venture capital funds requires realizing timely exits via an acquisition or initial public offering.

Corporate venture capital (CVC) investments are made when a unit of a corporation, specifically established as a registered investor, makes equity investments in startup ventures generally related to the corporate entities' own industry.

Angel investors are accredited high-net worth individuals who invest personal capital into young ventures at the earliest stages. Angel investors are often former entrepreneurs and business executives who identify promising startups in their area of expertise that may benefit from additional funding, guidance, or mentorship. While historically a highly independent and fragmented market, the angel investing landscape is trending toward more centralized angel networks.

Crowdfunding is where a large volume of online investors, with no need for accreditation, each contribute small amounts in return for fractional ownership in a startup at its earliest stages of formation. Crowdfunding has experienced rapid growth in recent years.

Accelerators/Incubators are programs that work with a cohort of entrepreneurs with a business idea or a nascent venture, and offer a mix of bootcamps, mentorship, work space and funding to launch these new ventures in return for an equity share.

Adapted from Drover et al, "A Review and Road Map of Entrepreneurial Equity Financing Research: Venture Capital, Corporate Venture Capital, Angel Investment, Crowdfunding and Accelerators," Journal of Management, July 2017

potential. The funding is typically provided in exchange for equity in the company.

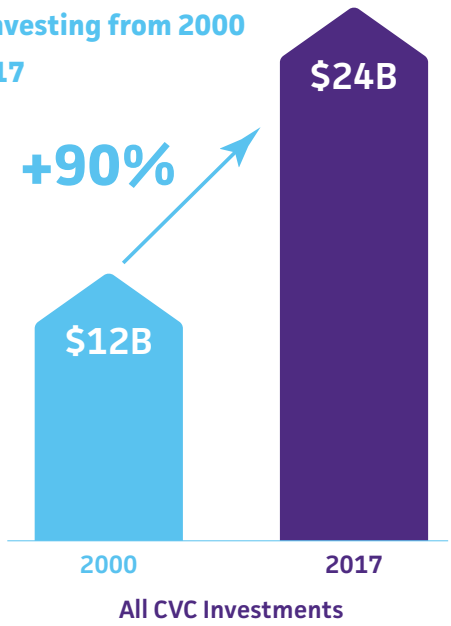
Corporate venture capital (CVC) is a unique subset of venture capital. CVC investments are made by an external entity established by a corporation specifically to invest in promising startup companies, usually related to the company's own industry. In addition to the financial investment, the CVC may also provide a range of management, technical, and strategic support to the startup. (For additional information, see text box regarding main sources of equity investment for startup ventures.)

While CVCs have been around since the 1960s, for the first four decades companies typically started CVC programs in periods of economic growth only to terminate them during subsequent economic downturns.[2] **Beginning in the early 2000s, this cyclical pattern of "boom and bust" gave way to a new era of sustained CVC activity.** One explanation for this shift is that corporations began to see CVCs as a unique mechanism to embrace innovation and stay competitive in today's global economy. The Boston Consulting Group explained this post-2000 evolution as follows:

> "In an economy where innovation spells the difference between success and failure, corporate venturing can spur tomorrow's innovations while it helps build an organization in which innovation is business as usual. Some of the world's most respected and successful corporations are already reaping the benefits of their venture investments, generating

profits and growth, and opening up new markets with innovations originally developed by their portfolio companies. They recognize that as competition intensifies, and uncertainty increases, CVC opens new strategic avenues. There is no denying that corporate venturing, like any other form of innovation, is a risky activity. But considering its game-changing potential, we believe the greater risk is not to engage in it at all."[3]

Significant growth in all CVC investing from 2000 to 2017



The value of the deals that CVCs have invested in nearly doubled since this evolutionary change in the corporate investment model, growing from $12.8 billion in 2000 to $24.3 billion in 2017.

CVC investments, as measured by the deals in which they participate, no longer ebb and flow but rather are now a sustained and rapidly-growing source of equity investment. This investment now exceeds the deal activity from angel investors, crowdfunding, and accelerator/incubator funding and is increasingly representing a greater share of total venture capital investments.

CVC focus reflects unique strategic objectives. Unlike what is typically found with other sources of equity investment, CVCs often have strategic objectives beyond obtaining a healthy return-on-investment. In a survey of CVCs in 2008-2009, the accounting firm EY found that 80 percent of CVC respondents sought to achieve a blend of financial and strategic success by working to achieve objectives aligned with their parent company's core business. An additional 17 percent of respondents were focused purely on achieving strategic advantages. Only 3 percent of CVCs responding said they were focused on financial success alone.[4]

A 2017 review of entrepreneurial equity financing research summarizes the existing literature:[5]

"Studying CVC at the aggregate level, scholars have found that an increase in total R&D expenditures within an industry is associated with a greater number of CVC investments in that industry ... Put differently, many established firms pursue CVC not merely as a way to generate high financial returns but, rather, as a critical vehicle to engage and nurture relationships with an external community: that of innovative entrepreneurial ventures."

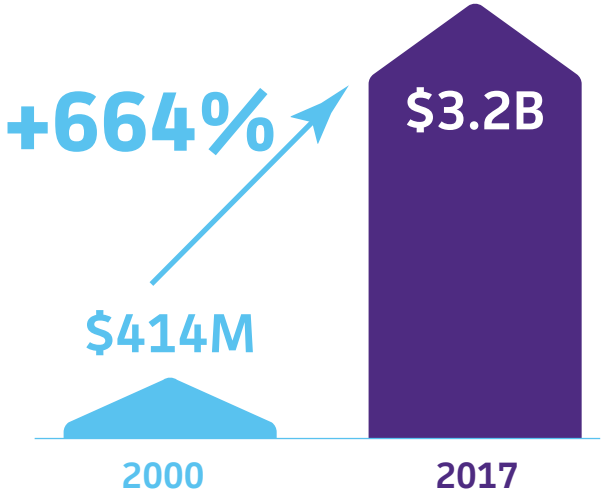
"Studying CVC at the aggregate level, scholars have found that an increase in total R&D expenditures within an industry is associated with a greater number of CVC investments in that industry ... Put differently, many established firms pursue CVC not merely as a way to generate high financial returns but, rather, as a critical vehicle to engage and nurture relationships with an external community: that of innovative entrepreneurial ventures."

Innovation-based Biopharmaceutical Companies Are Leaders in CVC Investment

As CVC investment has come of age, biopharmaceutical company-sponsored CVCs have led the growth in investment. This report sought to identify and describe CVCs that operate under the same corporate umbrella of PhRMA members. Fifteen CVCs were identified within the PitchBook investment database as being related to PhRMA members, and having investments within the 2000 to 2017 period. These PhRMA-member CVCs are distinct entities and function as a separate investment vehicle for these PhRMA member firms.[6] While a number of PhRMA member companies also make direct venture capital investments or are part of holding companies that make direct venture investments, those investments were outside the scope of this analysis.

Comparing 2000 to 2017, it becomes apparent how PhRMA-member companies' CVCs have evolved over time. In 2000, a mere $414 million out of the nearly $13 billion in total deal value involving CVC investment was undertaken by biopharmaceutical companies, with only 5 of the current 15 PhRMA-member CVCs in existence. By 2017, deals involving PhRMA-member CVC investments grew to $3.2 billion, an increase of over 660 percent, dwarfing the 90 percent growth rate across all CVC investments.

More than 660% growth in the total value of deals involving PhRMA-member CVCs from 2000 to 2017



All PhRMA CVC Investments

Of the 15 PhRMA-member CVCs, 12 (80 percent) have been in existence at least 10 years. Four of the 15 PhRMA-member CVCs were formed prior to 2000 with eleven established between 2000 to 2010. While there are some year-to-year fluctuations, the total value and number of deals involving PhRMA-member CVC investment have been on an upward trend since 2010, and in 2017 completed 64 deals to reach the nearly $3.2 billion (Figure 1).

Methodology: Capturing And Measuring Venture Investments

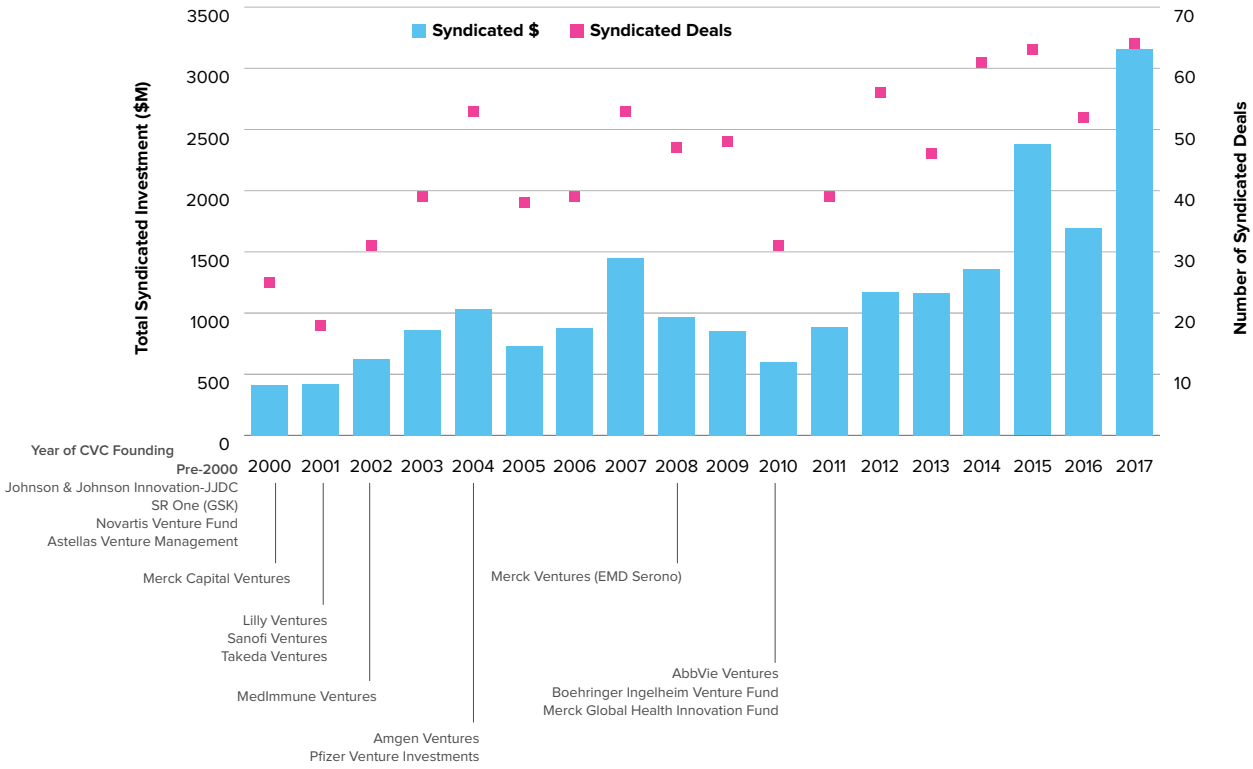
Throughout this report, the values (companies, deals, and investments) reported and discussed regarding overall venture investment trends and the specific nature of the 15 PhRMA-member CVCs were captured from the PitchBook investment database (https://pitchbook.com/) in September 2018.

PitchBook, like similar services, only reports the total value of a deal, not the individual amounts an investor (or each member of a syndicated or multi-investor deal) specifically invests.

A syndicated venture capital deal involves more than a single investor. Syndicated investments are typically made to increase the size of the investment, spread the risk among more investors, or to connect with resources, networks, or perspectives of additional investors.

This report tracks the growing value of deals that PhRMA-member CVCs have participated in as a way to gauge their growing impact.

Figure 1. PhRMA-member CVC Involvement in U.S. Syndicated Investments



Source: PitchBook and Corporate Information

This report examines the contributions and implications of the rise of PhRMA-member CVC investment on the functioning of our nation's ecosystem for medical innovation. It comes at a time of unprecedented scientific opportunity for biopharmaceutical innovation, but one that also presents significant challenges. In the next section, the report explores biopharmaceutical innovation and why the rise of these CVCs is an important complement to ongoing innovative biopharmaceutical industry R&D activities. Using specific data and illustrative examples, this report shows how PhRMA-member CVCs are helping support the growth of the overall medical innovation ecosystem..

Setting the Context: Growing PhRMA-member CVC activity comes at a time of unprecedented opportunity but rising challenges for medical innovation

Scientific and technological advances in biomedical research are fueling the development of new medicines to treat patients with some of the most complex diseases, including those for which there are currently no available treatment options. There are about 7,000 new medicines in development, with 70 percent being potentially first-in-class treatments for many diseases and conditions, and others offering more effective treatment options and fewer side-effects to improve the quality of life for patients.[7]

The U.S. currently stands as the global leader in biopharmaceutical innovation. This global leadership has resulted in the U.S. having a dynamic and interconnected ecosystem to develop, manufacture, and deliver new therapies to patients. The biopharmaceutical industry directly employs more than 800,000 workers with each direct biopharmaceutical job supporting nearly five additional jobs outside the industry. In total, the biopharmaceutical industry supported more than 4.7 million jobs across the U.S. economy in 2015 alone.[8] Additionally, there is a significant health dividend from this U.S. global leadership with new medicines under development often being introduced first in the U.S.[9]

Much of the R&D enterprise for the U.S. biopharmaceutical industry is generated by the members of PhRMA. PhRMA members are estimated to conduct more than $71 billion in R&D in 2017,[10] which accounts for most of the industry's overall R&D investment in the U.S.[11]

While these numbers are impressive on their own, a comparison with other industries demonstrates that the level of R&D investment by the biopharmaceutical industry far outpaces all other industries, particularly when considering the level of R&D investment per worker. In addition, the biopharmaceutical industry accounts for the single largest share of all self-funded R&D, representing 1 out of every 6 dollars spent on domestic R&D by U.S. businesses.[12]

The significant R&D investments by the biopharmaceutical industry reflect the lengthy, complex and highly regulated innovation process to bring new medicines to patients. In all phases of research, development, manufacturing, and delivery, the biopharmaceutical industry faces significant scientific and technical challenges, in addition to rigorous regulations.

Basic research into disease processes offers insights into potential new therapeutic approaches. To develop a specific lead compound, an enormous number of potential medicines having unique chemical structures and properties often must be screened. Once a potential medicine is identified, significant regulatory and scientific hurdles must be overcome before a promising discovery reaches patients. This includes rigorous pre-clinical testing, a series of multi-phase clinical trials where the drug product is tested in patients, and intensive regulatory review at FDA. Even if a product makes it through this process, it still may be subjected to post-approval testing and monitoring as the product enters the market. Finally, payers are increasingly demanding more evidence and testing before providing full coverage of certain therapeutics.

Only 12 percent of investigative medicines entering clinical trials are ultimately approved by the FDA—less than half of the percentage approved a mere decade ago.[13] Despite these high risks, the promise of positive returns from successfully navigating this rigorous process to bring new medical innovations to patients helps

Key Elements of the Drug Development Process

Drug Development builds upon insights into the underlying mechanism of a disease to identify potential therapeutic approaches. Once researchers identify a target they begin the search for a molecule that will specifically interact with this target to change the course of disease. They refine promising molecules in a process called lead optimization. When they have a lead compound preclinical testing can begin.

Preclinical Research extensively tests a lead compound in the lab and in animal models to determine if it safe enough for testing in humans. If key criteria are met, then an Investigational New Drug (IND) application is filed with the FDA to permit testing in humans.

Clinical Research in humans is a very rigorous multi-phase process that begins with a small number of healthy volunteers (20-80) in Phase I to determine the safety, tolerability and how the investigational compound behaves in the body. If it proves to be safe it moves into Phase II with a few hundred patient volunteers with the disease in question to assess the efficacy and dose response of the investigational compound, and finally, if there is an indication of efficacy, the investigational compound moves to large scale randomized and controlled testing in Phase III to assess its safety and efficacy in a larger group of patients (1,000-5,000).

Regulatory Review requires that all of the data collected from preclinical studies and the clinical trials be submitted to the FDA for review. The FDA weighs the benefits and risks of the potential medicine in deciding whether to grant approval. It is not unusual for the FDA to require additional clinical research testing before approval and/or to seek the advice of an independent expert panel on whether to approve the application. Only about 12 percent of the candidate medicines that make it into Phase I clinical trials will be approved by the FDA.

Post-Approval Research and Monitoring takes place after FDA approval. Every medicine is monitored as long as it is available to patients. The FDA often also requires long-term studies to collect ongoing safety and efficacy data in specific patient subgroups. Companies also conduct additional clinical trials to explore expanded uses and benefits of medicines over time.

Access and Coverage is increasingly becoming another hurdle impacting whether and when a medicine reaches patients. Simply being safe and effective is no longer sufficient to ensure coverage and payment. Health insurance companies require an ever-growing body of evidence, often including additional comparative data versus existing therapies, before they will begin to provide coverage and access to an FDA approved medicine.

fuel the interest of private venture capital to invest in biotech startups.

From the time a potentially promising candidate medicine is identified, it takes 10 to 15 years on average for a medicine to make its way through the entire R&D process to FDA approval. The average cost to develop a new medicine is estimated at $2.6 billion dollars, including the cost of failures, and evidence suggests these costs are on the rise and are even higher when accounting for the research that continues after a medicine has been approved.[14]

One contributor to increased costs is the increased complexity of the disease areas being tackled – from Alzheimer's Disease to deadly cancers to autoimmune diseases. As researchers tackle our most challenging and complex diseases, it is no surprise that the development hurdles mount as well. In particular, there is a growing focus on applying the molecular and genetic understanding of diseases to new drug and medical device strategies, such as immunotherapies and regenerative approaches. In addition, there are growing efforts to advance personalized medicine by combining diagnostics and new therapies

to deliver treatments based on an individual's specific genomic make-up.

All of these scientific advances enable researchers to address more complex diseases and medical conditions but also place additional challenges on the development process. For instance, the Center for the Study of Drug Development at Tufts University has found that clinical trial protocol design scope and complexity have steadily increased. Further, this trend will continue—and likely accelerate—as pharmaceutical and biotechnology companies target more difficult-to-treat and rare diseases, enroll more stratified patient populations, and collect higher volume and more diverse data—all of which will impact and contribute to increased challenges related to recruitment and retention of participants in clinical trials and lengthen the time and increase the costs related to drug development.[15]

Even with the significant and growing investment in R&D by PhRMA members, the long development times, scientific and regulatory uncertainties, and rising costs of bringing a new biopharmaceutical to market has created a challenge to the sustainability of U.S. biopharmaceutical innovation. As McKinsey & Company points out, "It's no secret that the biopharma industry has been grappling with diminishing R&D productivity … The return on investment for a typical biopharmaceutical portfolio today often will not even cover its cost of capital."[16]

At the same time, the pace of biopharmaceutical innovation is so intense with advances in genomics, immunotherapies, systems biology and more data-driven clinical insights, that as David Ricks, Chairman and CEO of Eli Lilly explains: "For the first time, we're seeing technical obsolescence in pharma, where the product life cycle is shorter than the intellectual-property cycle. That's already happening in virology and beginning to happen in oncology. The losers will be those that can't innovate fast enough."[17]

The emergence of PhRMA CVCs that directly invest in new startup companies is one tool to help address the challenges in biopharmaceutical innovation. While substantially smaller than the level of research and development investment being made directly by PhRMA members, most of the investment into biotech startups is used to fund R&D focused on newly emerging and still unproven areas of science.

Access to private venture-capital investment, including PhRMA-member CVC funding, is critical to helping these companies advance technologies forward. As Bio Link Direct explains:

> "Since 2000, VC has emerged as a driving force for the biotech-based innovations, and the surge continues. Hence, we got an impressive number of biotechnology companies making the industry reach another level … Biotechnology companies are set up by experts in research and development. More often than not, these individuals are far from any business sense. This element is taken care of by the VCs. They identify the factors of higher growth and allocate the available resources in the right direction. Next, a VC plays a primary role in setting milestones for a company. They ensure that these targets are achievable in the real world and give the company an edge over others. VCs research a lot before investing and thus are experts in competition analysis and monitoring."[18]

PhRMA companies are increasingly supporting this important facet of the biomedical R&D ecosystem through their CVC funds. These CVCs often combine financial support with additional, non-financial resources to create benefits for the biotech startup that go well beyond the dollars being provided. A closer examination of the trends and contributions of PhRMA-member CVCs reveal the significant role they play in supporting the growth of startup biopharmaceutical ventures and in complementing the efforts of traditional venture capital.

KEY TRENDLINES AND CONTRIBUTIONS: THE GROWING IMPORTANCE OF CVC ACTIVITY BY BIOPHARMACEUTICAL COMPANIES

A detailed analysis of the extensive PitchBook database on venture capital investments offers a unique view into how the CVC activity of innovation-based biopharmaceutical companies is unfolding and contributing to the medical innovation ecosystem.[19]

The data offers insights into both the level of venture capital investments at various stages as well as the economic results being generated by biotech companies. Supplementing this in-depth data analysis were interviews with seven of the managers of PhRMA-member CVCs – including AbbVie Ventures, Boehringer Ingelheim Venture Fund, Johnson & Johnson Innovation-JJDC, Inc., Lilly Ventures, Pfizer Venture Investments, Sanofi Ventures and SR One (GSK) – conducted by TEConomy as well as KRC Research. These interviews offered insights into the strategic focus, contributions, and challenges of PhRMA-member CVC efforts. A review of the growing academic studies and surveys on CVCs, including specific studies of biopharmaceutical company CVCs, also provided additional evidence of the growing impact and nature of biopharmaceutical CVC efforts.

As a result of this thorough analysis, this report concludes that biopharmaceutical CVCs are:

- A significant share of the overall activity in biopharmaceutical investment
- Doubling down on innovation in strategic areas of focus to their parent companies
- Active in early stage investments, and in recent years have helped reverse a troubling trend away from such investments in biotech
- Encouraging strong partnerships with other investors

- Providing opportunities in other areas of healthcare devices, technologies, and services beyond new drug therapies in strategic focus areas, and

- Having measurable impacts and broad benefits in advancing innovation by biotech startups

Biopharmaceutical CVCs are now a significant share of overall biopharmaceutical investment

Overall venture capital investment from all investors to emerging biopharmaceutical and biotech startup companies continues to reach new heights. Fueling this strong interest in biotech startups is the promise of a broad range of innovations to address unmet medical needs, such as immunotherapies, gene editing, gene and cell-based therapies and personalized medicine. In 2017, $12 billion was invested in biopharmaceutical startup companies across all types of venture investors, well above its past record of $10.4 billion set in 2015. Over the 2000 to 2017 period, a nearly six-fold increase in biopharmaceutical venture capital investment was achieved, growing from $2.2 billion in 2000 to $12.0 billion in 2017.

The emergence of CVC activity by PhRMA-member companies has been an important component of this increase, rising from a mere $304 million level of venture investment in 2000 to $2.4 billion

PhRMA-Member Corporate Venture Investment

Beyond the establishment of 15 specific CVCs, 32 PhRMA-member companies have made defined venture capital investments directly from corporate accounts, as opposed to CVC accounts. These efforts are a combination of both pre-cursor investments prior to the establishment of a formal CVC entity and specific investment approaches used by PhRMA members without a specific CVC entity and, in some instances, PhRMA members with CVCs. As with the CVCs, the corporate investments are typically made as part of syndicated deals. These direct PhRMA-member corporate venture capital investments are part of syndicated deals totaling:

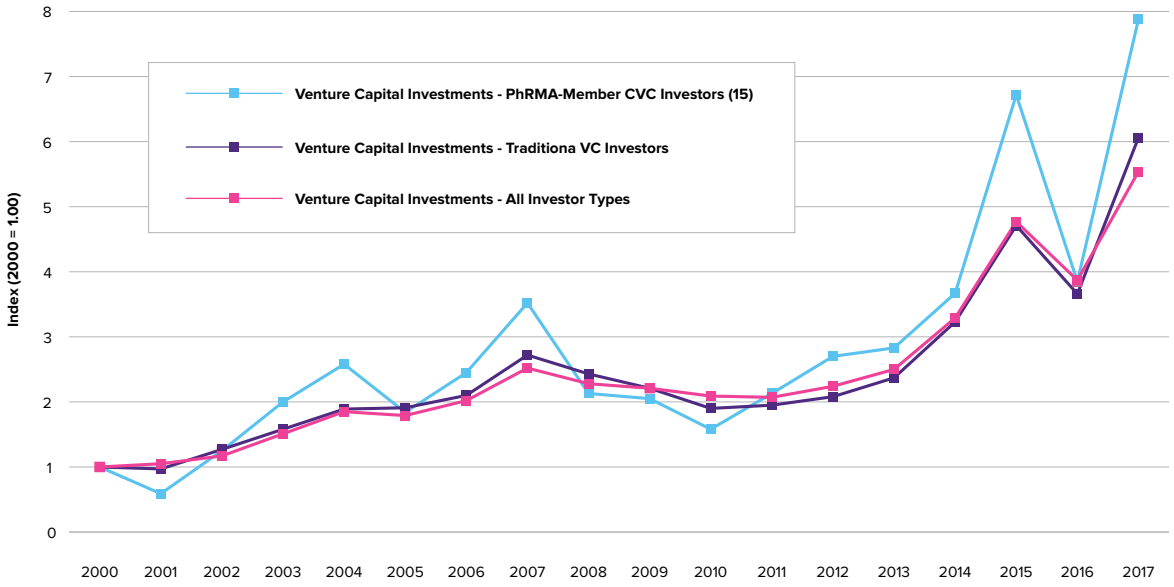
- $2.3 billion in 2017
- $7.0 billion from 2010-2017
- $9.3 billion from 2000-2017

Table 1. U.S. Biopharma VC Investments by Investor Participation Type, Key Years: 2000-2017

Total Syndicated Venture Capital Investments by Investor Type ($ Millions)	2000	2010	2015	2016	2017	Investment Growth	
						2000-2017	2010-2017
All Investor Types	$2,175	$4,537	$10,337	$8,413	$12,048	454%	166%
Traditional VC Investors	$1,817	$3,457	$8,550	$6,654	$11,008	506%	217%
PhRMA-Member CVC Investors (15)	$304	$482	$2,043	$1,172	$2,396	688%	397%

Source: TEConomy Partners analysis of PitchBook investment database. TEConomy uses "biopharma" to represent the specific Pharmaceutical and Biotechnology industry group as defined and captured within the PitchBook database. This industry group includes companies engaged in the R&D and production of pharmaceuticals, biotechnology (including areas such as genetics, molecular biology, etc.), drug discovery and related tools, and drug delivery mechanisms.

Figure 2. U.S. Venture Capital Trends by Investor Participation Type, 2000-2017 – Biopharma Sector



Source: TEConomy Partners analysis of PitchBook Venture Investment database

in 2017; a nearly 9-fold increase. In 2000, the investment deals involving PhRMA-member CVCs represented less than 14 percent of biopharmaceutical venture capital investment. In 2017, it stood at 20 percent of all biopharmaceutical investments -- which is a significant gain in light of the more than 450 percent growth in biopharmaceutical venture investments from all investor types over the 2000 to 2017 period. And the contribution of PhRMA-member CVC activity to the major rise of overall biopharmaceutical venture capital investment in recent years is even more significant – comprising 30 percent of the increase in biopharmaceutical venture capital investment from 2016 to 2017.

In its 2017 report on biotechnology industry trends, EY explains that:

"interest and support from corporate venture capitalists have been typical of the venture capital investment surge over the past several years."[20] By 2016, corporate venture capitalists participated in nearly half of all venture rounds.

As shown in Figure 2, from 2000 to 2017, CVC activity by large biopharmaceutical companies has more than kept pace with biopharmaceutical deals involving only traditional venture capital investors. ***In all but four of the past 18 years, the growth rate of PhRMA-member CVC investment activity has exceeded that of traditional venture capital firms.***

Biopharmaceutical CVCs are expanding investments in strategic areas aligned with the focus of their parent companies

Unlike traditional venture capital, where the primary objective is to generate high financial returns, biopharmaceutical CVC activity has multiple investment objectives. Research into CVC investment practices among U.S. and global biopharmaceutical companies found that highly important investment objectives included: obtaining a "window on technologies/market intelligence", accessing "breakthrough technology", "developing strategic relationships," as well as generating "financial return."[21]

Discussions with representatives of biopharmaceutical CVC similarly found that a key strategic objective was to invest in biotech companies to complement and deepen areas of strategic interest to the company. A particular value of startup biotech companies, noted by some biopharmaceutical CVC managers, is their close relationship to basic scientific advances taking place in university, federal lab, and non-profit research institutes that can spur "novel" technologies that have the potential to be transformative. As reported in Nature Biotechnology, "corporate venture capital invests in [startup] companies developing breakthrough technologies that the CVC believes have long-term disruptive potential."[22]

Biopharmaceutical CVC activity has been focused on companies that are working in disease areas with large unmet medical needs aligned to the areas of strategic focus of their parent companies. Out of the 507 diverse companies receiving funding between 2000 and 2017 by PhRMA-member CVCs, the leading disease areas are those associated with both large unmet medical needs and cutting-edge technologies, including:

- Cancer therapies – 131 venture-backed companies
- Neuroscience – 86 venture-backed companies
- Immunology and autoimmune – 85 venture-backed companies
- Virology and infectious diseases – 58 venture-backed companies
- Cardiovascular and circulatory – 57 venture-backed companies
- Metabolic disorders and diabetes – 57 venture-backed companies

Early stage investment in areas of strategic interest offers significant benefits for both the startup biotech company and the larger biopharmaceutical company. As a panelist during a Biopharm America discussion explained: "The big pharma gets potentially a board observer seat and the small biotech gets an expert in the field on their board."[23]

Venture Deals in 2017: Examples of Types of Novel Technologies/Areas Receiving Initial Investments from PhRMA-member CVCs

Company seeking to advance therapies to help children with rare, but severe and debilitating disorders of metabolism that leads to calcification affecting soft tissue and bone.

Company seeking to advance novel therapeutics for the treatment of urologic and gynecologic disorders.

Company that has developed a platform technology to remove brain myeloid cells associated with neurodegenerative diseases.

Company developing novel therapies using an enzyme-based drug platform to treat inflammatory bowel disease and promote blood cell reconstitution following bone marrow transplants.

Source: PitchBook and corporate websites.

Over time, this initial CVC investment can generate increased familiarity and longer-term relationships between the biotech company and the larger biopharmaceutical company that sponsors the CVC. For example, a PhRMA-member company CVC invested in a small company that makes a 3-D mapping system that discovers, interprets, and treats cardiac rhythm disorders. Two years later, the corporate parent of the CVC acquired the company, and today it comprises a significant portion of the electrophysiology market, with sales of around $2 billion.[24] Similarly, in interviews with TEConomy another PhRMA-member company CVC recounted a successful endeavor stemming from the CVCs investment in a biotech startup developing molecular imaging compounds for detecting and monitoring chronic human diseases. Years later, the former startup became a division of the biopharmaceutical company.

While primarily aligned with its broad corporate strategic focus, CVCs can also help examine new areas of interest. A notable example of this is the recent announcement by Pfizer to commit $600 million to its CVC arm. At least 25 percent, or $150 million, of the funds will be invested in neuroscience startups, despite an earlier decision by the biopharmaceutical company to shift its internal R&D spending away from this area. According to a statement from Pfizer:

> "By changing the way we invest in neuroscience, we hope to support an energized community of biotech entrepreneurs who are progressing the understanding of the molecular mechanisms of neurologic diseases and help advance potential treatments for people with neurological conditions."[25]

Biopharmaceutical CVCs are active in early stage investments, and in recent years have helped reverse a troubling trend away from such investments in emerging biopharma and biotech

Biopharmaceutical CVCs are active in both early and later stages of venture capital funding. Over the period of 2000 to 2017, PhRMA-member CVCs equally split their total investments between early and late stage investments. But this balance between early stage and later stage investments masks a highly dynamic environment facing venture capital markets.

Venture capital markets for biotech startups face the "tug and pull" between large potential value creation and significant risks associated with high development costs and uncertain outcomes. Not surprisingly, this has created an environment that can discourage early stage investments when a biotech startup is still involved in drug development or pre-clinical testing in favor of later stage investments when clinical trials activity is taking place and showing positive results.

From 2007 to 2015, traditional venture capital funds retreated substantially from early stage investment in biopharmaceutical startups. In each of these years, early stage investment fell below that of later stage investments for deals involving only traditional venture capital firms, reaching as low as 35 percent in 2012 and averaging a mere 42 percent on a year-to-year basis from 2007-2015. By comparison, in the earlier period of 2000-2006, early stage investment exceeded 50 percent in four years, reaching a high of 58 percent in 2002. Many biotech commentators raised concerns. For example, articles in Nature Biotechnology's "bioentrepreneur" section noted:

Examples of PhRMA-member CVC Early Participation in Companies Reaching Phase III Trials

CVC investment in novel therapeutics for patients based on the hypoxia inducible factor (HIF) technology. The company's lead product candidate, currently in a Phase III clinical trial, is an oral, investigational therapy in development for the treatment of anemia related to chronic kidney disease in both non-dialysis and dialysis patients,

CVC investment in medicines to treat inflammatory condition and metabolic diseases. Currently, the company is preparing to launch a Phase III trial to evaluate the efficacy and safety of the investigational drug as a potential treatment for Duchenne Muscular Dystrophy. The company is using a platform technology to help discover and develop medicines that can simultaneously target pathways in the inflammatory response.

CVC investment in medicines to treat cancer by targeting malignant cells both directly and through modulation of the tumor microenvironment, enabling cancer patients to begin treatment quickly. The FDA has granted fast track designation to the investigational drug for the potential treatment of patients with chronic lymphocytic leukemia. The investigational drug has the potential to be a first in class treatment for certain types of hematologic malignancies.

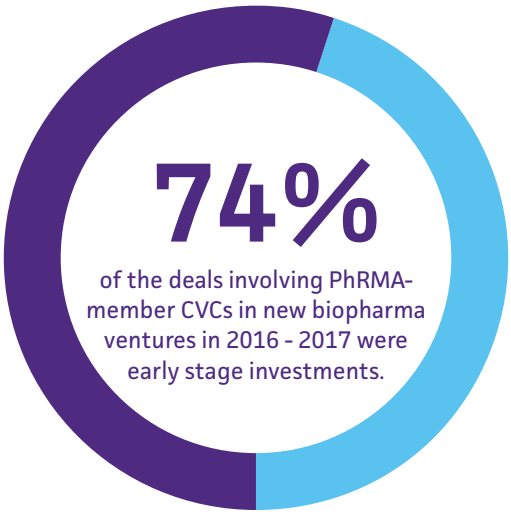
Source: PitchBook and corporate websites.

> "Following the economic downturns of 2008 and 2011, the profiles of those investing directly in biotech startups have changed; many traditional investors have curtailed their mandates and reduced their allocations to early-stage life science companies."[26]

> "In spite of consistently above average returns on biotech ventures, several traditional VC funds are shifting their investments away from the high-risk, early stage financing of biotech startups and into later-stage opportunities and existing portfolios. The fewer VC funds that do specialize in early stage biotech investments have consequently become increasingly more selective and unable to meet the greater demand for patient capital."[27]

In two specific years over the 2007-2015 period, the deals involving PhRMA-member CVCs had more than half of their funding in early stage biopharmaceutical investments, serving to offset the broader trends favoring later stage investments. In 2011, 73 percent of PhRMA-member CVC investments were in early stage deals compared to 48 percent for deals involving only traditional venture capital firms. Similarly, in 2009, 53 percent of PhRMA-member investments were in early stage deals compared to 40 percent for deals involving only traditional venture capital firms.

In more recent years, the pendulum has swung back in favor of early stage investments by venture capital investors. As EY reported in its 2017 review of biotech activity, early stage investing represented "the single biggest cause of optimism" in overall biotech financing.[28] PhRMA-member CVCs have been leading the charge towards more early stage funding for emerging biopharma firms. In the last two years (2016-2017), 74 percent of the investments in deals involving PhRMA-member CVCs in new



biopharma ventures were early stage investments compared to 59 percent for deals involving only traditional venture capital firms.

Interviews with representatives of biopharmaceutical CVCs help explain their orientation towards early stage investments. Below is a sampling of the comments made in these interviews:

- "We invest very early since our focus is on 'de-risking' novel technologies that have the potential to be transformative and have a significant impact on patient care in areas of strategic importance to our sponsoring companies. Then partnering can occur through more strategic relationships between the biotech startup and our parent, biopharmaceutical company. Therefore, corporate venture capital efforts are akin to a relay race where we are looking to pass the baton."

- "Because we are so early, we're investing in a process that will hit patients or will hit the market 10 to 30 years down the road. It's impossible to predict what policies or what the world will look like in 30 years. So hard core early stage investors look at a medical need. Is there a medical need out there that is clear, and are there novel approaches to address those medical needs?"

- "We are focusing on very early investments. Many of the companies we start, we're the first money in. And we have, as an investor then, the opportunity to help the company creating the data. If you invest in a later stage company, and they're in clinical trials already, the science is pretty much fixed. So, the focus of the company changes to clinical development. That's not as interesting for us."

Over the 2000 to 2017 period, the activity of PhRMA-member CVCs as "early investors" for emerging biopharmaceutical startups[29] had varying levels of intensity:

- Out of the 546 biopharmaceutical deals that PhRMA-member CVCs were investors, 278 or 51 percent were early stage investments, when the biopharmaceutical startup was typically involved in drug development, pre-clinical testing and Phase I clinical trials.

- In 126 out of the 278 early stage deals, the PhRMA-member CVCs invested, typically as part of an investor syndicate, in the first round of early stage investments for the emerging biopharmaceutical startups. This first round of early stage investment represents the initial funding by any venture investor in a startup company. In another 119 out of the 278 early stage deals, the PhRMA-member CVCs invested in the second round of early stage investing.

- In 52 out of the 278 early stage deals the PhRMA-member CVCs served as the lead investor, helping organize other investors and often taking a more active role in determining valuation and structure of the investment.

PhRMA-member CVCs have been widely engaged in helping to ensure the pipeline of biopharmaceutical investments is well-primed and, by doing so, often fill gaps in what traditional venture capitalists are willing to do on their own.

Biopharmaceutical CVCs encourage strong partnerships with other investors.

PhRMA-member CVCs are not trying to "crowd out" other venture investors, but instead typically co-invest, or what is commonly referred to as syndicate, with other venture investors. Indeed, 96 percent of the PhRMA-member CVC deals identified in PitchBook from 2000-2017 are syndicated with other venture investors. By co-investing, PhRMA-member CVCs are helping to catalyze early stage investments with other investors and then continue to participate in later rounds and stages of investment. As a result, deals with PhRMA-member CVCs tend to be larger than those without. On average, the deals involving PhRMA-member CVC provided nearly $24 million per deal compared to just over $14 million for deals not involving PhRMA-member CVCs.

PhRMA-member CVCs have co-invested with nearly 1,200 other venture investors since 2000. The greatest number of co-investments taking place in syndicated deals involves PhRMA-member CVCs joining together to advance a biotech startup—123 of the deals analyzed (15 percent) include two or more PhRMA-member CVCs, with one deal including five of the 15 PhRMA-member CVCs. These co-investments among biopharmaceutical CVCs are typically taking place in companies at the earliest stages of development, helping to de-risk novel technologies.

Other co-investors cover a wide range of traditional, niche, or regionally focused venture capital firms, as well as other CVCs and corporations that have made venture investments (see text box regarding biopharmaceutical "corporate" venture investing). Among the most active co-investors are leading venture capital firms with more than $3 billion under management, demonstrating the willingness of top traditional venture capital firms to co-invest with PhRMA-member CVCs. These leading venture capital firms drive more than 95 percent of all biotech startup investments each year. In slightly more than one out of every four deals, PhRMA-member CVCs are co-investing with leading venture capital firms in a syndicated deal that supports an emerging biopharmaceutical startup.

The result is that among traditional venture capitalists, biopharmaceutical CVC engagement is becoming recognized as a complement to their own efforts. As Marta New from Agent Capital explained at a recent Biopharm America conference: "We love when corporate VCs are around the table, and increasingly we're seeing that in earlier-stage deals, especially around platforms."[30]

Biopharmaceutical CVCs also invest in a broader range of healthcare-related startups.

Between 2000 and 2017, PhRMA-member CVCs have been investing across a broader range of startups involved with healthcare beyond biopharmaceutical development. This can include startups advancing new medical devices, such as surgical instruments or joint replacements, or companies developing remote monitoring solutions, or entities involved in the management and delivery of healthcare services, such as accountable care organizations. Since 2000, PhRMA-member CVC investments accounted for 5 percent of the total venture investments made in these areas, spanning 139 companies over 205 deals.

In recent years, there has been a sharp increase in PhRMA-member CVC investment in broader areas of healthcare, totaling $447 million in 2016 and $700 million in 2017. This two-year total represents just over 7 percent of total venture investments in healthcare devices, technologies, and services.

Among the key drivers of this increased investment by biopharmaceutical CVCs is a growing recognition of the convergence of digital technologies, to enable a new emphasis on patient-centered, value-based healthcare. Digital advances

Examples of PhRMA-member CVC investments in Health Tech and Digital Tech

Biopharma CVC investment in digital medicine technology intended to service the needs of health care providers and health systems. The company's products include ingestible sensors, a small wearable sensor patch, an application on a mobile device and a provider portal for data analytics, intended to enable providers and health systems to more effectively manage risk and ensure that outcomes are reliably achieved. In 2017 FDA granted the first approval of a drug-device combination product comprised of a tablet embedded with an Ingestible Event Marker (IEM) sensor.

Biopharma CVC investment in the developer of mobile health applications designed to monitor patient management. The company's mobile health applications use their secure and scalable based platforms to support monitoring and management of patients with cardiac-related issues and other health disorders. In 2018 the company received approval for a new cardiac monitoring technology.

Biopharma CVC investment in a company providing a "big data" analytics platform intended to develop analytic tools for precision medicine and population health. The company's big data analytics platform develops a machine learning system that collects patient data, including information from electronic medical records, connected health devices, medical and pharmacy claims, genomics and consumer behavior to identify which health interventions would be best suited for individual patients.

Source: PitchBook and corporate websites.

are expected to have far-reaching implications for the way new therapeutic treatments are developed and delivered, including supporting the development of personalized medicines, and the use of diagnostics, remote monitoring, or other patient services to support adherence and assess health outcomes once the medicine is used.[31]

As EY noted in its 2017 report on biotech trends, the use of artificial intelligence and other data-driven tools and tracking devices to help improve patient outcomes is on the rise. EY estimates that 70 percent of biopharmaceutical companies are planning to use mergers and acquisitions (M&A) to build digital capabilities over the next two to three years.[32]

Two rising vertical or "cross-cutting" investment areas capture this increased involvement of biopharmaceutical CVCs in the convergence of digital technologies to advance patient-centered, value-based healthcare:[33]

- **Health Technology** – representing companies that provide mobility and other information technologies to improve healthcare delivery while decreasing costs. This area focuses on the use of technology and services, including cloud computing, internet access and social mobility, to optimize patient-centric healthcare.
- **Digital Health** – representing companies engaged in building hardware and software solutions to empower individuals to more easily keep track of their health and offer healthcare providers new tools to communicate with and treat patients. This space includes a host of mobile applications designed to track fitness activity, sleep, nutrition, weight, and medication intake; telemedicine programs to make it easier to connect with health professionals; and technologies that integrate information from electronic health records (EHR), diagnostic testing and genomics to improve clinical outcomes and further personalized medicine approaches.

Since 2013, these two areas have become a growing area of investment for biopharmaceutical CVCs, with 22 deals in digital health and 37 deals in health tech investments, totaling $521 million and $768 million, respectively. Indeed, 79 percent of all digital health investments, and 77 percent of all health tech investments from the 2000-2017 period have occurred within the last five years.

PhRMA-member CVCs invested in **22 deals** in digital health amounting to **$521M** and **37 deals** in health tech investments totaling **$768M**

Biopharmaceutical CVCs are having measurable impacts and broad benefits in advancing innovation for emerging biopharmaceutical startups

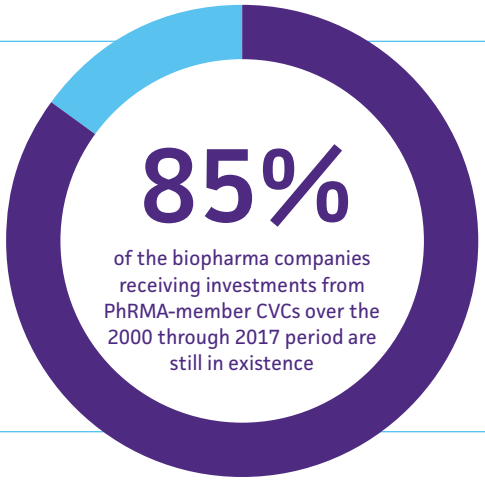
The track-record of success for startup companies benefitting from CVC investment demonstrates the impact of PhRMA-member CVC investments. PitchBook reports that of the 337 emerging biopharmaceutical startups that have received PhRMA-member CVC investments from 2000-2017, 85 percent are still in existence, including those involved in M&A activities. Nearly half (162) of the biopharmaceutical startups receiving investments from PhRMA-member CVCs are now generating revenues from product sales, with 32 being profitable. Another 70, or 21 percent, of startups receiving CVC investments have clinical trials under way.

The impact of PhRMA-member CVC investments is also reflected in broader economic output:

- Of the 147 emerging biopharmaceutical companies reporting employment data to PitchBook, the average employment was 22 employees at the time of their last investment.
- Of the 50 emerging biopharmaceutical companies reporting specific revenue earnings, they averaged $40.6 million annually at the time of their last investment.

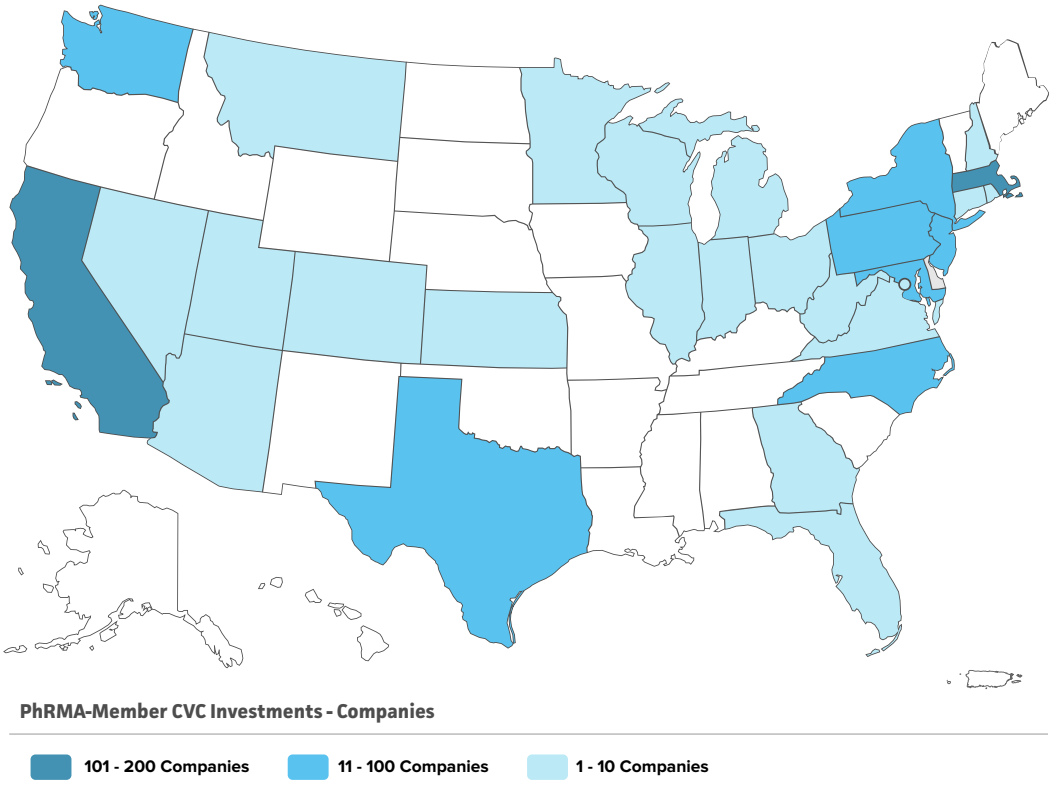
The overall PhRMA-member CVC investment footprint is distributed across the nation. In total, these CVC investments in 507 companies occurred in 29 states across the U.S. (Figure 3). Moreover, the pattern of investment does not simply reflect the distribution of biopharmaceutical industry employment. For example, Washington is

Successful-track record of start-ups receiving PhRMA-member CVC Investments



- **162** are now generating revenues from product sales
- **32** are profitable
- **70** are now in clinical trials to gain FDA approval for their novel medical products.

Figure 3. Distribution of PhRMA-member CVC U.S. Investments, 2000-2017: Companies



Source: TEConomy Partners analysis of PitchBook Venture Investment database

ranked 16th in overall biopharmaceutical industry employment, but ranks 3rd in the number of companies supported by biopharmaceutical CVC investments.[34]

Yet another measure of success is the higher share of initial public offerings (IPOs) generated by startups involving those companies backed by PhRMA-member CVCs. IPOs represent startups moving beyond private venture capital investments to generating funds from public markets, commonly referred to as "going public." It is viewed as a key mark of success for the company and its underlying innovations.

Of the 507 companies receiving PhRMA-member CVC investments, 84, or 17 percent, have gone public. The percentage of emerging biopharmaceutical companies that have gone public is even higher – 21 percent. By comparison, non-PhRMA-member CVC backed biopharmaceutical startups go public only 9 percent of the time. In other words, while PhRMA-member CVCs invested in 14 percent of all biopharmaceutical startups, those startups represent 40 percent of all biopharmaceutical startups that went public over the 2000 to 2017 period.

The success of biotech startups receiving CVC backing is reflected in the results of an in-depth analysis of 545 biotech startups in 2016. The study found that CVC backing is associated with higher patent and publication outcomes of entrepreneurial ventures versus companies that were solely VC backed. Compared to ventures that are solely VC-backed, CVC-backed ventures have 2.8 more

PhRMA-member CVCs invested in **14% of all biopharmaceutical startups,** those startups represent **40% of all biopharmaceutical startups** that went public over the 2000 to 2017 period.

patents per year and 2.05 more publications per year than solely VC-backed ventures.

The authors of the study explain:

> "This sheer magnitude of being affiliated with the [biopharmaceutical] corporate investor seems to be quite important. And when we dig slightly further into that, we look at a couple of mechanisms that seem to be associated with this evidence. The first one of them is … the ability to leverage knowledge, infrastructure, laboratories and so forth of the large corporation. The second one has to do with the ability to navigate clinical trials, compliance and other requirements that are important to taking the science and developing it into a drug that you and I can find in a marketplace."[35]

Discussions with managers of PhRMA-member CVCs confirm that the exposure biotech startups get to larger biopharmaceutical company experience, through both board participation and more informal troubleshooting and advice, can help these companies anticipate key hurdles and establish more effective strategies to navigate the regulatory and development issues inherent in clinical trial design, compliance, production scaling, and access to global markets.

Summing up the impact of biopharmaceutical CVCs is an article co-authored by Bain & Company and the Chair of Strategic Management and Innovation of ETH Zurich, one of the world's leading research universities: "The contribution of corporate VC investment to a [venture investment] syndicate is twofold: financial resources and highly specialized market knowledge of the pharmaceutical industry, which can be of decisive importance …"[36]

Examples of PhRMA-member CVC investments in Companies Getting New Drugs Approved

Biopharma CVC investment in novel small-molecule antibiotics intended to treat resistant infections.

Biopharma CVC investment in therapeutics intended for the treatment of rare and ultra-rare genetic diseases. The company's therapeutic products focus on metabolic and rare diseases that may affect small numbers of patients, but for which the medical need is high and there are no effective treatments.

Biopharma CVC investment in antibody therapeutics designed to treat infectious diseases. The company received FDA approval in 2016 for a medicine to treat anthrax exposure following a natural or intentional release of anthrax spores, enabling patients to prevent inhaled anthrax.

Source: PitchBook and corporate websites.

LOOKING FORWARD: ENSURING A BRIGHT FUTURE FOR MEDICAL INNOVATION

The growth of PhRMA-member CVCs as a strategic source of venture funding in the biopharmaceutical space has played an important role in helping to bring forward new medical advances for patients.

CVC investments increasingly complement the larger R&D investments being made by our nation's biopharmaceutical companies to develop medical innovations that improve the lives of patients.

While the trendlines have been generally positive on a year-by-year basis, the continued growth of biopharmaceutical CVCs cannot be taken for granted. Like other investors in startup biotech companies, biopharmaceutical CVCs face the high level of risk and uncertainty associated with lengthy and costly research and development timelines and increasing regulatory requirements that increase the costs and complexity of clinical trials. Moreover, biopharmaceutical R&D involves complex and promising science but with great uncertainty of success.

Public policies can play a role in shaping those risks. Discussions with representatives of biopharmaceutical CVCs reinforced the need to preserve and maintain:

- Strong intellectual property protections
- A well-functioning, science-based regulatory system
- Coverage and payment policies that value and support the use of new medical advances.

Strong intellectual property protections

Intellectual property protections, including both patents and statutory exclusivity protections, are key to supporting continued future medical innovation in the long term. Intellectual property protections are the lifeblood of innovation in pharmaceuticals. They are critical incentives for innovation, given the unique attributes of the biopharmaceutical

R&D process, which is lengthy, costly, and uncertain. The basic view of biopharmaceutical CVCs is that robust IP protection, makes a difference when considering investment decisions. As one biopharmaceutical CVC representative explained, "We can spend ten years of a 20-year patent on just development and not start selling anything until the last seven years because it has taken us 13 years to develop the drug. I think you would encourage more people to get involved in drug development if they could have longer periods of exclusivity." Indeed, in a separate interview, another CVC representative explained that, "[a] lot of how much we're willing to invest in a startup biotech depends on how much runway we have [exclusivity] to be able to realize a reasonable return on investment."

A well-functioning, science-based regulatory system

Given the rigorous regulatory standards needed to approve biopharmaceuticals in this country, it is not surprising that FDA is viewed as a critical factor in the investment landscape. As one biopharmaceutical CVC representative explained: "Anything that will impact how the FDA works has an impact on investment. And it's very important that the FDA is supported and has sufficient funding."

Another biopharmaceutical CVC representative explained the importance of the FDA keeping pace with the latest scientific developments through its review and approval process: "[C]ertain policy decisions from the FDA in certain therapeutic areas, particularly oncology, were beneficial—things like breakthrough designation and increasing use of fast track to show that it's possible to be able to get drugs approved with data that may be less than the traditional double blind randomized clinical trial."

As another biopharmaceutical CVC representatives explained, "[i]f the regulatory environment was seen as getting increasingly restrictive in terms of what's being required to get drugs approved, the probability of success starts to go even lower to be able to get drugs approved through certain divisions."

Coverage and payment policies that value and support the use of new medicines

Bringing new medicines to improve the lives of patients is not guaranteed upon FDA approval. As one biopharmaceutical CVC representative explained: "So, without having some kind of reimbursement for the innovation, if we don't have it, venture capital investment will dry out and stop." Often the process to get a new medicine reimbursed can be burdensome and uncertain. The chilling effects posed by current reimbursement approaches was explained by a member of the National Venture Capital Association in Congressional testimony for the 21st Century Cures Act:

"After our companies have worked through the costly and timely process of receiving FDA approval, they then must set their sights on securing coverage and reimbursement. This is an equally complex and unpredictable process which can add another three to five years to the development of a product. This means three to five more years before patients can actually benefit from a new

product and before the company can generate a meaningful revenue stream … The overall process of obtaining coverage and reimbursement represents a classic 'chicken and the egg' dilemma for the investment community. On the one hand, payors want to see more data and diffusion of a new technology until they agree to provide coverage for it. On the other, physicians and hospitals will not agree to use the product unless they get paid. Equally challenging, the data and utilization requirements are ambiguous at best."[37]

Biopharmaceutical investment, like the research and development process itself, is a risky endeavor and the outcomes are uncertain. While biopharmaceutical venture capital investing has been on the rise, with PhRMA-member CVCs playing an increasingly important role, it is important to not be complacent. Ensuring a regulatory and policy environment that protects intellectual property, reduces regulatory uncertainty, and fosters a coverage and payment system that values and supports new medicines is key to attracting robust investments in biopharmaceuticals and addressing today's most challenging diseases and meeting the needs of patients.

Endnotes

1 PhRMA members include: AbbVie, Alexion Pharmaceuticals, Inc., Alkermes plc., Allergan plc, Amgen Inc., Astellas Americas, AstraZeneca Pharmaceuticals LP, Bayer Corporation, Biogen, BioMarin Pharmaceutical Inc., Boehringer Ingelheim Pharmaceuticals, Inc., Bristol-Myers Squibb Company, Celgene Corporation, Daiichi Sankyo, Inc., Eisai Inc., Eli Lilly and Company, EMD Serono, GlaxoSmithKline, Incyte Corporation, Ipsen Biopharmaceuticals, Inc., Johnson & Johnson, Lundbeck Inc., Merck & Co., Inc., Merck Human Health Division - U.S. Human Health, Merck Research Laboratories, Merck Vaccine Division, Novartis Pharmaceuticals Corporation, Novo Nordisk Inc., Otsuka America Pharmaceutical, Inc. (OAPI), Otsuka Maryland Medicinal Laboratories (OMML), Otsuka Pharmaceutical Development & Commercialization, Inc. (OPDC), Pfizer Inc., Purdue Pharma L.P., Sanofi, Sanofi Pasteur, Sunovion Pharmaceuticals Inc., Takeda Pharmaceuticals USA, Inc., Teva US Specialty Medicines, and UCB.

2 Kauffman Foundation (2016). Basu, Benson and Dushnitsky (contributors), "Corporate Venture Capital: State of the Field," September 19, 2016, page 1. https://www.kauffman.org/microsites/state-of-the-field/topics/finance/equity/corporate-venture-capital.

3 Boston Consulting Group (2012). "Corporate Venture Capital: Avoid the Risk, Miss the Rewards," October 2012, page 16. https://www.bcg.com/documents/file120517.pdf.

4 EY (2009), Global Corporate Venture Capital Survey, 2008-2009, page 6. https://www.ey.com/Publication/vwLUAssets/SGM_VC_Global_corporate_survey_2008_2009/%24FILE/SGM_VC_Global_corporate_survey_2008_2009.pdf

5 Drover, et al (2017), "A Review and Road Map of Entrepreneurial Equity Financing Research: Venture Capital, Corporate Venture Capital, Angel Investment, Crowdfunding and Accelerators," Journal of Management, July 2017. https://www.scribd.com/document/382226010/A-Review-and-Road-Map-of-Entrepreneurial-Equity-Financing-Research-Venture-Capital-Corporate-Venture-Capital-Angel-Investment-Crowdfunding-and-Ac

6 The 15 PhRMA-member CVCs that were active and made U.S. investments during the 2000 2017 period captured in PitchBook include: AbbVie Ventures, Amgen Ventures, Astellas Venture Management, Boehringer Ingelheim Venture Fund, Johnson & Johnson Innovation – JJDC, Inc., Lilly Ventures, MedImmune Ventures, Merck Capital Ventures, Merck Global Health Innovation Fund, Merck Ventures (EMD Serono), Novartis Venture Fund, Pfizer Venture Investments, Sanofi Ventures, SR One (GSK), and Takeda Ventures.

7 Adis R&D Insight Database. Accessed June 2018.

8 TEConomy Partners (2017). The Economic Impact of the U.S. Biopharmaceutical Industry: 2015 National and State Estimates. http://phrma-docs.phrma.org/sites/default/files/pdf/biopharmaceuticaul-industry-economic-impact.pdf

9 TEConomy Partners (2016). Seizing a New Era of Medical Discovery: How Policymakers Can Embrace Practical Ideas that Help Lead to New Treatments and Cures, Forum on Medical Discovery. http://forumonmedicaldiscovery.org/wp-content/uploads/2016/07/Seizing-a-New-Era-of-Medical-Discovery-How-Policymakers-Can-Embrace-Practical-Ideas-that-Help-Lead-to-New-Treatments-and-Cures.pdf.

10 PhRMA (2018) 2018 PhRMA Annual Membership Survey. https://www.phrma.org/report/2018-phrma-annual-membership-survey

11 Research!America (2017). U.S. Investments in Medical and Health Research and Development 2013 – 2016. https://www.researchamerica.org/sites/default/files/RA-2017_InvestmentReport.pdf.

12 National Science Foundation, Business R&D and Innovation Survey, 2016. Data Table 2.

13 DiMasi JA, Grabowski HG, Hansen RA (2016). "Innovation in the pharmaceutical industry: new estimates of R&D costs." Journal of Health Economics, 47:20-33.

14 Ibid.

15 Tufts Center for the Study of Drug Development (2018). "Rising protocol complexity is hindering study performance, cost, and efficiency: Impact Report," July 17, 2018.

16 McKinsey & Company (2010). Pharmaceuticals and Medical Products. David et al, "New Frontiers in Pharma R&D Investment," February 2010.

17 McKinsey & Company (2017). "Innovating at the Speed of the 21st Century in Pharmaceuticals: Edited Summary of Discussion with David A. Ricks, Chairman and CEO of Eli Lilly," Elling and Tinkoff, November 2017.

18 BioLink Direct (2017). "The Role of Venture Capital in Biotech," June 20, 2017. See http://biolinkdirect.com/role-venture-capital-biotech-industry/

19 PitchBook, calculations by TEConomy Partners, LLC.

20 EY (2017). Biotechnology Report 2017: Staying the Course, page 54. https://www.ey.com/Publication/vwLUAssets/ey-biotechnology-report-2017-beyond-borders-staying-the-course/%24File/ey-biotechnology-report-2017-beyond-borders-staying-the-course.pdf

21 Von Krogh, et. al. (2012), "The Changing Face of Corporate Venturing in Biotechnology," Nature Biotechnology, Volume 30 Number 10. https://www.nature.com/articles/nbt.2383.

22 Ford and Nelsen (2013). "The View Beyond Venture Capital," Nature Biotechnology, December 19, 2013, page 4. https://www.nature.com/bioent/2013/131201/full/bioe.2013.15.html.

23 Osborne, R. (2018). "Pfizer Catalyzer? Pharma VC Board Seat More Good than Bad, 'Firsthand Look'," Bioworld, September 5, 2018. http://www.bioworld.com/content/pfizer-catalyzer-pharma-vc-board-seat-more-good-bad-firsthand-look-0.

24 Ioannou, L. (2018). "Big Pharma's Billion-Dollar Scramble to Invest in Start-Ups to Fuel Innovation," CNBC, March 18. https://www.cnbc.com/2018/03/26/big-pharmas-scramble-to-invest-in-start-ups-to-fuel-innovation.html

25 Pfizer, Inc. (2018). Pfizer to Expand Venture Investing with $600 Million Commitment to Pfizer Ventures. See https://www.pfizer.com/news/press-release/press-release-detail/pfizer_to_expand_venture_investing_with_600_million_commitment_to_pfizer_ventures-0

26 Ford and Nelson, op. cit., page 1.

27 Von Krogh, et al., op. cit., page 1.

28 EY, op. cit., page 52

29 In this context, the term "biopharmaceutical" refers to the Pharmaceutical and Biotechnology Industry Code within PitchBook.

30 Randy Osborne, op. cit., page 2.

31 See, for instance, Sam Marwaha et al., Biopharma in the Coming Era of 'Connected Health,' McKinsey on Business Technology, Number 26, Spring 2012, pg. 17.

32 EY, op. cit., page 15.

33 These two verticals are specified industry categories within PitchBook. Within these categories PitchBook may classify a single company in both verticals.

34 TEConomy Partners (2017), The Economic Impact of the U.S. Biopharmaceutical Industry: 2015 National and State Estimates.

35 Knowledge@Wharton (2016), "For Innovation Success, Choose a Corporate VC," transcript of a podcast interview with Gary Dushnitsky, a senior fellow at Wharton's Mack Institute for Innovation Management and a professor at the London Business School, January 19, 2016.

36 Von Krogh, op. cit., page 1.

37 Mike Carusi, Testimony before Subcommittee on Health, House Committee on Energy and Commerce, June 11, 2014. https://nvca.org/wp-content/uploads/2016/12/Mike-Carusi-testimony-CEC-Hearing-June-11-2014.pdf


TECONOMY
PARTNERS LLC