Key Facts

Research and Development (R&D)

Time to develop a drug = 10 to 15 years\(^1, 2, 3\)

Approvals

- Medicines approved 2000–2012 = more than 400\(^{10}, 11, 12\)
- In the 30 years since the Orphan Drug Act was established, more than 400 orphan drugs have been approved.\(^{13}\)
- Only 2 of 10 marketed drugs return revenues that match or exceed R&D costs.\(^{14}\)

Development Costs

Average cost to develop a drug (including the cost of failures):\(^4, 5\)
- Early 2000s = $1.2 billion* (some more recent studies estimate the costs to be even higher \(^6\))
- Late 1990s = $800 million*
- Mid 1980s = $320 million*
- 1970s = $140 million*

Medicines in Development

- Global development in 2011 = 5,400 compounds\(^15\)
- U.S. development 2013 = 3,400\(^16\) — an increase of 40% since 2005\(^17\)
- Potential first-in-class medicines** in clinical development globally = 70%\(^18\)

R&D Spending

<table>
<thead>
<tr>
<th>Year</th>
<th>PhRMA members(^7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>$48.5 billion (est.)</td>
</tr>
<tr>
<td>2011</td>
<td>$48.6 billion</td>
</tr>
<tr>
<td>2010</td>
<td>$50.7 billion</td>
</tr>
<tr>
<td>2009</td>
<td>$46.4 billion</td>
</tr>
<tr>
<td>2008</td>
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<tr>
<td>2007</td>
<td>$47.9 billion</td>
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<tr>
<td>2006</td>
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<td>$39.9 billion</td>
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<tr>
<td>2000</td>
<td>$26.0 billion</td>
</tr>
<tr>
<td>1990</td>
<td>$8.4 billion</td>
</tr>
<tr>
<td>1980</td>
<td>$2.0 billion</td>
</tr>
</tbody>
</table>

Value of Medicines

- **Cancer**: Since 1980, 83% of life expectancy gains for cancer patients are attributable to new treatments, including medicines.\(^19\) Another study found that medicines specifically account for 50% to 60% of increases in survival rates since 1975.\(^20\)
- **Cardiovascular Disease**: According to a 2013 statistics update by the American Heart Association, death rates for cardiovascular disease fell a dramatic 33% between 1999 and 2009.\(^21\)
- **HIV/AIDS**: Since the approval of antiretroviral treatments in 1995, the HIV/AIDS death rate has dropped by 85%.\(^22, 23\)

Economic Impact of the Biopharmaceutical Sector\(^9\)

- Direct jobs = more than 810,000
- Total jobs (including indirect and induced jobs) = nearly 3.4 million

Percentage of Sales That Went to R&D in 2012\(^8\)

- Domestic R&D as a percentage of domestic sales = 20.7%
- Total R&D as a percentage of total sales = 16.4%

Sales

- Generic share of prescriptions filled:\(^24\)
  - 2000 = 49%
  - 2012 = 84%

See inside back cover for references.

* Note: Data is adjusted to 2000 dollars based on correspondence with J.A. DiMasi.
** Note: First-in-class medicines are those that use a different mechanism of action from any other already approved medicine.
To enhance the content in the print version of this year’s Profile, we have included quick response (QR) codes that link you directly to additional materials online. You can find QR code readers for your smart phone or tablet in your device’s app store, or you can access the Industry Profile online at www.phrma.org/industryprofile2013.

Cover image: Neurons firing in the brain.
Today in America and around the world we confront daunting health care challenges. The incidence and costs of preventable and manageable chronic diseases like diabetes and asthma are growing. The medical needs of our rapidly aging population are unprecedented. And we face extremely complex diseases like cancer and Alzheimer’s disease.

Each of these alone represents an enormous challenge and, in combination, a threat to both individual health and to the U.S. economy. To overcome these challenges we will need many innovative solutions, and research in the biopharmaceutical sector offers an important part of the answer.

Biopharmaceutical research is an engine of progress in the fight against disease and in building a stronger economy. More importantly, drug discovery offers patients around the globe real hope — hope that a once-deadly disease may be prevented, treated, and even cured, hope that a patient may stop being a patient and live a longer, healthier life.

Researchers continue to work toward these goals in spite of many barriers. The science and technology of drug development are increasingly complex, and the length and cost of research and development have continued to grow. Regulatory and business environments add uncertainty to the process.

Still, researchers in our industry are inspired to improve life for patients. This is why biopharmaceutical research companies invested an estimated $48.5 billion in new R&D in 2012 — the largest R&D investment of any sector in the U.S. economy. PhRMA members invest in order to realize the promise of incredible advances in our understanding of basic biology; to help solve the puzzle of cancers and rare diseases; and to help reduce the cost and health burden of disease.

I am pleased to present the 2013 Biopharmaceutical Research Industry Profile, which lays out both the challenges we face and the progress we have made. I am proud of the story it tells of a sector striving to achieve the hope we all share for a longer life and a healthier future.

John J. Castellani
President and Chief Executive Officer
Pharmaceutical Research and Manufacturers of America
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Committed to Patients, Health, and the Economy

New medicines have been an important part of transforming many diseases in recent years. They are putting rheumatoid arthritis into remission, greatly increasing the chances of survival for children with cancer, curing hepatitis in many patients, and reducing hospitalizations for HIV patients.

The biopharmaceutical industry is a dynamic, knowledge-driven sector. The work of its researchers brings hope to millions of patients and benefits to local and national economies. Biopharmaceutical companies invest heavily in research and development; in the past year, Pharmaceutical Research and Manufacturers of America (PhRMA) members surpassed the $500 billion mark in research and development (R&D) spending since 2000.

Developing a new medicine is challenging and the chances of success are extremely low, particularly in recent years. The 44 new medicines approved by the U.S. Food and Drug Administration (FDA) in 2012 represented the highest total in 15 years, a proud landmark for an industry whose mission is to save and improve lives.

In addition to their health benefits, medicines are an important part of the solution to rising health care costs through their role in reducing the need for hospital stays, surgeries, and
other costly interventions. The biopharmaceutical sector also supports hundreds of thousands of high-quality, well-paying jobs in the United States that contribute significantly to the health of our communities and the nation's economy.

The 2013 Biopharmaceutical Research Industry Profile provides an overview of the essential contributions the industry makes to the lives and health of people and to the U.S. economy. Chapter 1 examines the enormous value of medicines developed by biopharmaceutical companies for patients around the world. Chapter 2 discusses the role that prescription medicines play in improving the quality and value of health care, and in controlling its cost. Chapter 3 describes the impact of the biopharmaceutical industry on local, state, and the national economies. Chapter 4 captures the R&D process that brings us new medicines. Chapter 5 reflects on our growing knowledge of disease, which is providing the most promising platform ever for developing new medicines and new ways to save lives. And Chapter 6 looks ahead at the hurdles facing the sector and how biopharmaceutical companies are meeting those challenges.
1 Impacting Patients
New medicines save and improve lives every day. For patients, new medicines can mean getting back to work, avoiding doctors’ visits and surgeries, feeling better, and living longer.

In recent years, we have seen accelerated progress in the fight against many diseases as a result of biopharmaceutical innovation. In 2012, the U.S. Food and Drug Administration (FDA) approved 44 new medicines\(^1,2\) — the largest number in 15 years.\(^3\) Of those, 39 were approved by the Center for Drug Evaluation and Research and 5 by the Center for Biologics Evaluation and Research.

Novel therapies were approved in a wide variety of disease areas, including:

- **Cystic Fibrosis**: The first therapy that targets the underlying cause of cystic fibrosis. This personalized medicine treats a subset of patients with a specific mutation.\(^5\)

- **Skin Cancer**: The first medicine approved for treatment of metastatic basal cell carcinoma, the most common form of skin cancer.\(^6\)

- **Tuberculosis**: The first new tuberculosis medicine in 40 years, which will be used in combination with other medicines to treat multi-drug resistant tuberculosis infection.\(^7\)

- **Leukemia**: Three new therapies that treat chronic myelogenous leukemia, a rare blood and bone marrow disease.\(^8\)

- **Cushing’s Disease**: Two new medicines to treat Cushing’s disease, a rare disease that affects the pituitary gland causing a host of problems throughout the body. One medicine treats patients with endogenous Cushing’s syndrome and the other is the first medicine that addresses the underlying mechanism of the disease.\(^9,10\)

- **Respiratory Distress Syndrome**: A new medicine to treat respiratory distress syndrome in premature infants.\(^11\)

These accomplishments could not have been achieved without the innovations of the biopharmaceutical industry and the dedication and skill of FDA’s drug review staff.\(^12\)
Fighting Rare Diseases

This year marks the 30th anniversary of the enactment of the Orphan Drug Act, which was pivotal in creating incentives for the development of new treatments for rare diseases. The Act transformed the landscape of drug development for rare diseases: more than 400 medicines have been approved to treat rare diseases since 1983, compared with fewer than 10 in the 1970s.\textsuperscript{13,14} Researchers have made tremendous progress against rare diseases in recent years. In fact, the FDA notes that approximately one-third of all new medicines approved in the last 5 years have been designated as “orphan drugs” — the term used for medicines that treat rare diseases affecting fewer than 200,000 patients in the United States.\textsuperscript{15} In 2012, 13 orphan drugs were approved by the FDA.\textsuperscript{16} Although each of the nearly 7,000 rare conditions affects a small number of people, their impact on public health is anything but small; rare diseases overall affect more than 30 million Americans.\textsuperscript{17} Because 85% to 90% of rare diseases are serious or life threatening, bringing new medicines to patients is especially important.\textsuperscript{18} (See Chapter 5, page 46 for information about treatments currently in development for rare diseases.)
Progress Against Disease

Medicines improve patients’ lives in many different ways. Appropriate use of medications can have a huge impact on the health and well-being of patients and their caregivers by extending life, halting or slowing disease progression, minimizing complications, improving quality of life, preventing hospitalizations and surgeries, preventing disease, and reducing side effects. Following are just a few specific examples of the positive impact therapies have had on patient care.

Extending Lives

Childhood Cancers: The chance of survival for children with cancer has greatly improved in recent years. The 5-year relative survival rate increased from 58% in the mid-1970s to 83% in the most recent time period (2002–2008) — a 25 percentage point increase.19 (See Figure 2.) The American Cancer Society noted that “survival for all invasive childhood cancers combined has improved markedly over the past 30 years due to new and improved treatments.”20

Slowing and Preventing Disease Progression

Cardiovascular Disease: Despite rising obesity levels, Americans have reached a milestone in controlling high cholesterol. The U.S. Centers for Disease Control and Prevention (CDC) reported in 2007 that U.S. adults reached an average cholesterol level in the ideal range (below 200) for the first time in 50 years.21 (See Figure 3.) Authors of the report attribute the drop to the increased use of cholesterol-lowering medicines in the over-60 population.22
Hepatitis C: This viral disease, which affects 3.2 million people in the United States, attacks the liver leading to many complications, including cirrhosis, liver transplants, liver cancer, and death. Sustained virologic response rates improved from 10% in the 1990s to 80% today among hepatitis C patients. Sustained virologic response, defined as the suppression of the virus below detectable levels for 24 weeks after treatment, rose as understanding of the disease grew and treatment moved to today’s triple therapy regimens, which include recently approved “direct acting antivirals.”

We are living in very exciting times. While years ago there were no specific therapies for liver diseases, we now have many different therapies for patients with different types of liver disease and at different stages of disease. One of the most exciting areas is the therapy of hepatitis C, one of the main causes of liver disease in the world.

Guadalupe Garcia-Tsao, M.D., President, American Association for the Study of Liver Diseases

Figure 2: Survival Rates for Childhood Cancers Have Increased 25 Percentage Points over the Last Several Decades

Figure 3: In 2007, the Average Cholesterol Level for Adults Reached the Ideal Range, Below 200 mg/dL


Protein enzymes, receptors, or channels identified by the pharmaceutical industry as ‘drugable targets’ have led to striking, remarkable, and repeated achievement.27

DRS. MYRON WEISFELDT AND SUSAN ZIEMAN, JOHNS HOPKINS UNIVERSITY, “ADVANCES IN THE PREVENTION AND TREATMENT OF CARDIOVASCULAR DISEASE,” HEALTH AFFAIRS, 2007
Preventing Hospitalizations

**HIV/AIDS:** Since anti-retroviral treatments became available in the mid-1990s, survival rates for HIV patients have grown rapidly, increasing the number of people living with the disease between 1996 and 2000 by 28%. Despite this increase in survival, hospitalization rates fell by 32% in this period. In more recent years, hospitalization rates have continued to fall. Between 2002 and 2007, the hospitalization rate fell from 35 per 100 HIV patients to 27 per 100 patients, a 23% drop.29

**Diabetes:** Over the last several years, many innovative medications for the treatment of diabetes have emerged, giving patients important tools for managing their disease. A recent study found that emergency room visits of patients who took their diabetes medicines as directed were 46% lower than for patients who took their medicines less than 50% of the time. Similarly, the hospitalization rate and the number of days spent in the hospital were 23% and 24% lower, respectively, for adherent patients.30

---

**HIV/AIDS**

**THEN...** “In the early years of the AIDS epidemic before ART (anti-retroviral treatment) was available, the median survival after an AIDS diagnosis was measured in weeks to months and patient care was confined to diagnosing and treating a complex array of opportunistic infections and AIDS-related types of cancer...”

**NOW...** “In stark contrast to the early and mid-1980s, if a person aged 20 years is newly infected with HIV today and guideline recommended therapy is initiated, researchers can predict by using mathematical modeling that this person will live at least an additional 50 years — that is, a close-to-normal life expectancy.”

► **Drs. Carl W. Dieffenbach and Anthony S. Fauci,** *Annals of Internal Medicine, 2011*

Learn about progress against HIV from an activist who has seen the disease go from acute and fatal to chronic and manageable.

Scan QR code ►
Improving Quality of Life

Rheumatoid Arthritis: Clinical remission is now possible for patients with severe rheumatoid arthritis (RA). A recent study found that patients treated with combination therapy consisting of both a new and older medicine had a 50% chance of complete clinical remission after 52 weeks of treatment, compared with 28% for those taking only the older medicine. These results would have been “unthinkable” prior to new disease-modifying biological medicines.

Rheumatoid Arthritis

THEN... “Previously the progression of RA from symptom onset to significant disability was often inevitable and, in some cases, rapid.”

NOW... “With the availability of medications that can slow or halt disease progression and prevent irreversible joint damage, joint replacement surgery is not always the ultimate outcome and patients with RA may live comfortable and productive lives on medical therapy.”

► Drs. Katherine Upchurch and Jonathan Kay, University of Massachusetts Medical School
The Evolving Value of Medicines

Advances against disease like those illustrated above are not typically driven by large, dramatic developments, but more commonly result from a series of incremental gains in knowledge over time. New medicines build on one another step by step. In addition, the best clinical role and full value of a therapy typically emerges years after initial approval as further research is conducted and physicians gain real-world experience. Initial FDA approval often marks the starting point for this additional research, generating a larger body of evidence to help us understand the full value of the medicine and how best to treat patients.

This step-wise transformation in knowledge has led to increased survival, improved patient outcomes, and enhanced quality of life for many patients. In fact, in recent years we have seen the transformation of several diseases that were once thought of as acute and sometimes fatal to chronic, manageable conditions for patients who have access to medication.

Some forms of cancer provide a useful illustration of the different pathways by which our understanding of value can evolve:

\begin{itemize}
  \item **Use earlier in treatment line or disease state**
  For example: Trastuzumab (Herceptin®) received an additional indication for use as a potential first-line adjuvant therapy, 10 years after originally being approved as a second-line treatment for HER2+ metastatic breast cancer.
  \item **Use in combination with other therapeutics or biomarkers**
  For example: Subsequent studies of Cetuximab (Erbitux®) indicated that mutations of the KRAS gene could predict response to treatment for patients with a form of metastatic colorectal cancer, allowing for more targeted treatment.
  \item **Use in additional indications**
  For example: Docetaxel (Taxotere®) was initially approved for the treatment of non-small cell lung cancer, but continued research revealed a significant survival benefit in squamous cell carcinoma of the head and neck; initial evaluation based on early trial results would have substantially underestimated its impact on survival by more than 4.5 years.
\end{itemize}

\begin{itemize}
  \item ⁴“CDER’s Novel Approvals in 2012.” The Pink Sheet, 7 January 2013.
\end{itemize}


Ibid.


Ibid.


Improving the Quality and Value of Health Care
Improving the Quality and Value of Health Care

Improving the quality and value of health care — and controlling its costs — are imperatives for the health of Americans and for our economy. Prescription medicines play an important role in achieving both of those goals, especially in light of our aging population and the large number of people living with chronic conditions.

With optimal use, medicines can improve health outcomes and help to reduce the need for costly health care services, such as emergency room admissions, hospital stays, surgeries, and long-term care. Patients are healthier, and unnecessary medical expenditures are avoided.

As more Americans gain access to health care, it is important that they also have access to the medicines they need. Suboptimal use of prescription medications remains a challenge, and there is a large opportunity for patients and their health care providers to improve the quality and the efficiency of the health care system by improving the use of medicines.

Better Use of Medicines Improves Outcomes

For patients to receive the clinical benefits of medicines, several actions must occur:

- Appropriate and timely diagnosis and prescribing
- Prompt initiation of therapy
- Adherence to prescribed medicines (i.e., patients must take the medicines as prescribed at the right dose and right time)
- Periodic reviews and updates of the medication regimen

All of these dimensions are key to achieving better health outcomes, particularly for patients with chronic diseases. For example:

- **Preventing Hospitalizations:** Poor adherence to prescribed medicines is associated with increased hospitalizations, nursing home admissions, and physician visits.\(^1\),\(^2\),\(^3\) For instance, research demonstrates that patients who did not consistently take their diabetes medicine were 2.5 times more likely to be hospitalized than were patients who took their medicine as directed more than 80% of the time.\(^4\)

- **Preventing Disease:** Nonadherent patients were 7%, 13%, and 42% more likely to develop coronary heart disease, cerebrovascular disease, and chronic heart failure, respectively, over 3 years than were patients who took antihypertension medicine as directed.\(^5\)

- **Preventing Adverse Events:** Providing counseling to patients to clarify their medication regimen following hospital discharge can dramatically reduce the likelihood of adverse drug events.\(^6\)
The Economic Value of Better Use of Medicines

Used appropriately, medicines also can generate positive economic outcomes across many common diseases. A wide range of studies have shown that improved use of recommended medications is associated with reduced total health care costs. In fact, the link between use of prescription medicines and spending on other health care services was recently acknowledged by the Congressional Budget Office (CBO). In 2012, the CBO announced a change to its scoring methodology to reflect savings in medical spending associated with increased use of medicines in Medicare. (For more on the value of better use of medicines in Medicare Part D, see sidebar on page 15.)

It is estimated that the cost of suboptimal medicine use including nonadherence, undertreatment, administration errors, and underdiagnosis is between $100 and $290 billion annually.

Examples of the medical savings resulting from better use of medicine include:

- **High Blood Pressure:** Treating patients with high blood pressure in accordance with clinical guidelines would result in fewer strokes and heart attacks, preventing up to 89,000 deaths and 420,000 hospitalizations annually and saving $15.6 billion a year. (See Figure 4.)

- **Diabetes:** Improving adherence to diabetes medicines would result in an estimated reduction of more than 1 million emergency room visits and hospitalizations annually, for potential savings of $8.3 billion each year.

- **High Cholesterol:** Research has shown that statin therapy reduces low-density lipoprotein cholesterol levels by an average of 19%. Over one year, this reduction in bad cholesterol was associated with roughly 40,000 fewer deaths, 60,000 fewer hospitalizations for...
Improving the Quality and Value of Health Care

CHAPTER 2

Improving the Quality and Value of Health Care

14

heart attacks, and 22,000 fewer hospitalizations for strokes in the United States. From an economic perspective, those prevented hospitalizations translated into gross savings of nearly $5 billion.13

---

**Chronic Conditions**:

For conditions such as diabetes, dyslipidemia, hypertension, and congestive heart failure, patients who had better adherence to prescribed medicines experienced savings of $3 to $10 in non-drug spending for each additional dollar spent on prescriptions — a net savings of $1,200 to $7,800 per patient per year.14 (See Figure 5.)

Another aspect of the economic impact of medicines is their potential to improve productivity in the workplace through reduced absenteeism or disability leave, which benefits both the individual patient and the economy as a whole. Several of the most common chronic conditions are estimated to cost the economy more than $1 trillion annually in lost productivity.15 Examples of improved productivity include:

- **Rheumatoid Arthritis**:
  Researchers at the Integrated Benefits Institute found that high cost sharing for rheumatoid arthritis medications decreased adherence and led to increased incidence and longer duration of short-term disability leave. Researchers estimated that lowering patient copays would improve medication adherence, reducing lost productivity among workers with this disease by 26%.16

- **Chronic Conditions**:
  Research shows that workers diagnosed with diabetes, hypertension, dyslipidemia, asthma, or chronic obstructive pulmonary disease who are adherent to prescribed medicines were absent up to 7 fewer days from work and used 5 fewer days of short-term disability compared with nonadherent workers.17

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**Gaps in Optimal Use of Medicines**

Poor use of medicines is a widespread challenge throughout the health care system. Because of the broad scope
Medicare Part D: Improving Seniors’ Access to Medicine and Reducing the Cost of Care

Passed into law in 2003, the Medicare prescription drug program (Part D) began in 2006. The program is working well and exceeding expectations. The current estimates for total spending over the first 10 years of the program are $346 billion lower than initial projections. Additionally, health outcomes for seniors have improved, and beneficiary satisfaction is high. Medicare Part D has improved access to needed medicines and reduced hospitalizations and use of other medical care.

A 2011 study in the *Journal of the American Medical Association* found that for those with limited prior drug coverage who subsequently enrolled in Part D, there was an average savings of $1,200 per beneficiary in total non-drug medical costs in both 2006 and 2007. (See Figure 6.) Better access to medicines through Medicare Part D also has led to declines in costly hospitalizations and skilled nursing care, which provides significant savings to the Medicare program.

Today, 32 million people, or almost two-thirds of all Medicare beneficiaries, are enrolled in a Part D plan and the overwhelming majority of them rate their coverage highly. A recent survey reported that 96% of respondents were satisfied with their Medicare drug coverage, and 96% said their coverage worked well.

To learn more about the successes of Medicare’s Part D program, visit [www.phrma.org/issues/medicare](http://www.phrma.org/issues/medicare).

**Figure 6: Gaining Drug Coverage Reduced Other Medical Spending**

The Medicare drug benefit increased access to medicines, reducing non-drug medical spending — an overall savings of $13.4 billion in 2007, the first full year of the program.

<table>
<thead>
<tr>
<th>Part A</th>
<th>Part B</th>
<th>Other Non-drug*</th>
<th>Total Non-drug Medical Spending</th>
</tr>
</thead>
<tbody>
<tr>
<td>-$816</td>
<td>-$268</td>
<td>-$140</td>
<td>-$1,224</td>
</tr>
</tbody>
</table>

*Home health, durable medical equipment, hospice, and outpatient institutional services.

of the problem, there is a significant opportunity for improving patients’ health and the efficiency of the health care system.

- More than 25% of newly written prescriptions, including those for high blood pressure, diabetes, and high cholesterol, are never brought to the pharmacy to be filled.26
- Approximately 50% of medications for chronic diseases are not taken as prescribed.27
- Among elderly patients, underuse of recommended medicines outweighs overuse by about 17 to 1.28

- A National Community Pharmacists Association poll showed that nearly 75% of adults do not follow their doctors’ prescription orders, including not filling the prescription in the first place or taking less than the recommended dose.29

Patients do not follow their doctors’ prescription recommendations for a wide variety of reasons. Patients may not believe that the treatment will help them or they may not adequately understand their illness and the need for treatment. Some patients may experience or fear potential side effects. Others suffer from cognitive or physical impairments that can reduce their adherence to medication regimens. Complex medication regimens, limited access to medicines, and poor relationships between prescribers and patients may also contribute to nonadherence.30

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

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

- **26 million** Americans with **DIABETES**
  - **19 million** are **DIAGNOSED**
  - **7 million** are **UNDIAGNOSED**
  - **16 million** are **TREATED**
    - Blood sugar control (diet and exercise, medicines)
    - Testing to prevent complications
  - **3 million** are diagnosed but **NOT TREATED**
  - **8 million** are treated and have their disease **CONTROLLED**
  - **8 million** receive some treatment but their disease is **NOT SUCCESSFULLY CONTROLLED**
  - **18 million** have **UNCONTROLLED** diabetes

stakeholders have taken on the challenge in differing ways. For example:

- To reduce their medical costs, employers and health plans are focusing on comprehensive medication management and decreasing cost sharing, which can pose a significant barrier to taking prescribed medicines.\(^{31}\)

- Advances in information technology are enabling pharmacies to synchronize refills for patients who have multiple prescriptions to reduce the number of times a patient must go to the pharmacy. Some pharmacies now send out reminders to patients when they need to pick up a prescription and allow physicians to access their patients’ medication fill histories to prevent drug interactions.

- The Centers for Medicare and Medicaid Services is tracking medication adherence rates for Part D Medicare Advantage and standalone prescription drug plans.

- Biopharmaceutical companies are continuing to develop innovative new therapies that make it easier for patients to take medicines by simplifying dosing regimens or reducing side effects.

There is no single solution to improving use of medicines. With diverse approaches, patients will gain more value from the medicines prescribed to keep them healthy.


8. Ibid.


3 Supporting the Economy
Supporting the Economy

The biopharmaceutical industry continues to make major contributions to the U.S. economy. This sector generates high-quality jobs and powers economic output for the U.S. economy, serving as “the foundation upon which one of the United States’ most dynamic innovation and business ecosystems is built.” The U.S. biopharmaceutical sector employs more than 810,000 workers, supports a total of nearly 3.4 million jobs across the country, and contributes nearly $790 billion in economic output on an annual basis when direct, indirect, and induced effects are considered.

These economic impacts are driven by the industry’s research and development (R&D) enterprise. The U.S. biopharmaceutical sector accounts for the single largest share of all U.S. business R&D, representing nearly 20% of all domestic R&D funded by U.S. businesses, according to data from the National Science Foundation.

The high number of jobs that are supported indirectly reflects the fact that the industry is a “jobs multiplier,” meaning that each biopharmaceutical sector job supports a total of four jobs throughout the economy. The industry helps support a vibrant scientific and economic ecosystem that is vital to the U.S. economy and our country’s competitiveness in the global market. Biopharmaceutical companies put down roots in communities across the country, helping to generate jobs across a whole range of sectors, from suppliers to retail to personal services.

The jobs the industry creates have high wages and require a workforce with diverse skills and educational levels, from Ph.D. scientists, to entry-level technicians, to support staff of all kinds.
In accomplishing the mission of bringing new medical treatments to the market, the biopharmaceutical industry sustains a very large-scale supply chain — both in R&D and in support of the production and distribution of biopharmaceutical products.

To provide insight into the breadth and depth of the industry’s impact in the form of business relationships with vendors large and small, a recent analysis aggregated data from 17 innovative biopharmaceutical companies across 17 states. The analysis found that in 2011, these biopharmaceutical companies spent approximately $53 billion in transactions with vendors and suppliers in these states. The recipient companies provided services and supplies to the industry. Although just a snapshot of the sector’s total impact, these findings demonstrate the importance of a strong and vibrant biopharmaceutical industry in helping other businesses to grow and contribute to a strong local economy.

Vendor data from this analysis, broken down by congressional and state legislative district, can be viewed at www.weworkforhealth.org.

**Mapping the Impact**

The biopharmaceutical sector supported nearly 3.4 million jobs across the economy in 2009, including about 3.3 million in other sectors.

**Biopharma Jobs**
More than 810,000 Jobs in the U.S. Biopharmaceutical Sector

**Total Jobs Supported**
Nearly 3.4 million total U.S. Jobs Supported by the Biopharmaceutical Sector

**Supporting the Economy**

**Figure 9: The Ripple Effect of High-Value Biopharmaceutical Jobs**

Each direct biopharmaceutical job supports 3 additional jobs in other sectors.

Science, technology, engineering, and mathematics (STEM) workers drive our nation’s innovation and competitiveness by generating new ideas, new companies, and new industries. STEM workers play a key role in the sustained growth and stability of the U.S. economy and are critical components to helping the U.S. win the future. 

— U.S. Department of Commerce

In 2011, the more than 810,000 direct jobs generated $89.9 billion in total personal income—averaging $110,490 in wages and benefits per worker. This was twice the average U.S. private sector compensation of $54,455, an indication of the high-quality jobs the biopharmaceutical industry provides to U.S. workers.

Boosting State and Regional Economies

Clinical trials are the most costly portion of the drug development process, usually accounting for 45% to 75% of the $1.2 billion average cost of developing a new medicine. Trials on average last 7 years and represent a large investment into the communities where they are conducted. Biopharmaceutical companies collaborate with local research institutions across the country — including clinical research centers, university medical schools, hospitals, and foundations — to carry out clinical trials, providing patients access to potential new treatments as well as creating local jobs.

A PhRMA program called “Research in Your Backyard” helps to illustrate the impact trials have on communities around the country. Sixteen state reports developed by the program have been released, highlighting the biopharmaceutical economic impact on these communities through clinical trials. For example, in Washington State, job growth in the biopharmaceutical industry grew 12% from 2007 through 2011, compared with a 2% decline in jobs for all other industries. Since 1999,
biopharmaceutical companies working with local research institutions have conducted, or are conducting:

- Nearly 3,500 clinical trials in Maryland, including 1,775 for six major chronic diseases (asthma, cancer, diabetes, heart disease, mental illness, and stroke)\(^9\)
- More than 3,000 trials in Colorado, including 1,400 for major chronic diseases\(^10\)
- More than 3,600 trials in Georgia, including 1,800 targeting major chronic diseases\(^11\)
- More than 3,400 trials in Virginia, including more than 1,500 for major chronic diseases\(^12\)

Although clinical trials provide an economic boost for communities, their primary benefit is to offer patients potential therapeutic options. Clinical trials may provide a new avenue of care for some chronic disease sufferers who are searching for the medicines that are best for them.

**Ripple Effect of Industry R&D Support**

Biopharmaceutical R&D continues to have a strong impact on the overall U.S. economy. PhRMA members have invested more than half a trillion dollars in R&D since 2000, including an estimated $48.5 billion in 2012 alone.\(^13\) The impacts of this spending and the sector’s broad support for biomedical research ripple across the economy.

Support for the R&D enterprise extends beyond the confines of any given company. In addition to supporting science, technology, engineering, and mathematics (STEM) education

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“The STEM fields and those who work in them are critical engines of innovation and growth: according to one recent estimate, while only about five percent of the U.S. workforce is employed in STEM fields, the STEM workforce accounts for more than fifty percent of the nation’s sustained economic growth.”

U.S. Department of Labor
STEM Jobs and Education: A Critical Focus for Today and Tomorrow

Science, technology, engineering, and mathematics (STEM) education is critical to continued U.S. global leadership. A workforce with strong STEM skills is essential to providing an adequate supply of workers with the skills necessary for the increasingly complex mission of developing 21st century medicines, and for the U.S. biopharmaceutical industry to maintain its competitive edge globally.

From 2001 to 2008, the biopharmaceutical industry outperformed other major STEM industries in generating jobs, and it is one of the few high-tech manufacturing sectors projected to add STEM-related jobs between 2010 and 2020. However, many of these high-wage, high-value jobs may go unfilled if the United States continues to fall behind other countries in the quality of STEM education it provides its students. Improvements in this area would not only help the industry but also would benefit American workers as the average earnings for STEM workers are nearly twice as high as those of all workers, and STEM workers are also much less likely to experience joblessness. Increasingly, biopharmaceutical companies are supporting STEM efforts around the country in many ways, including providing scholarships, mentoring students in local school districts, and funding and supporting teacher workshops and other professional development in STEM fields.
(see sidebar on page 24), innovative biopharmaceutical companies are engaged in a range of precompetitive research collaborations and partnerships with academic medical centers as well as increasingly supporting start-up and emerging companies through the establishment of corporate venture capital funds. These innovative collaborations not only help to ensure a robust future for the industry and the biopharmaceutical ecosystem, but benefit the larger national economy as well.

**Partnerships Across Sectors**

In recent years, biopharmaceutical companies have formed a growing number of partnerships with researchers in government, academia, smaller companies, and other parts of the biomedical ecosystem. The close and synergistic relationship between sectors in the biomedical research ecosystem is critical to ensuring a robust national biomedical research capacity in the United States.

The Tufts Center for the Study of Drug Development recently conducted an analysis of more than 3,000 partnerships of biopharmaceutical companies with academic medical centers (AMCs). The analysis found that the partnerships benefit both industry and academia by providing opportunities for the sectors to work together to explore promising new technologies and address scientific problems that may lead to breakthroughs in treatments for the most challenging diseases and conditions. According to a report by PwC’s Health Research Institute, “all large pharmaceutical companies have established at least one AMC partnership, often specific to a disease,” and the number of partnerships is rising as the industry adopts a more collaborative approach to R&D.

These relationships vary significantly and are continually evolving. Common partnership models include unrestricted research support, academic drug discovery centers, and precompetitive research centers, which incorporate a collaborative research model that brings together various institutions that ordinarily are commercial competitors to perform early-stage research collectively.

One prominent example of a precompetitive research collaboration is the Alzheimer's Disease Neuroimaging Initiative (ADNI), which includes federal agencies, nonprofit organizations, and industry members. The goal is to identify physical changes in the brain prior to the onset of Alzheimer's disease, track their progression, establish quality standards for imaging data collection and sharing, and 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.20

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**The industry is funding and working collaboratively with the academic component of the public sector on basic research that contributes broadly across the entire spectrum of biomedical R&D, not just for products in its portfolio.**

Tufts Center for the Study of Drug Development, 2012
Corporate Venture Capital Investments

Venture capital (VC) and other forms of private capital are a key form of financing for start-up and emerging biopharmaceutical companies.

As traditional VC has recently declined due to several factors, including regulatory challenges and concerns about coverage and payment for new medical innovations, the corporate venture arms of established biopharmaceutical companies have become an increasingly important source of capital to help fill this gap. Between 2010 and 2012, biopharmaceutical corporate venture capital funds invested nearly $1.2 billion in biotechnology start-ups. And corporate venture activity is on the rise. According to a recent report by the Boston Consulting Group, 63% of the 30 largest biopharmaceutical companies currently participate in corporate venture capital investments — up from 50% in 2007.

Corporate venture funds may provide biotech startups with strategic benefits beyond investment capital. These include the opportunity to access technology, research knowledge and capacity, drug development expertise, marketing competence, and (often) a global presence... Corporate venturing by multinational pharmaceutical and large biotech companies is playing an increasingly important role in financing the development of early stage innovation... and an essential role in the sustainability of the biotech ecosystem, advancing the future of pharmaceutical innovation and biotech entrepreneurship.

Ensuring Access to Needed Medicines

The Partnership for Prescription Assistance

The biopharmaceutical industry has long provided access to medicines for patients who cannot afford them. The Partnership for Prescription Assistance (PPA) has helped nearly 8 million uninsured and financially struggling patients gain free and confidential access to 475 public and private patient assistance programs, including nearly 200 that are offered by pharmaceutical companies. PPA member programs offer more than 2,500 brand-name medicines and generic drugs. More than 1,300 major national, state, and local organizations have joined the PPA, including the American Academy for Family Physicians, American Cancer Society, American College of Emergency Physicians, Easter Seals, National Association of Chain Drug Stores, United Way, and the Urban League.

Patients can learn about and apply to the PPA by visiting www.pparx.org or calling toll-free 1-888-4PPA-NOW. The call center can provide help in English, Spanish, and about 150 other languages.

Rx Response

Ensuring access to medicines following a major disaster is a critical priority for biopharmaceutical companies. In the aftermath of Hurricane Katrina, the industry realized that the absence of a single point of contact through which federal and state officials could reach the biopharmaceutical supply chain was a serious problem.

Rx Response is a unique collaborative initiative that brings together biopharmaceutical companies, distributors, and dispensers, along with the American Red Cross, to help ensure the continued flow of medicines following a major disaster. In the 6 years since its inception, Rx Response has become an indispensable homeland security and public health asset. In October 2012, Rx Response was activated to address threats to the supply chain posed by Super Storm Sandy.

Among its most valuable resources is the Pharmacy Status Reporting Tool, an online resource that maps the location of open pharmacies in disaster-stricken areas. For additional disaster planning resources and more information about Rx Response, visit RxResponse at www.rxresponse.org.

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2Battelle Technology Partnership Practice. "The Economic Impact of the U.S. Biopharmaceutical Industry." Washington, DC: Battelle Technology Partnership Practice, July 2013. Note: The economic impact estimates developed by Battelle and presented here reflect several methodological refinements and thus are not directly comparable to previous estimates prepared for PhRMA. These estimates now more accurately capture the core functions of today’s innovative biopharmaceutical industry and better capture headquarters’ jobs.


CHAPTER 3

Supporting the Economy


Discovering and developing new medicines is a long, complex, and costly process, but biopharmaceutical researchers devote their careers to this often frustrating but tremendously gratifying task. The research and development (R&D) process is the road to new medicines — and more often than not it entails many turns, stops, and starts. Substantial progress typically occurs in increments over time, as advances build on each other.

In 2012, Pharmaceutical Research and Manufacturers of America (PhRMA) member companies invested an estimated $48.5 billion in R&D. This strong investment is part of the industry’s ongoing commitment to innovation; since 2000, PhRMA members have spent more than half a trillion dollars on R&D. PhRMA members’ yearly investments represent the majority of all biopharmaceutical R&D spending in the United States.

According to the Congressional Budget Office, “The pharmaceutical industry is one of the most research-intensive industries in the United States. Pharmaceutical firms invest
as much as five times more in research and development, relative to their sales, than the average U.S. manufacturing firm.\textsuperscript{4}

Today, more than 5,000 medicines are in clinical trials globally or in U.S. Food and Drug Administration (FDA) review.\textsuperscript{5} All of these have the potential to benefit U.S. patients, and each must undergo the same rigorous process to determine safety and efficacy for patient use. (For more information about the many innovative medicines in the pipeline, see Chapter 5.)
Overview of the R&D Process

For those who do not work directly in drug development, the difficulty of the process can be hard to grasp. Numbers can help give a sense of the gauntlet of challenges each candidate medicine must pass through, and those numbers are daunting:

- On average, it takes about 10 to 15 years for a new medicine to complete the journey from initial discovery to the marketplace.⁶⁻⁷⁻⁸
- For every 5,000 to 10,000 compounds that enter the pipeline, only one receives approval. Even medicines that reach clinical trials have only a 16% chance of being approved.⁹

The process is costly. The average R&D investment for each new medicine is $1.2 billion, including the cost of failures,¹⁰ with more recent studies estimating the costs to be even higher.¹¹

Each potential new medicine goes through a long series of steps on its way to patients. Figure 11 outlines this process.

Drug Discovery

The first step in developing a new medicine is to understand the disease or condition as thoroughly as possible. The entire biomedical research community contributes to this body of knowledge. In the United States, we are fortunate to have a dynamic, collaborative research ecosystem that includes researchers from government, industry, and academia.

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Figure 11: The Research and Development Process
From the earliest stages of basic research to drug approval, this collaborative ecosystem is among our greatest strengths in moving medical advances forward and making the United States the worldwide leader in biopharmaceutical innovation. (For more information on this ecosystem and these partnerships, see page 25 in Chapter 3 and Figure 12 below.)

Basic research provides clues about how to treat diseases and potential ways to target the symptoms or underlying causes. Armed with an idea, researchers work to understand biological targets for a potential medicine. A drug target can be a protein, RNA, DNA, or other molecule that is somehow involved in the disease. The investigators conduct studies in cells, tissues, and animal models to determine whether the target can be influenced by a medicine.

Then researchers look for a lead compound — a promising molecule that could influence the target and, potentially, become a medicine. They do this in various ways, including creating a molecule from scratch, using high-throughput screening techniques to select a few promising possibilities from among thousands of potential candidates, finding compounds from nature, and using biotechnology to genetically engineer living systems to produce disease-fighting molecules.

Even at this early stage, investigators already are thinking about the final product. Issues such as the formulation (or "recipe") of a medicine and its delivery system (for example, whether it is taken in pill form, injected, or inhaled) are critical if a compound is to become a successful new medicine.
Preclinical Testing

The drug discovery phase whittles down thousands of compounds to a few hundred promising possibilities that are ready for preclinical testing. In this stage, scientists conduct laboratory and animal studies to determine whether a compound is suitable for human testing. At the end of this process, which can take several years, around five compounds move to the next stage of testing in humans. The company files an Investigational New Drug Application with the FDA to begin clinical trials.

Clinical Trials

During this stage, a compound is tested in human volunteers. The clinical trials process occurs in several phases and takes on average 6 to 7 years. A potential medicine must successfully complete each phase before being submitted to the FDA for review.

Because this process involves both benefits and risks, companies take great care to protect the safety of trial participants and to ensure that they are thoroughly informed about the trial and its potential risks so that they can provide informed consent to participate, as required by federal regulations. Companies also ensure that the trials are conducted correctly and with integrity and that clinical trial results are disclosed at the appropriate time.

Clinical Trial Principles

PhRMA members have had a longstanding commitment to sponsoring clinical research that fully complies with all legal and regulatory requirements as well as international agreements. In addition, PhRMA has set out voluntary principles to fortify member companies’ commitment to the highest standards for ethics and transparency in the conduct of clinical trials. PhRMA’s Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results are designed to help ensure that clinical research conducted by America’s pharmaceutical research and biotechnology companies continues to be carefully conducted and that meaningful medical research results are communicated to health care professionals and patients.

Learn more about PhRMA’s Principles on Conduct of Clinical Trials.
Scan QR code ▶
The study design and the informed consent are reviewed, approved, and monitored by an Institutional Review Board (IRB). The IRB is made up of physicians, researchers, and members of the community. Its role is to make sure that the study is ethical and the rights and welfare of participants are protected. This includes ensuring that research risks are minimized and are reasonable in relation to any potential benefits.12

Following is a general description of the three primary phases of clinical research:

- **Phase 1** trials test a compound in a small group (e.g., 20 to 100) of healthy volunteers to determine the safety of the compound.
- **Phase 2** trials test the compound in a somewhat larger group (e.g., 100 to 500) of volunteers who have the disease or condition the compound is designed to treat. Phase 2 trials determine effectiveness of the compound, examine possible short-term side effects and risks, and identify optimal dose and schedule.
- **Phase 3** trials test the compound in a much larger group (e.g., 1,000 to 5,000) of participants to generate statistically significant information about safety and efficacy and to determine the overall benefit-risk ratio.

**FDA Review and Approval**

If the results of all three clinical trial phases indicate that the compound is safe and effective, the company submits a New Drug Application or Biologics License Application to the FDA. This application, which includes reams of data from all stages of testing, is a request for FDA approval to market the new medicine.

Scientists at the FDA carefully review all the data from all of the studies on the compound and, after weighing the benefits and risks of the potential medicine, decide whether to grant approval. Occasionally, the FDA will ask for additional research before granting approval or convene an independent expert panel to consider data presented by the FDA and the company. The panel will then advise the agency on whether to approve the application and under what conditions.

**Manufacturing**

Approved medicines may be used by millions of people or a small, specific population. Medicines often are in the marketplace for many years. As a result, manufacturing facilities must be carefully planned so that medicines can be consistently and efficiently produced. Manufacturing facilities must be constructed to the highest standards to ensure that safety and quality are built into each step of the manufacturing process.13 Companies must adhere to FDA's Good Manufacturing Practices regulations, and they also must constantly update, overhaul, or even rebuild facilities when new medicines are approved, as each new medicine is manufactured differently.
Drug Lifecycle

The R&D process is part of a larger prescription drug lifecycle. The cycle begins with the initial development of the medicine and it ends with generic drugs. Generics provide low-cost access to effective medicines for many years. But we would not have generics if innovator companies did not commit the time, resources, and investment to research and develop new, innovative medicines.

After FDA approval, the average effective patent life of a brand name medicine is about 12 years. Competition often begins soon after approval, with generics frequently coming to the market even earlier through patent challenges, and other competing brand drugs commonly coming to market. During the period of patent protection, the medicine must earn enough revenue to fund the drug development pipeline for other candidates that may someday become new drugs. Only 2 of every 10 brand name medicines earn sufficient revenues to recoup average R&D costs.

After patent protection expires, other companies are allowed to sell generic copies of the innovative drug. These medicines, which are often adopted rapidly, can be offered at low cost because the generic companies can base their approval on the extensive research already conducted to develop the brand name medicine. Today, we estimate that 84% of all drug prescriptions are filled generically, yielding a savings of $1.1 trillion dollars in the past decade.

With the passage of the Affordable Care Act, an abbreviated approval pathway was created for biosimilars, which will further increase competition.

Post-Approval Research and Monitoring

Research on a new medicine does not end when the discovery and development phases are over and the product is on the market. On the contrary, companies conduct extensive post-approval research to monitor safety and long-term side effects in patients using the medicine. The FDA requires that companies monitor a medicine for as long as it stays on the market and submit periodic reports on safety issues. Companies must report any adverse events that occur from use of the medicine.

FDA sometimes requires companies to conduct phase 4 clinical trials, which evaluate long-term safety or effects in specific patient subgroups. Companies may conduct post-approval studies to assess the benefits of a medicine for different populations or in other disease areas. In some cases, they may also develop improved delivery systems or dosage forms.

This research phase is critical to improving researchers’ and clinicians’ understanding of a medicine’s potential uses and its full benefits for health and quality of life. Continued research can show whether a medicine has a greater impact on an outcome when it is used earlier in a disease, in combination with other medicines, in different disease indications, or in combination with specific biomarkers (see the section “The Evolving Value of Medicines” in Chapter 1, page 9).

The Evolving R&D Process

As science advances and opens new doors, the R&D process continually changes and adapts. New scientific advances are bringing greater promise but also increasing complexity. Here are just a few examples of the forces that are changing the R&D process:

Working on the molecular level: In recent years, scientists’ deepening understanding of the molecular and genetic underpinnings of disease has brought unprecedented opportunities and dramatically changed many aspects of drug development.
Researching more complex diseases:
Increasingly, clinical investigators are exploring treatment options for more complex diseases such as neurological disorders, cancer, and many rare diseases. For example, in 2003 there were 26 medicines in development for Alzheimer’s disease in the United States; today there are 94.\textsuperscript{18,19} New scientific opportunities make these new avenues of exploration possible, but the complexities of these uncharted areas also can in some cases mean that research projects are less likely to succeed.

Advancing personalized medicine:
With the emergence of personalized medicine — in which the use of a medicine is linked to a diagnostic to determine if a patient will respond well to a medicine — the R&D process has become more complex. Drug developers must coordinate research on a new medicine along with a corresponding diagnostic.

In this increasingly complicated research scheme, it is necessary to dig deeper into how each patient may respond to a therapy and to keep pace with expanding regulatory requirements. As a result of these changes, the burden of executing a clinical trial is growing, with more procedures required, more data collected, more numerous and complex eligibility criteria for study enrollment, and longer study duration.\textsuperscript{20} (See Figure 13.) In fact, the form used to collect data from each patient expanded in length by 227\% between 2000 and 2011, reflecting the growing challenges of conducting clinical trials.\textsuperscript{21}

Recruitment of patient volunteers is also an ongoing and growing challenge for researchers. Difficulty recruiting volunteers extends the original timeline of phase 2 to 4 trials by nearly double on average across all therapeutic areas.\textsuperscript{22}

The increased complexity of the research environment has contributed to the rising costs of clinical research.\textsuperscript{23} Treatment failures and setbacks also contribute to the cost of research. According to the Tufts Center for the Study of Drug Development, the cost of developing a drug (including the cost of failures) grew from $800 million in
the late 1990s to about $1.2 billion in the early 2000s.24 (See Figure 14.) Other more recent studies have put the total cost even higher.25

Adapting to Changes and Challenges

The biopharmaceutical industry is continually adapting to produce innovative treatments more efficiently. Researchers are exploring ways to reduce development times and increase the odds of success using new research tools, new approaches to patient recruitment, and sophisticated methods of analyzing data.

Companies are working to develop innovative partnerships and collaborative relationships with researchers in academia, government, and in other companies. Precompetitive partnerships, which seek to advance basic research, are a growing part of this approach.26

Improving the clinical trials process is another area of active exploration. For example, phase 0 or “microdosing” trials allow researchers to test a very small dose in fewer human volunteers to eliminate more quickly drug candidates that may be metabolically or biologically ineffective.

No one change will transform the R&D process on its own, but with many diverse efforts biopharmaceutical companies will continue to improve the process of innovation.

Companies are developing “new approaches to designing and conducting global clinical trials, including simplifying protocols, maximizing investigational site performance, and reducing the number of protocol amendments.”27

“
Learning from Setbacks in Alzheimer’s Disease Research

Not only do successes build over time, but so do lessons learned from seemingly failed projects and research. Alzheimer’s disease is commonly considered one of the most devastating conditions anyone can face and is the sixth leading cause of death in the United States.\(^{28}\) The disease progressively robs people of their memory, their personality, and their health.\(^{29}\) What’s more, the Alzheimer’s Association projects that the disease will cost the U.S. health care system $1.1 trillion annually by 2050.\(^{30}\)

Today’s medicines can address symptoms of Alzheimer’s, but medicines that prevent or slow the disease are needed. Although researchers continue to discover and learn more, the underlying causes and mechanisms of this disease remain elusive, and the complex nature of the disease presents huge challenges to scientists.

Since 1998, biopharmaceutical companies have made 101 unsuccessful attempts to develop medicines to treat Alzheimer’s while, in the same period, only three medicines have been approved. That means that for every success, companies have experienced 34 so-called “failures.”\(^{31}\) (See Figure 15.) Although these setbacks may be disheartening, they are certainly not failures because they contribute valuable knowledge about Alzheimer’s that can be used as building blocks to point researchers in more fruitful directions.


Figure 15: Unsuccessful Alzheimer’s Drugs in Development, 1998 – 2011

Total unsuccessful drugs=101

Recognizing Researchers and Patient Advocates for Alzheimer’s Disease

In September 2012, PhRMA bestowed the first annual Research and Hope Award, honoring individuals and organizations in academia, the biopharmaceutical research sector, as well as the patient and caregiving communities that have contributed significantly to the advancement of medical progress and patient care for Alzheimer’s. Information about the award recipients is available at www.phrma.org/awards.

Biopharmaceutical researchers are responding to this complex scientific challenge and are committed to finding treatments for Alzheimer’s disease. There are nearly 100 new medicines in development in the United States. As researchers examine the science and clinical data behind both the successes and the stumbling blocks, there is hope for a future in which this devastating disease can be managed successfully or even cured or prevented altogether.
In 1992, the Prescription Drug User Fee Act (PDUFA) authorized the FDA to collect user fees from the biopharmaceutical industry to hire additional drug reviewers and safety specialists. These funds supplement Congressional appropriations. In its first 20 years, PDUFA has helped to bring more than 1,500 new medicines to market. It also has increased FDA’s staffing and resources and preserved and strengthened FDA’s high safety standards, resulting in a drop in approval times for new medicines from 29 months in the early 1990s to an estimated 10 months in 2010.34,35

In 2012, the fifth authorization of PDUFA (called PDUFA-V) was enacted as part of the Food and Drug Administration Safety and Innovation Act. In addition to enabling more timely patient access to safe and effective new medicines, PDUFA-V promotes future research and prepares the FDA for a 21st century regulatory framework. It also supports the development of a framework to facilitate evaluations of the benefits and risks of new medicines (including orphan drugs) and integrates patient perspectives into the review process.

Congress also acted last year to make two provisions affecting pediatric research permanent. These provisions, the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA), work together to encourage pediatric research. The combination of BPCA and PREA, often referred to as the “carrot” and “stick” approach, has resulted in a wealth of useful information about administering drugs to children, including information on dosing, safety, and efficacy. Together, BPCA and PREA have driven research and greatly advanced American children’s medical care. Making these two provisions permanent will help create a more predictable and efficient pediatric drug development process, resulting in continued progress to develop new medicines for children. BPCA and PREA already have resulted in significant accomplishments:

- As of December 2012, 193 drugs have received pediatric exclusivity under BPCA.36,37
- Following the reauthorization of BPCA and PREA in 2007 and through June 2012, 405 pediatric studies were completed, involving 174,273 patients.38
- Since 1998, BPCA and PREA have resulted in 463 labeling changes reflecting important pediatric information.39

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35Ibid.


A Promising Pipeline
Our growing understanding of human disease gives us the most promising platform ever to find medicines that treat disease in new ways. Today, more than 5,000 medicines are in development globally, all of which have the potential to help patients in the United States and around the world.1 (See Figure 16.) According to another data source, there are 3,400 medicines in development today just in the United States, an increase of 40% since 2005.2,3 The quantity and quality of new drugs in the pipeline reflect a robust research ecosystem. Both basic research and the biopharmaceutical pipeline are thriving. As a result, the potential for new treatments and cures for patients is unprecedented.

Biopharmaceutical researchers are working tirelessly to develop medicines that attack diseases in novel ways. They are exploring new scientific approaches while expanding their knowledge and understanding of human diseases. The increase in the number and variety of scientific tools over the last 20 years has enabled researchers to better understand the molecular and genetic bases of disease and to develop targeted treatments that work more precisely and effectively. Researchers are steadily applying this knowledge to a range of different diseases and conditions, and the result is unprecedented potential for improvements in human health around the world.

Examining the Pipeline

According to a recent report by Analysis Group, which uses various data sources to examine innovation in the pipeline from several different angles, 70% of the more than 5,000 new molecular entities (NMEs) being investigated are potential first-in-class medicines, meaning that they are in a unique pharmacologic class distinct from any other marketed drugs.4 Such medicines offer new potential treatment options for patients, particularly for those who have not responded to existing therapies or for whom no existing treatment options are available. These medicines may improve the outlook for patients by providing greater efficacy or fewer side effects. Subsequent medicines in the class may provide patients with different side effect or efficacy profiles.
These data “hint at an exciting new Spring of medical innovation for patients. The last thing we want to do — or can afford to do — is stop it cold.”

► JOHN C. LECHLEITER, PH.D., CHAIRMAN, PRESIDENT, CHIEF EXECUTIVE OFFICER, ELI LILLY AND COMPANY

Figure 16: Medicines in Development by Regulatory Phase

In 2011, 5,408 medicines* were in clinical development worldwide.

Because many of the 5,408 medicines in development are in trials for more than one indication, the total number of projects in development is close to 8,000.

*Defined as single products which are counted exactly once regardless of the number of indications pursued.

The proportion of projects in development that could become first-in-class varies by therapeutic area but is particularly high in areas such as neurology (84%), cancer (80%), and psychiatry (79%).6 (See Figure 17.) The high number of potential first-in-class drugs being researched in these areas likely reflects researchers’ growing knowledge of the underpinnings of these disease areas and new opportunities for advances.

According to Analysis Group, biopharmaceutical companies are making significant progress in a number of key areas:7

- **Rare diseases.** There are nearly 7,000 rare diseases—many of which are serious or life-threatening and have few treatment options. In 2011, 1,795 projects in development focused on rare diseases, which each affect fewer than 200,000 persons in the United States. The U.S. Food and Drug Administration (FDA) designations of orphan drugs in development have been increasing. In the past 10 years, an average of 140 drugs were designated as orphan drugs each year compared with 64 in the previous 10 years.9

- **Diseases that do not yet have approved treatments.** Scientists are increasingly developing medicines for diseases for which no therapies have been approved in the last 10 years and that have significant gaps in treatment options. For example, there are 61 medicines in development for amyotrophic lateral sclerosis or Lou Gehrig’s disease, 41 for small cell lung cancer, 19 for sickle cell disease, and 158 for ovarian cancer.10

- **Medicines that are among the first to apply new scientific strategies to address disease.** New discoveries in basic science are leading to new therapeutic approaches that were never before possible. Among the potential new approaches under investigation today are:
If you’re a patient with a terrible disease, a serious cancer or something like that, I think you ought to take heart from what we are seeing.

— Janet Woodcock, M.D., Director of the U.S. Food and Drug Administration’s Center for Drug Evaluation and Research

**RNAi therapy.** While most drugs target proteins such as enzymes and cellular receptors, this new approach opens up opportunities to target RNA, which carries genetic information to create proteins in the cell. Antisense RNA interference (RNAi) therapy can help to silence harmful gene expression. In the past 20 years, this work has advanced from the laboratory bench to the bedside, and two RNAi therapies already have been approved. More than 127 RNAi projects are in the pipeline.11

**Therapeutic cancer vaccines.** Unlike traditional vaccines, these new vaccines harness the power of the immune system to fight cancer rather than to prevent it. This idea first emerged in the late 1990s, and the first therapeutic cancer vaccine was approved in 2010. More than 20 therapeutic vaccines for cancer are in development.12,13

**Figure 18: Number of Projects with Orphan Drug Designation by Year 1983–2011**

Our progress in understanding the specific pathways of disease has identified hundreds of new targets for potentially life-saving drugs that hold the potential to treat individual patients much more effectively. The result of this understanding is an emerging paradigm shift for the development of new medicines.15

➤ Mark McClellan, M.D., Ph.D., Engelberg Center for Health Care Reform, Brookings Institution, and Ellen Sigal, Ph.D., Friends of Cancer Research, 2012
New Horizons in Personalized Medicine

Personalized medicine presents a new set of tools to help diagnose and treat patients based on our growing understanding of the genetic and molecular basis of disease. This approach is becoming more widespread, particularly in the treatment of cancer, and it holds potential to prevent disease, find the correct treatment more quickly, prevent side effects, improve patients’ quality of life, and treat disease more effectively. As the overall cost of health care continues to rise, personalized medicine could help to control costs by reducing unnecessary treatments and side effects.16

The role of personalized medicine is growing. According to the Personalized Medicine Coalition, there were 13 prominent examples of personalized medicines, treatments, and diagnostics available in 2006; by 2011, there were 72.17 Likewise, a 2010 survey by the Tufts Center for the Study of Drug Development found that companies saw a roughly 75% increase in personalized medicine investment between 2005 and 2010 and expected to see an additional 53% increase from 2010 to 2015.18 Of the companies surveyed, 94% of biopharmaceutical companies are investing in personalized medicine research, and 12% to 50% of the products in their pipelines are personalized medicines.19

The industry as a whole is committed to pushing strongly ahead ... Early indications show that development of personalized medicines is commanding more resources and fomenting more corresponding organization change than is generally appreciated outside the industry.20

► Tufts Center for the Study of Drug Development, 2010
Spotlight on Medicines in the Pipeline

Treating a Dangerous Mutation in Infants

Hypophosphatasia is a rare inherited bone disease that is caused by a genetic mutation. The mutation results in low levels of an enzyme called alkaline phosphatase. This deficiency hinders the formation of bones and teeth and can result in substantial skeletal abnormalities. No medicine has been approved for this disease. A potential therapy in development would provide the enzyme necessary for proper bone growth in those with this devastating, rare disease.  

Addressing Difficult-to-Treat Symptoms of Schizophrenia

Schizophrenia is a severe and complex mental illness that impairs the patient mentally and emotionally. Although some medicines target symptoms like hallucinations and delusions, they are generally not able to improve other symptoms such as lack of motivation and interest in social activities. A new medicine in development could be the first in a new class that has the potential to target these difficult-to-treat symptoms by improving transmission of a chemical needed in the brain for proper communication between neurons.
Looking Ahead

Despite an extremely promising scientific landscape and ongoing positive impact of the biopharmaceutical sector on patients, the health care system, and the economy, the biopharmaceutical industry faces growing challenges.

**Higher Hurdles**

**Changing Science**
The drug development process is becoming more costly and complex. In part, this is due to today's need for medicines to treat increasingly challenging and costly chronic diseases, such as arthritis, cancer, diabetes, and neurodegenerative disorders. Scientific opportunities are leading researchers to focus on increasingly complex diseases and new approaches such as personalized medicine. This sophisticated science requires equally sophisticated tools, technologies, and expertise.

**Regulatory Environment**
Today's regulatory environment requires complex and extensive research to establish the safety and effectiveness of new medicines and an ever-growing amount of information on each new medicine. This typically means that companies must sponsor clinical trials with large numbers of participants. Patient recruitment and retention in clinical trials are continuing challenges.

**International Competition**
Many countries are now focusing on building an innovative biomedical sector because they recognize its benefits for their economies and their patients — posing a challenge to U.S. leadership in biomedical research. They are forming industry clusters, often in partnership with regional governments. They are also helping to grow their knowledge-based economies through strategies such as building research and development (R&D) infrastructure; emphasizing science, technology, engineering, and math (STEM) education; ensuring access to financial capital; and building and retaining a skilled workforce.1 For example:

- **Singapore** invested significantly in R&D infrastructure, most famously by creating the Biopolis Research Park. More than 30 companies have located to Biopolis, including many well-known multinational companies.2

- **China** has increased R&D investment by 10% each year over the last decade for a total investment of $154 billion — second only to the United States. China also has established programs and incentives to attract talented scientists and foreign investment.3

**Meeting Challenges**
America's biopharmaceutical companies are adapting and seeking creative solutions to meet these growing economic, scientific, business, regulatory, and policy challenges. For example, companies are working to make the clinical trials process as efficient as possible and are focusing on diseases with the greatest unmet needs. They are developing partnerships and unique collaborations to expand the capacity to address complex disease targets. Companies are also working with the U.S. Food and Drug Administration, the National Institutes of Health, and related research agencies.
to advance regulatory science and to foster the integration of emerging data and innovation into the development and review of new medicines.

These responses, combined with positive, forward-looking public policies that sustain a market-based system and incentives for innovators, such as strong intellectual property protections, will help ensure America’s continued role as the worldwide leader in biopharmaceutical research.

To foster innovation and the medical advances and economic impact that go with it, we must:

- Continue to advance regulatory science and foster the integration of emerging scientific data and innovative approaches into the development and review of new medicines more efficiently, promoting public health in areas such as biomarkers, pharmacogenomics, and rare and orphan drug development.

- Advance medical innovation policies as a solution to health-system problems. For example, to help realize the potential of medical innovation as a solution for improving patient outcomes and controlling rising health care costs, it is important to recognize across all policy areas that the full value of medical advances emerges over time, and to support the ability of physicians and patients to choose from the full range of medically appropriate treatment options.

- Support coverage and payment policies that foster the introduction and availability of new medical advances to America’s patients.

- Support the development of STEM workers to increase the nation’s ability to develop and manufacture tomorrow’s new treatments and to compete globally.

- Support strong intellectual property rights and enforcement in the United States and abroad.

- Sustain U.S. global leadership in the biosciences through economic, trade, and related policies to promote a level playing field globally.


2 Ibid.

3 Ibid.
The challenges facing the biopharmaceutical industry are many and substantial — complex scientific issues, an evolving regulatory environment, and stiff competition at home and abroad. But the scientific opportunities and the promise of medicines in the pipeline are remarkable. And the positive impact of the industry is far reaching.

The biopharmaceutical sector is meeting the challenges before it with innovative scientific work, creative approaches to building and sustaining the industry, and an unending commitment to saving lives and improving the health and quality of life of patients.

This commitment is reflected in the many advances that we have already seen across a wide spectrum of diseases that affect millions. And it brings many benefits such as good jobs and economic investment to communities and states across the nation. The future holds great promise for continued advancements, and with sustained support for innovation, the U.S. biopharmaceutical sector will continue to lead the world.
PhRMA: 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 more than $500 billion in research and development into medical innovations since 2000, and an estimated $48.5 billion in 2012 alone. This investment also helps drive the industry’s significant contributions to the U.S. 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, D.C., 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

To learn more about PhRMA, go to www.PhRMA.org/about.
PhRMA Member Companies
Full Members & Research Associate Members

Members & Subsidiaries

**AbbVie, Inc.**
North Chicago, IL

**Alkermes plc**
Waltham, MA

**Amgen Inc.**
Thousand Oaks, CA

**Astellas Pharma US, Inc.**
Northbrook, IL

**AstraZeneca Pharmaceuticals LP**
Wilmington, DE

**Bausch + Lomb**
Rochester, NY

**Bayer**
Wayne, NJ

**Biogen Idec Inc.**
Weston, MA

**Boehringer Ingelheim Pharmaceuticals, Inc.**
Ridgefield, CT

**Bristol-Myers Squibb Company**
New York, NY

**Celgene Corporation**
Summit, NJ

**Cubist Pharmaceuticals, Inc.**
Lexington, MA

**Daiichi Sankyo, Inc.**
Parsippany, NJ

**Dendreon Corporation**
Seattle, WA

**Eisai Inc.**
Woodcliff Lake, NJ

**EMD Serono**
Rockland, MA

**Endo Pharmaceuticals, Inc.**
Chadds Ford, PA

**GlaxoSmithKline**
Research Triangle Park, NC

**Johnson & Johnson**
New Brunswick, NJ

**Eli Lilly and Company**
Indianapolis, IN

**Lundbeck Inc.**
Deerfield, IL

**Merck & Co., Inc.**
Whitehouse Station, NJ
Merck Human Health Division
Merck Research Laboratories
Merck Vaccine Division
Novartis Pharmaceuticals Corporation  
East Hanover, NJ

Novo Nordisk Inc.  
Princeton, NJ

Otsuka America Pharmaceutical  
Princeton, NJ
  Otsuka America Pharmaceutical, Inc. (OAPI)  
  Otsuka Pharmaceutical Development & Commercialization, Inc. (OPDC)  
  Otsuka Maryland Medicinal Laboratories, Inc. (OMML)

Pfizer Inc.  
New York, NY

Purdue Pharma L.P.  
Stamford, CT

Sanofi U.S.  
Bridgewater, NJ  
Sanofi Pasteur

Sunovion Pharmaceuticals Inc.  
Marlborough, MA

Sigma-Tau Pharmaceuticals, Inc.  
Gaithersburg, MD

Takeda Pharmaceuticals U.S.A., Inc.  
Deerfield, IL

Research Associate Members

Arena Pharmaceuticals, Inc.  
San Diego, CA

Auxilium Pharmaceuticals, Inc.  
Chesterbrook, PA

BioMarin Pharmaceutical Inc.  
Novato, CA

CSL Behring, LLC  
King of Prussia, PA

Ferring Pharmaceuticals, Inc.  
Parsippany, NJ

Grifols USA, LLC  
Los Angeles, CA

Horizon Pharma, Inc.  
Deerfield, IL

Ikaria, Inc.  
Hampton, NJ

Ipsen Pharmaceuticals Inc.  
Basking Ridge, NJ
Onyx Pharmaceuticals
South San Francisco, CA

Orexigen Therapeutics, Inc.
La Jolla, CA

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

XOMA Corporation
Berkeley, CA
PhRMA Annual Membership Survey

Definition of Terms

Research and Development Expenditure Definitions

R&D Expenditures: Expenditures within PhRMA member companies’ U.S. and/or foreign research laboratories plus research and development (R&D) funds contracted or granted to commercial laboratories, private practitioners, consultants, educational and nonprofit research institutions, manufacturing and other companies, or other research-performing organizations located inside/outside of the U.S. Includes basic and applied research, as well as developmental activities carried on or supported in the pharmaceutical, biological, chemical, medical, and related sciences, including psychology and psychiatry, if the purpose of such activities is concerned ultimately with the utilization of scientific principles in understanding diseases or in improving health. Includes the total cost incurred for all pharmaceutical R&D activities, including salaries, materials, supplies used, and a fair share of overhead, as well as the cost of developing quality control. However, it does not include the cost of routine quality control activities, capital expenditures, or any costs incurred for drug or medical R&D conducted under a grant or contract for other companies or organizations.

Domestic R&D: Expenditures within the United States by all PhRMA member companies.

R&D Abroad: Expenditures outside the United States by U.S.-owned PhRMA member companies and R&D conducted abroad by the U.S. divisions of foreign-owned PhRMA member companies. R&D performed abroad by the foreign divisions of foreign-owned PhRMA member companies is excluded.

Prehuman/Preclinical Testing: From synthesis to first testing in humans.

Phase 1/2/3 Clinical Testing: From first testing in designated phase to first testing in subsequent phase.

Approval Phase: From New Drug Application (NDA)/Biologic License Application (BLA) submission to NDA/BLA decision.

Phase 4 Clinical Testing: Any post-marketing R&D activities performed.

Uncategorized: Represents data for which detailed classifications were unavailable.
Sales Definitions

Sales: Product sales calculated as billed, free on board (FOB) plant or warehouse less cash discounts, Medicaid rebates, returns, and allowances. These include all marketing expenses except transportation costs. Also included is the sales value of products bought and resold without further processing or repackaging, as well as the dollar value of products made from the firm’s own materials for other manufacturers’ resale. Excluded are all royalty payments, interest, and other income.

Domestic Sales: Sales generated within the United States by all PhRMA member companies.

- Private Sector: Sales through regular marketing channels for end use other than by government agency administration or distribution.

- Public Sector: Sales or shipments made directly to federal, state, or local government agencies, hospitals, and clinics.

Sales Abroad: Sales generated outside the United States by U.S.-owned PhRMA member companies, and sales generated abroad by the U.S. divisions of foreign-owned PhRMA member companies. Sales generated abroad by the foreign divisions of foreign-owned PhRMA member companies are excluded.
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### TABLE 1: Domestic R&D and R&D Abroad, PhRMA Member Companies: 1975–2012

(dollar figures in millions)

<table>
<thead>
<tr>
<th>Year</th>
<th>Domestic R&amp;D</th>
<th>Annual Percentage Change</th>
<th>R&amp;D Abroad*</th>
<th>Annual Percentage Change</th>
<th>Total R&amp;D</th>
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**Average**

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<th>Domestic R&amp;D</th>
<th>R&amp;D Abroad*</th>
<th>Total R&amp;D</th>
<th>Annual Percentage Change</th>
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<td>10.8%</td>
<td>12.2%</td>
<td>11.1%</td>
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*R&D Abroad includes expenditures outside the United States by U.S.-owned PhRMA member companies and R&D conducted abroad by the U.S. divisions of foreign-owned PhRMA member companies. R&D performed abroad by the foreign divisions of foreign-owned PhRMA member companies are excluded. Domestic R&D, however, includes R&D expenditures within the United States by all PhRMA member companies.

**Estimated.

***R&D Abroad affected by merger and acquisition activity.

Note: All figures include company-financed R&D only. Total values may be affected by rounding.

<table>
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<tr>
<th>Year</th>
<th>Domestic R&amp;D as a Percentage of Domestic Sales</th>
<th>Total R&amp;D as a Percentage of Total Sales</th>
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<td>14.4</td>
</tr>
<tr>
<td>1989</td>
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<td>14.8</td>
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<tr>
<td>1988</td>
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<td>14.1</td>
</tr>
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<td>1987</td>
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<tr>
<td>1986</td>
<td>16.4</td>
<td>12.9</td>
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<td>1985</td>
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<td>12.9</td>
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<td>1984</td>
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<td>11.8</td>
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<tr>
<td>1982</td>
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<td>10.9</td>
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<tr>
<td>1981</td>
<td>14.8</td>
<td>10.0</td>
</tr>
<tr>
<td>1980</td>
<td>13.1</td>
<td>8.9</td>
</tr>
<tr>
<td>1979</td>
<td>12.5</td>
<td>8.6</td>
</tr>
<tr>
<td>1978</td>
<td>12.2</td>
<td>8.5</td>
</tr>
<tr>
<td>1977</td>
<td>12.4</td>
<td>9.0</td>
</tr>
<tr>
<td>1976</td>
<td>12.4</td>
<td>8.9</td>
</tr>
<tr>
<td>1975</td>
<td>12.7</td>
<td>9.0</td>
</tr>
</tbody>
</table>

*Estimated.
**Revised in 2007 to reflect updated data.
TABLE 3: Domestic R&D and R&D Abroad,* PhRMA Member Companies: 2011

(dollar figures in millions)

<table>
<thead>
<tr>
<th>R&amp;D Expenditures for Human-use Pharmaceuticals</th>
<th>Dollars</th>
<th>Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Domestic</td>
<td>$35,923.9</td>
<td>73.8%</td>
</tr>
<tr>
<td>Abroad*</td>
<td>$11,982.5</td>
<td>24.6%</td>
</tr>
<tr>
<td><strong>Total Human-use R&amp;D</strong></td>
<td><strong>$47,906.4</strong></td>
<td><strong>98.5%</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>R&amp;D Expenditures for Veterinary-use Pharmaceuticals</th>
<th>Dollars</th>
<th>Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Domestic</td>
<td>$449.7</td>
<td>0.9%</td>
</tr>
<tr>
<td>Abroad*</td>
<td>$288.9</td>
<td>0.6%</td>
</tr>
<tr>
<td><strong>Total Vet-use R&amp;D</strong></td>
<td><strong>$738.7</strong></td>
<td><strong>1.5%</strong></td>
</tr>
</tbody>
</table>

**TOTAL R&D** $48,645.0 100.0%

*R&D abroad includes expenditures outside the United States by U.S.-owned PhRMA member companies and R&D conducted abroad by the U.S. divisions of foreign-owned PhRMA member companies. R&D performed abroad by the foreign divisions of foreign-owned PhRMA member companies are excluded. Domestic R&D, however, includes R&D expenditures within the United States by all PhRMA member companies.

Note: All figures include company-financed R&D only. Total values may be affected by rounding.


---

TABLE 4: R&D by Function, PhRMA Member Companies: 2011

(dollar figures in millions)

<table>
<thead>
<tr>
<th>Function</th>
<th>Dollars</th>
<th>Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prehuman/Preclinical</td>
<td>$10,466.3</td>
<td>21.5%</td>
</tr>
<tr>
<td>Phase 1</td>
<td>4,211.0</td>
<td>8.7%</td>
</tr>
<tr>
<td>Phase 2</td>
<td>6,096.4</td>
<td>12.5%</td>
</tr>
<tr>
<td>Phase 3</td>
<td>17,392.9</td>
<td>35.8%</td>
</tr>
<tr>
<td>Approval</td>
<td>4,033.4</td>
<td>8.3%</td>
</tr>
<tr>
<td>Phase 4</td>
<td>4,760.9</td>
<td>9.8%</td>
</tr>
<tr>
<td>Uncategorized</td>
<td>1,684.0</td>
<td>3.5%</td>
</tr>
<tr>
<td><strong>TOTAL R&amp;D</strong></td>
<td><strong>$48,645.0</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

Note: All figures include company-financed R&D only. Total values may be affected by rounding.

### TABLE 5: R&D by Geographic Area, PhRMA Member Companies: 2011

(dollar figures in millions)

<table>
<thead>
<tr>
<th>Geographic Area*</th>
<th>Dollars</th>
<th>Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Egypt</td>
<td>$3.7</td>
<td>0.0%</td>
</tr>
<tr>
<td>South Africa</td>
<td>50.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Other Africa</td>
<td>5.2</td>
<td>0.0</td>
</tr>
<tr>
<td>Americas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>$36,373.6</td>
<td>74.8%</td>
</tr>
<tr>
<td>Canada</td>
<td>781.0</td>
<td>1.6</td>
</tr>
<tr>
<td>Mexico</td>
<td>114.6</td>
<td>0.2</td>
</tr>
<tr>
<td>Brazil</td>
<td>181.1</td>
<td>0.4</td>
</tr>
<tr>
<td>Argentina</td>
<td>101.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Venezuela</td>
<td>5.3</td>
<td>0.0</td>
</tr>
<tr>
<td>Columbia</td>
<td>29.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Chile</td>
<td>21.5</td>
<td>0.0</td>
</tr>
<tr>
<td>Peru</td>
<td>16.9</td>
<td>0.0</td>
</tr>
<tr>
<td>Other Latin America</td>
<td>77.6</td>
<td>0.2</td>
</tr>
</tbody>
</table>

| Asia-Pacific     |          |       |
| Japan            | $1,027.7 | 2.1%  |
| China            | 327.6    | 0.7   |
| India            | 48.7     | 0.1   |
| Taiwan           | 38.7     | 0.1   |
| South Korea      | 103.9    | 0.2   |
| Other Asia-Pacific| 272.3 | 0.6 |

| Australia        |          |       |
| Australia and New Zealand | $274.7 | 0.6% |

| Europe           |          |       |
| France           | $509.6   | 1.0%  |
| Germany          | 659.2    | 1.4   |
| Italy            | 190.6    | 0.4   |
| Spain            | 230.7    | 0.5   |
| United Kingdom   | 1,770.5  | 3.6   |
| Other Western European | 4,009.6 | 8.2 |
| Czech Republic   | 50.6     | 0.1   |
| Hungary          | 40.1     | 0.1   |
| Poland           | 73.5     | 0.2   |
| Turkey           | 48.2     | 0.1   |
| Russia           | 73.3     | 0.2   |
| Central and Eastern Europe | 538.7 | 1.1 |

| Middle East      |          |       |
| Saudi Arabia     | $7.3     | 0.0%  |

| Middle East       |          |       |
| Other countries, United Arab Emirates, Iraq, Iran, Kuwait, Israel, Jordan, Syria, Afghanistan, and Qatar | 74.8 | 0.2 |

| Uncategorized      | $513.6   | 1.1%  |

| TOTAL R&D         | $48,645.00 | 100.0% |

---

*R&D abroad includes expenditures outside the United States by U.S.-owned PhRMA member companies and R&D conducted abroad by the U.S. divisions of foreign-owned PhRMA member companies, R&D performed abroad by the foreign divisions of foreign-owned PhRMA member companies are excluded. Domestic R&D, however, includes R&D expenditures within the United States by all PhRMA member companies.

Note: All figures include company-financed R&D only. Total values may be affected by rounding.

### TABLE 6: Domestic Sales and Sales Abroad, *PhRMA Member Companies: 1975–2012*

(dollar figures in millions)

<table>
<thead>
<tr>
<th>Year</th>
<th>Domestic Sales</th>
<th>Annual Percentage Change</th>
<th>Sales Abroad*</th>
<th>Annual Percentage Change</th>
<th>Total Sales</th>
<th>Annual Percentage Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012**</td>
<td>$177,506.9</td>
<td>-3.9%</td>
<td>$117,293.1</td>
<td>10.0%</td>
<td>$294,800.0</td>
<td>1.2%</td>
</tr>
<tr>
<td>2011</td>
<td>187,870.7</td>
<td>3.7</td>
<td>117,138.5</td>
<td>12.0</td>
<td>305,009.2</td>
<td>10.4</td>
</tr>
<tr>
<td>2010</td>
<td>184,660.3</td>
<td>2.0</td>
<td>106,593.2</td>
<td>10.0</td>
<td>291,253.5</td>
<td>5.4</td>
</tr>
<tr>
<td>2009</td>
<td>181,116.8</td>
<td>-1.1</td>
<td>95,162.5</td>
<td>-7.5</td>
<td>276,279.3</td>
<td>-3.4</td>
</tr>
<tr>
<td>2008</td>
<td>183,167.2</td>
<td>-1.1</td>
<td>102,842.4</td>
<td>16.6</td>
<td>286,009.6</td>
<td>4.6</td>
</tr>
<tr>
<td>2007</td>
<td>185,209.2</td>
<td>4.2</td>
<td>88,213.4</td>
<td>14.8</td>
<td>273,422.6</td>
<td>7.4</td>
</tr>
<tr>
<td>2006</td>
<td>177,736.3</td>
<td>7.0</td>
<td>76,870.2</td>
<td>10.0</td>
<td>254,606.4</td>
<td>7.9</td>
</tr>
<tr>
<td>2005</td>
<td>166,155.5</td>
<td>3.4</td>
<td>69,810.1</td>
<td>0.1</td>
<td>236,065.6</td>
<td>2.4</td>
</tr>
<tr>
<td>2004***</td>
<td>160,751.0</td>
<td>8.6</td>
<td>69,806.9</td>
<td>14.6</td>
<td>230,557.9</td>
<td>10.3</td>
</tr>
<tr>
<td>2003***</td>
<td>148,038.6</td>
<td>6.4</td>
<td>60,914.4</td>
<td>0.1</td>
<td>208,953.0</td>
<td>8.4</td>
</tr>
<tr>
<td>2002</td>
<td>139,136.4</td>
<td>6.4</td>
<td>53,697.4</td>
<td>12.1</td>
<td>192,833.8</td>
<td>8.0</td>
</tr>
<tr>
<td>2001</td>
<td>130,715.9</td>
<td>12.8</td>
<td>47,886.9</td>
<td>5.9</td>
<td>178,602.8</td>
<td>10.9</td>
</tr>
<tr>
<td>2000</td>
<td>115,881.8</td>
<td>14.2</td>
<td>45,199.5</td>
<td>1.6</td>
<td>161,081.3</td>
<td>10.4</td>
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<tr>
<td>1999</td>
<td>104,618.1</td>
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<td>44,496.6</td>
<td>2.7</td>
<td>145,958.4</td>
<td>17.1</td>
</tr>
<tr>
<td>1998</td>
<td>81,289.2</td>
<td>13.3</td>
<td>43,320.1</td>
<td>10.8</td>
<td>124,609.4</td>
<td>12.4</td>
</tr>
<tr>
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<td>71,761.9</td>
<td>10.8</td>
<td>39,086.2</td>
<td>6.1</td>
<td>110,848.1</td>
<td>9.1</td>
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<tr>
<td>1996</td>
<td>64,741.4</td>
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<td>36,838.7</td>
<td>8.7</td>
<td>101,580.1</td>
<td>11.6</td>
</tr>
<tr>
<td>1995</td>
<td>57,145.5</td>
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<td>33,893.5</td>
<td>****</td>
<td>91,039.0</td>
<td>****</td>
</tr>
<tr>
<td>1994</td>
<td>50,740.4</td>
<td>4.4</td>
<td>28,870.7</td>
<td>1.5</td>
<td>77,611.1</td>
<td>3.4</td>
</tr>
<tr>
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<td>48,590.9</td>
<td>1.0</td>
<td>26,467.3</td>
<td>2.8</td>
<td>75,058.2</td>
<td>1.7</td>
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<tr>
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<td>48,095.5</td>
<td>8.6</td>
<td>25,744.2</td>
<td>15.8</td>
<td>73,839.7</td>
<td>11.0</td>
</tr>
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<td>44,304.5</td>
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<td>22,231.1</td>
<td>12.1</td>
<td>66,535.6</td>
<td>14.1</td>
</tr>
<tr>
<td>1990</td>
<td>38,486.7</td>
<td>17.7</td>
<td>19,838.3</td>
<td>18.0</td>
<td>58,325.0</td>
<td>17.8</td>
</tr>
<tr>
<td>1989</td>
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<td>16,817.9</td>
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<td>49,524.5</td>
<td>7.1</td>
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<tr>
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<td>10.4</td>
<td>17,649.3</td>
<td>17.1</td>
<td>46,231.9</td>
<td>12.9</td>
</tr>
<tr>
<td>1987</td>
<td>25,879.1</td>
<td>9.4</td>
<td>15,064.8</td>
<td>15.6</td>
<td>40,947.5</td>
<td>11.6</td>
</tr>
<tr>
<td>1986</td>
<td>23,658.8</td>
<td>14.1</td>
<td>13,030.5</td>
<td>19.9</td>
<td>36,689.3</td>
<td>16.1</td>
</tr>
<tr>
<td>1985</td>
<td>20,742.5</td>
<td>9.0</td>
<td>10,872.3</td>
<td>4.0</td>
<td>31,614.8</td>
<td>7.3</td>
</tr>
<tr>
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<td>19,026.1</td>
<td>13.2</td>
<td>10,450.9</td>
<td>0.4</td>
<td>29,477.0</td>
<td>8.3</td>
</tr>
<tr>
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<td>16,805.0</td>
<td>14.0</td>
<td>10,411.2</td>
<td>-2.4</td>
<td>27,216.2</td>
<td>7.1</td>
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<td>14,743.9</td>
<td>16.4</td>
<td>10,667.4</td>
<td>0.1</td>
<td>25,411.3</td>
<td>9.0</td>
</tr>
<tr>
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<td>12,665.0</td>
<td>7.4</td>
<td>10,658.3</td>
<td>1.4</td>
<td>23,323.3</td>
<td>4.6</td>
</tr>
<tr>
<td>1980</td>
<td>11,788.6</td>
<td>10.7</td>
<td>10,515.4</td>
<td>26.9</td>
<td>22,304.0</td>
<td>17.8</td>
</tr>
<tr>
<td>1979</td>
<td>10,651.3</td>
<td>11.2</td>
<td>8,287.8</td>
<td>21.0</td>
<td>18,939.1</td>
<td>15.3</td>
</tr>
<tr>
<td>1978</td>
<td>9,580.5</td>
<td>12.0</td>
<td>6,850.4</td>
<td>22.2</td>
<td>16,430.9</td>
<td>16.1</td>
</tr>
<tr>
<td>1977</td>
<td>8,550.4</td>
<td>7.5</td>
<td>5,605.0</td>
<td>10.2</td>
<td>14,155.4</td>
<td>8.6</td>
</tr>
<tr>
<td>1976</td>
<td>7,951.0</td>
<td>11.4</td>
<td>5,084.3</td>
<td>9.7</td>
<td>13,035.3</td>
<td>10.8</td>
</tr>
<tr>
<td>1975</td>
<td>7,135.7</td>
<td>10.3</td>
<td>4,633.3</td>
<td>19.1</td>
<td>11,769.0</td>
<td>13.6</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td></td>
<td>9.4%</td>
<td></td>
<td>9.9%</td>
<td></td>
<td>9.4%</td>
</tr>
</tbody>
</table>

*Sales Abroad includes sales generated outside the United States by U.S.-owned PhRMA member companies and sales generated abroad by the U.S. divisions of foreign-owned PhRMA member companies. Sales generated abroad by the foreign divisions of foreign-owned PhRMA member companies are excluded. Domestic sales, however, includes sales generated within the United States by all PhRMA member companies.

**Estimated.

***Revised in 2007 to reflect updated data.

****Sales abroad affected by merger and acquisition activity.

Note: Total values may be affected by rounding.

### TABLE 7: Sales by Geographic Area, PhRMA Member Companies: 2011

(dollar figures in millions)

<table>
<thead>
<tr>
<th>Geographic Area*</th>
<th>Dollars</th>
<th>Share</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Africa</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Egypt</td>
<td>$347.7</td>
<td>0.1%</td>
</tr>
<tr>
<td>South Africa</td>
<td>872.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Other Africa</td>
<td>1,327.8</td>
<td>0.4</td>
</tr>
<tr>
<td><strong>Americas</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>$187,870.7</td>
<td>61.6%</td>
</tr>
<tr>
<td>Canada</td>
<td>6,793.0</td>
<td>2.2</td>
</tr>
<tr>
<td>Mexico</td>
<td>2,576.9</td>
<td>0.8</td>
</tr>
<tr>
<td>Brazil</td>
<td>4,387.4</td>
<td>1.4</td>
</tr>
<tr>
<td>Argentina</td>
<td>873.9</td>
<td>0.3</td>
</tr>
<tr>
<td>Venezuela</td>
<td>1,323.2</td>
<td>0.4</td>
</tr>
<tr>
<td>Columbia</td>
<td>771.4</td>
<td>0.3</td>
</tr>
<tr>
<td>Chile</td>
<td>320.8</td>
<td>0.1</td>
</tr>
<tr>
<td>Peru</td>
<td>167.6</td>
<td>0.1</td>
</tr>
<tr>
<td>Other Latin America</td>
<td>1,449.8</td>
<td>0.5</td>
</tr>
<tr>
<td>(Other South America, Central America, and all Caribbean nations)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Asia-Pacific</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td>$17,556.4</td>
<td>5.8%</td>
</tr>
<tr>
<td>China</td>
<td>3,391.2</td>
<td>1.1</td>
</tr>
<tr>
<td>India</td>
<td>1,635.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Taiwan</td>
<td>1,152.2</td>
<td>0.4</td>
</tr>
<tr>
<td>South Korea</td>
<td>2,669.7</td>
<td>0.9</td>
</tr>
<tr>
<td>Other Asia-Pacific</td>
<td>2,003.6</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>Australia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Australia and New Zealand</td>
<td>$4,008.7</td>
<td>1.3%</td>
</tr>
<tr>
<td><strong>Europe</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>France</td>
<td>$9,947.9</td>
<td>3.3%</td>
</tr>
<tr>
<td>Germany</td>
<td>8,127.0</td>
<td>2.7</td>
</tr>
<tr>
<td>Italy</td>
<td>6,761.6</td>
<td>2.2</td>
</tr>
<tr>
<td>Spain</td>
<td>5,976.2</td>
<td>2.0</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>6,037.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Other Western European</td>
<td>11,825.3</td>
<td>3.9</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>687.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Hungary</td>
<td>499.9</td>
<td>0.2</td>
</tr>
<tr>
<td>Poland</td>
<td>942.5</td>
<td>0.3</td>
</tr>
<tr>
<td>Turkey</td>
<td>1,518.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Russia</td>
<td>1,816.9</td>
<td>0.6</td>
</tr>
<tr>
<td>Central and Eastern Europe</td>
<td>(Cyprus, Estonia, Slovenia, Bulgaria, Lithuania, Latvia, Romania, Slovakia, Malta, and other Eastern European countries and the Newly Independent States)</td>
<td>5,576.4</td>
</tr>
<tr>
<td><strong>Middle East</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>$716.3</td>
<td>0.2%</td>
</tr>
<tr>
<td>Middle East</td>
<td>(Yemen, United Arab Emirates, Iraq, Iran, Kosovo, Israel, Jordan, Syria, Afghanistan, and Qatar)</td>
<td>1,268.8</td>
</tr>
<tr>
<td><strong>Uncategorized</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$1,808.3</td>
<td>0.6%</td>
</tr>
<tr>
<td><strong>TOTAL SALES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$305,009.2</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

*Sales abroad include expenditures outside the United States by U.S.-owned PhRMA member companies and sales generated abroad by the U.S. divisions of foreign-owned PhRMA member companies. Sales generated abroad by the foreign divisions of foreign-owned PhRMA member companies are excluded. Domestic sales, however, include sales generated within the United States by all PhRMA member companies.

Note: Total values may be affected by rounding.


16Adis Insight. Customized analysis for PhRMA based on R&D Insight Database. October 2011.


