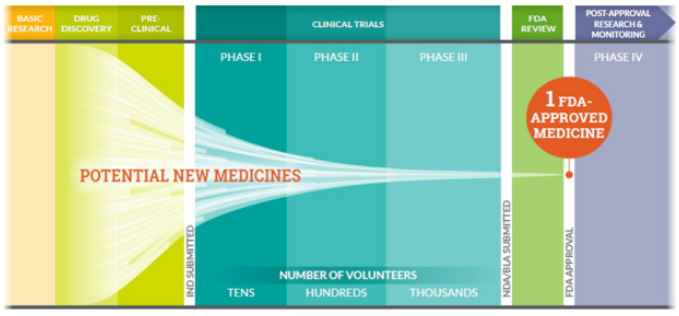
THE DYNAMIC U.S. RESEARCH AND DEVELOPMENT ECOSYSTEM

The rapid pace of scientific and technological advances and our growing understanding of the underlying mechanisms of disease are fueling the development of new treatments and cures for patients. In turn, scientific, technical, and regulatory challenges related to drug development create complexities as companies often focus their research and development (R&D) where the science is difficult and the failure risks are higher. As scientific complexities create new challenges, research-based biopharmaceutical companies are committed to realizing the promise of the pipeline and are working with stakeholders across the dynamic U.S. R&D ecosystem to leverage new scientific and technological advances to bring innovative medicines to patients. With about 8,000 medicines in clinical development globally—of which 74 percent have the potential to be first-in-class treatments—the future has never been brighter.[1, 2]

AMERICA'S BIOPHARMACEUTICAL COMPANIES PLAY CENTRAL ROLE IN R&D ECOSYSTEM

U.S. biopharmaceutical companies play a central role in the biomedical research ecosystem. The complex system is marked by collaborations across industry, academic institutions, government agencies, venture capital firms, nonprofit foundations and others. Biopharmaceutical companies today are engaging in a wide range of partnerships to move science forward in new and promising ways. In fact, the collaborative ecosystem that exists is among our country's greatest strengths in moving medical advances forward and makes the United States the worldwide leader in biopharmaceutical innovation.

THE COMPLEX BIOPHARMACEUTICAL R&D PROCESS



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

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

The R&D process typically begins with the screening of an enormous number of potential medicines followed by clinical trials alone which can take up to 7 years. On average it takes 10 to 15 years for a medicine to make its way from the start of the R&D process to approval by the U.S. Food and Drug Administration (FDA). And only 12 percent of investigational medicines entering clinical trials are ultimately approved by the FDA.[3]

The average cost to develop a new medicine is estimated at $2.6 billion dollars, including the cost of those that fail. The cost of development has more than doubled over the past decade.[4] Over this same period, rapid scientific and technical advances, alongside increasing regulatory burdens, are resulting in more complex clinical trials. For example, one study found that between 2001 and 2015, the total number of endpoints within a typical Phase III trial grew 86 percent and the number of procedures (including routine exams, blood work and x-rays) grew by 70 percent.[5] Despite these challenges, biopharmaceutical research companies remain committed to bringing important new treatment options to patients. PhRMA member companies themselves have invested more than half a trillion dollars in R&D since 2000.[6]

BIOPHARMACEUTICAL RESEARCH AND DEVELOPMENT PROCESS

Discovery: The road to a new medicine begins with selecting a disease target based on an understanding of the underlying mechanisms of the disease and emerging science. Researchers search for a candidate medicine that may have activity on the chosen target.

Preclinical Development: Researchers run the potential medicine through a battery of lab tests to understand the activity and safety of the medicine before moving to clinical studies.

Clinical Development: Before moving to studies in humans, the sponsor company submits an Investigational New Drug Application to the FDA outlining the preclinical findings and clinical plans. Clinical trials are conducted in 3 phases:

- Phase I trials examine safety as well as how the medicine is broken down in the body in a small group of healthy volunteers.
- Phase II trials include larger numbers of patient volunteers to assess safety, dosing and effectiveness.
- Phase III trials are in a large group of patient volunteers to generate statistically significant information on the efficacy of the candidate medicine.

FDA Review/Approval: If the potential medicine successfully passes through clinical trials, the sponsor submits a New Drug Application or Biologics License Application to the FDA, which reviews the data and determines whether the medicine is safe, effective and ready for approval.

Ongoing Study of the Medicine: Research does not end when the discovery and development phases are completed and the medicine is on the market. On the contrary, companies conduct extensive post-approval research to monitor safety and long-term side effects. They may also pursue research into new indications for the medicine in different disease areas, age groups, or patient populations.

THE EVOLVING R&D PROCESS

Researchers are constantly seeking to refine the R&D process in response to new scientific and technological advances and evolving regulatory requirements. Increasing acceptance of innovative clinical trial designs, appropriate integration of the patient perspective and advancing the use of real-world evidence all hold potential in speeding the development and regulatory review process and in enhancing the competitive marketplace through the introduction of innovative new medicines. While new scientific advances bring greater promise and complexity, the process is inherently fraught with a high degree of scientific and regulatory uncertainty, and there are often research setbacks. For example, between 1998 and 2017, 146 potential medicines for the treatment of Alzheimer's disease did not make it through clinical trials, with only four gaining FDA approval.[7] Despite these challenges, researchers remain committed to conquering challenging diseases such as Alzheimer's. Today, there are 92 Alzheimer medicines in clinical development or awaiting FDA review.[8]

PROVIDING HOPE TO PATIENTS

By all accounts, we are in an unprecedented period of medical discovery, driving new cures and treatments for many of our most costly and debilitating diseases and providing options that allow many to live longer, healthier lives. However, in many ways, our work is just getting started. Realizing the promise and potential of the pipeline will require increased collaboration and convergence across a range of sectors and fields to harness novel scientific approaches, massive amounts of data and computational capabilities, and a range of new technologies.

It is critical that we have a policy and regulatory environment that promotes innovation to fulfill the promise that these scientific opportunities represent for patients. To continue to advance medical discovery, we need to ensure a well-functioning, science-based regulatory system that keeps pace with the latest advances and ensures the timely review, approval and introduction of new medicines. This will be critical not only in improving the lives of patients, but also in maintaining U.S. global leadership in biomedical innovation and sustaining and growing U.S. jobs.

1 Adis R&D Insight Database. June 2019.

2 G Long, Analysis Group, "The Biopharmaceutical Pipeline: Innovative Therapies in Clinical Development," July 2017.

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

4 JA DiMasi , Grabowski, RW Hansen. Innovation in the pharmaceutical industry: New estimates of R&D costs. J Health Econ. 2016;47:20-33.

5 KA Getz, RA Campo. New benchmarks characterizing growth in protocol design complexity. Therapeutic Innovation & Regul Sci. 2018;52(1):22-28.

6 PhRMA annual membership survey. Washington, DC: PhRMA.

7 PhRMA. Researching Alzheimer's Disease: Setbacks and Stepping Stones. Fall 2018.

8 PhRMA. Medicines in Development for Neurological Disorders. April 2018.