SPURRING INNOVATION
IN RARE DISEASES

What are Rare Diseases?

Although rare diseases each may individually only impact a relatively small number of patients, defined as less than 200,000 in the United States, their impact on public health is far-reaching.[i] While the median number of patients with each rare disease is less than 10,000, rare diseases affect 30 million Americans – about 1 in 10.[iiiii]

Approximately 7,000 different rare diseases are known today,[iv] with many more still to be identified,[v] and it is estimated that 80% of rare diseases are genetic in origin.[vi] Accordingly, rare diseases are often biologically complex and much remains unknown about the underlying causes and the clinical course of many individual rare diseases despite recent progress. Even within a particular rare disease, there can be many variations or subtypes resulting in different clinical manifestations and disease progression. Additionally, 85% to 90% of rare diseases are considered "serious or life threatening."[vii]

Although researchers have made tremendous progress in advancing innovation for rare diseases, 95% of rare diseases still do not have a treatment option, representing a significant unmet need for patients.

RARE DISEASES BY THE NUMBERS

RARE DISEASES AFFECT **30 MILLION AMERICANS–**

THAT'S 1 IN 10[viii]

Approximately

7,000

DIFFERENT RARE DISEASES EXIST TODAY[ix]

The FDA has approved more than

575 ORPHAN DRUGS

since the passage of the Orphan Drug Act[x]

There is still tremendous unmet need, with approved treatments available for

ONLY 5% OF ALL RARE DISEASES[xi]

PROMISE IN THE PIPELINE:

Currently there are **more than**

560

MEDICINES IN DEVELOPMENT FOR RARE DISEASES[xii]

Rare Disease Drug Development: Challenges and Complexities

Developing medicines to treat rare diseases is particularly challenging. The complex biology of many rare diseases presents a challenge for scientists, making it difficult to design and implement a drug development program. Additionally, due to the inherently small population of patients with a rare disease, recruiting for and conducting clinical studies can be very difficult.[xiii]

Despite these challenges, America's biopharmaceutical researchers have leveraged new technologies and the growing scientific understanding of many rare diseases to develop groundbreaking therapies in recent years.

Facilitating Rare Disease Drug Development

The Orphan Drug Act (ODA) has been crucial in driving innovation in the treatment of rare diseases. Since the passage of the ODA in 1983, the FDA has approved more than 575 orphan drugs, in contrast to fewer than 10 medicines for rare diseases in the decade prior.[xiv] However, there remains a great need for new treatments.

The ODA has sought to provide incentives for R&D to develop medicines aimed at treating diseases for which there was no reasonable expectation that sales of the drug in the United States could support the development of the drug. These incentives include an R&D tax credit for 50% of clinical trial costs, as well as an exclusive right to market the drug for the orphan indication for 7 years upon FDA approval.[xv]

In addition, federal funding is available through grants and contracts to perform clinical trials of orphan products, and the Act created the Office of Orphan Products Developmentxvi at the FDA, which is intended to ensure close coordination between the FDA and biopharmaceutical manufacturers as they develop orphan medicines for review and approval by the FDA.

Harnessing Innovation in Rare Disease Treatment: 2016 Advances

In 2016, progress continued for patients with rare diseases. Nine of the 22 novel new drugs approved in 2016 at FDA's Center for Drug Evaluation and Research (CDER) were for rare diseases.[xvii]

The new medicines help patients across a variety of disease areas, including genetic disorders and rare forms of cancer. Many of the new medicines offer treatment options where there were few or none previously available. Of these medicines, five were first-in-class treatments, offering patients an entirely new way to tackle their disease.

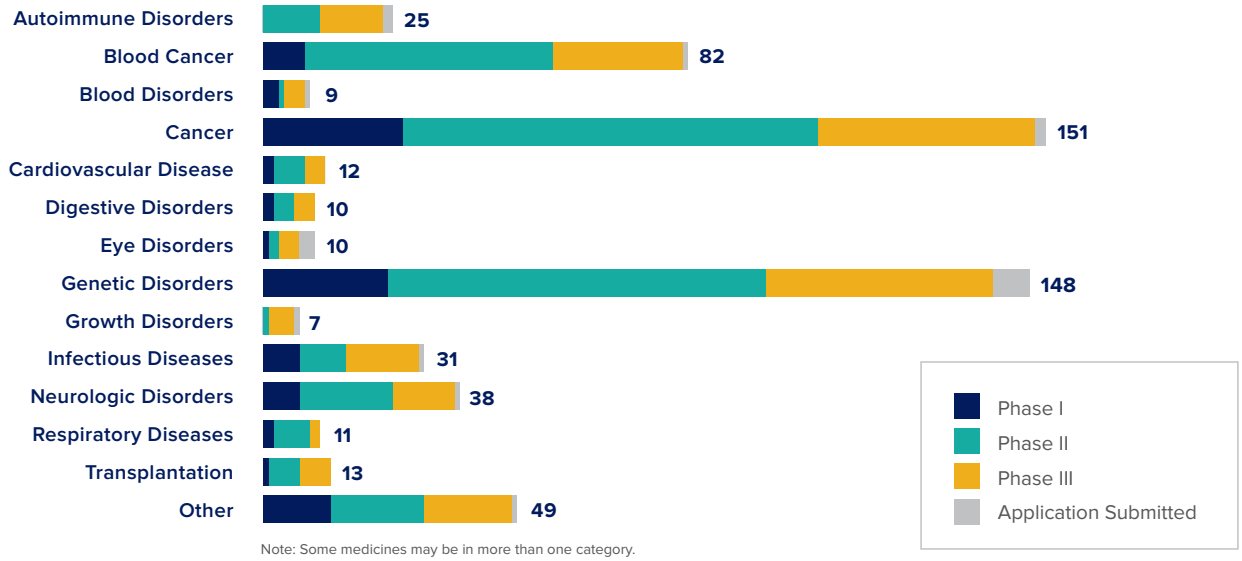
In recent years some noteworthy advances included:

- The first treatments directed at treating the underlying causes of cystic fibrosis.[xviii]
- Significant advances in targeted therapies for many forms of blood cancer, including chronic lymphocytic leukemia, chronic myelogenous leukemia, and multiple myeloma.[xix xx]
- New medicines that can prevent or slow the impact of several extremely rare, devastating conditions, including pulmonary arterial hypertension, hereditary angioedema, and Gaucher disease.[xxi]
- The first therapies available to treat many rare pediatric diseases, including a progressive, metabolic disease called hypophosphatasia (HPP), an inherited genetic disease called lysosomal acid lipase (LAL) deficiency, and neuroblastoma, a rare form of cancer that occurs in nerve cells and the brain.[xxii xxiiixxiv]

Spurring Continued Innovation for Patients

We've seen incredible advances in the development of medicines to treat patients with rare diseases. Despite this progress, there remains substantial unmet need for patients, as only 5% of rare diseases today have available treatment options. The biopharmaceutical industry is committed to advancing new medicines for patients with rare diseases, and the pipeline has never been more promising. There are more than 560 medicines currently in development for rare diseases.[xxv] Unprecedented scientific potential makes this a promising time for many patients with rare diseases. Maintaining incentives for research and development into these complex and challenging disease areas is critical in order to bring new medicines to patients.

MEDICINES IN DEVELOPMENT FOR RARE DISEASES



Note: Some medicines may be in more than one category.

The Role of PDUFA VI in Fostering Advances in Rare Disease

The Prescription Drug User Fee Act (PDUFA) has been essential in ensuring that the FDA has the resources to support the efficient review of new drug applications, including those to treat rare diseases. For nearly 25 years, PDUFA has helped FDA fulfill its central mission – to promote and protect the public health – by ensuring that the Agency has the necessary resources and expertise to bring safe and effective innovative medicines to patients in a timely manner. The reauthorization of PDUFA in 2017 includes several provisions that will be particularly impactful in driving continued innovation in rare diseases, equipping the FDA with knowledge and regulatory tools to keep pace with the latest scientific and medical advances, such as:

Patient-Focused Drug Development

Rare diseases are incredibly unique, impacting patients in a variety of ways. Incorporating the patient perspective into the clinical research process is integral in ensuring that trials are assessing the outcomes that matter most to patients.

Biomarker Qualification

As scientists develop a greater understanding of rare diseases, novel biomarkers are emerging as important ways to measure disease activity; an unambiguous qualification pathway for biomarkers will increase the usage of these endpoints.

Innovative Clinical Trial Designs

In rare diseases especially, where a large clinical study may be very difficult to conduct, increased clarity on the acceptance of emerging alternative trial designs will help accelerate clinical research.

More on Progress Against Rare Diseases

A recent PhRMA report, *A Decade of Innovation in Rare Diseases*, examines the significant progress made over the past decade (2005-2015) across a broad range of diseases, where medicines for rare diseases are having a tremendous impact for patients. Find out more at: http://www.phrma.org/sites/default/files/pdf/PhRMA-Decade-of-Innovation-Rare-Diseases.pdf

Learn more about promising rare disease medicines in the pipeline: http://phrma-docs.phrma.org/sites/default/files/pdf/medicines-in-development-report-rare-diseases.pdf

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