SPURRING INNOVATION **IN RARE DISEASES**

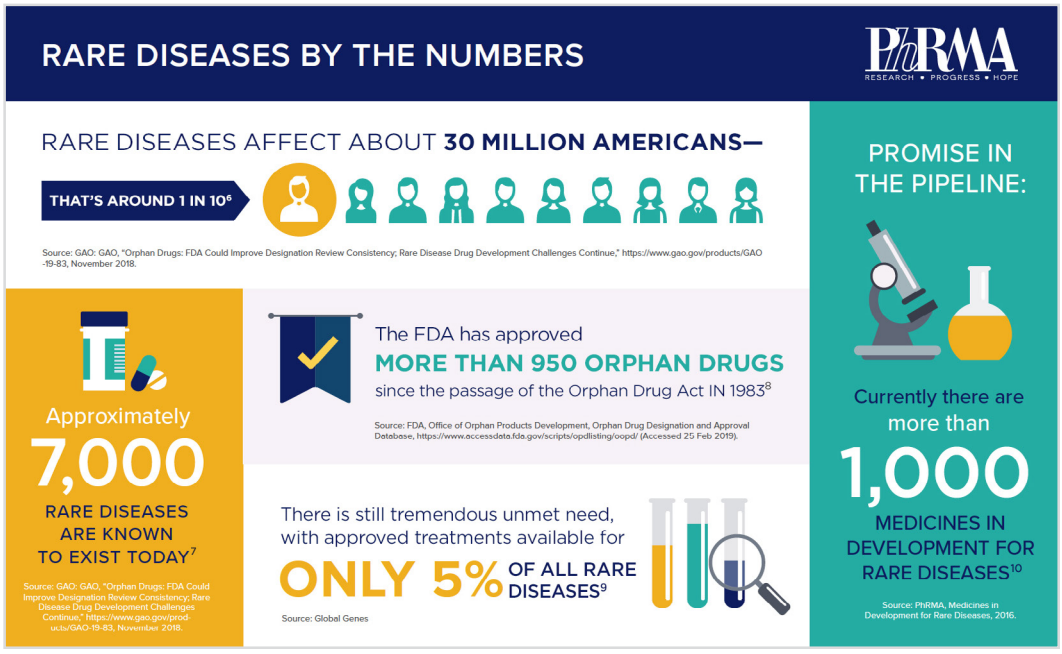
What Are Rare Diseases?

Although rare diseases each may individually only impact a relatively small number of patients, their impact on public health is far-reaching.[1] Collectively, rare diseases affect about 30 million Americans – or roughly 1 in 10.[2,3] In the U.S., a disease that affects fewer than 200,000 Americans is considered a rare or "orphan" disease.

Approximately 7,000 different rare diseases are known today, with many more still to be identified. It is estimated that 80% of rare diseases are genetic in origin and the vast majority impact children.[4] Additionally, 85% to 90% of rare diseases are considered "serious or life threatening."[5]

Although researchers have made tremendous progress in advancing innovation for rare diseases, 95% of these diseases still do not have a treatment option and significant unmet needs remain for patients. Rare diseases are often biologically complex and much remains unknown about the underlying causes and the natural history of many of these unique conditions. Even within a particular rare disease, there can be many variations or subtypes resulting in different clinical manifestations and disease progressions which can translate to a highly heterogeneous patient population and a need for individually tailored treatment approaches. A lack of good diagnostics accessible by patients, may be an additional barrier that limits the ability to understand many of these complex diseases in such small and specific patient populations.

Rare Disease Drug Development: Challenges and Complexities



Developing medicines to treat rare diseases is particularly challenging. The complex biology and heterogeneity of many rare diseases presents unique hurdles for scientists, making it difficult to design and implement a drug development program particularly as the natural history of these diseases are often poorly or incompletely understood. Additionally, due to the inherently small population of patients with a rare disease, recruiting for and conducting clinical trials can be very difficult.[11] In fact, trials for rare diseases overall require engaging more investigative sites with relatively fewer patients, underscoring the difficulties of identifying these patients and enrolling them in trials. Owing to these range of challenges, on average, it typically takes four years longer for rare disease medicines to successfully advance through clinical trials and to FDA approval relative to non-rare disease medicines.[12]

Despite these challenges, America's biopharmaceutical companies are leveraging new technologies and growing scientific understanding to develop groundbreaking therapies for rare diseases. In fact, about 30% of the medicines in the drug development pipeline are focused on rare diseases.[13]

Facilitating Rare Disease Drug Development

The Orphan Drug Act (ODA) has been crucial in driving innovation in the treatment of rare diseases. The ODA was enacted in 1983 to address the lack of incentives to foster development of new treatments for rare diseases and, under the current law, a disease affecting fewer than 200,000 individuals in the United States constitutes a rare disease.

The policies under current law to encourage orphan drug development include an R&D tax credit for 25% of clinical trial costs, as well as an exclusive right to market the drug for the intended orphan disease for seven years upon FDA approval.[14] In addition, federal funding is available through grants to perform clinical trials of orphan products, which is particularly critical for small and emerging companies. Since the passage of the ODA in 1983, the FDA has approved more than 950 orphan drugs, in contrast to fewer than 10 medicines for rare diseases in the decade prior to its enactment.[15] While the ODA has encouraged incredible progress, given the inherent challenges associated with orphan drug development and the tremendous need that remains, the policies first established by the ODA have never been more critically needed in driving new treatments for patients.

Additionally, the Prescription Drug User Fee Act (PDUFA) helps further advance the development and review of safe and effective new medicines, including those for rare diseases. The most **recent reauthorization of PDUFA** supports the efforts of CDER's Rare Diseases Program[16] to "facilitate, support, and accelerate the development of drug and biologic products for the benefit of patients with rare disorders."[17]

Harnessing Innovation in Rare Disease Treatment: Recent Advances

In 2020, progress continued for patients with rare diseases. 31 (of the 53) novel new drugs approved in 2020 by FDA's Center for Drug Evaluation and Research (CDER) were for rare diseases or conditions.[18,19] There were also several medicines approved by Center for Biologic Evaluation and Research (CBER) that brought significant treatment advances to patients.[20]

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 the medicines approved at CDER to treat rare diseases, 11 were first-in-class treatments, offering patients an entirely new way to tackle their disease.[21]

Among the approvals in 2020 for rare disease therapies are new medicines to treat many dangerous and painful inflammatory conditions such as Still's Disease, a rare form of arthritis affecting the entire body, and another condition of the skin and bones, affecting newborns in the first days of life. 2020 also ushered in new treatments for infectious diseases such as Ebola and a first-time therapy for pediatric patients with a devastating parasitic infection called Chagas disease which can lead to congestive heart failure. In addition, the FDA approved eight new treatments for rare forms of cancer. For example, a first-time treatment was approved for patients, two years of age and older, with a debilitating genetic disorder typically beginning early in life that causes tumors to grow on nerves.[22]

These approvals build on a many noteworthy rare disease advances in recent years, including:

- The first treatments directed at treating the underlying causes of cystic fibrosis (CF), based on rare genetic mutations.[23] Today, treatments are available for patients with a range of mutations associated with the disease, including the most common which is estimated to represent 90% of the CF population.[24]
- Significant advances in targeted therapies for many forms of rare blood cancer, such as chronic lymphocytic leukemia, chronic myeloid leukemia, follicular lymphoma, acute myeloid leukemia, and multiple myeloma and many more.[25,26]
- A growing range of medicines providing options to patients that can prevent or slow the impact of several extremely rare, devastating conditions, including pulmonary arterial hypertension, hereditary angioedema, and Gaucher disease.[27]
- A gene therapy to providing a first-time treatment for a rare inherited retinal disease that commonly leads to blindness.[28]
- In 2019, the first gene therapy to treat children less than two years of age with the most common form of spinal muscular atrophy (SMA), which is the leading genetic cause of infant mortality.[29]
- Today there are three FDA approved therapies available providing a range of treatment options for this highly heterogeneous disease.

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 conditions, and the pipeline has never been more promising. There are more than 1,000 medicines currently in development for rare diseases and conditions.[30]

Unprecedented scientific potential makes this a promising time for many patients with rare diseases. Maintaining incentives as provided in the ODA to ensure continued progress into the many complex and challenging disease areas where we lack treatments is critical to improving the lives of patients.

Learn more on Progress against Rare Diseases at PhRMA.org/RareDiseases

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