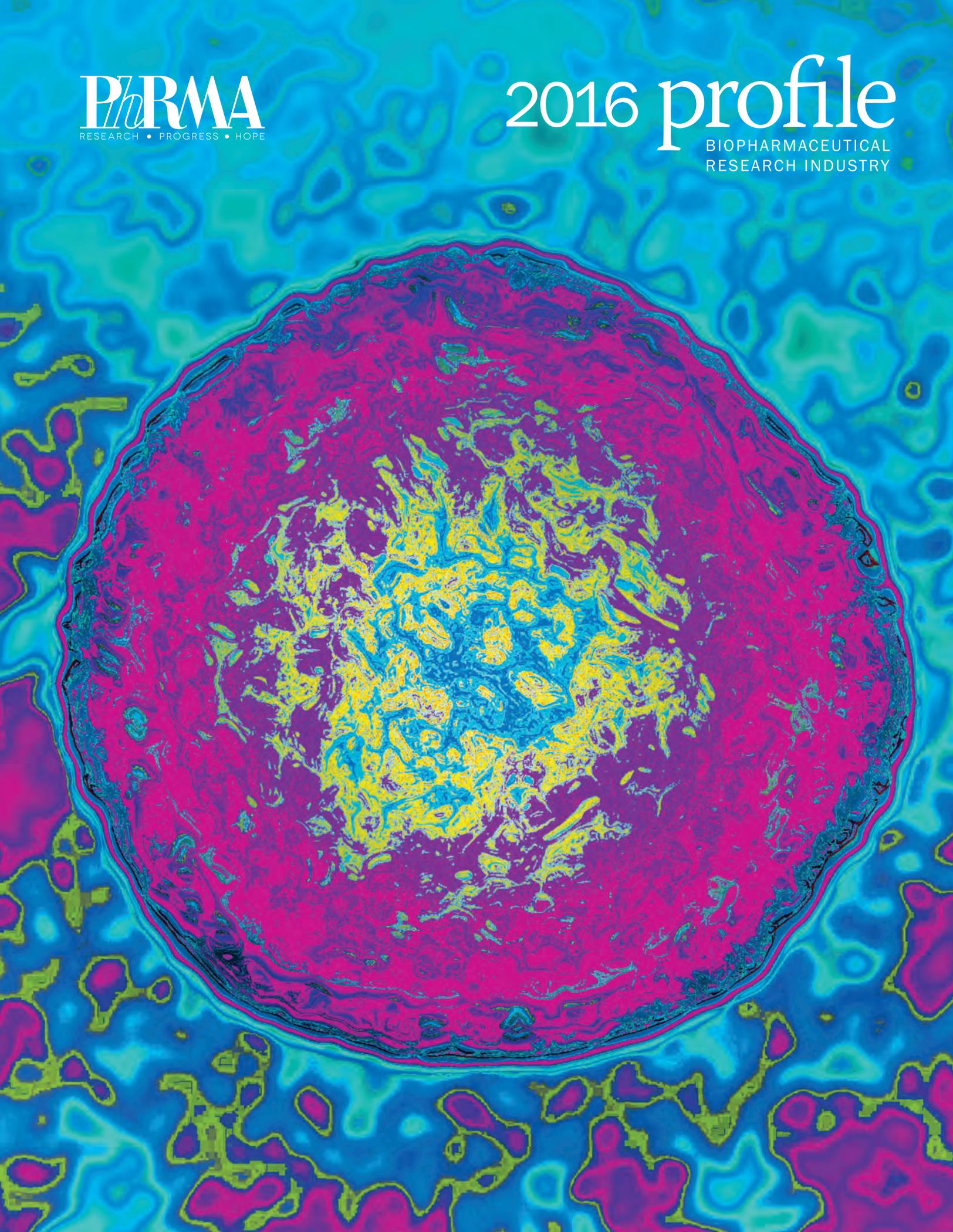


**PhARMA**  
RESEARCH • PROGRESS • HOPE

# 2016 profile

BIOPHARMACEUTICAL  
RESEARCH INDUSTRY



# Key Facts 2016

## RESEARCH AND DEVELOPMENT (R&D)<sup>1</sup>

Average time to develop a drug = **10 to 15 years**

Percentage of drugs entering clinical trials resulting in an approved medicine = less than **12%**

## PERCENTAGE OF SALES THAT WENT TO R&D IN 2015<sup>5</sup>

Domestic R&D as a percentage of domestic sales = **24.8%**

Total R&D as a percentage of total sales = **19.8%**

## MEDICINES IN DEVELOPMENT

Medicines in development globally = **7,000**<sup>14</sup>

Potential first-in-class medicines\*\* across the pipeline = an average of **70%**<sup>15</sup>

Medicines in development to treat rare diseases = more than **450**<sup>16</sup>

## DEVELOPMENT COSTS

Average cost to develop a drug (including the cost of failures):<sup>2</sup>

2000s–early 2010s = **\$2.6 billion**

1990s–early 2000s = **\$1.0 billion\***

1980s = **\$413 million**

1970s = **\$179 million**

## ECONOMIC IMPACT OF THE BIOPHARMACEUTICAL SECTOR<sup>6</sup>

Direct jobs = about **854,000**

Total jobs (including indirect and induced jobs) = more than **4.4 million**

## VALUE OF MEDICINES

**Cancer:** Since peaking in the 1990s, cancer death rates have declined **23%**.<sup>17</sup> Approximately **83%** of survival gains in cancer are attributable to new treatments, including medicines.<sup>18</sup>

**Hepatitis C:** Just five years ago, treatment options for hepatitis C came with debilitating side effects and cured only half of patients over a course of treatment lasting up to 48 weeks.<sup>19</sup> Today, a range of treatment options are available offering cure rates upwards of **90%**, with minimal side effects, in as few as 8 weeks.<sup>20</sup>

**HIV/AIDS:** Since the introduction of highly active antiretroviral treatment (HAART), the HIV/AIDS death rate has dropped **87%**.<sup>21</sup> As a result of HAART and all the medical innovations that followed, it is estimated that **862,000** premature deaths were avoided in the United States alone.<sup>22</sup>

## R&D SPENDING

Year	PhRMA members <sup>3</sup>
2015	\$58.8 billion (est.)
2014	\$53.3 billion
2013	\$51.6 billion
2012	\$49.6 billion
2011	\$48.6 billion
2010	\$50.7 billion
2009	\$46.4 billion
2008	\$47.4 billion
2007	\$47.9 billion
2006	\$43.0 billion
2005	\$39.9 billion
2000	\$26.0 billion
1990	\$8.4 billion
1980	\$2.0 billion



## APPROVALS

Novel medicines approved 2015 = **56**<sup>7,8</sup>

Medicines approved since 2000 = more than **550**<sup>9,10,11</sup>

In the 30 years since the Orphan Drug Act was established, more than **500** orphan drugs have been approved, with nearly **300** approved in the last decade alone<sup>12</sup>

Only **2 of 10** marketed drugs return revenues that match or exceed R&D costs<sup>13</sup>

## SALES

Generic share of prescriptions filled:<sup>4</sup>

2000 = **49%**

2015 = **91%**



<sup>1</sup>Previous research by the same author estimated average R&D costs in the early 2000s at \$1.2 billion in constant 2000 dollars [see DiMasi JA, Grabowski HG. The cost of biopharmaceutical R&D: Is biotech different? *Managerial and Decision Economics*. 2007;28:469–479]. That estimate was based on the same underlying survey as the author's estimates for the 1990s to early 2000s reported here (\$800 million in constant 2000 dollars), but updated for changes in the cost of capital.

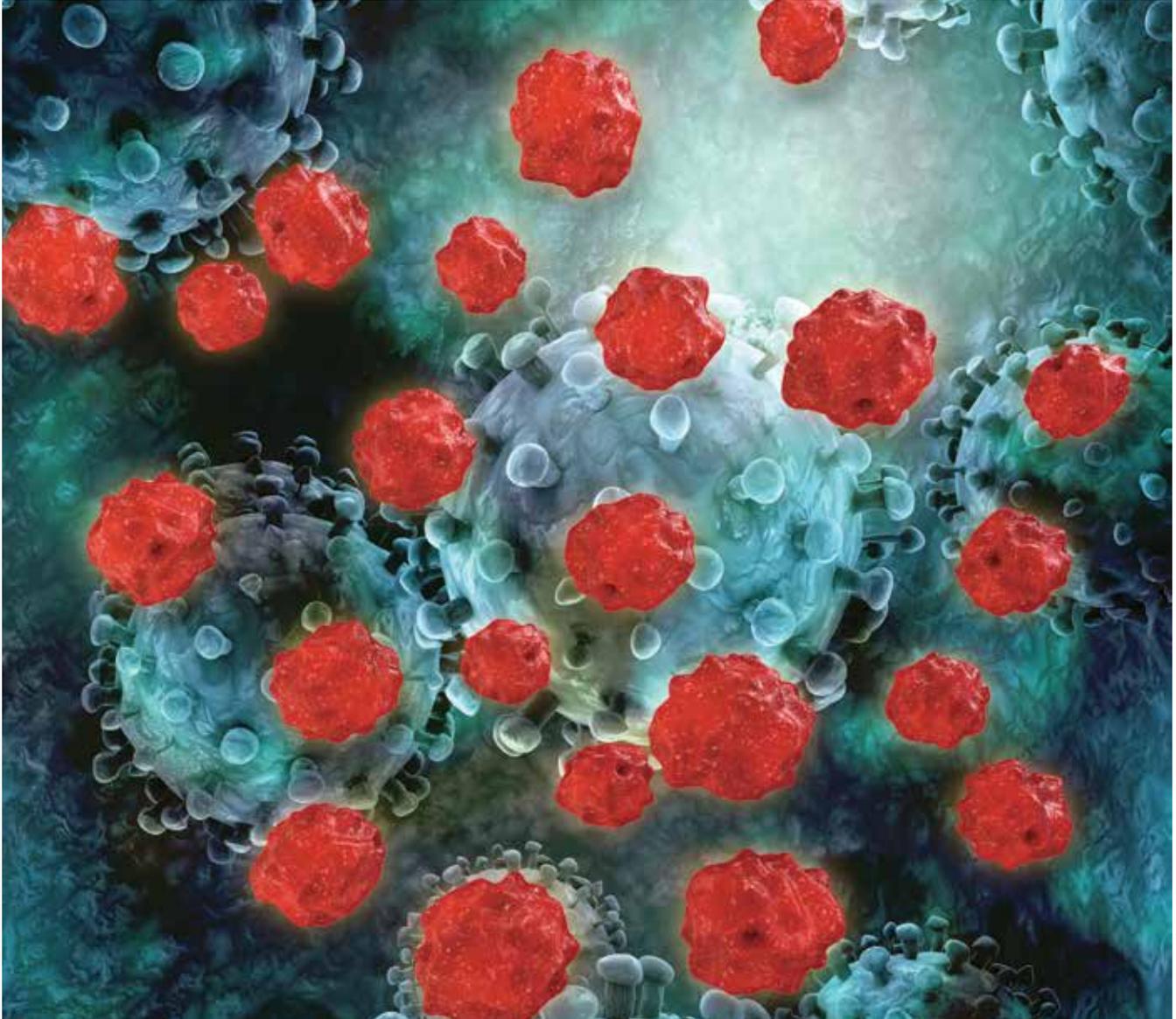
<sup>2</sup>Note: First-in-class medicines are those that use a different mechanism of action from any other already approved medicine.



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# PhRMA

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Pharmaceutical Research and Manufacturers of America.

2016 biopharmaceutical research industry profile.

Washington, DC: PhRMA; April 2016.

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Cover image: Hepatitis C Virus (HCV)

# President and CEO's Introduction to the 2016 Profile



The biopharmaceutical industry is at a pivotal time in medical discovery, which has enormous potential to further revolutionize the treatment of costly and debilitating diseases like

Alzheimer's, cancer, heart disease, and hepatitis C. Our ability to harness recent scientific advances continues to accelerate, and the potential benefits to patients are becoming clearer.

Much of this progress is attributed to a deeper, molecular-level understanding of all different kinds of disease. More than 7,000 medicines are in clinical development around the world right now—more than there have ever been—and 70% of medicines have the potential to be first-in-class therapies. From 2000 to 2015, this pipeline spawned more than 550 new medicines that were approved by the US Food and Drug Administration (FDA).

This progress is generating a ripple effect across the entire health care system and the *2016 Biopharmaceutical Research Industry Profile* details a US business sector delivering greater value than ever before by:

- **Transforming Patients' Lives:** Decades of promise and progress are now paying off in new medicines that cure 90% of treated hepatitis C patients, help increase survival

rates across cancer and other disease groups, and turn previously acute fatal diagnoses like HIV/AIDS into manageable chronic conditions (*see Chapter 1*).

- **Lowering Projected Health Care Costs:** New medicines continue to help avoid costly hospitalizations and expensive surgeries—arguably delivering greater value than any other component of the US health care system (*see Chapter 2*).
- **Strengthening the US Economy:** The biopharmaceutical industry supports the hard work of more than 4.4 million American workers—about 854,000 of them directly. The economic output from these jobs was valued at more than \$1.2 trillion in 2014, and their pioneering work is exported around the globe, helping keep America ahead of its economic competitors (*see Chapter 3*).
- **Helping Improve the Drug Review and Approval Process:** Biopharmaceutical companies are exploring ways to incorporate robust, science-based understanding of patient perspectives into decisions that promote innovation and the drug development process (*see Chapter 4*).
- **Investing For the Long Term:** PhRMA members are making greater research and development investments than at any other time in the industry's history, investing more than \$58.8 billion in 2015 alone (*see Chapter 5*).

The biopharmaceutical industry, government, and other stakeholders can extend this progress in 2016 and beyond by working collaboratively to:

- **Modernize the Drug Discovery and Development Process:** Pro-patient, pro-science, pro-market reforms at the FDA would enhance competition, drive greater efficiency in drug development and discovery, and help hold down costs.
- **Promote Value-Driven Health Care:** Regulatory barriers impede open communication by manufacturers, predictability regarding the biopharmaceutical pipeline, and innovative contracting. Value-driven payment for prescription medicines can promote efficiency and affordability by ensuring that more patients receive the best treatment the first time around.
- **Engage and Empower Consumers:** We need to make more information on health care out-of-pocket costs and quality available to patients. In addition, vulnerable patients should have the protection of enforceable, commonsense rules that prevent discrimination and remove barriers to access.

- **Address Market Distortions:** The 340B Drug Pricing program and the risk adjuster for commercial insurance that does not account for prescription drug costs are just two programs requiring reform to help preserve the safety net, revive the health care market, and improve affordable access to medicines for patients.

As the burden of chronic disease continues to grow, these treatment advances, and those to come, will continue to play a central role in alleviating the burden for patients and caregivers, as well as the health care system. We owe it to America's patients to continue this progress, underscoring the need to maintain a robust ecosystem that fosters and encourages the development of tomorrow's treatments and cures.

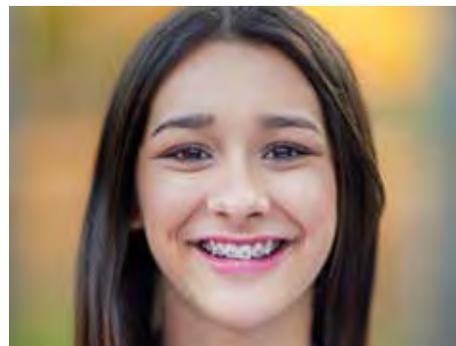
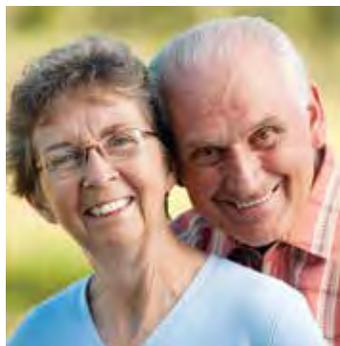


**Stephen J. Ubl**

President and Chief Executive Officer

Pharmaceutical Research and Manufacturers of America

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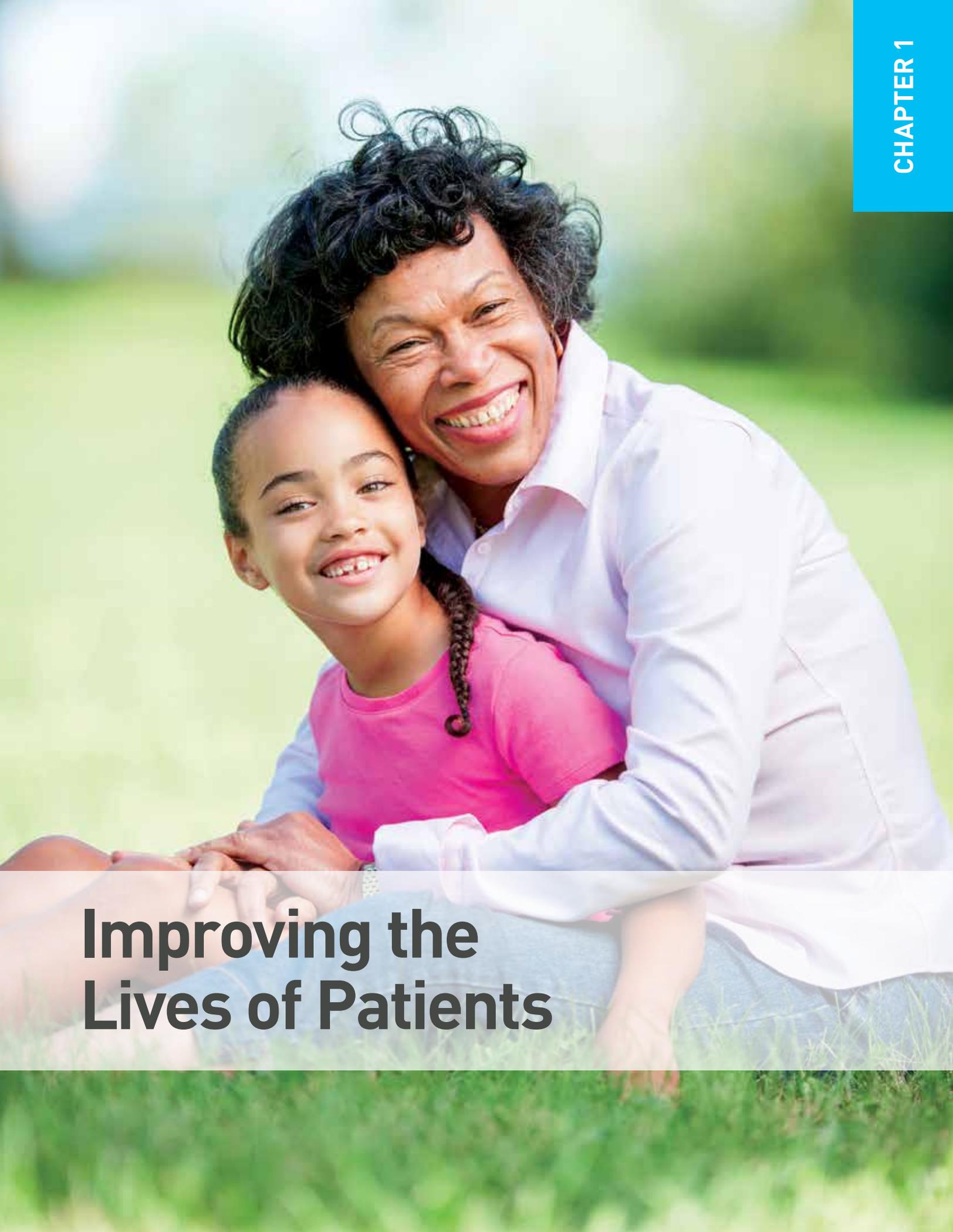
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A photograph of a woman with dark, curly hair and a young girl sitting on a grassy field. The woman is wearing a white long-sleeved shirt and has her arms around the girl, who is wearing a pink shirt. Both are smiling warmly at the camera. The background is a soft-focus green field.

# Improving the Lives of Patients

# Improving the Lives of Patients



In recent years, many new treatment options have emerged that are having a profound impact on the lives of patients. Many of these advances transform what were once considered fatal illnesses into manageable conditions and, in some cases, may even cure a disease. Often new medicines fill an important unmet need or provide an effective alternative where there previously were none. Many recent advances also facilitate adherence to treatment, halt disease progression, and help prevent serious

complications, thus enabling patients to live longer, healthier lives.

Last year was an exceptionally strong year for biopharmaceutical innovation. The US Food and Drug Administration (FDA) approved 56 new medicines, including 45 new medicines approved by the Center for Drug Evaluation and Research (CDER)—the highest number of approvals in almost two decades, giving patients even greater hope for the future (see Figure 1).<sup>1,2</sup>

Among CDER's approvals, 36% were first-in-class medicines, representing entirely new ways of treating disease.<sup>3</sup> This incredible progress reflects a harnessing of scientific breakthroughs and our improved understanding of today's most complex and challenging diseases.

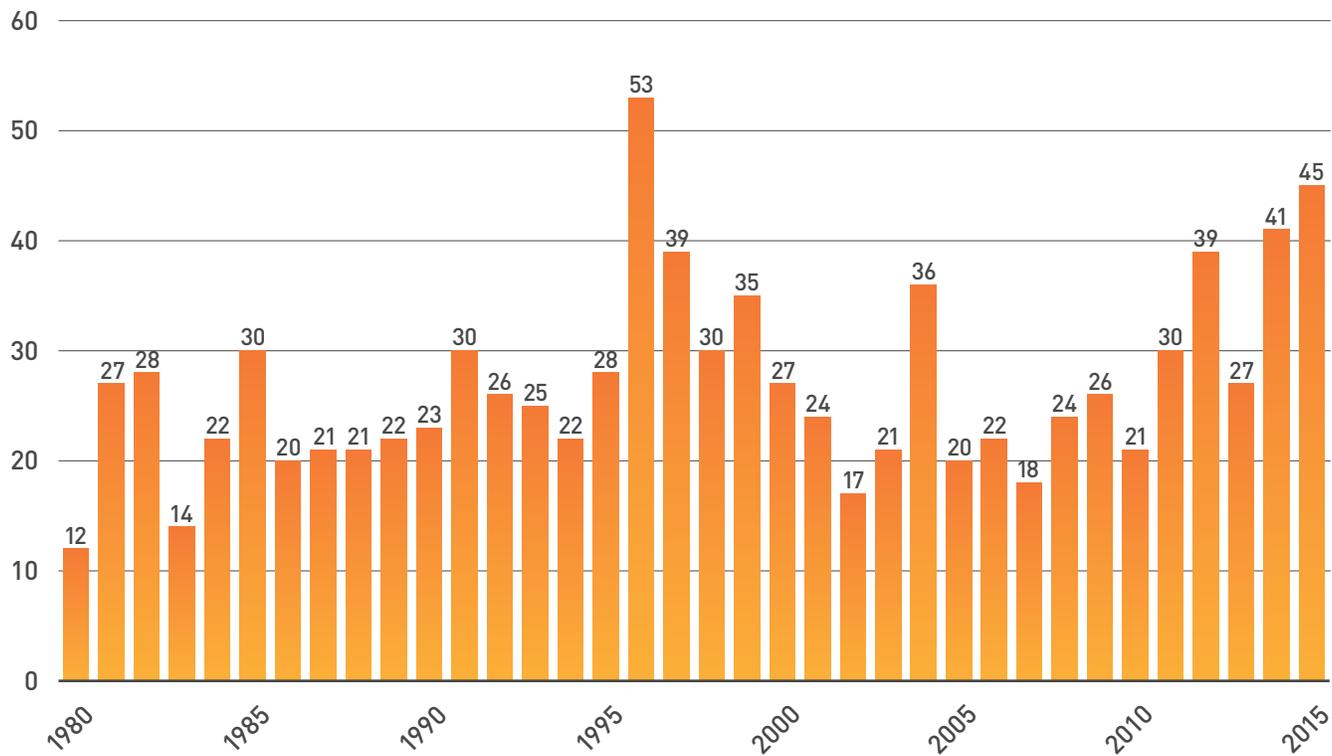
In 2015, novel therapies were approved across a broad range of disease areas. A few examples of important new treatment options brought to patients this year include:

**Advanced Melanoma:** Two new medicines for the treatment of melanoma—the most aggressive and deadly form of skin cancer—became available to patients. One of these treatments, a personalized



medicine approved for use in combination with another targeted therapy, prevents and slows cancer cell growth in melanoma patients who have a specific genetic abnormality. The other medicine is the first FDA-approved oncolytic virus therapy. This medicine uses a genetically modified herpes virus and is injected directly into

**FIGURE 1: FDA Approved Medicines\***



\*Medicines approved by the FDA's Center for Drug Evaluation and Research (CDER).

Sources: US Food and Drug Administration. Summary of NDA approvals and receipts, 1938 to the present. <http://www.fda.gov/aboutfda/whatwedo/history/productregulation/summaryofndaapprovalsreceipts1938tothepresent/default.htm>. Published January 18, 2013. Accessed March 2016; US Food and Drug Administration. New drugs at FDA: CDER's new molecular entities and new therapeutic biological products. <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugInnovation/ucm20025676.htm>. Updated February 8, 2016. Accessed March 2016.

melanoma lesions, where it replicates inside cancer cells and causes the cancer cells to rupture and die.<sup>4,5</sup>

**Asthma:** A new drug to treat asthma in patients with a history of severe asthma attacks despite previously receiving other treatments is now available. The new medicine limits severe asthma attacks by reducing the levels of blood eosinophils—a type of white blood cell that contributes to the development of asthma. The therapy offers an important new treatment option to the more than 22 million people in the United States with asthma, a condition which causes debilitating inflammation in the airways of the lungs.<sup>6</sup>



**Diabetes:** A brand new type of long-acting insulin became available for patients with either type 1 or type 2 diabetes. The insulin provides patients with up to 42 hours of activity, significantly longer than previously available long-acting insulins, and it can be administered at any point during the day, reducing the burden associated with daily injections.<sup>7,8</sup> Only half of patients treated for diabetes have control of their disease. New

medicines that decrease the complexity of treatment and support patient adherence represent important advancements for these patients.<sup>9</sup>

**Schizophrenia/Bipolar Disorder:** Access to a broad range of treatment options and dosage forms is important for patients struggling with mental health disorders because the effects of medications can vary among patients. Two new treatments were approved in 2015 for mental health disorders. One is an oral medicine used to treat both schizophrenia and bipolar disorder, and one is an injected medicine for patients with schizophrenia that has once-monthly and six-week dosing options. The dose variations of this new treatment provide greater flexibility to patients with this debilitating illness as well as for the family members and health care professionals who are involved in their care.<sup>10,11,12</sup>

**High Cholesterol:** Two new medicines from a new class of cholesterol-lowering therapies, called pro-protein convertase subtilisin kexin type 9 (PCSK9) inhibitors, became available for patients with difficult-to-treat forms of high cholesterol. The self-injected medicines inhibit a protein that reduces the liver's ability to break down cholesterol. These medicines are approved for use in combination with a special diet and statin therapy in adults with a genetic condition known as familial hypercholesterolemia (FH) or patients with clinical atherosclerotic cardiovascular disease who require additional lowering of cholesterol. Patients with FH have cholesterol levels that range as much as 2 to 5 times greater than those of a healthy individual.<sup>13,14</sup> This new class of medicines has been shown to lower cholesterol levels by as much as 60%.<sup>15,16</sup>



**Cardiovascular Disease:** Two new medicines for the treatment of heart failure became available to patients in 2015. Heart failure is the most common diagnosis among elderly Medicare patients and the primary cause of hospital readmission within 60 days of discharge.<sup>17</sup> The condition affects 5.1 million Americans and is a leading cause of death and disability. One medicine was approved to reduce hospitalizations in patients with worsening heart failure.<sup>18</sup> The second medication has been shown to reduce the rate of cardiovascular death and heart failure-related hospitalizations in patients with the condition.<sup>19</sup>

**Rare Diseases:** Nearly half of all medicines approved in 2015 were for rare conditions, which affect 200,000 or fewer people in the United

States. This is noteworthy, given over the last 5 years an average of more than 35% of novel FDA drug approvals were medicines treating rare diseases.<sup>20</sup> Many of these medicines were approved for pediatric patients (see sidebar: Providing Treatments for Pediatric Patients with Rare Diseases).<sup>21</sup>

Below are a few examples of novel orphan drug approvals:

- **Multiple Myeloma:** Four new treatments became available to patients this year, including two first-in-class medicines. Multiple myeloma is a rare form of bone marrow cancer that occurs in infection-fighting white blood cells. The first-in-class medicines work through different

mechanisms to help activate the body's own immune system to attack the cancerous cells and have showed significant clinical impact by reducing the size of tumors.<sup>22,23,24</sup>

- **Cystic Fibrosis:** A first-in-class treatment became available for patients with the mutation F508del, which is known to be the

most common cause of cystic fibrosis.<sup>25</sup> Great advances have been made in recent years in the treatment of cystic fibrosis in highly targeted patient populations based on the genetic mutation that causes their disease. These treatments target the underlying cause of the disease rather than just the symptoms.<sup>26</sup>

## PROVIDING TREATMENTS FOR PEDIATRIC PATIENTS WITH RARE DISEASES

FDA approved several new medicines for pediatric patients in 2015, including many offering treatment options for conditions that previously had few or no options.

The first therapy for the treatment of a rare, progressive, metabolic disease called **hypophosphatasia (HPP)** was approved.<sup>27</sup> In its most severe form, this genetic condition affects 1 in 100,000 newborns and is characterized by defective bone mineralization that can lead to softening of the bones and skeletal abnormalities. HPP patients who took this new medicine had improved survival and also demonstrated improvements in bone growth and health.

Another notable pediatric advance was the approval of a new treatment for children with high-risk **neuroblastoma**, a rare form of cancer that occurs in nerve tissue, often starting in nerve cells located in the adrenal glands, abdomen, spine, or pelvis. CDER's Office of Hematology and Oncology Products noted that the medicine "fulfills a critical need by providing a treatment option that prolongs survival in children with high-risk neuroblastoma."<sup>28</sup>

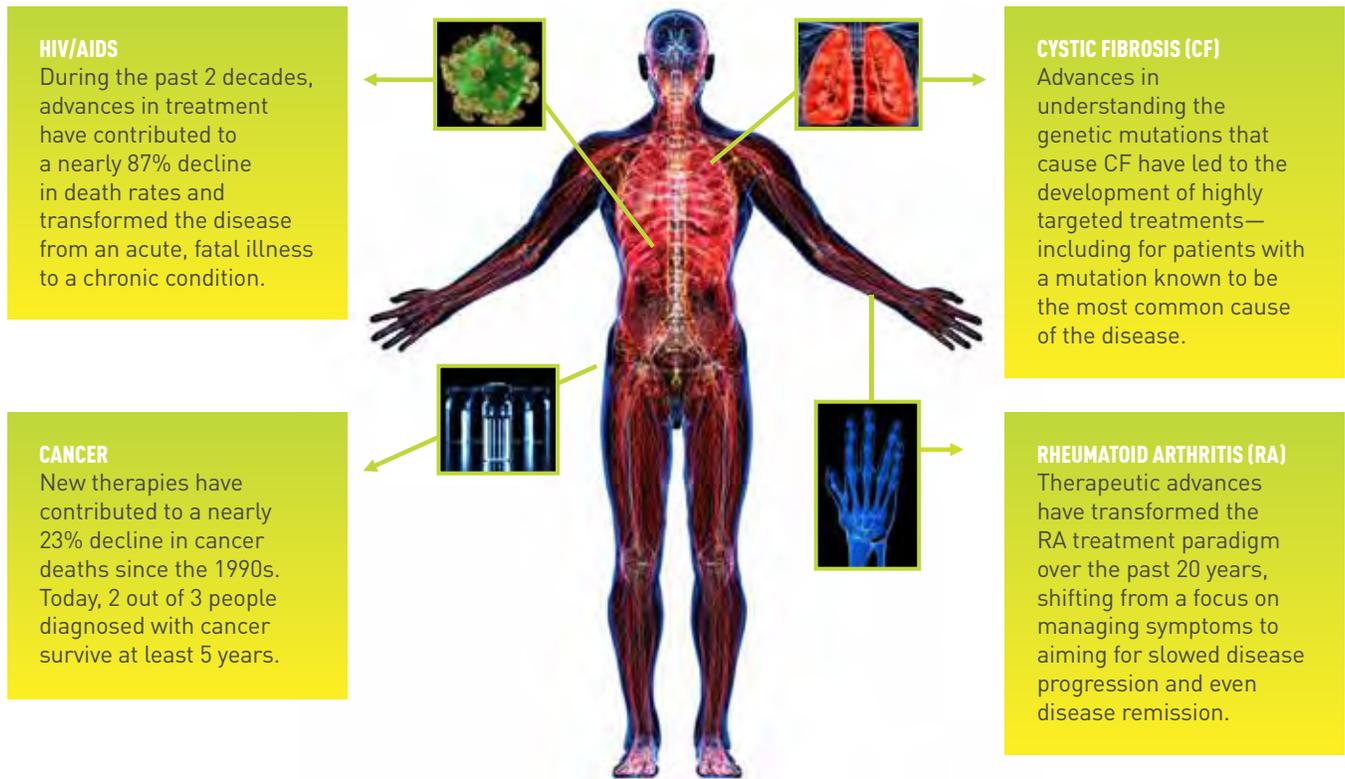
The first therapy for the treatment of a rare inherited genetic disease called **lysosomal acid lipase (LAL) deficiency** was approved.<sup>29</sup> Patients with LAL deficiency have little or no activity of an enzyme that breaks up fatty material in cells. Disruption of this breakdown process results in the buildup of fats in important organs and leads to liver and cardiovascular disease. LAL often appears during infancy and progresses rapidly. The new medicine helps replace and replenish the deficient enzyme.

FDA granted approval for the first treatment ever for an ultra-rare, inherited metabolic disease called **hereditary orotic aciduria (HOA)**.<sup>30</sup> Patients with HOA are deficient in an enzyme that is necessary for producing uridine, which reduces their ability to produce ribonucleic acid. Characteristics or symptoms of the disease include developmental delays, failure to thrive, blood abnormalities, and urinary tract obstructions. This new medicine is intended to replace uridine and helps patients maintain stability across a variety of hematologic blood parameters.

**“These patients for the first time ever have access to a treatment that may improve their lives and chances of survival.”**

—JANET WOODCOCK, MD, DIRECTOR OF THE FDA'S CENTER FOR DRUG EVALUATION AND RESEARCH<sup>31</sup>

**FIGURE 2: Medicines Are Transforming the Treatment of Many Diseases**



Sources: US Food and Drug Administration (FDA). FDA approves new treatment for cystic fibrosis. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm453565.htm>. Published July 2, 2015. Accessed April 2016; Augustyn C, Walker B, Goss TF; Boston Healthcare Associates. Recognizing the value of innovation in the treatment of rheumatoid arthritis. <http://www.phrma.org/sites/default/files/pdf/BHARWhitepaperMarch2013.pdf>. Published March 2013. Accessed April 2016; National Institutes of Health (NIH), National Cancer Institute (NCI). Cancer statistics. <http://seer.cancer.gov/faststats/selections.php?#Output>. Accessed April 2016; American Cancer Society. Cancer treatment & survivorship facts & figures 2014-2015. <http://www.cancer.org/acs/groups/content/@research/documents/document/acspc-042801.pdf>. Published 2014. Accessed April 2016; Bastian BA; US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System. Deaths: final data for 2013. Natl Vital Statistics Rep. 2016;64(2). [http://origin.glb.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64\\_02.pdf](http://origin.glb.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64_02.pdf). Accessed April 2016.

## PROGRESS AGAINST DISEASE

Medicines are transforming care for patients fighting debilitating diseases like cancer, hepatitis C, cardiovascular disease, and more (see Figure 2). Here are just a few examples of the positive effects new and innovative therapies are having on patient care.

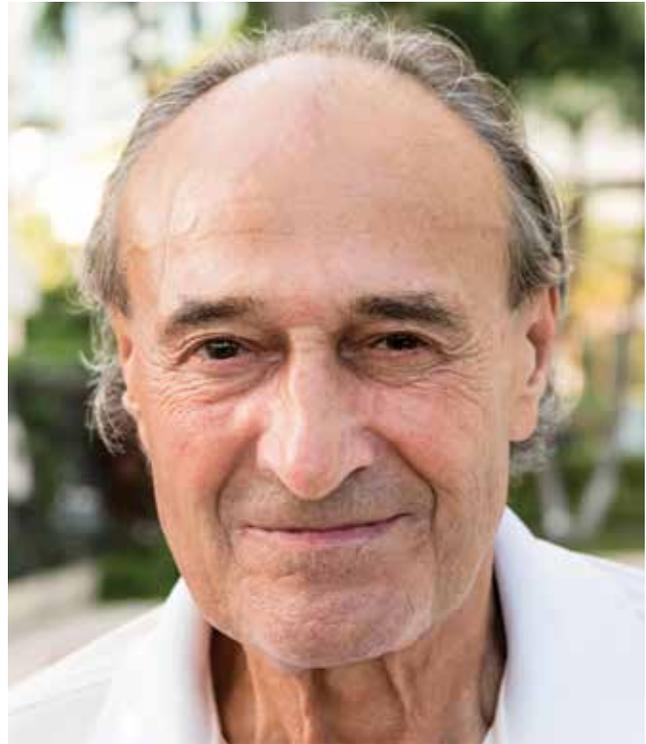
### Extending Lives

**Cardiovascular Disease (CVD):** Tremendous strides have been made in reducing CVD morbidity and mortality (see Figure 3). In the past decade, the death rate from heart disease has fallen about 38%, and the death rate from stroke has



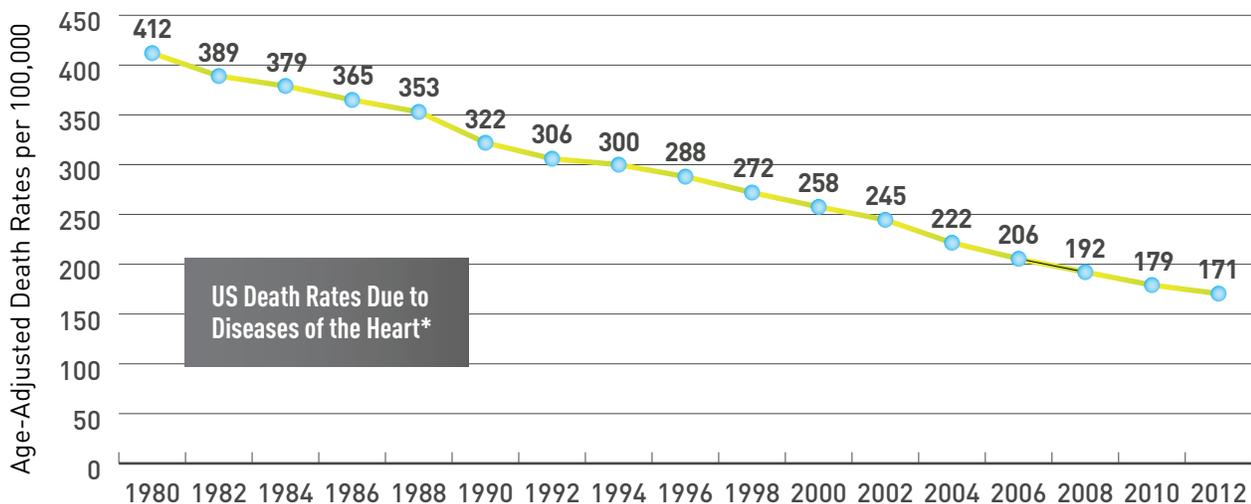
fallen about 34%.<sup>32</sup> Stroke, which was the third leading cause of death in Americans for more than 50 years, dropped to fourth in 2008 due in part to improvements in new drug treatments.<sup>33</sup> High cholesterol remains a leading cause of CVD. In 2007, Americans reached average cholesterol levels in the ideal range (below 200) for the first time in 50 years, due to increased use of cholesterol-lowering medicines by older Americans.<sup>34</sup> For more information on how new treatments are helping patients better manage their cholesterol, see sidebar: Advances in Treating High Cholesterol: Then and Now.

**Cancer:** New medicines are a driving force behind recent gains in the life expectancy of cancer patients. According to the American Cancer



**FIGURE 3: Cardiovascular Disease: Declining Rates of Death**

Tremendous strides have been made in reducing cardiovascular disease morbidity and mortality, thanks in part to new medicines. The death rate from heart disease has declined about 38% over the past decade alone.



\*Age-adjusted death rates based on Year 2000 US Standard Population. 1980-1998 causes of death are classified by the International Classification of Diseases, Ninth Revision (ICD-9). Beginning in 1999, causes of death have been classified by the International Classification of Diseases, Tenth Revision (ICD-10).

Sources: US Department of Health and Human Services (HHS), Centers for Disease Control and Prevention (CDC). Vital signs: avoidable deaths from heart disease, stroke, and hypertensive disease—United States, 2001-2010. *Morbidity & Mortality Weekly Rep.* 2013;62(35):721-727; CDC, National Center for Health Statistics (NCHS), National Vital Statistics System. Age-adjusted death rates for 72 selected causes by race and sex using year 2000 standard population: United States, 1979-98. <http://www.cdc.gov/nchs/data/mortab/aadr7998s.pdf>. Accessed April 2016; Xu J, Murphy SL, Kochanek KD, Bastian BA; US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System. Deaths: final data for 2013. *Natl Vital Statistics Rep.* 2016;64(2). [http://origin.glb.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64\\_02.pdf](http://origin.glb.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64_02.pdf). Accessed April 2016.

## ADVANCES IN TREATING HIGH CHOLESTEROL: THEN AND NOW<sup>35</sup>

The introduction of statin therapy nearly 30 years ago transformed treatment of high cholesterol for many patients. Yet, some continued to face challenges, including those with dangerously high cholesterol levels resulting from a genetic condition known as familial hypercholesterolemia (FH). Advances over the past decade have provided important new treatment options for these patients.

### Then

- In addition to diet and exercise, most patients were able to manage cholesterol with statin therapy, which offered patient cholesterol reductions ranging from 30% to 50%.
- Other cholesterol-lowering agents were also available to patients, which may have been used individually or as adjunctive therapy along with statins to achieve greater reductions in cholesterol levels.
- Some patients continued to struggle, particularly those with cholesterol levels ranging as high as two to five times greater than those of a healthy individual, which is often the case for individuals who have FH.

### Now

- Patients continue to benefit from the mainstays of treatment, including statins and other lipid-lowering agents.
- Patients with extremely high cholesterol levels—including individuals with FH—have four additional treatment options stemming from three entirely new classes of medicines, offering reductions in cholesterol ranging as high as 77%.
- There are 40 medicines currently in development to treat patients with high cholesterol, offering to further reduce substantial heart disease-related burden and mortality.

For more information about advances in treatment of chronic conditions like high cholesterol, visit <http://phrma.org/sites/default/files/pdf/decade-of-innovation-chronic-disease.pdf>

Society, the United States has witnessed a 23% decline in cancer deaths since the early 1990s, translating to 1.5 million lives saved, due in large part to early diagnosis and treatment advances. Today, two out of three people diagnosed with cancer survive for at least 5 years.<sup>36</sup>

Until the late 1990s, clinicians had three main treatment options available to fight cancer: surgery, radiation, and chemotherapy. In the last 2 decades, researchers have identified two new types of medicines, targeted therapies and immunotherapies, which are contributing greatly to improvements in treating many forms

of cancer.<sup>37</sup> According to the American Cancer Society, the most marked survival gains for cancer patients in recent decades have been in blood and lymphatic cancers; these gains are attributed to “improvements in treatment protocols, including the discovery of targeted therapies.” Of particular note are improvements in survival for acute lymphocytic leukemia (ALL).<sup>38</sup> The 5-year survival rate for ALL has increased from 41% in the mid-1970s to 70% between 2005 and 2011.<sup>39</sup> Another striking example of the advances made in blood cancer treatment is the survival rate for patients with chronic myeloid leukemia (CML). In 1999, only 30% of patients with CML survived for 5 years.

However, use of a new generation of targeted cancer medicines, known as tyrosine kinase inhibitors, has resulted in nearly 90% of CML patients living at least 5 years.<sup>40</sup>

### **Preventing Disease Complications**

**Hepatitis C (HCV):** Hepatitis C is a devastating, slowly progressing viral disease that can lead to serious complications, including cirrhosis, advanced liver disease, liver cancer, and in some cases, may cause patients to need a liver transplant.<sup>41</sup> Just 5 years ago, the only treatment available to patients with hepatitis C was a challenging course of interferon treatment over 24 to 48 weeks, which cured only half of patients and caused debilitating side effects.<sup>42</sup> Today, available treatment options offer cure rates over 90% in as little as 8 weeks, and patients with the most common form of the disease, as well as less common forms, can also choose from a range of oral treatments that do not require the use of interferon, allowing patients to avoid its accompanying side effects.<sup>43</sup> What's more, a study found that with current screening guidelines and the availability of today's treatments, HCV could become a rare disease in the United States by 2036. The same study estimated that 78,800 cases of liver cancer, 9,900 liver transplants, and 126,500 liver-related deaths could be avoided by 2050 with the availability of new and effective treatments for HCV.<sup>44</sup>

### **Preventing Unnecessary Hospitalizations**

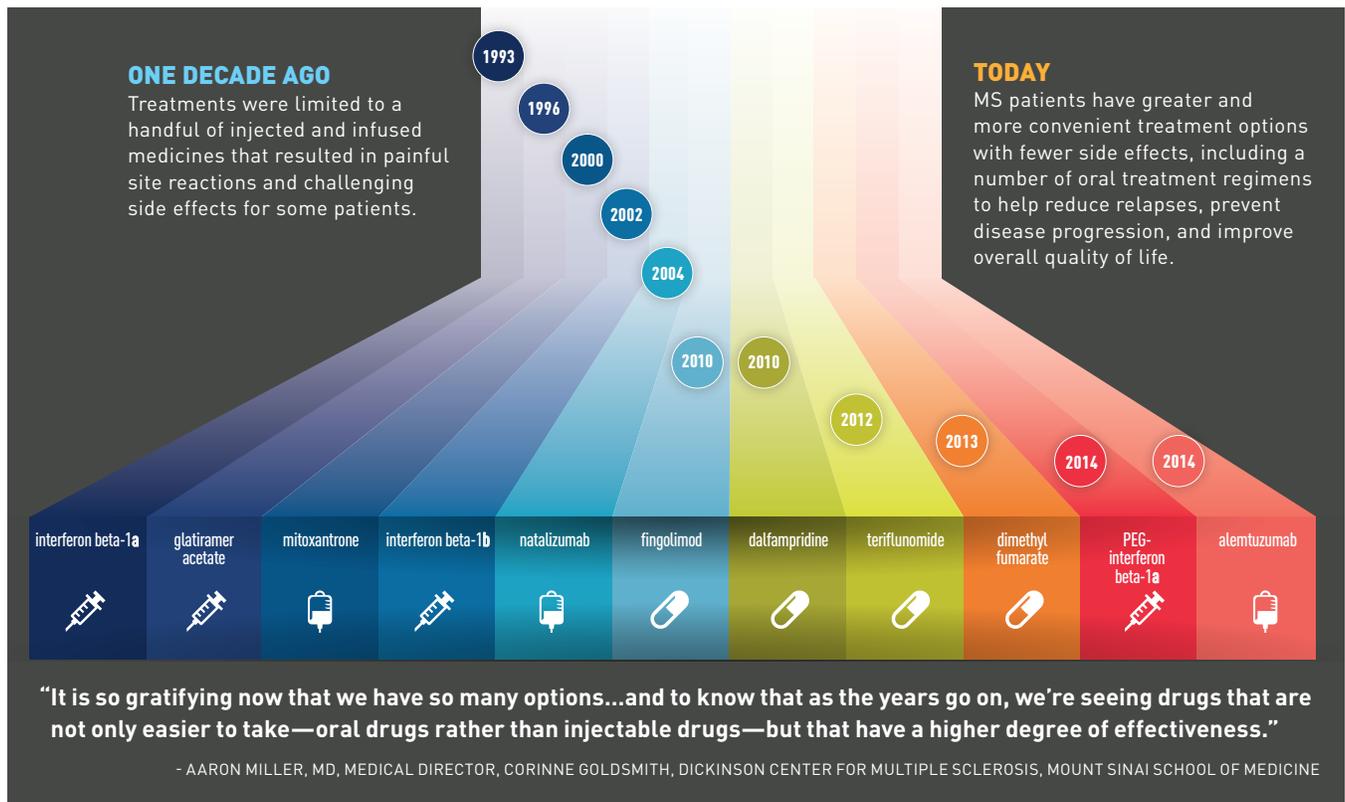
**Diabetes:** For many, diabetes requires constant monitoring, multiple daily insulin injections, coordination of multiple oral medicines, and a carefully planned daily routine to avoid serious disease complications, such as heart disease,

kidney failure, vision or hearing loss, and, in some situations, foot or leg amputation. Successful management of diabetes remains a lifelong challenge, and just half of patients treated have control of their disease.<sup>45</sup>



Advances in treating diabetes offer better or more sustained glycemic control, reduced pill burden, more convenient delivery mechanisms, less frequent injections, and simplified daily routines. These advances can have a significant impact on the lives of diabetes patients and can help to facilitate better adherence to treatment. Research demonstrates that diabetes patients who took their medicines as directed were able to avoid unnecessary hospitalizations. One study showed that improved adherence to diabetes medications was associated with a lower likelihood of subsequent hospitalizations or emergency department visits. Similarly the study found decreased adherence to these medicines is associated with a higher likelihood of hospitalizations and emergency department visits. Based on these findings, the study estimates that good adherence to prescribed diabetes treatment regimens could avoid 341,000 hospitalizations and 699,000 emergency department visits annually.<sup>46</sup>

**FIGURE 4: A Decade of Innovation in Multiple Sclerosis: Expanded Treatment Options Improve Outcomes for Patients**



Source: PhRMA. A decade of innovation in chronic diseases: 2006–2016. <http://phrma.org/sites/default/files/pdf/decade-of-innovation-chronic-disease.pdf>. Published 2016. Accessed March 2016.

### Improving Quality of Life

**Multiple Sclerosis (MS):** The number of treatment options for MS patients has expanded dramatically in recent years—including more convenient oral treatment options—to help patients not only prevent relapses and slow disease progression, but to more effectively manage disease symptoms and improve overall quality of life (see Figure 4). This is particularly valuable as different treatments can sometimes produce different effects in MS patients.<sup>47</sup>

The availability of medications that help to better manage the disease is remarkably valuable for MS patients suffering from diminished quality of life and significant work-related

impairments. Improvements in treatment are also incredibly valuable to society at large. In fact, productivity losses may constitute the largest portion of the societal burden attributed to MS with absenteeism, lost work hours, and early retirement accounting for 44% of the total



economic burden of the disease in the United States.<sup>48</sup> Treatment advances offering better overall disease management may help to prevent much of this burden.

## **THE NATURE OF MEDICAL PROGRESS**

We have made great progress in the fight against many diseases. The approval of a new medicine marks an important milestone providing tremendous benefits to patients. But many medicines go on to offer additional benefits that were not known at the time the medicine was initially approved. A full understanding of a medicine's benefits to patients evolves over time as researchers and clinicians continue to learn even more about a new medicine once it reaches patients and additional research is conducted post-approval. Often, a medicine is found to provide additional benefit when it is used earlier in the development of the disease, in combination with other medicines, or paired with a diagnostic test to better guide appropriate treatment. In addition, through continued research, a medicine may prove to be effective in other disease areas. This evolution of value over time is evident across a number of disease areas, including HIV/AIDS and rheumatoid arthritis, and has been particularly noticeable in many cancer treatments. For example, a targeted therapy for metastatic non-small lung cancer (crizotinib) was granted an accelerated approval by the FDA for patients with a particular genetic mutation after demonstrating that the treatment yielded significant tumor shrinkage. Two years later, the FDA updated the labeling to reflect the clinical benefit of crizotinib that had been revealed through ongoing studies: patients receiving the medicine experienced prolonged progression-free survival.<sup>49</sup>

Because of the life-threatening, progressive nature of cancer, investigational therapies in clinical trials are often tested first in patients with advanced stages of cancer who have exhausted existing standard treatment options. This creates a theoretical "ceiling" on the amount of clinical benefit that can usually be observed during initial clinical research. As additional testing is conducted following FDA approval, a therapy may demonstrate efficacy earlier in the course of treatment or stage of the disease. For example, bortezomib was initially approved to treat patients with multiple myeloma who had already received two prior therapies and were not responding. Ongoing data revealed greater benefits when bortezomib was given earlier in the progression of the disease, and the label was updated for use as a first-line treatment.<sup>50</sup>



## **THE IMPORTANCE OF PROVIDING PATIENTS WITH CHOICE OF MEDICINES**

Having a variety of therapeutic options available is important as physicians and patients work together to create individual treatment plans for a patient's particular disease or condition. For a variety of reasons, including biological differences or differences in lifestyle and diet, patients with the same disease may respond differently when given the same medicine. Seemingly small differences among similar medicines, such as in formulation or dosing, can also affect the way the medicine works for a particular patient, impact adherence, and ultimately a patient's quality of life. For example, for some patients with HIV/AIDS, the ability to take a combination of therapies in a single pill has made adherence to a treatment regimen exponentially simpler. As we learn more about the underlying biology of diseases, it has also become clear many diseases are able to develop resistance or adapt and evade forms of treatment after prolonged use. For this reason, having a succession of available treatment options can be important. For example, patients with chronic myelogenous leukemia have several treatment options available within a single class (i.e., tyrosine kinase inhibitors). This provides patients with a range of treatment options, which are necessary if their cancer develops resistance over time to their current therapies.



## **PERSONALIZING TREATMENT**

Growing understanding of the underlying genetic and biological factors causing diseases is enabling a new era in targeted health care. Through personalized, or precision medicine, physicians and researchers are better able to direct patient care along the full spectrum of health care, from risk assessment and prevention to detection, diagnosis, treatment, and disease management. In recent years, we have seen tremendous advances in personalized medicine. In 2015, more than 25% of new drug approvals were personalized medicines, with 35% of 2015 cancer approvals alone being personalized medicines.<sup>51</sup> These medicines are shifting the treatment paradigm for patients, enabling increasingly precise assessment of which medical treatments and procedures will be best for each patient.

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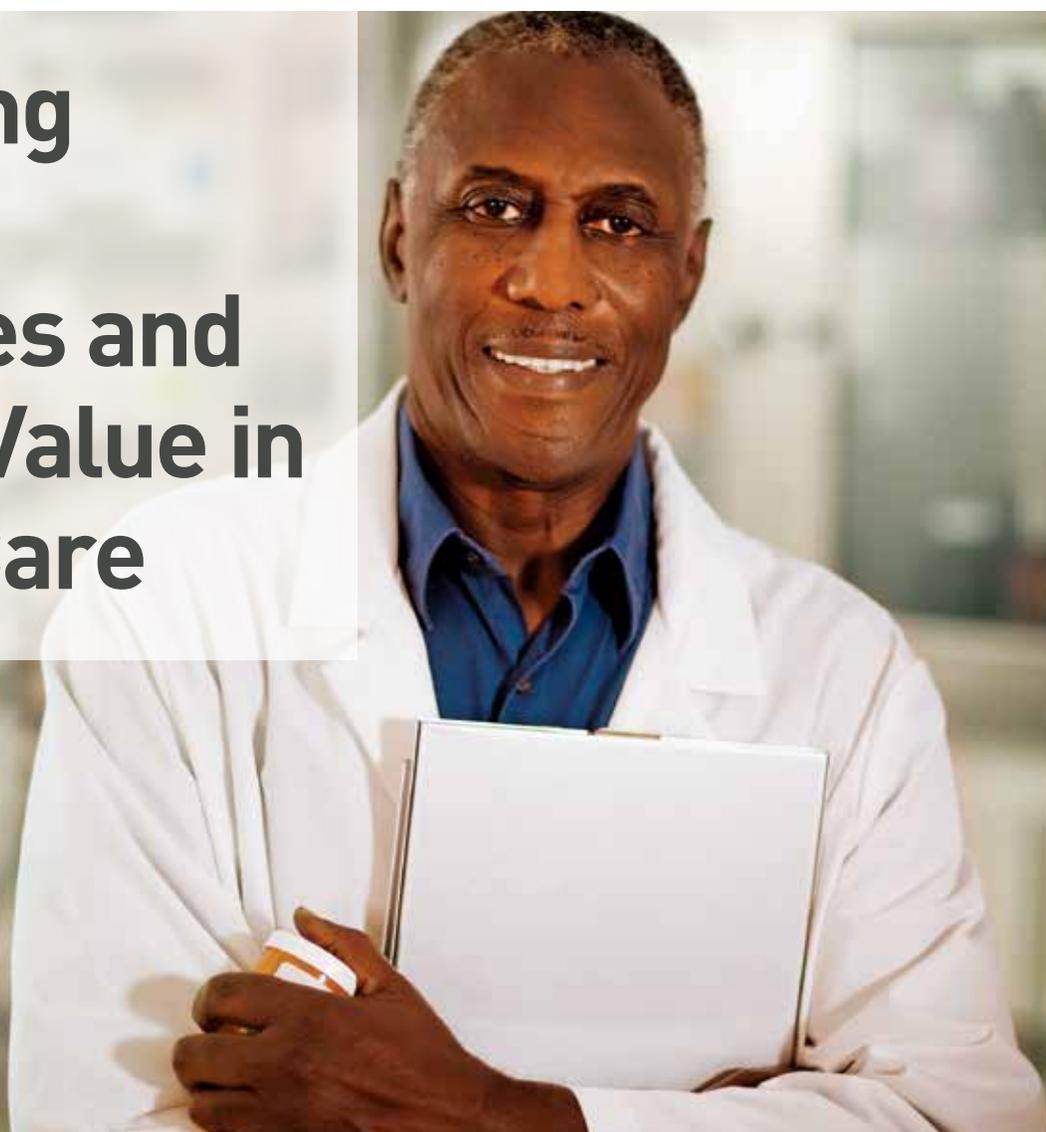
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# Improving Health Outcomes and Driving Value in Health Care

# Improving Health Outcomes and Driving Value in Health Care



**T**remendous medical advances in recent years demonstrate the important role medicines play in treating many debilitating diseases and conditions. But prescription medicines are not only improving and saving the lives of millions of patients, they are also driving substantial value in the United States health care system. Unlike most other health care services, medicines when used appropriately allow patients to avoid other costlier services, such as emergency room visits, hospital stays, surgeries,

and long-term care. Likewise, medicines produce substantial savings in avoided health care costs. Moving forward, medicines will continue to provide the best opportunity to improve health outcomes and drive value and quality in health care.

Importantly, even as remarkable advances in medicine over the years have yielded incredible value for patients and society, spending on prescription medicines has remained a small share of total health care expenditures. In fact, retail prescription medicines account for the

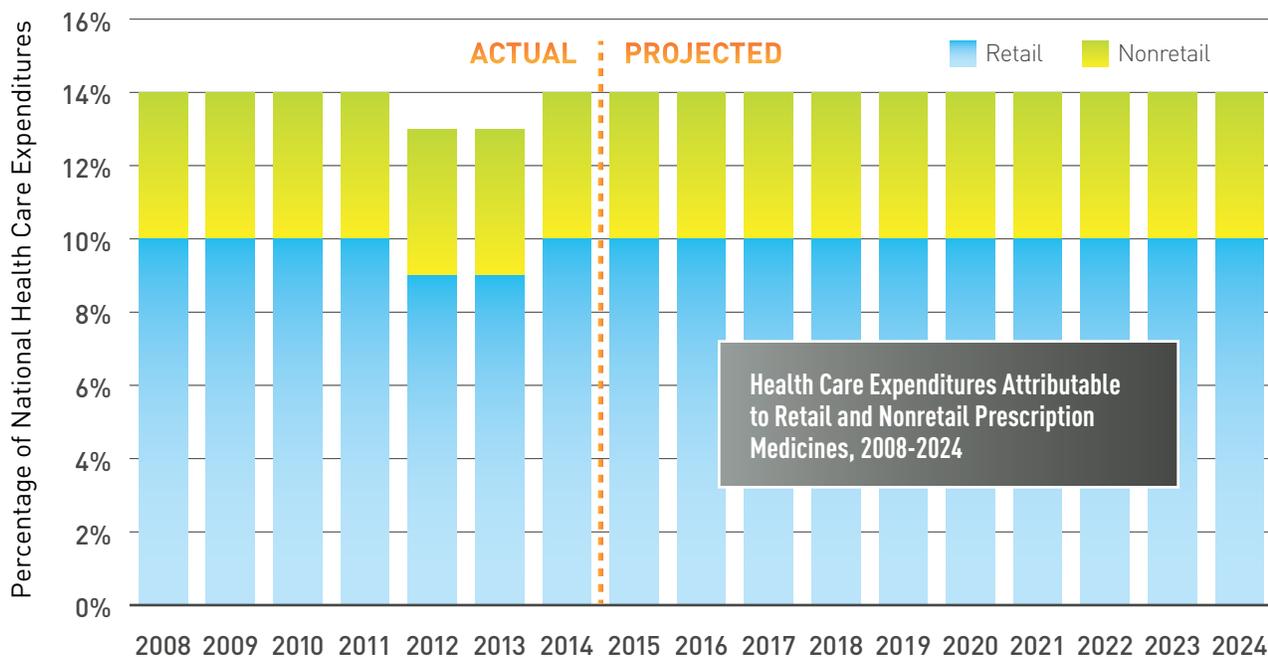


same percentage of health care spending today as in 1960—just 10%.<sup>1</sup> And total spending (retail and nonretail) on medicines is projected to remain stable as a percentage of total health care spending (13 to 14%) in the years ahead, even as numerous new medicines are brought to patients (see Figure 5).<sup>2,3</sup> This is possible because the competitive marketplace in the United States

works to control the costs of medicines (see sidebar: Market Dynamics Contain Costs of Prescription Medicines).

Not only do medicines allow patients to live longer, healthier lives and avoid serious complications and associated medical costs, but they also allow patients to more actively engage in the workforce and the economy at large. Despite the many benefits that medicines provide, significant gaps in appropriate use of medicines remain. However, where there are gaps there are also opportunities to improve patient care. Looking forward, it will remain critically important that the care patients receive provides them with the medicines they need to live longer, healthier, and more productive lives.

**FIGURE 5: Medicines Are Expected to Account for a Stable Share of Total Health Care Expenditures Through the Next Decade**



Retail prescription medicines are those filled at retail pharmacies or through mail service. Nonretail prescription medicines are those purchased through physicians' offices, clinics, and hospitals and are typically administered to the patient by the provider.

Source: Altarum Institute. Center for Sustainable Health Spending data brief: a ten year projection of the prescription drug share of national health expenditures including non-retail. [http://altarum.org/sites/default/files/uploaded-publication-files/Non-Retail%20Rx%20Forecast%20Data%20Brief\\_with%20Addendum.pdf](http://altarum.org/sites/default/files/uploaded-publication-files/Non-Retail%20Rx%20Forecast%20Data%20Brief_with%20Addendum.pdf). Published October 2014; addendum update August 2015. Accessed April 2016.

## MARKET DYNAMICS CONTAIN COSTS OF PRESCRIPTION MEDICINES

Since 2000, more than 550 new medicines have become available, providing important treatment options to millions of patients with serious, unmet medical needs.<sup>4,5</sup> Yet, total prescription drug costs have remained and are expected to remain a small and stable share of health care spending. This is possible because the dynamics of the market-based system in the United States promote incentives for continued innovation and patient access to needed medicines while leveraging competition to achieve cost containment.

One of the reasons that spending on medicines remains a consistent share of health care spending while new medicines reach patients year after year is because the prescription drug life cycle works to control costs. Although new medicines generate a large share of the medical advances that patients need and society demands, older medicines remain highly useful, lose their intellectual property and regulatory protections, and generate even more substantial cost savings. In fact, following generic market entry, prices typically fall by 90%.<sup>6</sup> For example, the price of a common statin, atorvastatin, dropped by about 92% when generic alternatives came to market.<sup>7</sup> And today, most statins used by patients are generic. Price drops like this occur in no other part of the health care sector. By comparison, the average charge for a procedure used to treat cardiovascular disease, percutaneous transluminal coronary angioplasty (PTCA), increased by 66% in less than 10 years.<sup>8</sup>

The competitive market-based system in the United States is also structured to take advantage of savings from brand competition once new medicines reach the market. Multiple companies are often simultaneously competing to research, develop, and secure FDA approval of first-in-class treatments, and drug development is more competitive than ever. In fact, 88% of first-in-class medicines launched between 2005 and 2011 already had a competitor in Phase II clinical development at the time of their launch, compared to 63% of first-in-class medicines launched between 1998 and 2004. Once launched, the time a medicine is alone in its class has continued to shrink, from 4.7 years for drugs approved between 1998 and 2004, to 2.3 years for drugs approved between 2005 and 2011.<sup>9</sup>

Following generic entry, the US market continues to drive long-term affordability by taking maximum advantage of the savings provided by these medicines. Today, more than 90% of all medicines prescribed in the United States are generic medicines.<sup>10</sup> Continued competitive pressure resulting from the loss of intellectual property protection and the entry of more generics and biosimilars is expected to continue to fuel this dynamic in the years ahead. Between now and 2020, an estimated \$93 billion of US brand sales are projected to face generic competition.<sup>11</sup> This type of built-in cost containment exists in no other part of the US health care system (see Figure 6).

## THE HEALTH IMPACT OF BETTER USE OF MEDICINES

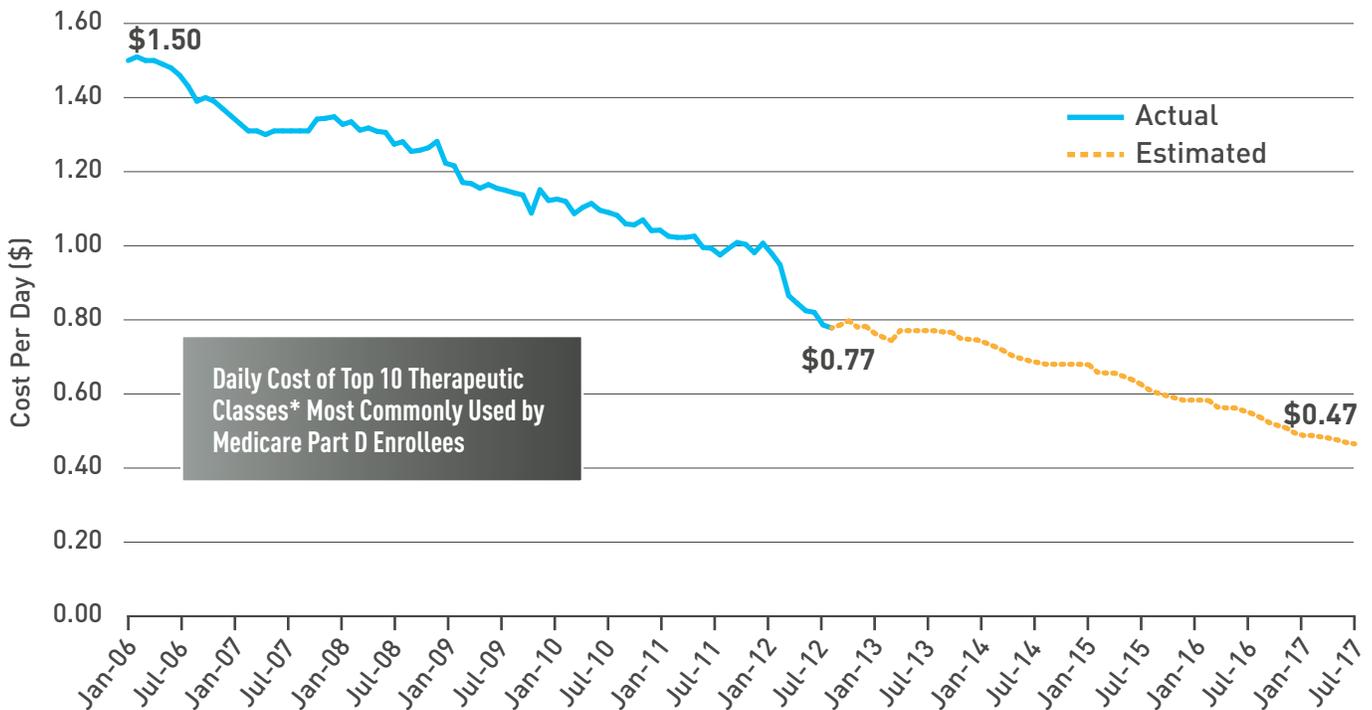
Medicines, when used appropriately, play a central role in improving patient health and outcomes. A large body of evidence clearly demonstrates that better use of medicines results in a number of improved health-related outcomes, including decreases in mortality, prevention of

disease complications, as well as unnecessary hospitalizations and other health care services:

**Decreasing Mortality:** Expansion of prescription drug coverage through the Medicare Part D program has improved use of medicines and had a profound impact on saving and extending the lives of millions of American seniors. Since

**FIGURE 6: Savings From the Prescription Drug Lifecycle Reduce Treatment Costs for the Most Common Conditions**

Incredible advances by innovative pharmaceutical companies, resulting from pioneering scientific work and large-scale investments, eventually lead to lower-cost generics that bring long-term value to consumers.



\*Ten therapeutic classes most commonly used by Part D enrollees in 2006 were lipid regulators, angiotensin-converting-enzyme inhibitors, calcium channel blockers, beta blockers, proton pump inhibitors, thyroid hormone, angiotensin II, codeine and combination products, antidepressants, and seizure disorder medications.

Source: Kleinrock M. *Daily Cost of Medicare Part D: December 2013 Update*. Danbury, CT: IMS Institute for Healthcare Informatics; December 2013.

the implementation of the program, on average, 22,100 lives were saved each year between 2006 and 2014, and nearly 200,000 Medicare beneficiaries have lived at least 1 year longer, with an average increase in longevity of 3.3 years.<sup>12</sup>

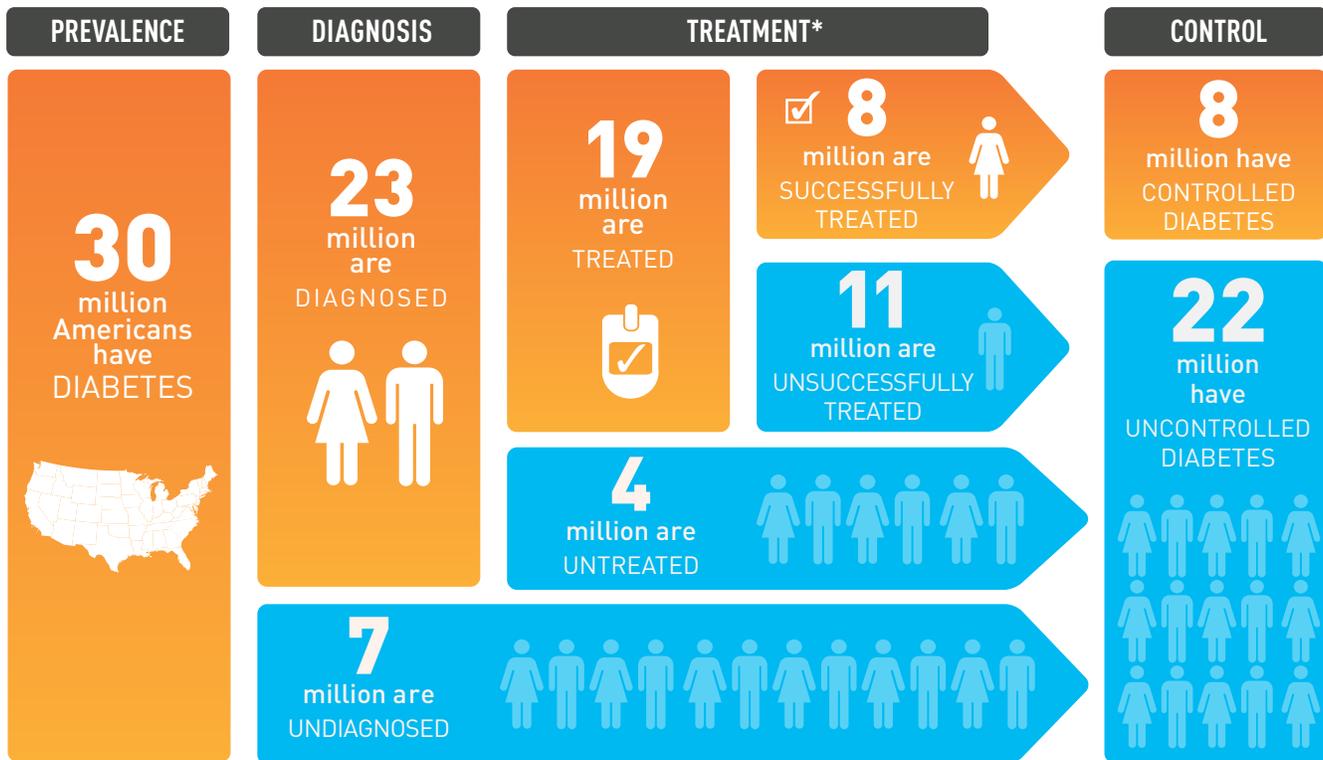
**Preventing Disease Complications and Hospitalizations:**

A wealth of evidence underscores the crucial role that medicines and proper adherence play in preventing disease complications and unnecessary use of medical services such as emergency department visits and hospitalizations. Examples in specific disease categories follow.

- Asthma:** Children with asthma enrolled in Medicaid whose prescriptions were filled after a hospital discharge faced a reduced risk of early readmission. In fact, one study of these children found the risk of being readmitted to the hospital within 14 days was 33% and 41% less for those filling a prescription for a beta antagonist and inhaled steroid, respectively, compared with those whose prescriptions were not filled.<sup>13</sup> Similarly, children on Medicaid who had lower adherence to long-term controller medications had 21% higher risk of experiencing an emergency department visit and a 70% higher risk of being hospitalized

**FIGURE 7: Diabetes: An Example of Underdiagnosis and Undertreatment**

Uncontrolled diabetes can lead to kidney failure, amputation, blindness, and stroke.



\*Treatment includes blood sugar control (medicines, diet, and exercise) and testing to prevent complications. Data rounded to whole numbers.  
 Source: IHS Life Sciences analysis based on Centers for Disease Control and Prevention data. National Health and Nutrition Examination Survey, 2013-2014. [http://www.cdc.gov/nchs/nhanes/search/nhanes13\\_14.aspx](http://www.cdc.gov/nchs/nhanes/search/nhanes13_14.aspx). Accessed April 2016.

within 3 months after being initially prescribed the controller medication relative to children with better adherence.<sup>14</sup>

- Diabetes:** For many patients, successful management of diabetes requires constant and diligent monitoring, multiple daily injections, coordination of multiple oral medicines, and a carefully planned daily routine to avoid serious complications. This challenge underscores the importance of medicines that reduce burdens to patients and improve adherence (see Figure 7). Among diabetes patients, adherence is associated with fewer emergency department visits and lower rates of complications,

including heart attack, amputation, and vision impairment/blindness (retinopathy).<sup>15</sup>

- Cystic Fibrosis (CF):** CF is a life-threatening rare disease primarily affecting the lungs and digestive system. Research shows more than twice as many patients who were poorly adherent to pulmonary medications for their condition experienced a pulmonary embolism relative to those with good adherence.<sup>16</sup> Poor adherence to pulmonary medications has also been shown to be associated with higher use of acute health care services. Patients with low adherence were hospitalized 35% more often than those with high adherence.<sup>17</sup>

## THE ECONOMIC VALUE OF BETTER USE OF MEDICINES

The appropriate use of medicine can keep patients healthy and reduce the need for medical services—saving money for both patients and the nation’s health care system.<sup>18,19,20</sup> Likewise, inappropriate use of medicines can result in unnecessary medical care, increased health care costs, and poor patient outcomes. For example, misuse and abuse of prescription medicines results in unnecessary use of health care services, increased hospitalizations, and greater health care costs. Evidence suggests that inappropriate use—such as poor medication adherence, suboptimal prescribing, and medication errors—result in an estimated \$213 billion in avoidable health care costs each year, representing 8% of the nation’s health care spending and providing an opportunity



to produce substantial savings for the health system at large.<sup>21</sup>

Improved use of medicines increases prescription drug spending, but these costs are often offset by reductions in other health care spending. Due to a growing body of evidence, in 2012 the Congressional Budget Office (CBO) revised its methodology for estimating the federal budget impact of policy changes to recognize reductions in other medical expenditures associated with increased use of prescription medicines in Medicare.<sup>22</sup>

Since the CBO announcement, the evidence has continued to develop and grow, broadening the potential cost offsets attributed to use of medicines. In fact, a recent study suggests the savings due to better use of medicines in Medicare may be 3 to 6 times greater than estimated by CBO in 4 common chronic conditions—heart failure, diabetes, hypertension, and high cholesterol.<sup>23</sup> New evidence also suggests increased use of medicines is associated with reductions in expenditures from avoided use of inpatient and outpatient services in the Medicaid population.<sup>24</sup>

In addition to producing savings from avoided health care costs, better use of medicines also improves health and overall quality of life, which can lead to improved productivity through reduced absenteeism and use of disability leave. Improvements in worker productivity also yield important contributions to the economy at large.

Several examples across a range of conditions illustrate the savings realized by patients and the health care system as a result of better use of

medicines as well as improvements in employee productivity:

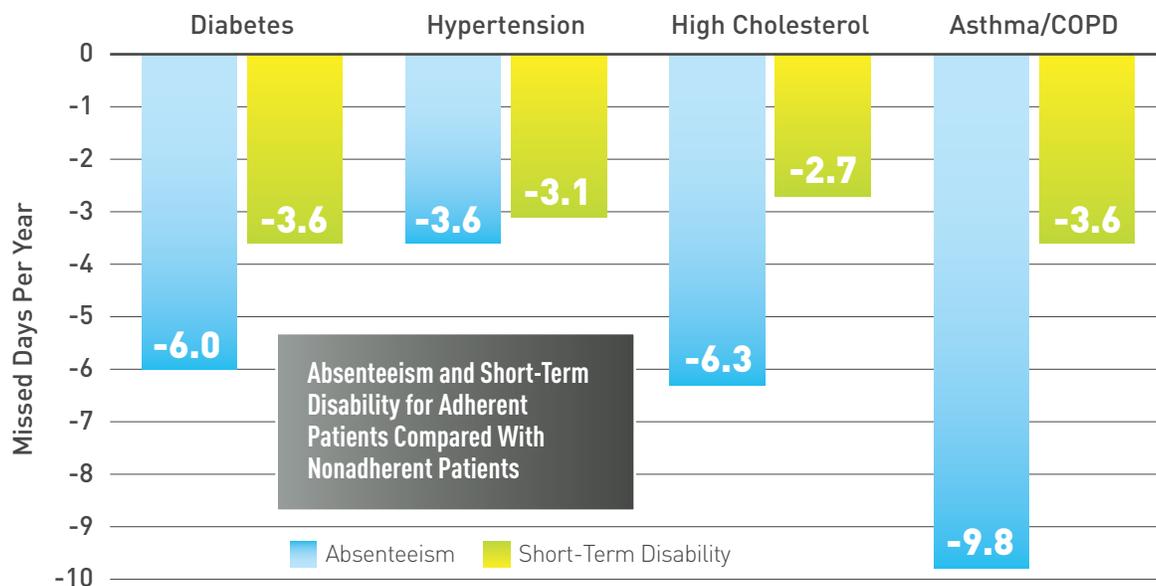
**Multiple Chronic Conditions:** Research shows spending \$1 more on medicines for adherent patients with multiple chronic conditions—including congestive heart failure, high blood pressure, diabetes, and high cholesterol—can generate \$3 to \$10 in savings on emergency room visits and inpatient hospitalizations.<sup>25</sup> Research also suggests health plans demonstrating better patient adherence display significantly better performance on patient outcomes, including lower spending and fewer complications from congestive heart failure or diabetes. In fact, the study found plans with low medication adherence rates could save \$4 billion and \$19 billion annually

by improving adherence of their enrollees with heart failure and diabetes, respectively.<sup>26</sup> Another study found patients with diabetes, hypertension, high cholesterol, asthma, or chronic obstructive pulmonary disease who took medicines as prescribed missed fewer days of work and needed less short-term disability than patients who did not take their medicines (see Figure 8).<sup>27</sup>

**Diabetes:** A study of Medicare patients with diabetes found 15% and 19% net cost savings per patient associated with good adherence to oral antidiabetic drugs and antihypertensives, respectively. Good adherence was associated with nearly \$5,000 in reduced medical spending and \$4,000 in total Medicare spending for these therapeutic areas, over 2 years.<sup>28</sup>

**FIGURE 8: Improving Adherence Increases Employee Productivity**

For workers with asthma/chronic obstructive pulmonary disease (COPD), better adherence results in more than \$3,100 in savings on average per worker annually.



Source: Carls GS, Roebuck MC, Brennan TA, Slezak JA, Matlin OS, Gibson TB. Impact of medication adherence on absenteeism and short-term disability for five chronic diseases. *J Occup Environ Med.* 2012;54(7):792-805.

**Crohn's Disease:** Patients with Crohn's disease have an autoimmune condition that impairs the digestive system. A study of adults using a biologic medicine for the disease found that drug-related costs were offset by lower hospitalization and outpatient visit costs. Adherent patients spent \$13,097 in direct medical costs, but less adherent patients spent \$20,068 in direct medical costs during the same period.<sup>29</sup> Another study of Crohn's disease patients found that adherence to the same biologic medicine was associated with lower total health care costs. Specifically, average total costs were \$41,713 for adherent patients and were \$47,411 for nonadherent patients. Broken down further, these costs were \$2,458 versus \$17,634 for hospitalizations, \$7,357 versus \$10,909 for outpatient visits, and \$236 versus \$458 for emergency room visits.<sup>30</sup> Patients with Crohn's disease also suffer a number of work-related impairments due to physical effects and the poor quality of life associated with the disease. One study examining Crohn's patients treated by a biologic medicine tested in clinical trials measured a number of work-related outcomes and found a 9% decrease in absenteeism and a 25% reduction in total work impairment compared to those who were not being treated with the medicine.<sup>31</sup>



**Multiple Sclerosis (MS):** A study of employed adults with MS found that improving medication adherence significantly decreased urgent-care use, days of work lost, and direct and indirect costs. In fact, a 10 percentage point increase in adherence decreased the likelihood of an inpatient or emergency room visit by 9% to 19%, days of work loss by 3% to 8%, and direct and indirect costs by 3% to 5%.<sup>32</sup>

### **GAPS IN OPTIMAL USE OF MEDICINES**

Despite the value provided to patients, gaps in appropriate use of medicines remain. A National Community Pharmacists Association survey showed that nearly 75% of adults do not follow their doctors' prescription orders, including not filling their prescriptions or taking less than the recommended dose.<sup>33</sup> A number of factors, such as complexity of treatment regimens and limited access, create additional barriers to the optimal use of medicines.

The complexity of treatment regimens and poor relationships or communication challenges between prescribers and patients can negatively affect patients' ability to follow the prescribers' instructions for their medications. Patients often do not fully understand their illness or the need for treatment. They may suffer from mental illness or cognitive or physical impairments that contribute to poor adherence to prescribed treatment. Patients with multiple chronic conditions often have trouble managing complicated treatment regimens. Additionally, underuse is a common problem among elderly patients; researchers report that elderly patients are 17 times more likely to underuse prescribed medicines than to overuse them.<sup>34</sup>

Limited access to, or coverage of, medicines may also contribute to gaps in appropriate use. Insurers are increasingly using high deductibles, coinsurance, and multiple tiers resulting in high out-of-pocket costs for some patients. High cost-sharing for medications may limit patients' access to needed treatments, reduce adherence, and lead to poor health outcomes.<sup>35</sup> Out-of-pocket spending for prescription medications can represent a disproportionate share of total health care costs borne directly by patients, especially those who are low-income or chronically ill.

**Insurers are increasingly using tools that place a disproportionate cost-sharing burden on some patients:**

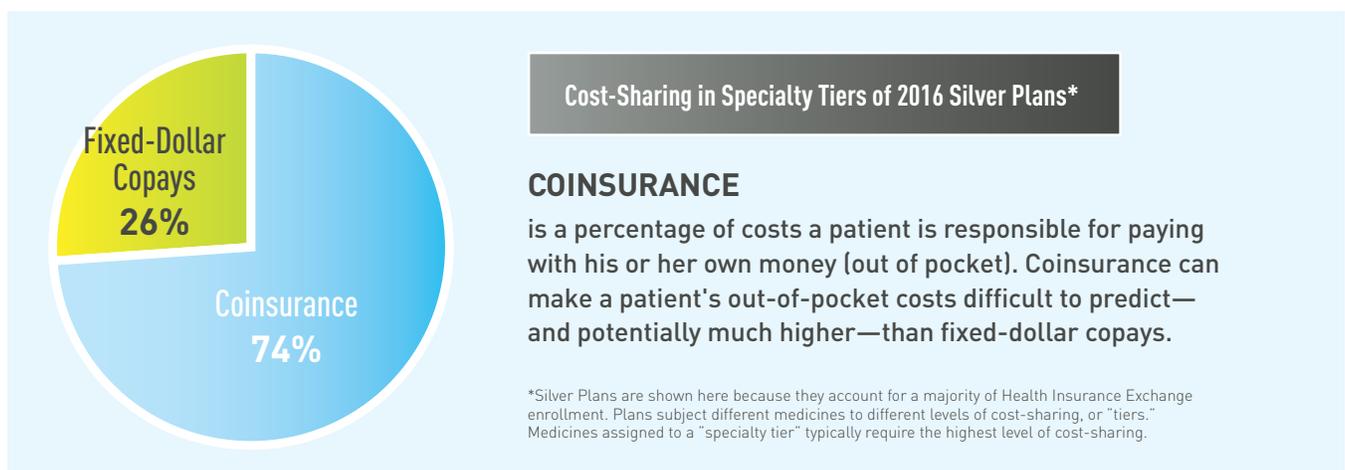
- Drugs placed on higher tiers are subject to higher cost-sharing. From 2000 to 2015, average copays for first-tier, or generic, drugs have risen about 38%, while cost sharing for

second- and third-tier products has increased 107% and 86%, respectively. Over the past decade, plans have been also increasingly introducing benefit design structures with four or more tiers.<sup>36</sup>

- The most frequently purchased type of health insurance exchange plan under the Affordable Care Act commonly requires patients to pay coinsurance rather than a fixed copay amount for medicines placed on the highest cost-sharing tier.<sup>37</sup> Coinsurance can make patients' out-of-pocket costs difficult to predict and can pose challenges as these costs must be paid up front at the pharmacy before a patient can obtain a prescription (see Figure 9).
- Increasingly, health plans are requiring patients to pay a combined deductible for prescription medicines before their drug coverage goes

**FIGURE 9: Plans Often Charge Patients a Percentage of a Medicine's Total Cost Rather Than Fixed-Dollar Copays**

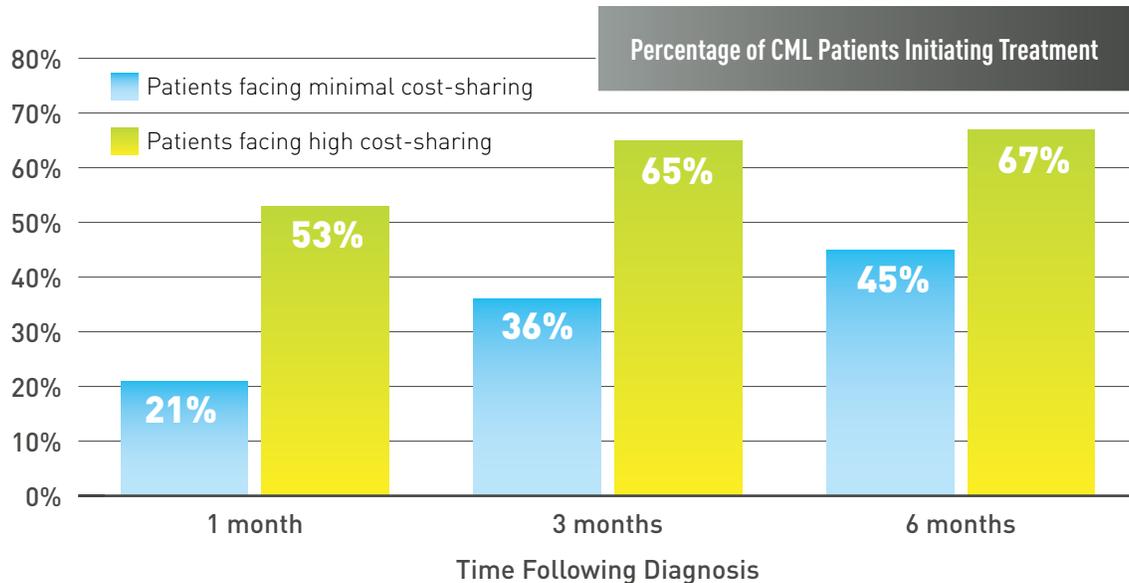
In the most frequently purchased type of Health Insurance Exchange plan, coinsurance for certain medicines is common: 74% of these plans require enrollees to pay a percentage of a specialty tier medicine's total cost, with 36% of plans requiring patients to pay coinsurance of more than 30% of the cost.



Source: Avalere Health PlanScape®, a proprietary analysis of exchange plan features, December 2015. This analysis is based on data collected by Managed Markets Insight & Technology, LLC.

**FIGURE 10: Patients Facing High Cost Sharing Commonly Do Not Initiate Treatment**

Chronic myeloid leukemia patients facing high out-of-pocket costs for medicines on a specialty tier are less likely to initiate drug therapy than patients receiving a cost sharing subsidy and take twice as long to initiate treatment.



Source: Doshi JA, Li P, Ladage VP, Pettit AR, Taylor EA. Impact of cost sharing on specialty drug utilization and outcomes: a review of the evidence and future directions. *Am J Managed Care*. 2016;22(3):188-197. <http://www.ajmc.com/journals/issue/2016/2016-vol22-n3/Impact-of-Cost-Sharing-on-Specialty-Drug-Utilization-and-Outcomes-A-Review-of-the-Evidence-and-Future-Directions>. Accessed March 2016.

into effect. The share of commercial plans subjecting prescription medicines to a deductible increased from 23% in 2012 to 46% in 2015. Plans with prescription drug deductibles also tend to have higher copays than plans that don't subject medicines to a deductible, particularly for brand medicines.<sup>38</sup>

**Adherence decreases as out-of-pocket cost increases:** Research shows for every \$10 increase in out-of-pocket costs for prescription drugs, adherence decreases by approximately 4%, with the effect depending on the therapeutic class of the medication and the severity of the condition.<sup>39</sup> One study found that doubling medication copayments for a variety of health conditions reduced medication adherence rates by 25% to 45%.<sup>40</sup> A recent study shows that chronic

myeloid leukemia patients facing high cost sharing for medicines on a specialty tier are less likely to initiate drug therapy following a diagnosis than patients receiving a cost-sharing subsidy to help minimize out-of-pocket costs. On average, patients facing high out-of-pocket costs took twice as long to initiate therapy (see Figure 10).<sup>41</sup>

**Higher copays are linked to increased hospitalizations and spending:**<sup>42</sup> For example, research shows that patients with acute coronary syndrome (ACS) who faced higher cost-sharing were less likely to adopt—and more likely to discontinue—therapy within the first year following stent implantation. Subsequently, plans with high cost-sharing had a \$2,180 increase in rehospitalization costs per patient with ACS in that time compared to lower cost-sharing plans.<sup>43</sup>

Although there are many barriers to the optimal use of medicines, there are also significant opportunities to improve patient health and the efficiency of the health care system by closing existing gaps in the use of medicines.

A large body of research supports the important role that appropriate use of medicines plays in

improving health outcomes for patients and often in producing cost offsets in other areas of health care. Also critical to achieving these outcomes is access to quality prescription drug coverage. Quality coverage is essential to ensuring patients can access the medicines they need to achieve better health outcomes and improved quality of life (see sidebar: Access Better Coverage).

## ACCESS BETTER COVERAGE

A well-informed consumer is an engaged and empowered patient. More information on health care out-of-pocket costs and quality needs to be made available to patients. In addition, vulnerable patients should have the protection of enforceable, common sense rules that prevent discrimination. These steps will improve both coverage and access and will help make medicines more affordable for patients.

While more needs to be done, AccessBetterCoverage.org can help. This site, developed by PhRMA, provides resources—in English and Spanish—to help consumers better understand and navigate their insurance coverage, including how needed prescription medicines are covered.

For more information visit [www.AccessBetterCoverage.org](http://www.AccessBetterCoverage.org)

## PARTNERSHIP FOR PRESCRIPTION ASSISTANCE (PPA)

Patients should not have to worry about whether they can afford the care they need.

Despite more Americans having insurance, many still face affordability issues that put their ability to stay on a needed therapy at risk. Maintaining patient access is important for everyone. Patient assistance programs sponsored by America's biopharmaceutical research companies are one option to help patients maintain access to needed medicines.

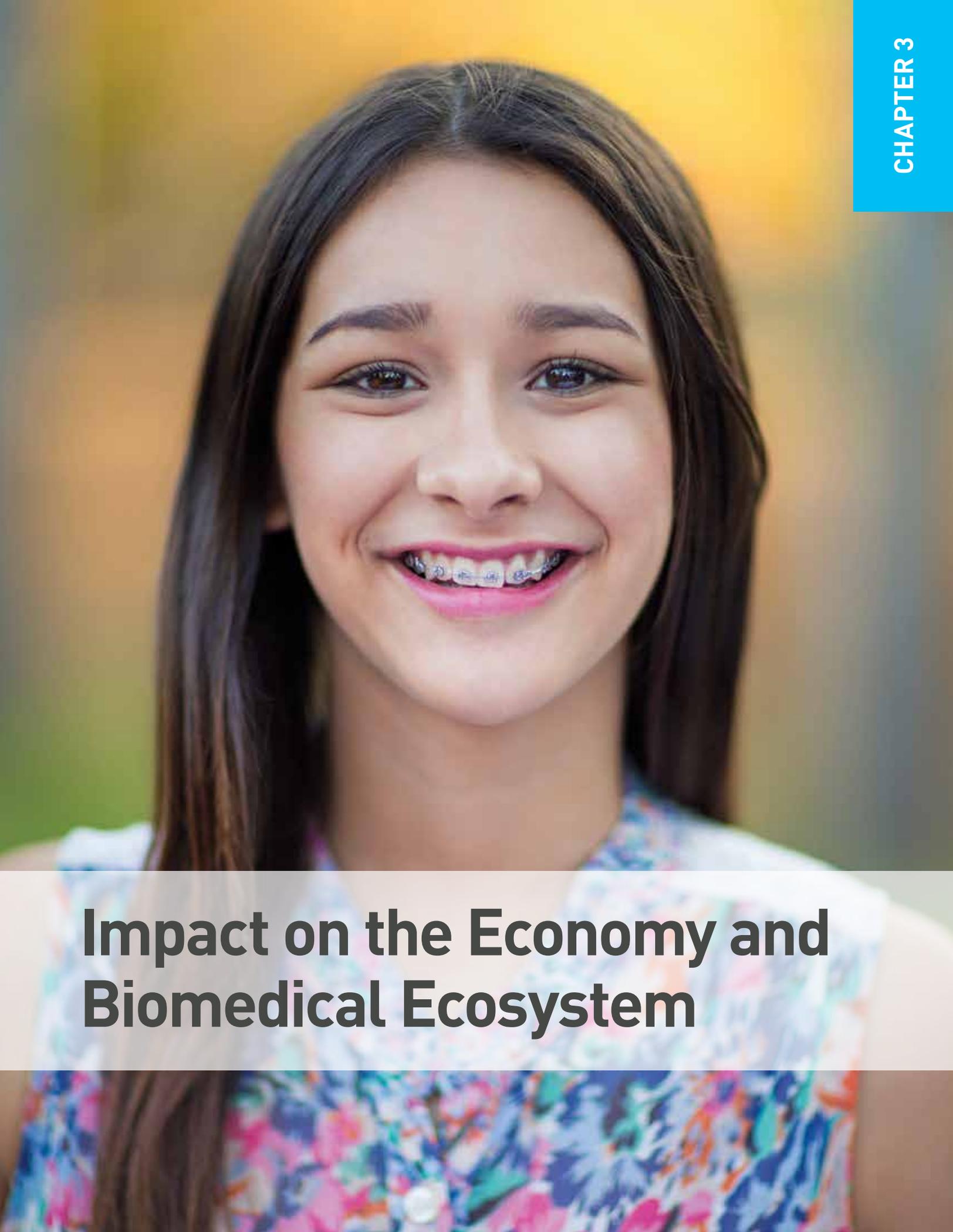
Since 2005, the Partnership for Prescription Assistance (PPA) has helped nearly 9.5 million patients access patient assistance programs. Sponsored by America's biopharmaceutical research companies, the PPA is a single point of access to information on hundreds of public and private patient assistance programs, including nearly 200 programs offered by biopharmaceutical companies. The PPA's easy-to-use website—[www.pparx.org](http://www.pparx.org)—makes it simple for a patient or patient advocate to complete the online application with basic information. The PPA then matches the patient with assistance programs for which he or she may be eligible.

Each month, more than 60,000 people visit PPA online to find patient assistance programs and much more. Through its online free clinic finder, PPA has connected more than 300,000 patients with free health care clinics across the country. As the website has evolved, the clinic finder has become a user-friendly resource that offers an interactive map and directions to nearly 10,000 free health care clinics throughout the United States.

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# Impact on the Economy and Biomedical Ecosystem

# Impact on the Economy and Biomedical Ecosystem



Over the past 30 years, the US biopharmaceutical research sector has been a world leader in the development of new medicines, and it continues to drive biopharmaceutical innovation for patients. Biopharmaceutical innovation generates high-quality jobs and powers economic output and exports for the US economy, serving as “the foundation upon which one of the United States’ most dynamic innovation and business ecosystems is built.”<sup>1</sup> These immense

economic contributions and the nation’s position as the global leader in biopharmaceutical innovation are driven by the industry’s investment in the research and development (R&D) enterprise.

As the most R&D-intensive industry in the US economy, the biopharmaceutical sector is committed to addressing the unmet needs of patients in the United States and around the world. Sitting at the heart of the US R&D

enterprise, biopharmaceutical companies are harnessing new scientific and technological advances and collaborating with key stakeholders across the biomedical ecosystem to ensure patients obtain the medicines they need.

## DRIVING ECONOMIC GROWTH AND GLOBAL COMPETITIVENESS

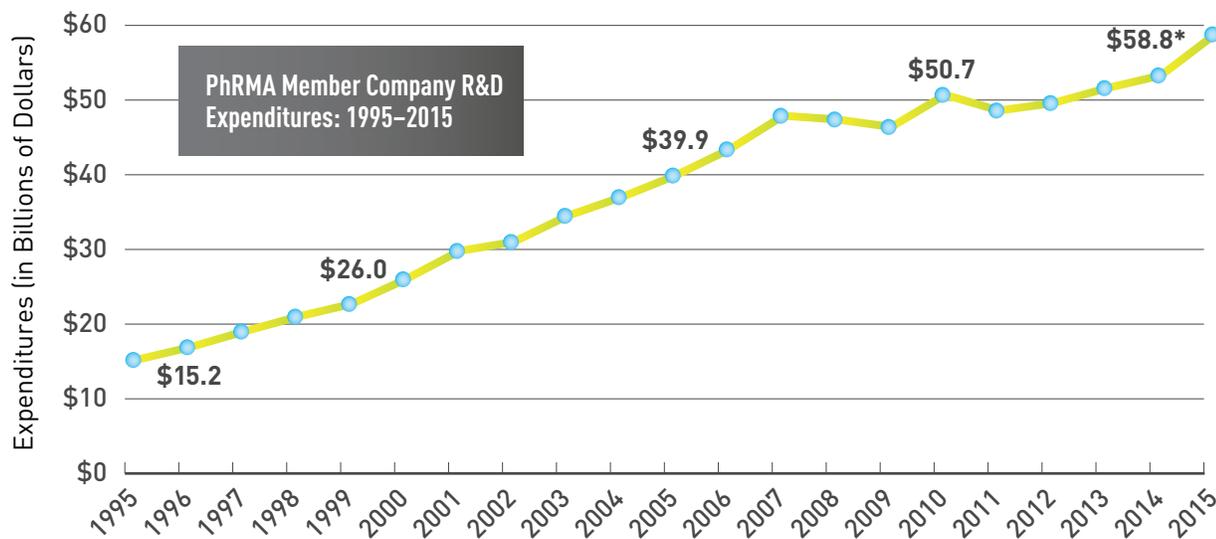
PhRMA member companies invested an estimated \$58.8 billion in R&D in 2015, representing the majority of all biopharmaceutical R&D spending in the United States (see Figure 11).<sup>2,3</sup> In fact, the sector accounts for the single largest share of all US business R&D, accounting for approximately 17% of all R&D spending by US businesses.<sup>4</sup>

Relative to other manufacturing industries, the biopharmaceutical industry invests 12 times more in R&D per employee and had the highest

growth rate in R&D investment (25%) across all manufacturing industries between 2000 and 2012.<sup>5</sup>

Not only are the significant investments of the US biopharmaceutical sector bringing new medicines to patients, but they are fueling tremendous contributions to the US economy. The biopharmaceutical industry puts down roots in communities across the country, creating high-quality, high-wage R&D and manufacturing jobs that generate a powerful multiplier effect across the US economy. Today, the industry employs nearly 854,000 workers and supports more than 4.4 million jobs across the country. Each job at a biopharmaceutical research company supports more than four additional jobs across the US economy, ranging from construction and business services to retail stores and childcare providers. The wages of employees working in the

**FIGURE 11: PhRMA Member Company R&D Investment**



\*Estimated fiscal year 2015

Sources: Congressional Budget Office (CBO). A CBO study: research and development in the pharmaceutical industry. [www.cbo.gov/sites/default/files/cbofiles/ftpdocs/76xx/doc7615/10-02-drug-r-d.pdf](http://www.cbo.gov/sites/default/files/cbofiles/ftpdocs/76xx/doc7615/10-02-drug-r-d.pdf). Published October 2006. Accessed April 2016; Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA Annual Membership Survey, 1995-2015. Washington, DC: PhRMA; 2016.

biopharmaceutical sector are also significantly higher than the average for all private sector industries; individuals directly employed in the industry earned an average of \$123,108 in wages and benefits, more than twice the average compensation (\$57,149) of American workers generally. What's more, the biopharmaceutical sector generates nearly \$1.2 trillion in economic output annually when direct, indirect, and induced effects are considered (see Figure 12).<sup>6</sup>

Biopharmaceutical exports are another strong indicator of the industry's growing economic contributions. In 2015, US biopharmaceutical goods exports totaled \$47 billion. And these exports have grown in recent years, nearly tripling between 2003 and 2015.<sup>7</sup> Among the most R&D-intensive manufacturing industries, the biopharmaceutical sector outpaces other sectors with a 9.9% annual growth rate in exports relative to an average annual growth rate of 4.6%.<sup>8</sup>

**FIGURE 12: The Economic Reach of the US Biopharmaceutical Industry**

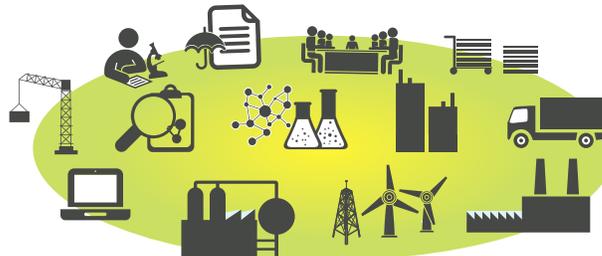
Every biopharmaceutical sector job supports more than 4 additional jobs outside the industry.

**854,000**  
direct jobs



Innovative Biopharmaceutical Industry

**1,710,000**  
indirect jobs



Vendors and Suppliers

**1,882,000**  
induced jobs



Additional Private Economic Activity

**4,446,000**  
TOTAL JOBS

The biopharmaceutical industry supported more than 4.4 million jobs across the US economy in 2014.

Source: TEconomy Partners; for PhRMA. *The Economic Impact of the US Biopharmaceutical Industry*. Columbus, OH: TEconomy Partners; April 2016.

R&D-intensive industries, such as the biopharmaceutical industry, critically rely on patents and other intellectual property (IP) incentives to produce innovations and to support the high-skill, high-wage jobs that generate significant contributions to the US economy (see sidebar: Supporting STEM Jobs in the US Economy). In fact, industries relying heavily on IP have an outsized impact on the economy and consistently outperform other industries across a number of economic indicators. Thus, IP protections are key to driving the profound impact the biopharmaceutical industry has on the US economy as well as maintaining US leadership in the development of medicines in an increasingly knowledge-based and competitive global economy.<sup>9</sup>

Continued growth of the biopharmaceutical research enterprise is needed to ensure the United States maintains its position as the world leader in biomedical innovation. Currently, the IP related to more than half of new medicines is invented in the United States.<sup>10</sup> And US researchers author the largest share of worldwide biomedical peer-reviewed publications.<sup>11</sup> The innovative biopharmaceutical

industry is uniquely positioned to help maintain US leadership in new technologies and scientific breakthroughs that will continue to create high-quality, high-wage R&D and manufacturing jobs and enhance America's global competitiveness in the future.

## **ECONOMIC IMPACT OF CLINICAL TRIALS**

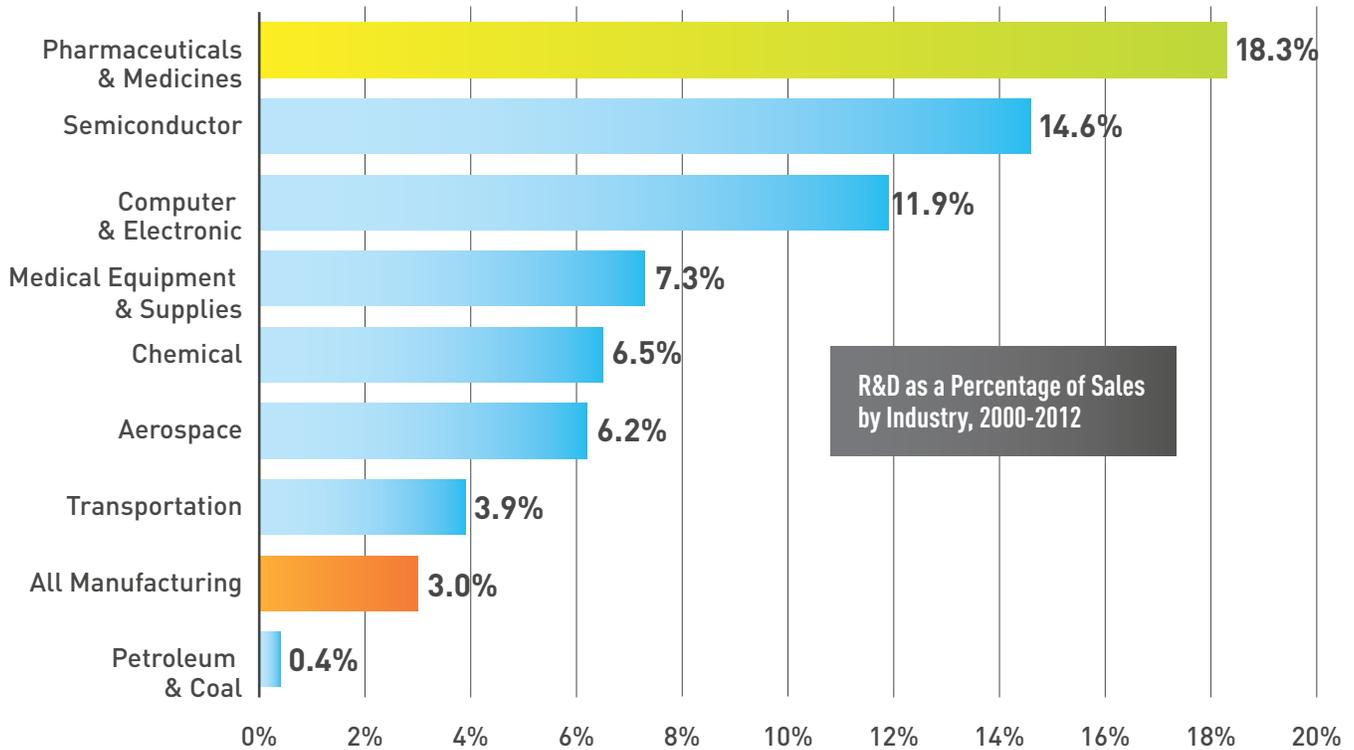
Of the billions of dollars spent on R&D each year by the biopharmaceutical industry, the majority is spent on clinical research. In the United States, the industry is responsible for the vast majority of this development work, accounting for roughly 90% of all spending on clinical trials to test medicines and medical devices.<sup>14</sup> Industry-funded clinical trials are typically conducted in collaboration with a broad range of local institutions, including academic medical research centers, contract research organizations, university medical and pharmacy schools, hospitals, and foundations. Perhaps no partner is more critical to the R&D process than patients, and our nation's innovative biopharmaceutical companies are increasingly seeking to incorporate the patient perspective throughout all elements of the R&D process.

### **SUPPORTING STEM JOBS IN THE US ECONOMY**

Continued scientific and technological innovations are critical to fostering sustained economic growth and global competitiveness. A key element of harnessing new scientific discoveries to build technological advances is a 21st century workforce with educational qualifications and professional mastery in science, technology, engineering, and mathematics (STEM). According to the Department of Labor, the STEM workforce accounts "for more than 50 percent of the nation's sustained economic growth."<sup>12</sup> As an industry rooted in science, the biopharmaceutical industry is a leading employer of the US-based STEM workforce, employing nearly 13% of the nation's manufacturing R&D workforce—the highest share among all manufacturing industries (see Figure 13).<sup>13</sup>

**FIGURE 13: The Biopharmaceutical Sector Invests More in R&D Relative to Sales Than Other Manufacturing Industries**

The biopharmaceutical sector invests more in R&D relative to sales than any other manufacturing industry, investing more than 6 times the average for all manufacturing industries.



Source: Pham ND; NDP Analytics. IP-intensive manufacturing industries: driving US economic growth. <http://www.ndpanalytics.com/ip-intensive-manufacturing-industries-driving-us-economic-growth-2015>. Published March 2015. Accessed March 2016.

Beyond the profound value provided to patients and society by new medicines, the major resource investments, as well as the time and expertise required to operate clinical trials and conduct related research, have a significant impact on communities across the country, creating jobs and sustaining and growing local economies (see sidebar: States Increasingly Seek to Attract and Support the Biopharmaceutical Industry).

In 2013, the biopharmaceutical industry sponsored 6,199 clinical trials of medicines in the United States, involving a total of 1.1 million

volunteer participants. Biopharmaceutical company-sponsored clinical trials occurred in all 50 states and the District of Columbia. The industry spent nearly \$10 billion in these clinical trial locations in 2013. This is in addition to the significant resources invested in clinical trial-related activities, such as trial management and data analysis functions occurring within companies and their contractors. In addition, research activities in the field supported \$25 billion in economic activity in communities throughout the United States, the result of an economic ripple effect spurred by the expenditures of clinical trial vendors and

## STATES INCREASINGLY SEEK TO ATTRACT AND SUPPORT THE BIOPHARMACEUTICAL INDUSTRY

As a major contributor to local economies, the biopharmaceutical industry is increasingly becoming the focus of state economic development plans. This is not surprising given the industry supports high-wage, high-value jobs that generate new income to states while also yielding broader economic growth potential. A forthcoming report from TEconomy Partners highlights the rise of state practices to pursue integrated, cutting-edge economic development programs focused on innovation, through the attraction and retention of the biopharmaceutical industry. Increasingly, states are putting in place a wide array of development initiatives to serve their established and emerging biopharmaceutical companies with access to R&D incentives and infrastructure, technology commercialization and entrepreneurial development services, trained workforce, and other shared development needs.<sup>15</sup>



contractors, as well as consumer spending by industry and vendor employees.<sup>16</sup>

### VENTURE CAPITAL INVESTMENTS

In addition to contributing immensely to the US economy, biopharmaceutical companies are dedicated to ensuring the industry continues to innovate and produce new or improved medicines for patients. Emerging biopharmaceutical companies, which are important contributors to the creation of these new medicines, rely

on venture capital (VC) and other forms of private capital to lay a solid foundation for their future success. Even with the recent uptick in VC investment—US biopharmaceutical VC investments in 2015 surpassed record highs achieved in 2007—the future of medical innovation remains uncertain as these investments did not keep pace with VC investments across all industries.<sup>17</sup> In fact, biopharmaceutical's share of total VC dropped 37% over the last decade—indicating that investors are shifting their investments from biopharmaceuticals to other industries.<sup>18</sup>

More problematic is the growing funding gap for early-stage biopharmaceutical companies, which are particularly vulnerable to funding challenges as they are most sensitive to changes in the business operating environment, such as increased costs of capital and regulatory and manufacturing setbacks. This gap in early-stage funding has grown due to several factors, including increasing regulatory burdens, concerns about coverage and payment for new medical innovations, and uncertainties related to IP rights and their enforcement. According to recent data,

**FIGURE 14:** The Biopharmaceutical Industry Supports a Broader Ecosystem Through Corporate Venture Capital



Source: PricewaterhouseCoopers and National Venture Capital Association. MoneyTree report: Biotechnology investing by corporate venture capital groups 1995-2015. March 2016.

early-stage biopharmaceutical start-ups have experienced rapid declines in funding over the past decade, with first-round investment and deals as a share of total biopharmaceutical VC investment dropping by about 20%.<sup>19</sup> As a 2014 report by Deloitte notes, “If these trends are sustained it will further encourage financiers to invest their capital elsewhere, and for an industry that heavily relies on small-cap firms and venture capital to fuel innovation, this could negatively impact the ecosystem in a permanent way.”<sup>20</sup>

However, the corporate venture arms of established biopharmaceutical companies are stepping in to help fill this gap—just one example of how the nation’s innovative biopharmaceutical companies seek to support and grow the R&D ecosystem. Corporate VC investments have steadily grown over the last decade—increasing by over 130% since 2006. In fact, established

biopharmaceutical companies have invested more than \$6 billion in emerging biotechnology firms in the decade between 2006 and 2015 (see Figure 14). Much of this significant investment has been directed toward early-stage companies, with corporate venture arms participating in nearly 30% of early-stage deals in 2015, up from 13% in 2007.<sup>21</sup>



## RESPONDING TO SOCIETAL NEED

Increasingly, the biopharmaceutical industry is harnessing growing scientific and technological advances and collaborating across the life sciences ecosystem to ensure patients obtain the medicines they need.



### Meeting Unmet Medical Need for Patients:

Effectively leveraging growing scientific knowledge and emerging technologies to treat and cure disease requires collaboration and information exchange among the best and the brightest throughout the R&D ecosystem. Biopharmaceutical companies are increasingly working in strategic partnerships with other key stakeholders to create efficiencies and accelerate the R&D process to address a number of areas of unmet need for patients.

A forthcoming report from Deloitte explores how R&D partnerships are increasingly more open and collaborative. To pursue breakthrough discoveries in very difficult disease areas, three or more parties frequently are coming together with shared incentives to pool risks and rewards. Collaborations focused on driving a single molecule forward through clinical trials and to market remain common and effective,

but there are also many stakeholders pursuing scientific discovery in larger consortiums driven by common interests to solve the toughest unanswered therapeutic challenges and develop platform technologies that speed and enhance development of new treatments for patients.<sup>22</sup>

One exciting example of an innovative research collaboration is the Alzheimer's Disease Neuroimaging Initiative (ADNI). Historically, developing medicines to treat Alzheimer's disease, and many other neurological conditions, has been fraught with many challenges and setbacks due in large part to the complexity of these diseases. The ADNI collaboration is working to address these challenges to accelerate progress against this debilitating disease. A collaboration among federal agencies, nonprofit organizations, and industry members, ADNI aims to use neuroimaging to identify physical changes in the brain before the onset of the disease and to track the progression of these changes. The initiative also will establish quality standards for imaging data collection and sharing, and will validate biomarkers to be used in clinical trials. Data collected from ADNI are made available at no cost to other researchers to analyze and use when designing Alzheimer's disease clinical trials and research projects.<sup>23</sup>

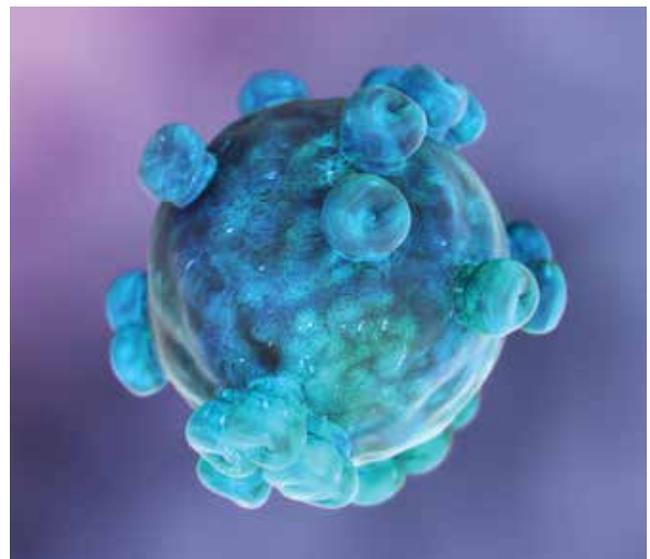
Research collaborations such as these demonstrate the commitment of researchers across the life sciences ecosystem to collectively tackle the most complex and challenging diseases of our time in order to bring new medicines to patients.

### Combating Serious Public Health Threats:

Epidemics or outbreaks of infectious disease can range in severity and impact. The public health threat posed by these rapidly evolving disease outbreaks makes close coordination and collaboration even more important, as stakeholders work to accelerate research and to protect patients and their families. The biopharmaceutical industry is committed to advancing novel vaccine and therapeutic options for infectious diseases.

The industry's swift response to the Ebola virus is evidence of this commitment. In coordination with researchers around the world, across both public and private sectors, biopharmaceutical companies have been working to develop new ways to prevent the spread of Ebola and to treat patients with the disease. Although on average it takes 10 to 15 years to develop a new medicine, biopharmaceutical researchers have been working to compress that timeline for Ebola projects in their pipelines. Conducting clinical research in an infectious disease that has an unusual origin, unpredictable mechanisms to spread, and occurs in seemingly sporadic episodes creates many challenges for researchers as they look to identify and recruit patients and produce adequate supplies of medicines. Additionally, the fragmented infrastructure, in terms of electricity and transportation, in many underdeveloped countries makes it difficult to provide basic medical care, let alone conduct clinical trials.<sup>24</sup> The biopharmaceutical industry works with public health and regulatory agencies to find innovative solutions to these and many other complicated clinical research challenges.

The rapid evolution in our understanding of the impact of the Zika virus has triggered tremendous global coordination to accelerate vaccine options that may prevent the spread of this mosquito-borne, tropical disease. Many biopharmaceutical companies working in infectious disease have research platforms that are ongoing for vaccines that combat viruses in the same family as Zika, including dengue virus, chikungunya virus, and yellow fever. Building upon their existing platforms, these companies are exploring ways to leverage their infrastructure and growing knowledge base to help develop a vaccine for Zika.<sup>25</sup> These companies are coordinating closely with scientific and public health organizations around the world to assess the feasibility of various discovery and preclinical streams, and are collaborating to find ways to accelerate what is normally a very difficult and cumbersome clinical development process.



Additionally, in times of acute public health threats, such as recent outbreaks of Ebola and the Zika virus, the industry works collaboratively across both public and private

## MOBILIZING TO STOP PUBLIC HEALTH EPIDEMICS<sup>26</sup>

Each year, leaders at the Cleveland Clinic develop a list of the top 10 medical innovations they believe will shape health care over the next 12 months. Topping the list for 2015 was the progress scientists, physicians, and public health officials made toward developing new vaccines to curtail and prevent public health epidemics. These transformative efforts by researchers and the public health community were particularly evident in 2014 as they faced the urgency of the Ebola epidemic in West Africa and outbreaks of bacterial meningococcal (Meningococcal B) in the United States.

The Ebola epidemic that started in 2014 killed more than 10,000 people in Sierra Leone, Guinea, and Liberia. The global community came together and coordinated unprecedented information-sharing to accelerate vaccine development. A phase III trial of one of the most promising vaccines, involving 4,000 people who had direct exposure to the virus, showed 100% protection after 10 days. At least five other candidate vaccines are in other phases of testing and experts at Cleveland Clinic expect a safe and effective vaccine soon.

Outbreaks of Meningococcal B occurred at two US universities in 2014. Meningococcal B is a particularly aggressive and dangerous disease that is highly contagious and can lead to death within 24 hours. Ten percent of infections are fatal and those that aren't can lead to devastating complications, including loss of limbs and sensory or neurological problems. The serious public health threat posed by the outbreaks fueled a race in the scientific and medical communities to develop an effective vaccine to prevent the spread of the disease. Today, two effective vaccines for Meningococcal B have been approved by the FDA and are available. Thousands of students at both universities were successfully vaccinated and the ability to prevent Meningococcal B is available to everyone.

**"The rapid scientific response to recent epidemics indicates that we've achieved a new level of sophistication in the area of vaccine development."**

—STEVEN GORDON, MD, CHAIR OF THE DEPARTMENT OF INFECTIOUS DISEASE AT CLEVELAND CLINIC

sectors to assist patients and their families through humanitarian and public health outreach. For example, in response to Ebola, PhRMA member companies sought to expand capacity on the ground in West Africa and donated medical products to assist affected patients. Companies are also providing funding to relief organizations for infrastructure improvements, medical products, and protective equipment for health care workers, as well as donating funds for disease education and prevention efforts within the region.

Biopharmaceutical research companies collaborate and mobilize in the face of public health threats (see sidebar: Mobilizing to Stop Public Health Epidemics).

**Helping Patients in Times of Disaster:** During major disasters, people must have access to critical medicines. Building resilience in communities supports health and creates economic strength so that if disaster strikes quality of life returns to normal as fast as possible.

Healthcare Ready, formerly known as Rx Response, helps to strengthen health care supply chains through collaboration with public health and private sectors by addressing pressing issues before, during, and after disasters. As the convener of industry and government, Healthcare Ready safeguards patient health by offering solutions to critical problems and providing best practices to facilitate health care preparedness and response.

Since its inception in the aftermath of hurricane Katrina over a decade ago, Healthcare Ready has helped companies, government agencies, and other organizations quickly and effectively address health care supply chain concerns before, during, and after disasters. In addition, Healthcare Ready offers Rx Open, an online resource that maps the location of open pharmacies in disaster-stricken areas. Please visit [www.healthcareready.org](http://www.healthcareready.org) for more information.

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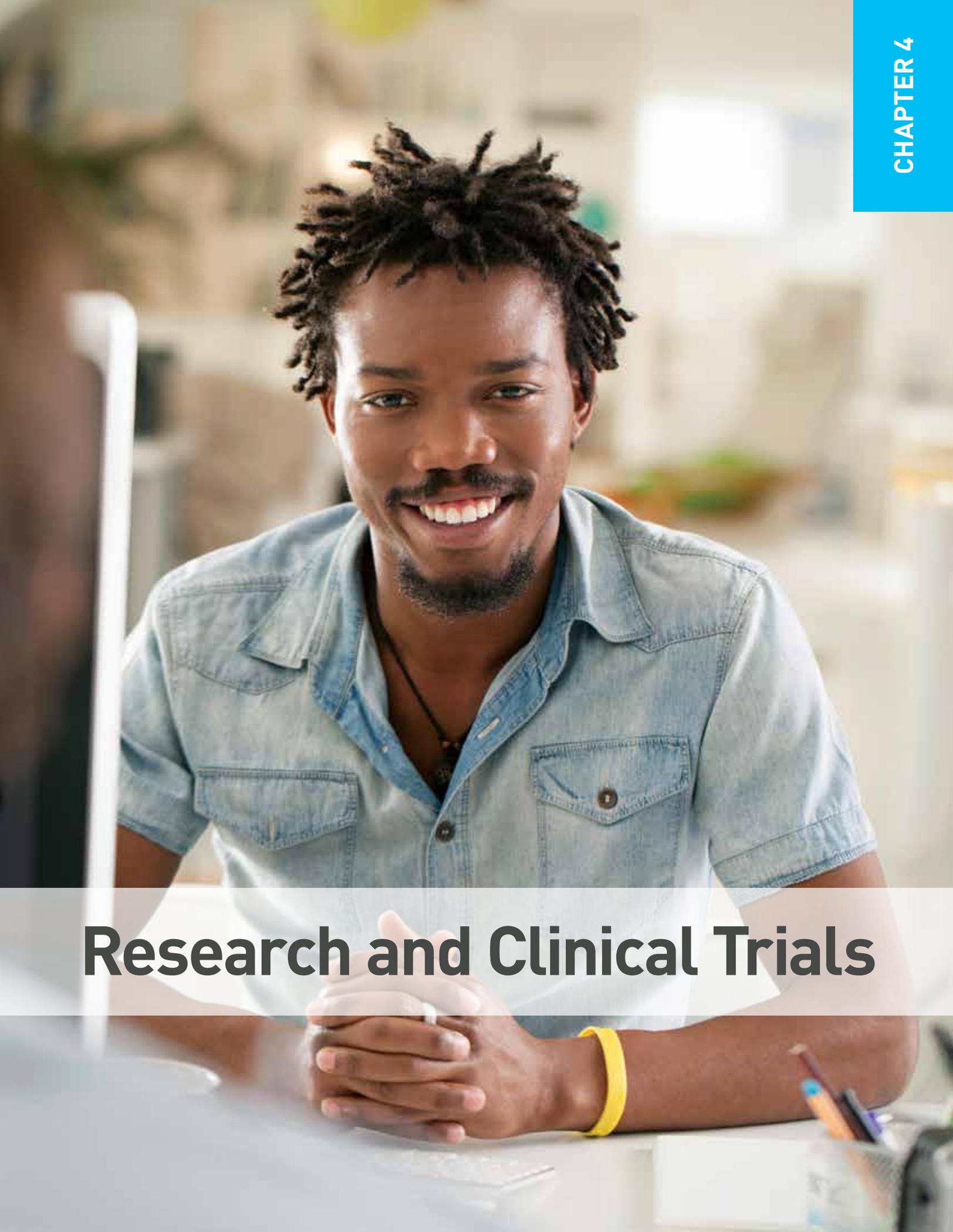
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A young Black man with short dreadlocks is smiling warmly at the camera. He is wearing a light blue denim button-down shirt and has his hands clasped on a white desk. A yellow wristband is visible on his left wrist. The background is a blurred office environment with a computer monitor on the left and a pen holder on the desk to the right.

# Research and Clinical Trials

# Research and Clinical Trials



**S**cientific and technological advances and growing understanding of the underlying mechanisms of disease are fueling the development of new treatments and cures for patients. At the same time, the costs, time, and complexities of biopharmaceutical research have also increased, introducing additional challenges in the research and development (R&D) process.

The drug development process begins with the screening of an enormous number of potential

medicines with some companies screening compound libraries numbering in the millions. From the time a potentially promising candidate medicine is identified and optimized, on average it takes 10 to 15 years for a medicine to make its way through the entire R&D process to US Food and Drug Administration (FDA) approval. And only 12% of investigative medicines entering clinical trials are ultimately approved by the FDA. The average cost to develop a new medicine is estimated at \$2.6 billion dollars, including the cost of failures. Evidence suggests these costs

are on the rise and even higher when accounting for the cost of research that continues after a medicine has been approved. In fact, the cost of development has more than doubled over the last decade (see Figure 15).<sup>1</sup>

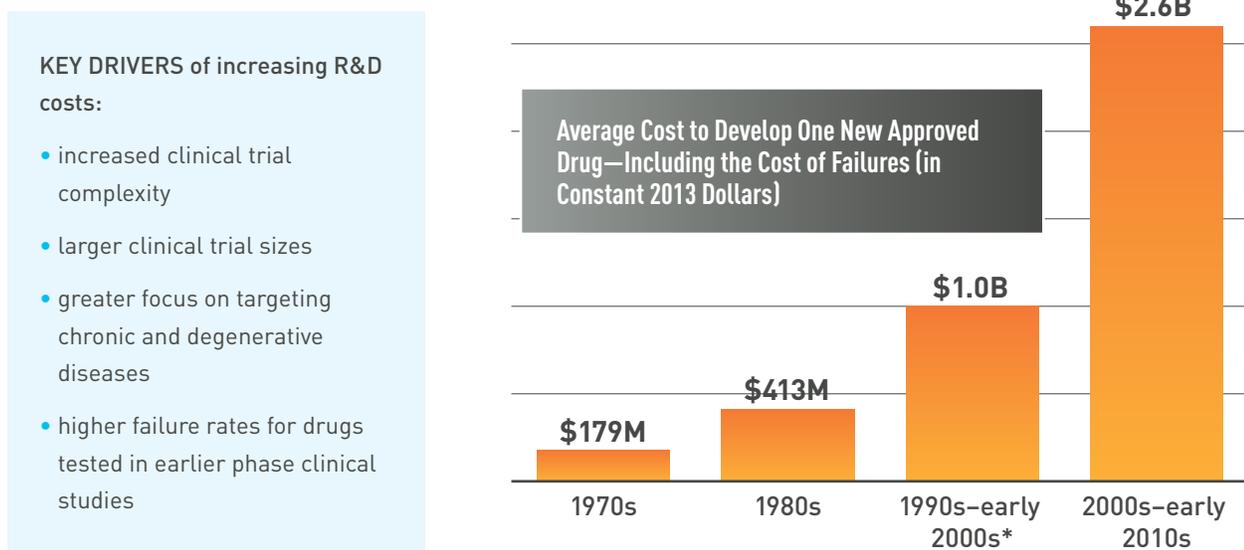
In light of these challenges, the nation’s innovative biopharmaceutical research companies remain committed to bringing new and important treatment options to patients and are working to introduce new efficiencies in the R&D process. PhRMA members alone invested an estimated \$58.8 billion in R&D in 2015 and have invested more than half a trillion since 2000.<sup>2</sup> One of the nation’s most R&D intensive enterprises, the biopharmaceutical sector represents the single largest share of business R&D, accounting for approximately 17% of all

R&D spending by US businesses.<sup>3</sup> Today, there are more than 7,000 medicines in development globally, with the potential to address serious unmet needs of patients with a variety of complex and challenging diseases.<sup>4</sup>

### OVERVIEW OF THE R&D PROCESS

Although millions of potential drug candidates may be screened and assessed early in the R&D process, many compounds ultimately fail to make it through the R&D pipeline. Candidate medicines must navigate a lengthy, complicated, multi-step process before being approved by the FDA and delivered to patients. And the journey does not end with FDA approval; ongoing research and data collection, as the medicine is used in a clinical setting and examined in any required post-approval studies, will continue to provide

**FIGURE 15: The Costs of Drug Development Have More Than Doubled Over the Past Decade**

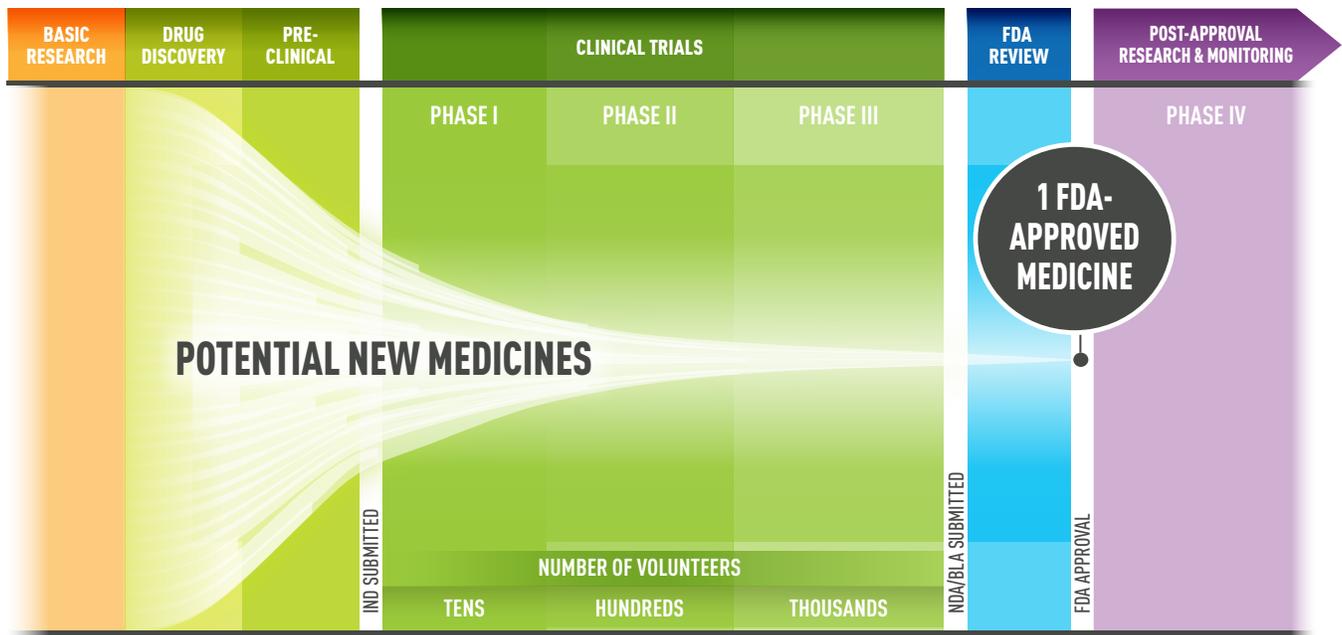


\*Previous research by same author estimated average R&D costs in the early 2000s at \$1.2 billion in constant 2000 dollars (see DiMasi JA, Grabowski HG. The cost of biopharmaceutical R&D: is biotech different? *Managerial and Decision Economics*. 2007;28: 469-479). That estimate is based on the same underlying survey as the author’s estimates for the 1990s to early 2000s reported here (\$800 million in constant 2000 dollars), but updated for changes in the cost of capital.

Source: DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: new estimates of R&D costs. *J Health Economics*. 2016;47:20-33.

**FIGURE 16: The Lengthy, Costly, and Uncertain Biopharmaceutical Research and Development Process**

From drug discovery through FDA approval, developing a new medicine on average takes 10 to 15 years and costs \$2.6 billion.\* Less than 12% of the candidate medicines that make it into phase I clinical trials are approved by the FDA.



Key: IND: Investigational New Drug Application, NDA: New Drug Application, BLA: Biologics License Application

\* The average R&D cost required to bring a new, FDA-approved medicine to patients is estimated to be \$2.6 billion over the past decade (in 2013 dollars), including the cost of the many potential medicines that do not make it through to FDA approval.

Sources: PhRMA adaptation based on DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: new estimates of R&D costs. *J Health Economics*. 2016;47:20-33; DiMasi JA, Grabowski HG, Hansen RW; Tufts Center for the Study of Drug Development. Innovation in the pharmaceutical industry: new estimates of R&D costs. In: Briefing: Cost of Developing a New Drug. [http://csdd.tufts.edu/files/uploads/Tufts\\_CSDD\\_briefing\\_on\\_RD\\_cost\\_study\\_-\\_Nov\\_18\\_2014.pdf](http://csdd.tufts.edu/files/uploads/Tufts_CSDD_briefing_on_RD_cost_study_-_Nov_18_2014.pdf). Published November 18, 2014. Accessed April 2016; US Food and Drug Administration. US Food and Drug Administration drug approval process. <http://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/UCM284393.pdf>. Accessed April 2016.

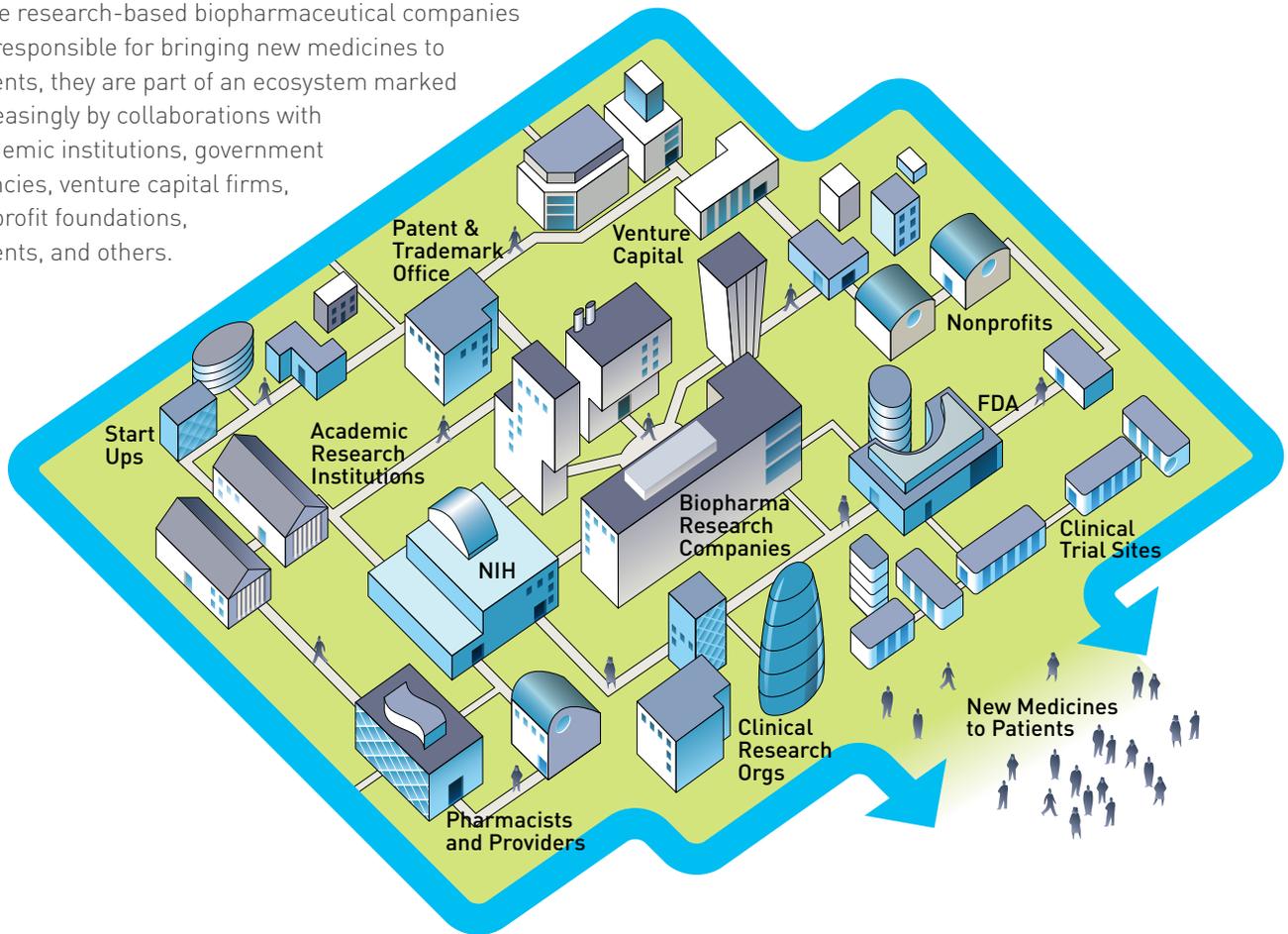
important insights (see Figure 16). These findings can lead to expanded treatment options and mean greater hope for patients.

Innovative biopharmaceutical companies are increasingly incorporating the patient perspective into all stages of drug development, including patient insights on their diseases, symptoms, and treatment options. Finding ways to incorporate a robust, science-based understanding of patient perspectives into decisions that promote innovation and expedite drug development is becoming a critical focus of the R&D process.

America’s innovative biopharmaceutical companies are the heart of a dynamic R&D ecosystem that includes academic researchers, the National Institutes of Health (NIH), the FDA, nonprofit patient and disease groups, clinical research organizations, clinical trial centers, health care providers, venture and other private capital investors, among others. This diverse group of individuals and organizations work in concert to advance novel science and therapeutics and to move potential new medicines through the R&D pipeline to FDA approval for patient use (see Figure 17).

**FIGURE 17: Innovative Biopharmaceutical Companies Sit at the Heart of a Dynamic R&D Ecosystem in the United States**

While research-based biopharmaceutical companies are responsible for bringing new medicines to patients, they are part of an ecosystem marked increasingly by collaborations with academic institutions, government agencies, venture capital firms, nonprofit foundations, patients, and others.



## Drug Discovery

The first step in the biopharmaceutical R&D process is to identify diseases and conditions for which new or expanded treatment options are needed. By understanding the mechanisms of disease, researchers are able to hone in on specific drug targets. They then look for a promising candidate compound that offers the potential to affect that target and eventually become a medicine. Even at this early stage, researchers are already thinking about the final product and the best ways to manufacture and deliver the potential new medicine to patients.

## Preclinical Testing

Before studying a potential medicine in humans, the most promising candidates are selected and optimized for preclinical testing. Researchers conduct a series of laboratory and animal studies to test how the medicine works and assess its safety. This usually takes several years, and in the end, only a few compounds move on to clinical studies in humans.

## Clinical Trials

After successfully completing preclinical studies, scientists file an Investigational New Drug



application with the FDA, outlining the preclinical study results and a detailed plan for the clinical study program in humans. These studies—known as clinical trials—are designed to demonstrate the medicine’s safety and efficacy. The sponsoring company works closely with an independent institutional review board (IRB) composed of physicians, researchers, and members of the general public to ensure the clinical trials are ethical and the rights and welfare of participants are protected at all times. Furthermore, the IRB ensures research risks are minimized and reasonable in relation to potential benefits.<sup>5</sup> Biopharmaceutical companies take tremendous

care to protect trial participants and ensure they are informed of potential benefits and risks associated with clinical trial participation.

Clinical trials occur in phases, and a potential medicine must complete each phase successfully before undergoing FDA review and approval. In the end, only 12% of candidate medicines that enter clinical trials are actually approved.<sup>6,7</sup>

- **Phase I** trials test the candidate medicine in a small group (e.g., 100 or less) of healthy volunteers to assess the compound’s safety and how it is best metabolized or processed in the body.
- **Phase II** trials involve a somewhat larger group of patient volunteers (100 to 500) living with the disease or condition the compound is designed to target. In addition to examining the compound’s safety and possible short-term side effects, phase II trials also evaluate the compound’s effectiveness and identify optimal dosing.

## SPOTLIGHT ON THE PRESCRIPTION DRUG USER FEE ACT (PDUFA)

Conducting a thorough review of a marketing application for a new medicine is a complex process. By the mid- to late-1980s, in light of the emerging AIDS epidemic, there was increased frustration that the slow process of drug review and approval was delaying patient access to important new medicines.<sup>8</sup> PDUFA was enacted in 1992 and subsequently renewed in 1997 (PDUFA II), 2002 (PDUFA III), 2007 (PDUFA IV), and 2012 (PDUFA V). The legislation authorizes the FDA to collect user fees from companies submitting applications for novel new medicines to provide for the appropriate levels of technical and scientific expertise to efficiently conduct reviews of human drug applications at the FDA and accelerate application review timelines.<sup>9</sup> To ensure timely reviews, FDA is held to specific performance benchmarks—10 months for standard reviews and 6 months for priority reviews. PDUFA has had a significant impact on reducing the so-called “drug lag,” and in 2015 the FDA’s Center for Drug Evaluation and Research approved 96% of applications within the benchmark review timelines.<sup>10</sup> PDUFA agreements also contain several procedural and processing goals that aim to improve communication and coordination between the FDA and innovative biopharmaceutical companies.<sup>11</sup>

- **Phase III** trials test the compound in a much larger group of patients (usually in the thousands). The purpose of these studies is to generate a wealth of statistically significant information about the safety and efficacy of a candidate medicine to determine the overall benefit–risk ratio.

### **FDA Review and Approval**

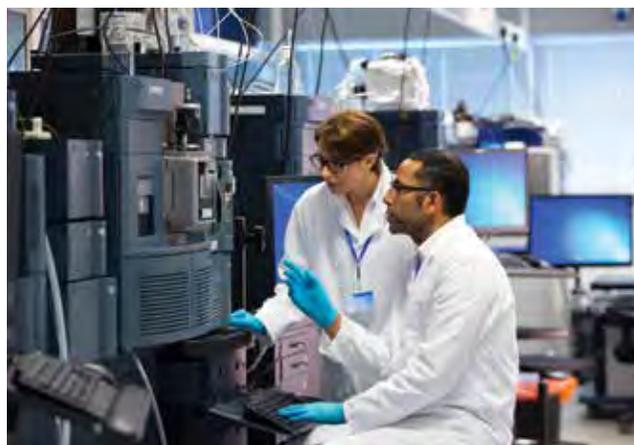
If clinical trial results show the compound is safe and effective, the sponsoring company submits a New Drug Application or a Biologics License Application to the FDA seeking review and approval to market the drug. The application presents an analysis of the results gathered throughout the clinical trials and earlier preclinical testing. It also includes proposals for manufacturing and labeling the new medicine.

FDA scientists carefully review the application, and after weighing the compound’s benefits and risks, they decide whether or not to grant approval. Sometimes the FDA will request additional research data before granting approval. Other times it will convene an independent panel of experts to examine data presented by the FDA and the sponsoring company. The panel then advises the agency on whether or not the application should be approved or if additional research is needed to test the medicine’s safety and efficacy. FDA then makes a final decision on whether to approve a new therapy.

### **Manufacturing**

At the same time the candidate compound is navigating the clinical trial process, company scientists are working to identify the best way to manufacture and package the new medicine

for patients. A new medicine will be taken by a larger group of patients than those participating in a clinical trial, so careful planning is required to ensure consistent product quality when production is scaled up. This process also includes ensuring enough medicine can be produced continuously in order to be available for patients as needed.



Manufacturing facilities are constructed to the highest standards to ensure that safety and quality are built into each step of the manufacturing process.<sup>12</sup> Companies must adhere to FDA’s Current Good Manufacturing Practices regulations. They also must constantly update, overhaul, or even rebuild facilities when new medicines are approved because each new medicine is manufactured differently. Many biopharmaceutical companies use the latest green manufacturing approaches to streamline the process and reduce the use of resources such as energy and water—lowering operating costs while protecting the environment at the same time.<sup>13</sup>

In recent years, rapid changes in molecular science have revolutionized the biopharmaceutical industry. The advent of personalized or targeted therapies, the increased prevalence of large

molecule medicines, and the enormous growth in the number of treatments for orphan diseases are having a profound impact on how medicines are created and manufactured on a large scale. To capitalize on the shifting global landscape, companies are investing in the latest innovative manufacturing techniques—from raw materials to finished drug products. These advances—including use of continuous manufacturing, process analytical technology, single-use systems, and other new technologies—are driving manufacturing flexibility and scalability while simultaneously improving quality and efficiency. These advanced techniques are efficiently helping to deliver higher quality medicines to patients

and supporting the nation’s standing as a global leader in innovation.<sup>14</sup>

### **Phase IV and Other Post-Approval Research and Monitoring**

Research on a new medicine doesn’t stop when it receives FDA approval. The FDA requires companies to conduct long-term safety monitoring of approved medicines and may ask companies to collect ongoing safety and efficacy data for specific subgroups of patients. Companies may conduct post-approval studies to evaluate a medicine’s benefits in additional patient groups, beyond those studied in the original clinical trials, or to evaluate efficacy in related

## **PUBLIC/PRIVATE ROLES IN THE DRUG DEVELOPMENT PROCESS<sup>15</sup>**

The United States is the worldwide leader in biopharmaceutical innovation. Government research has always played an important role in laying the groundwork for drug development. In fact, the collaborative ecosystem that exists in the United States between the government, academia, and biopharmaceutical companies is among our country’s greatest strengths in moving medical advances forward.

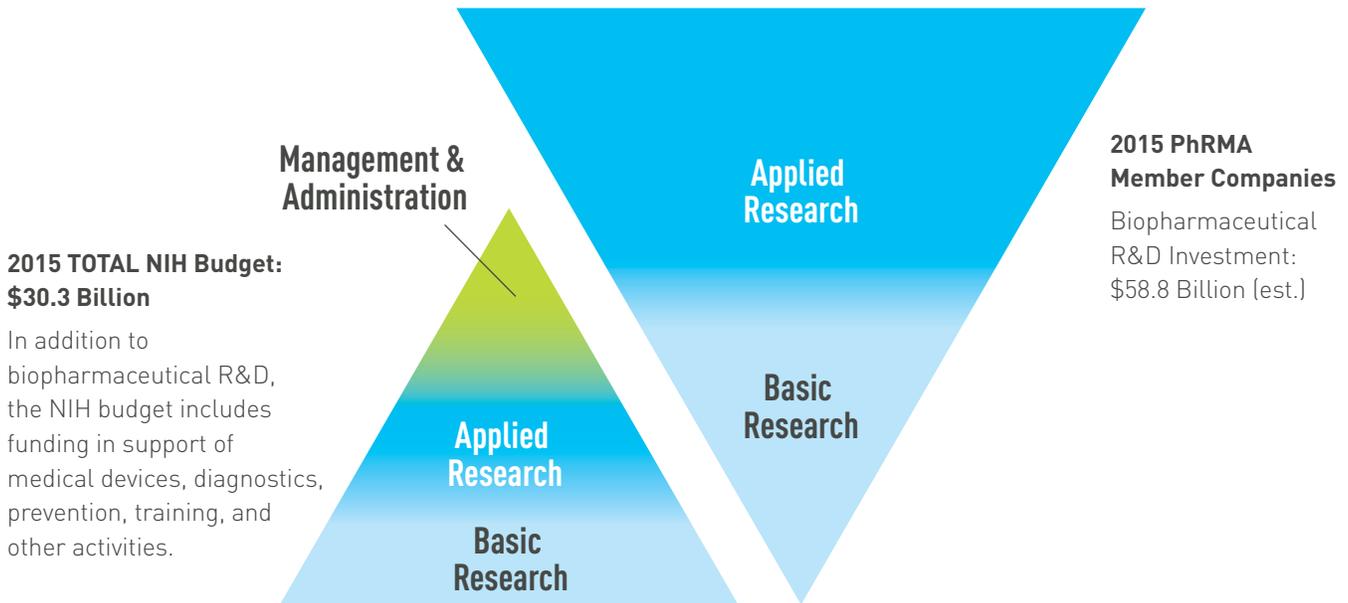
The role of government in the development of new medicines is largely indirect because biopharmaceutical companies build on basic research and translate those findings into therapies for patients. The NIH Office of Technology Transfer reinforces the large role of applied research by private companies and others in translating basic research findings into advances for patients, reminding us basic research is necessary but not sufficient for producing new medicines (see Figure 18).

**“Today, most important developments in medical science typically begin in laboratories, such as the discovery of specific new biological molecules, processes, or pathways, or innovative applications of existing knowledge. In most cases, these discoveries in and of themselves have limited effect beyond meeting a fairly narrow research goal. Their real impact for public health generally comes after several more significant steps—including further R&D, testing, approval by appropriate regulatory bodies (such as the FDA), manufacturing, and distribution.” (emphasis added)**

—NIH OFFICE OF TECHNOLOGY TRANSFER<sup>16</sup>

**FIGURE 18: Biopharmaceutical Companies Do the Vast Majority of Research to Translate Basic Science into New Medicines**

While basic science is often initiated in government and academia, it is biopharmaceutical firms that provide the necessary critical mass, expertise, and experience needed to develop new medicines.



Total National Institutes of Health (NIH) spending is for fiscal year 2015. In addition to funding for basic and applied research, the total NIH budget includes funding in support of prevention (eg, suicide prevention), diagnostics and medical devices, Superfund Research Program activities, training and education (eg, dental), program evaluation, management and support, buildings and facilities, and other activities. PhRMA member companies' R&D spending is estimated for calendar year 2015. PhRMA member companies account for the majority of private biopharmaceutical R&D spending. Nonmember company data are not included.

Sources: Chakravarthy R, Cotter K, DiMasi J, Milne C-P, Wendel N; Tufts Center for the Study of Drug Development. Public and private sector contributions to the research & development of the most transformational drugs of the last 25 years. <http://csdd.tufts.edu/files/uploads/PubPrivPaper2015.pdf>. Published January 2015. Accessed April 2016; Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA Annual Membership Survey, 1995-2015. Washington, DC: PhRMA; 2016; National Institutes of Health (NIH), Office of Budget. FY 2016 president's budget request. NIH Office of Budget Web site. <https://officeofbudget.od.nih.gov/br2016.html>. Accessed April 2016.

disease areas. Researchers also study longer-term benefits and risks and assess whether or not possible adjustments may deliver even greater value to patients, including the development of improved delivery or dosages. Further, such information can inform future efforts to discover and develop even better medicines for patients.

**THE EVOLVING R&D PROCESS**

The R&D process constantly adapts and changes as new science emerges and as the policy environment also shifts and changes. With new scientific advances comes greater promise and increased complexity, as well as greater

uncertainty for biopharmaceutical companies. This is particularly evident as they focus on complex disease areas of greatest scientific risk, such as Alzheimer's disease. Growing complexity of clinical trials, uncertainty concerning intellectual property (IP) rights, changing coverage and reimbursement requirements from payers, and continued challenges related to capital and investment are driving an increasingly complex and costly R&D process. A few examples of forces changing the R&D process include:

- **Complexity of Science:** Scientists' ever-deepening understanding of the biologic

causes of disease yields new opportunities while also changing numerous aspects of the drug development process. For example, personalized medicine offers enormous potential to revolutionize the treatment paradigm, but the complex nature of the development process for these exceptionally precise treatments and diagnostic tests requires changes in how medicines are identified, studied, and manufactured.

- **Research on Complex Diseases:** Investigators continue to explore potential new treatment options for more complex diseases such as neurological disorders, cancer, and many rare diseases for which few or no treatments exist. For example, the number of Alzheimer’s disease medicines in development jumped from 26 in 2003 to 82 today.<sup>17,18</sup> Science has always been, and always will be, about exploration, but

with exploration comes the inevitable setbacks inherent in the research of complex diseases.

- **Regulatory Environment:** The regulatory requirements and growing complexity of clinical trials translates into more numerous and more complex eligibility criteria for study enrollment, increased site visits and required procedures, longer study duration, and more rigorous data collection requirements. Recruiting patients for clinical trials can also be challenging, especially as science reveals molecular identifiers of various diseases that allow researchers to focus on increasingly narrow and specific patient populations. The form researchers use to collect data from each trial participant more than doubled in length between 2000 and 2011, underscoring the increased efforts required from the clinical trial research community (see Figure 19).<sup>19</sup>

**FIGURE 19: The Complexity of Clinical Trials Has Increased**

During the last decade, clinical trial designs and procedures have become much more complex, demanding more staff time and effort, and discouraging patient enrollment and retention.

TRENDS IN CLINICAL TRIAL PROTOCOL COMPLEXITY	2000–2003	2008–2011	Increase in Complexity
Total procedures per trial protocol (median) (eg, bloodwork, routine exams, x-rays)	105.9	166.6	57%
Total investigative site work burden (median units)	28.9	47.5	64%
Total eligibility criteria	31	46	48%
Clinical trial treatment period (median days)*	140	175	25%
Number of case report form pages per protocol (median)	55	171	211%

\*These numbers reflect the “treatment duration” of the protocol only.

Sources: Getz KA, Campo RA, Kaitin KI. Variability in protocol design complexity by phase and therapeutic area. *Drug Inf J.* 2011;45(4):413-420; updated data provided through correspondence with Tufts Center for the Study of Drug Development.

- Incorporating the Patient Perspective:**  
 Biopharmaceutical companies are working on integrating patient perspectives into the drug development process. Incorporating patient

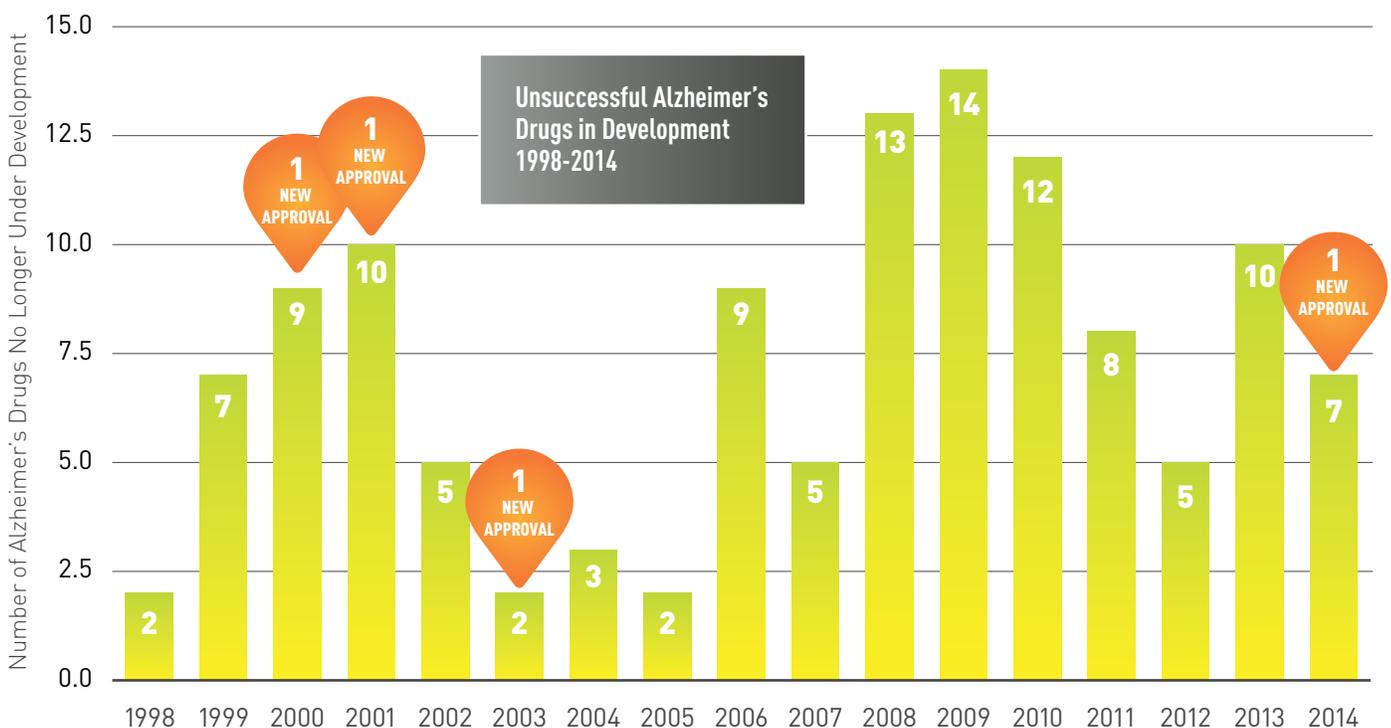
views on the outcomes that matter most to them, in terms of quality of life, day-to-day impact, and new therapy's benefits and risks, allows researchers to develop medicines that

## RESEARCHING ALZHEIMER'S MEDICINES: SETBACKS AND STEPPING STONES

Although a number of recent scientific advances have led to innovative treatments for patients, for many disease areas, the more we learn about a disease the greater our appreciation for a disease's complexity and mystery. Such has been the case with Alzheimer's disease, where just four new medicines were approved during the same period where there were 123 so-called "failures," where medicines did not make it through the development process (see Figure 20). Although frustrating, these setbacks give researchers important insights that give them a better understanding of the disease and inform research on other medicines in development. This is an inherent part of biopharmaceutical research. A PhRMA report exploring these crucial stepping stones is available at <http://www.phrma.org/sites/default/files/pdf/alzheimersetbacksreportfinal912.pdf>.

**FIGURE 20: Setbacks in Alzheimer's Disease Research Provide Stepping Stones for Future Innovation**

Since 1998, 123 medicines in development for the treatment of Alzheimer's disease have not made it through clinical trials, with only 4 gaining FDA approval. These setbacks highlight the complexity of the R&D process. Though disappointing, they provide important knowledge to fuel future research.



Source: Pharmaceutical Research and Manufacturers of America (PhRMA). Researching Alzheimer's medicines: setbacks and stepping stones. <http://phrma.org/sites/default/files/pdf/alzheimers-setbacks-and-stepping-stones.pdf>. Published 2015. Accessed April 2016.

## STRATEGIES TO ADAPT TO NEW CHALLENGES IN THE R&D PROCESS

To address the increasing challenges, costs, and uncertainties associated with the drug discovery and development process, biopharmaceutical companies are retooling their R&D capabilities to ensure the efficient discovery and development of the next generation of medicines. Although more progress is needed, these efforts have begun to bear fruit in the form of FDA-approved innovative new medicines. Tufts Center for the Study of Drug Development examined innovative approaches biopharmaceutical companies are taking to improve the efficiency and productivity of their research efforts. These approaches include:

- **Improving validation of drug targets**—the process of clearly defining the role of proteins, genes, and other molecules involved in disease pathogens.
- **Increasing integration of information technology infrastructure and real world data into the R&D process** by integrating, storing, interrogating, and analyzing large datasets from multiple sources to develop more targeted therapies and personalized medicines.
- **Exploring new clinical trial approaches such as adaptive clinical trial design**, allowing drug developers to adjust clinical trial design elements after a trial is underway using interim data collecting.<sup>20</sup>

achieve outcomes that are more meaningful for patients.

- **Coverage and Payment Uncertainty:** Both in the United States and abroad, coverage and payment policies for new medicines affect the amount of capital available for R&D investment. With this comes an element of uncertainty that may diminish future R&D. Reimbursement hurdles create new challenges in designing clinical trials in which trial endpoints meet regulatory requirements but do not necessarily meet the standards of public and private payers. Incorporating the patient voice earlier in the drug development process may help in delivering value-driven health care, as stakeholders work together to reconcile what payers value and what patients value from their medicines.
- **Intellectual Property:** Both in the United States and abroad, adequate IP rights and

their enforcement remains a challenge. New threats to the strength and enforceability of patents as well as the repeated calls to reduce the data exclusivity period for innovative biologics are increasing business uncertainty for established and emerging biopharmaceutical companies, negatively impacting their ability to make long-term R&D investment decisions. Without adequate IP protection, companies will not be able to make the significant investments needed to bring new medicines to patients due to uncertainty about their ability to recoup costs and fund new research.

### ADAPTING AND EVOLVING

Increasingly, biopharmaceutical researchers are exploring innovative ways to reduce development times and boost the odds of success, including using new research tools, unique approaches to trial recruitment, and more sophisticated

data collection and analysis methods. In fact, industry researchers are leveraging the power of collaboration to conquer the most perplexing scientific and technological challenges. More than ever, biopharmaceutical researchers are joining forces with academic medical research centers, governmental institutions, nonprofit organizations, patient advocacy groups, and others to share risk and to exchange intellectual, financial, and in-kind resources to advance the science and drive innovation for patients. In addition, precompetitive partnerships and risk-sharing consortia continue to emerge as innovative means of collaboration and information-sharing.<sup>21</sup> New platforms for data collection and data sharing will also have a significant impact on biopharmaceutical R&D, enabling closer collaboration and creating greater efficiency.

Biopharmaceutical companies in collaboration with other companies, regulatory bodies, clinical research organizations, patient and disease groups, academic medical research centers, and others are also actively exploring innovative clinical trial designs and methodologies that may provide more flexible and efficient pathways for clinical development. By capitalizing on the strengths of each partner and leveraging new strategies, these

innovations can translate into a more efficient use of resources and, most importantly, accelerate the discovery and development of new treatment options for patients.



For example, researchers are using adaptive clinical trials to adjust specific elements of a given trial, such as dosing, number of participants, and the patient population, after a trial is already underway to create efficiencies. Lung-MAP—a first-of-its-kind clinical trial collaboration—uses a multi-drug, targeted screening approach to match patients through genetic information to one of several different investigational medicines that treat recurrent squamous cell lung cancer.

**"Biopharmaceutical companies...are using a wide variety of innovative approaches to adapt the R&D and manufacturing process to the changing scientific landscape. These innovative approaches to drug discovery, development, and manufacturing shed light on a resilient enterprise making progress in improving the quality, performance, and efficiency of R&D and manufacturing."**

—TUFTS CENTER FOR THE STUDY OF DRUG DEVELOPMENT<sup>22</sup>



The FDA, National Cancer Institute, SWOG Cancer Research, Friends of Cancer Research, the Foundation for the NIH, Foundation Medicine, and numerous lung cancer advocacy groups have joined forces with at least five different biopharmaceutical companies to build the infrastructure necessary to drive such a novel design. Patients undergo targeted screening that directs them to specific studies testing different investigational medicines. All studies operate under a single master study protocol that allows more efficient information sharing

and study conduct.<sup>23</sup> This innovative approach to clinical research is anticipated to both improve access to promising therapies for patients and ease the significant clinical trial recruitment and infrastructure burdens of traditional clinical trials.

America's innovative biopharmaceutical companies continue to strive to accelerate the pace of innovation and deliver effective medicines to patients quickly and efficiently. By investing more time, energy, and resources in collaboration across the R&D ecosystem and leveraging more sophisticated research and manufacturing tools, our nation's innovative biopharmaceutical companies continue to advance the science forward. But even more important, with the ever expanding drug development pipeline and continued high levels of R&D investment, potential new medicines continue to offer tremendous promise and hope for patients.

**“Traditional clinical trials have long imposed significant recruitment and infrastructure burdens on researchers and patients, with frustratingly slow results. This master protocol will allow multiple enrollees to be tested once and assigned to a treatment most likely to work for them, rather than separate tests for separate trials with most patients ineligible. This strategy will validate biomarkers and facilitate drug development in one infrastructure, to more rapidly provide safer and more effective treatments to patients.”**

—MARIA FREIRE, PhD, PRESIDENT AND EXECUTIVE DIRECTOR OF THE FOUNDATION FOR THE NIH<sup>24</sup>

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# The Promise of the Pipeline

# The Promise of the Pipeline



**T**he rapid pace of scientific advances is giving patients unprecedented hope. Researchers are leveraging growing knowledge of the biological basis of disease and harnessing technological advances across the biopharmaceutical ecosystem to usher in a new era of treatment possibilities. This commitment to bringing new medicines to patients is evidenced by the robust pipeline of medicines currently in development. Today, more than 7,000 medicines targeting a

broad array of disease areas and conditions are in clinical development around the world (see Figure 21).<sup>1</sup> Many of these medicines have the potential to meet substantial unmet patient need. In fact, experts estimate 70% are potential first-in-class medicines with a mechanism of action distinct from any other marketed drug.<sup>2</sup>

Researchers are also leveraging their understanding of the molecular basis of disease to develop a new wave of targeted therapies.

Today, 42% of medicines in development have the potential to be personalized medicines, and 73% of cancer medicines have the potential to be personalized medicines.<sup>3</sup> For patients lacking treatment options or those for whom existing therapies have been unsuccessful, these potential medicines hold great promise in helping them live longer, healthier lives. But what's more, these medicines offer to alter the trajectory of some of the most complex and challenging diseases of our time.

### EXAMINING THE PIPELINE

Novel scientific approaches employed across the biopharmaceutical pipeline are giving patients new sources of hope. Here are just a

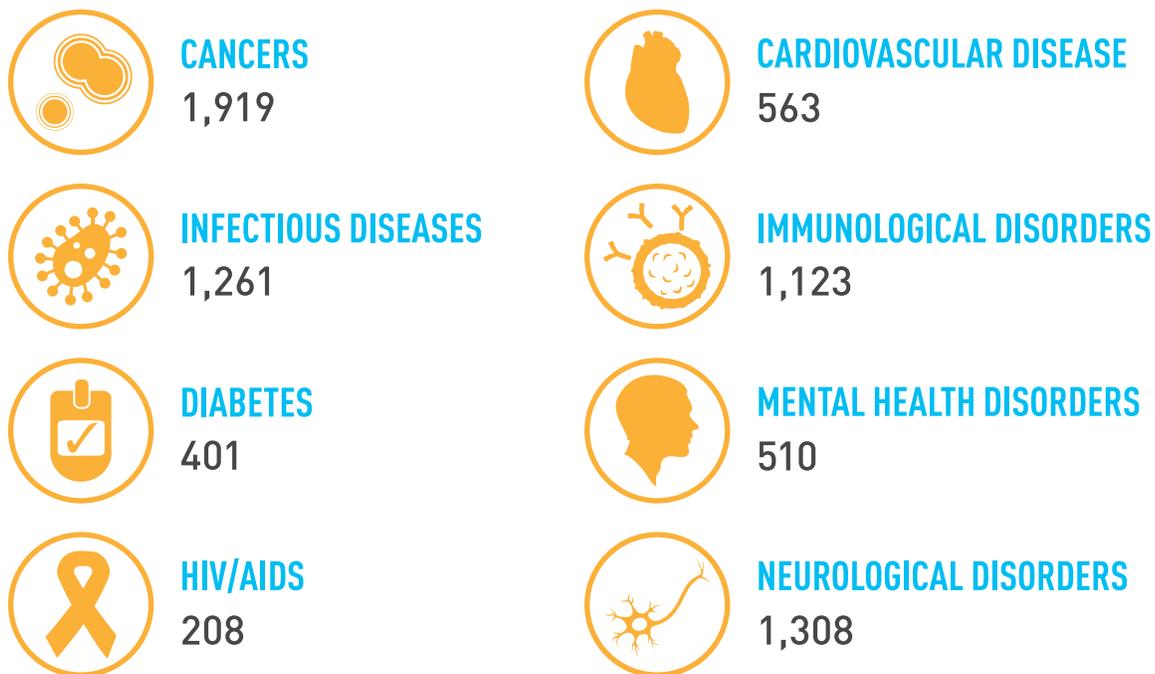
few examples of how researchers are exploring innovative strategies to deliver new medicines to patients across a broad range of complex diseases and conditions.

#### Multiple Sclerosis

Multiple sclerosis (MS) is a debilitating, chronic autoimmune disorder, which generally leads to disability. In MS, the immune system mistakenly attacks myelin, a substance that coats nerve fibers, resulting in a disruption of communication between the brain and the body. Common symptoms include fatigue, walking difficulties, numbness, spasticity, muscle stiffness, weakness, vision problems, sexual problems, bowel problems, pain, and cognitive and emotional

**FIGURE 21: More Than 7,000 Medicines in Development Globally**

Biopharmaceutical researchers are working on new medicines\* for many diseases, including:



\*Defined as single products that are counted exactly once regardless of the number of indications pursued

Source: Adis R&D Insight Database. Accessed March 2016.

changes. Approximately 400,000 Americans and 2.3 million people worldwide struggle with the condition. The vast majority of patients experience a relapsing–remitting form of the disease. However, about 10% of patients experience a progressive form of the disease in which there are no distinct relapses or remissions.<sup>4</sup>

The past several decades have yielded a number of effective treatments for patients with relapsing MS. However, there are no available treatments that treat the cause of the progressive form of the disease. The development of medicines for neurological conditions like MS has historically been challenging because these conditions are complex. Today the science is helping researchers navigate these complexities, offering significant hope for patients. More than 40 medicines are in development to treat MS—including for patients with the progressive form of the disease—with the potential to transform the treatment landscape.<sup>5</sup>

As just one exciting example, research findings suggest that anti-LINGO-1 antibodies may protect the nerves damaged by MS. Anti-LINGO-1 blocks a protein called LINGO-1. Because LINGO-1 is part of a pathway that inhibits the production of myelin, myelin growth is spurred when LINGO-1 is blocked. The medicine is being explored in both relapsing and progressive MS, and it may emerge as the first-ever treatment for patients with the progressive form of the disease.<sup>6</sup>

## Rare Diseases

Rare diseases are defined as those affecting fewer than 200,000 Americans. Collectively, however, rare diseases affect 30 million people—or 1 in 10 Americans.<sup>7</sup> There are currently about 7,000

known rare diseases, half of which affect children.<sup>8</sup> Unfortunately, rare diseases are often difficult to diagnose and in many cases few or no treatment options exist. Currently, approved treatment options are only available for approximately 5% of patients with rare diseases, indicating the substantial unmet patient need that remains.<sup>9</sup>



Approximately 80% of these conditions are caused by abnormalities in a person’s genes.<sup>10</sup> Researchers continue to learn more about the underlying genetic causes of these complex diseases, and today more than 450 medicines are under development to treat these conditions.<sup>11</sup>

For example, viral-based gene therapies are demonstrating considerable promise as a potential platform to target rare diseases. The process for these therapies involves removing stem cells from a patient, using a modified virus as a vehicle to insert a therapeutic gene into the removed cells, and returning the altered cells to the patient. Diseases best suited to this process are those caused by mutations in a single gene.

An investigational gene therapy appears to be yielding success against two rare blood disorders: sickle cell disease and beta-thalassemia. Another investigational medicine using the same platform is also showing promise against childhood cerebral adrenoleukodystrophy, a rare disorder affecting the nervous system of one in 20,000 boys.<sup>12</sup>

### **Blood Cancers**

More than 162,000 Americans are diagnosed with blood cancer each year, accounting for 9% of all new cancer diagnoses. In recent years, science has advanced quickly and opened up opportunities for more precise treatments as our understanding of the underlying causes of these diseases and our ability to treat them has grown. For example, just a few decades ago, blood cancers were known collectively as “diseases of the blood.” Today, we know blood cancers consist of at least 35 types of leukemia and 50 different lymphomas—all of which vary based upon genetic differences.<sup>13</sup>

Despite considerable research and clinical progress in the treatment of these diseases, an

unmet need remains for many patients. Today, 240 medicines are in development to treat leukemia, lymphoma, and other blood cancers.<sup>14</sup>

Chimeric antigen receptor (CAR) T-cell immunotherapy is an emerging cellular immunological approach demonstrating remarkable potential in clinical trials to help patients with blood cancers. CAR T-cell therapy involves removing immune-boosting T-cells from a patient, engineering them so they are able to recognize and kill cancer cells, and returning the engineered cells to the patient. A number of promising candidates in the pipeline target cancerous cells in patients with acute lymphoblastic leukemia, diffuse large B-cell lymphoma, and a range of other blood cancers.<sup>15</sup>



### **HIGHLIGHTING CANCER METABOLISM-TARGETING DRUGS**

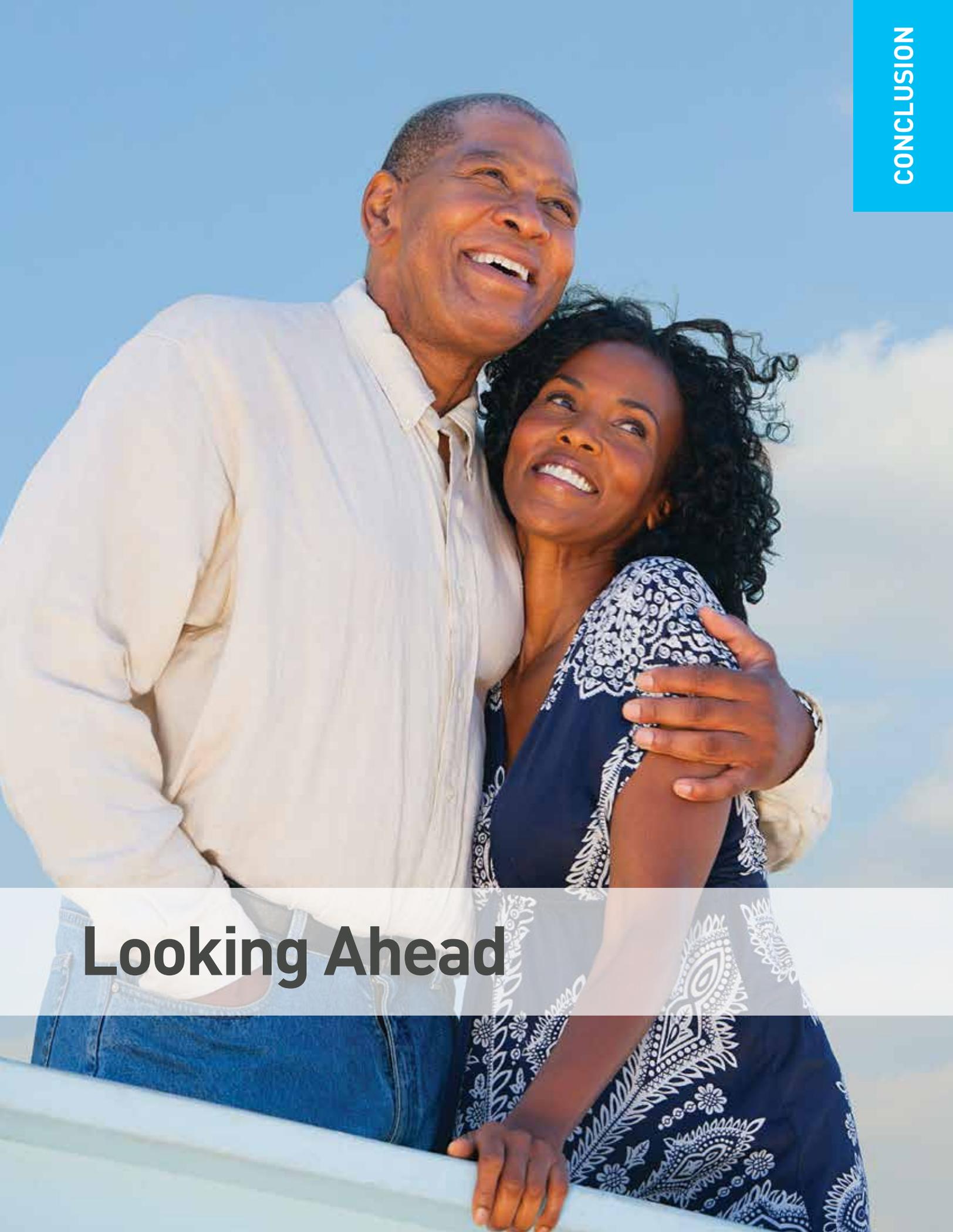
A new approach in cancer therapy has the potential to be broadly applicable across a wide range of cancers. Researchers have long understood the metabolism of cancer cells is aggressively ramped up relative to normal cell metabolism, enabling mutated cancer cells to grow exponentially at the expense of healthy surrounding tissue. A number of investigative medicines in clinical development aim to disrupt cancer cell metabolism and impede cell growth. Some of these medicines target genetic mutations involved in metabolic processes that may be more prevalent in certain cancers. Other cancer metabolism-targeting drugs in development aim to disrupt metabolic functions that occur in most types of cancer. The latter approach works by cutting off the energy supply to cancer cells, causing the cells to die. Medicines targeting cancer metabolism are being explored by researchers to address a range of different cancers, including acute myeloid leukemia, glioma, lung cancer, pancreatic cancer, breast cancer, and many other blood cancers and solid tumors; these medicines and the many being explored in combination with other cancer therapies offer tremendous hope for patients.<sup>16</sup>

The tremendous promise evident in today's biopharmaceutical pipeline represents not only the ever-growing knowledge of the genetic and biological basis of disease, but also the dedication of researchers to translate this incredible science into new and potentially

life-saving medicines for patients. Innovative approaches target a broad range of diseases, and this chapter highlights just a few examples of how researchers are striving to transform the lives of patients and the trajectory of today's most complex and challenging diseases.

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A photograph of a man and a woman, both smiling and looking towards the right. The man is wearing a white button-down shirt and blue jeans, and has his arm around the woman's shoulder. The woman is wearing a dark blue dress with a white pattern. They appear to be on a boat, with a white railing visible at the bottom. The background is a bright blue sky with some clouds.

# Looking Ahead

# Looking Ahead



**N**ew medicines are revolutionizing health care and helping millions of patients live longer, healthier lives. As innovative biopharmaceutical companies harness and translate new scientific and technological advances into new medicines, our industry with more than 7,000 medicines in development will continue to bring new hope to patients.

Delivering on this promise is not only critical to patients but central to sustaining and driving economic growth and US global competitiveness. A robust policy and regulatory framework is needed to ensure that companies can deliver on the promise of the pipeline. The framework includes the need for strong intellectual property (IP) rights and enforcement of IP rights both within the United States and abroad through

strong trade agreements. Trade agreements must promote a level playing field globally, as trade and innovation policies are increasingly entwined in the growing globalized economy.

The introduction of medical advances that are critical to improving patients' lives will also require a well-functioning, science-based regulatory system that fosters the timely review, approval, and introduction of medical advances. It will also require a regulatory system that embraces scientific and technological advances like new innovative clinical trial networks, incorporates patient-reported outcomes, and supports the development of personalized medicines and diagnostics.

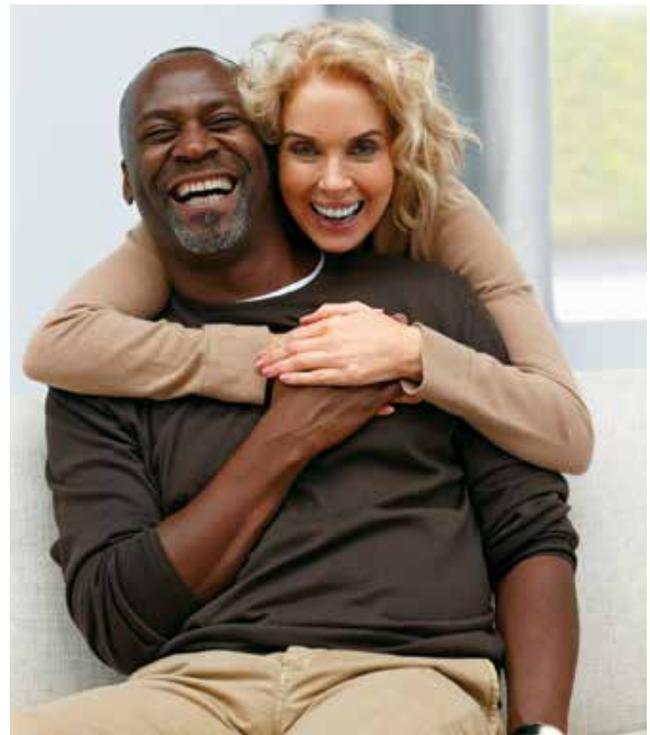
Public policies also need to foster the health care market's shift to new value-based payment incentives that would provide better value for patients and the health care system. New, value-based payment models would pay providers and other stakeholders for value, recognize the value of innovation in health care, create payment incentives based on care that patients value, and remove regulatory barriers to innovators' participation as partners in value-based health care. This will lead to better outcomes for patients, support continued innovation, and provide an alternative to proposals that rely on centralized government interventions that restrict patient access and impede continued innovation.

Consumers must also be empowered in the delivery of their care because a well-informed consumer is better equipped to judge value. This includes broader access to information on health care out-of-pocket costs and quality. In addition, vulnerable patients should have the protection of

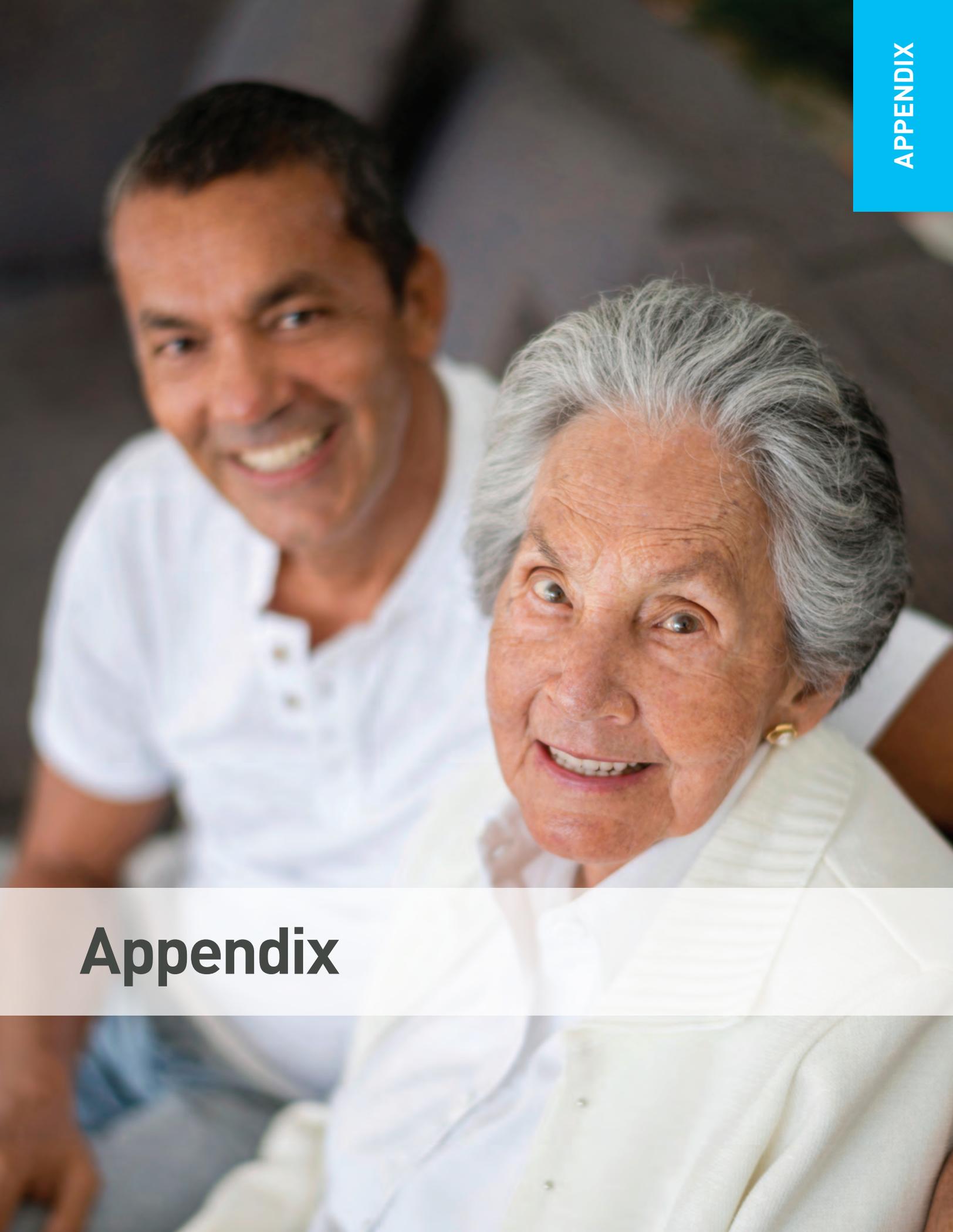
enforceable, common-sense rules that prevent discrimination and remove barriers to access. These steps will improve coverage and access and help make medicines more affordable to patients.

The United States hosts a dynamic, collaborative research ecosystem among government, academia, biopharmaceutical companies, and others. We must ensure that public policies sustain and grow this system, which is the envy of the world.

The biopharmaceutical industry is committed to working across the innovation ecosystem and supporting pragmatic, patient-centric approaches to building a stronger and more sustainable US health care system. Addressing health care holistically, we can build a sustainable, science-based health care system that stops the growth of chronic disease and harnesses today's hopes to discover tomorrow's cures.







# Appendix

# PhRMA: Who We Are, Mission, and Annual Membership Survey



## WHO WE ARE

The Pharmaceutical Research and Manufacturers of America (PhRMA) represents the country's leading biopharmaceutical companies, which are committed to discovering and developing medicines that save and improve lives. The work of the biopharmaceutical research sector brings hope to millions of patients, allowing them to live longer, healthier lives, while helping to manage health care costs. PhRMA member companies have invested nearly \$700 billion in research and development into medical innovations since 2000, and an estimated \$58.8 billion in 2015 alone. This investment also helps drive the industry's significant contributions to the US economy, including the generation of hundreds of thousands of American jobs and vital support for local communities.

## OUR MISSION

PhRMA's mission is to conduct effective advocacy for public policies that encourage discovery of important new medicines for patients by pharmaceutical and biotechnology research

companies. To accomplish this mission, PhRMA is dedicated to achieving these goals in Washington, DC, the states, and the world:

- Broad patient access to safe and effective medicines through a free market, without price controls
- Strong intellectual property incentives
- Transparent, efficient regulation and a free flow of information to patients

## PHRMA ANNUAL MEMBERSHIP SURVEY

Please visit <http://www.phrma.org/annual-membership-survey-results> for the following annual survey results:

### R&D, PhRMA Member Companies

**Table 1:** Domestic R&D and R&D Abroad, PhRMA Member Companies: 1980–2015

**Table 2:** R&D as a Percentage of Sales, PhRMA Member Companies: 1980–2015

**Table 3:** Domestic R&D and R&D Abroad, Human and Veterinary Use: 2014

**Table 4:** R&D by Function: 2014

**Table 5:** R&D by Geographic Area: 2014

### Sales, PhRMA Member Companies

**Table 6:** Domestic Sales and Sales Abroad: 1980–2015

**Table 7:** Sales by Geographic Area: 2014

# PhRMA Leadership 2016-2017



**PRESIDENT & CEO**  
**Stephen J. Ubl**  
PhRMA



**CHAIRMAN OF THE BOARD**  
**George A. Scangos, PhD**  
Chief Executive Officer  
Biogen



**CHAIRMAN-ELECT**  
**Joaquin Duato**  
Worldwide Chairman  
Pharmaceuticals Group  
Johnson & Johnson



**TREASURER**  
**Joseph Jimenez**  
Chief Executive Officer  
Novartis AG

## BOARD MEMBERSHIP



**Carlos Alban**  
Executive Vice President,  
Commercial Operations  
AbbVie



**Werner Baumann**  
Chairman of the Board  
of Management  
Bayer AG



**Robert A. Bradway**  
Chairman and  
Chief Executive Officer  
Amgen



**Olivier Brandicourt, MD**  
Chief Executive Officer  
Sanofi



**Giovanni Caforio, MD**  
Chief Executive Officer  
Bristol-Myers Squibb  
Company



**William H. Carson, MD**  
President and  
Chief Executive Officer  
Otsuka Pharmaceutical  
Development and  
Commercialization, Inc.



**Paul R. Fonteyne**  
President and  
Chief Executive Officer  
Boehringer Ingelheim  
USA Corporation



**Kenneth C. Frazier**  
Chairman, President and  
Chief Executive Officer  
Merck and Co., Inc.



**Belén Garijo, MD**  
Member of the Executive  
Board and Chief Executive  
Officer  
Merck Healthcare  
EMD Serono



**Glenn J. Gormley,  
MD, PhD**  
Chairman of the Board  
and President  
Daiichi Sankyo, Inc.



**Peter Greenleaf**  
Chief Executive Officer  
Sucampo Pharmaceuticals,  
Inc.



**Jesper Høiland**  
Executive Vice President  
Novo Nordisk USA

## BOARD MEMBERSHIP (continued)



**Robert Hugin**  
Chairman and  
Chief Executive Officer  
Celgene Corporation



**John C. Lechleiter, PhD**  
Chairman, President and  
Chief Executive Officer  
Eli Lilly and Company



**Yuji Matsue**  
Chairman and  
Chief Executive Officer  
Eisai Inc.  
Corporate Officer and  
Vice President  
Eisai Co., Ltd.



**Clive A. Meanwell,  
MD, PhD**  
Chairman and  
Chief Executive Officer  
The Medicines Company



**Michael A. Narachi**  
President and  
Chief Executive Officer  
Orexigen Therapeutics, Inc.



**Richard F. Pops**  
Chairman and  
Chief Executive Officer  
Alkermes plc



**Ian Read**  
Chairman and  
Chief Executive Officer  
Pfizer Inc



**James Robinson**  
President, Americas  
Operations  
Astellas Pharma US, Inc.



**Brent Saunders**  
Chief Executive Officer and  
President  
Allergan plc



**Staffan Schüberg**  
Executive Vice President &  
Chief Commercial Officer  
Lundbeck LLC



**Ramona Sequeira**  
President  
Takeda Pharmaceuticals  
U.S.A., Inc.



**Pascal Soriot**  
Executive Director and  
Chief Executive Officer  
AstraZeneca PLC



**Nobuhiko Tamura, MS**  
Vice Chair and President  
Sunovion Pharmaceuticals  
Inc.



**Mark Timney**  
President and  
Chief Executive Officer  
Purdue Pharma L.P.



**Mark Trudeau**  
President and  
Chief Executive Officer  
Mallinckrodt  
Pharmaceuticals



**Timothy Walbert**  
Chairman, President and  
Chief Executive Officer  
Horizon Pharma plc



**Sir Andrew Witty**  
Chief Executive Officer  
GlaxoSmithKline

**Vacant**  
Sigma-Tau  
Pharmaceuticals, Inc.

# PhRMA Member Companies

## FULL MEMBERS

### **AbbVie Inc.**

North Chicago, IL

### **Alkermes plc**

Waltham, MA

### **Allergan plc.**

Parsippany, NJ

### **Amgen Inc.**

Thousand Oaks, CA

### **Astellas Pharma US, Inc.**

Northbrook, IL

### **AstraZeneca Pharmaceuticals LP**

Wilmington, DE

### **Bayer Corporation**

Whippany, NJ

### **Biogen Inc.**

Weston, MA

### **Boehringer Ingelheim Pharmaceuticals, Inc.**

Ridgefield, CT

### **Bristol-Myers Squibb Company**

New York, NY

### **Celgene Corporation**

Summit, NJ

### **Daiichi Sankyo, Inc.**

Parsippany, NJ

### **Eisai Inc.**

Woodcliff Lake, NJ

### **Eli Lilly and Company**

Indianapolis, IN

### **EMD Serono**

Rockland, MA

### **GlaxoSmithKline**

Research Triangle Park, NC

### **Johnson & Johnson**

New Brunswick, NJ

### **Lundbeck LLC**

Deerfield, IL

### **Mallinckrodt Pharmaceuticals**

Hazelwood, MO

### **Merck & Co., Inc.**

Kenilworth, NJ

### **Novartis Pharmaceuticals Corporation**

New York, NY

### **Novo Nordisk Inc.**

Plainsboro, NJ

### **Orexigen Therapeutics, Inc.**

La Jolla, CA

### **Otsuka America Pharmaceutical, Inc.**

Princeton, NJ

### **Pfizer Inc.**

New York, NY

### **Purdue Pharma L.P.**

Stamford, CT

### **Sanofi**

Bridgewater, NJ

### **Sigma-Tau Pharmaceuticals, Inc.**

Gaithersburg, MD

### **Sunovion Pharmaceuticals Inc.**

Marlborough, MA

### **Takeda Pharmaceuticals U.S.A., Inc.**

Deerfield, IL

### **The Medicines Company**

Parsippany, NJ

## RESEARCH ASSOCIATE MEMBERS

**ACADIA Pharmaceuticals Inc.**

San Diego, CA

**Aerie Pharmaceuticals, Inc.**

Durham, NC

**AMAG Pharmaceuticals, Inc.**

Waltham, MA

**Avanir Pharmaceuticals, Inc.**

Aliso Viejo, CA

**BioMarin Pharmaceutical Inc.**

Novato, CA

**CSL Behring, LLC**

King of Prussia, PA

**Esperion Therapeutics, Inc.**

Ann Arbor, MI

**Ferring Pharmaceuticals Inc.**

Parsippany, NJ

**Grifols USA, LLC**

Los Angeles, CA

**Horizon Pharma plc**

Deerfield, IL

**Ipsen Biopharmaceuticals, Inc.**

Basking Ridge, NJ

**Marathon Pharmaceuticals, LLC**

Northbrook, IL

**Shionogi Inc.**

Florham Park, NJ

**Sucampo Pharmaceuticals, Inc.**

Bethesda, MD

**Theravance, Inc.**

South San Francisco, CA

**Vifor Pharma**

Basking Ridge, NJ

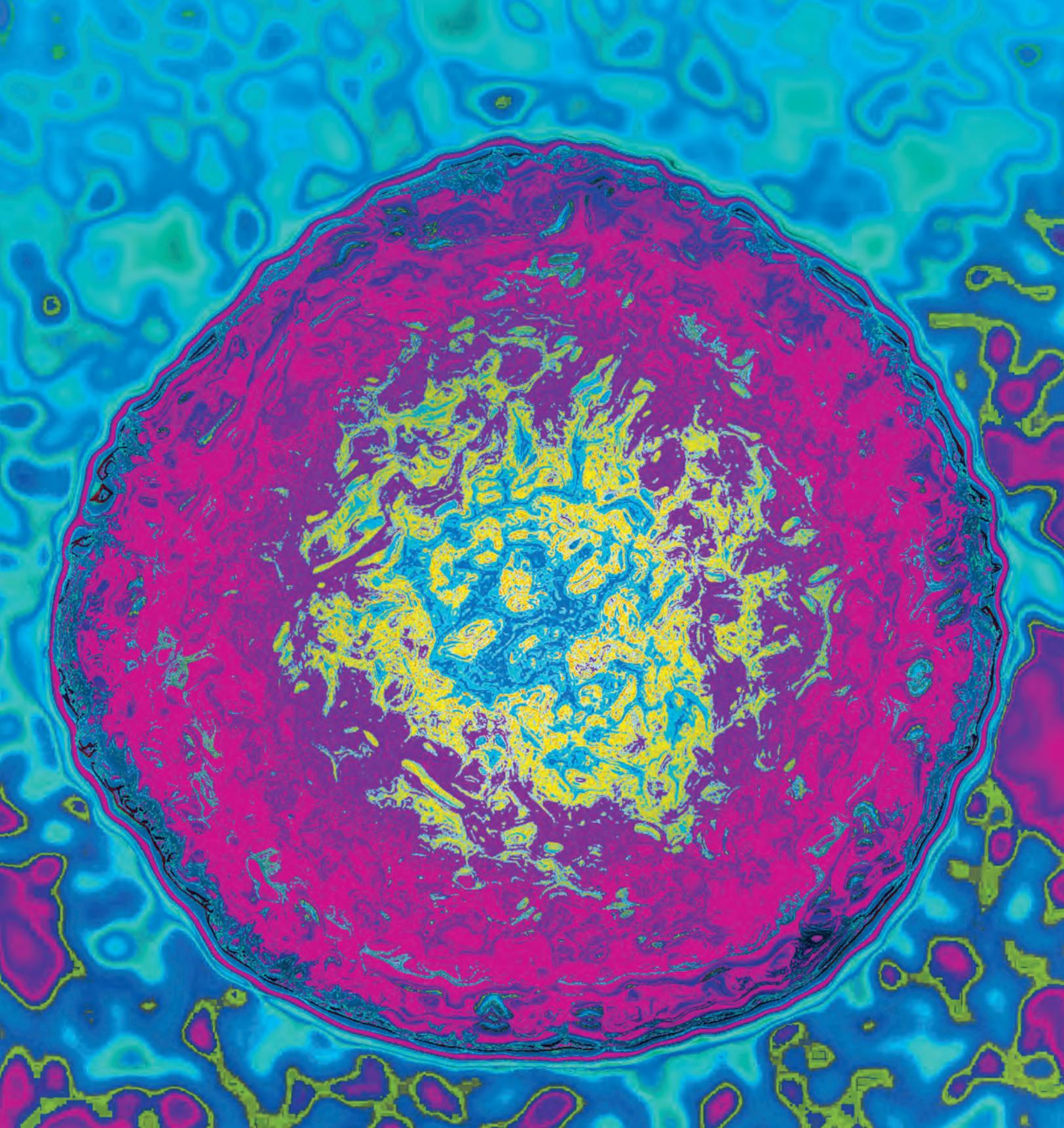
**VIVUS, Inc.**

Mountain View, CA



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