

### JUST THE FACTS

**30**  
MILLION

Americans — about 1 in 10 — are living with a rare disease<sup>1</sup>

**APPROXIMATELY**  
**7,000**

rare diseases are known to exist today<sup>1</sup>

**FDA APPROVED**  
**MORE THAN**  
**500**

orphan drugs since the passage of the Orphan Drug Act<sup>2</sup>

**ONLY**  
**5%**

of rare diseases have an approved treatment<sup>1</sup>



IN PARTNERSHIP WITH



# MEDICINES IN DEVELOPMENT FOR RARE DISEASES

A REPORT ON ORPHAN DRUGS IN THE PIPELINE

## More Than 560 Medicines in Development for Rare Diseases

Rare diseases, when taken together, are not that rare at all. In fact, 30 million Americans, or 10 percent of the population, have one of the 7,000 known rare diseases, of which 80 percent are genetic in origin. Half of those affected worldwide are children.<sup>1</sup> A disease is generally defined as “rare” when, by itself, it affects fewer than 200,000 people in the United States.<sup>1</sup> However, many rare diseases impact significantly smaller groups of patients, sometimes as small as a few hundred.

Simply getting to a diagnosis can be a complicated, lengthy and frustrating journey for people with a rare disease. Many health care providers may have limited experience with the identification and diagnosis of rare diseases. Also, diagnosis before symptom onset or diagnosis early in the disease can be very challenging.

Developing medicines for patients with rare diseases presents one of the most scientifically complicated health challenges of our time. The underlying biological mechanisms of a rare disease are often complex, making it difficult to design and implement research and development strategies. Additionally, due to the inherently small population

of patients with a rare disease, recruiting for and conducting clinical studies can be difficult.

For many rare diseases, there are gaps in knowledge regarding the natural history of disease. This gap in scientific and medical knowledge presents challenges when trying to research, diagnose, and develop medicines for rare diseases. The underlying biology of the disease may be very complex and poorly understood, and research to fill in the gaps can be difficult and time-consuming given the small numbers of people with the rare disease. Continued research and improved understanding of rare diseases will accelerate the development of medicines for rare diseases.

### 2015: Banner Year FOR RARE DISEASES



**47%**  
of new drug approvals were for rare diseases

**8**  
first-in-class treatments, representing entirely new ways for treating disease

**5**  
new medicines for pediatric patients

**11**  
new cancer therapies

New treatments for cystic fibrosis, difficult-to-treat high cholesterol, and several enzyme deficiency disorders

Source: U.S. FDA, "Novel Drugs Summary 2015."

[www.PhRMA.org](http://www.PhRMA.org)



(cont. from page 1)

Despite these challenges, this is a time of progress and hope. Biopharmaceutical researchers have leveraged new technologies and the growing scientific understanding of many rare diseases to develop groundbreaking therapies over the last 10 years.<sup>3</sup>

In the past decade, more than 230 new orphan drugs<sup>4</sup> were approved by the U.S. Food and Drug Administration (FDA).<sup>2</sup> In 2015 alone, nearly half (47 percent) of novel new drug approvals were for rare diseases, including therapies for cancer, cystic fibrosis, difficult to treat high cholesterol, and several enzyme deficiency disorders. Many of the new medicines provide treatment options for patients where there were few or none previously available.

Today, biopharmaceutical research companies are continuing that progress with 566 medicines<sup>5</sup> in development for patients with rare diseases. The medicines listed in this report are either in clinical trials or under review by the FDA. The medicines in development include:

- 151 for rare cancers and 82 for rare blood cancers, accounting for 40 percent of all rare disease medicines in development.
- 148 for genetic disorders, including cystic fibrosis and spinal muscular atrophy.
- 38 for neurological disorders, including amyotrophic lateral sclerosis (ALS) and seizures.
- 31 for infectious diseases, including rare bacterial infections and hepatitis.
- 25 for autoimmune diseases, including systemic sclerosis and juvenile arthritis.

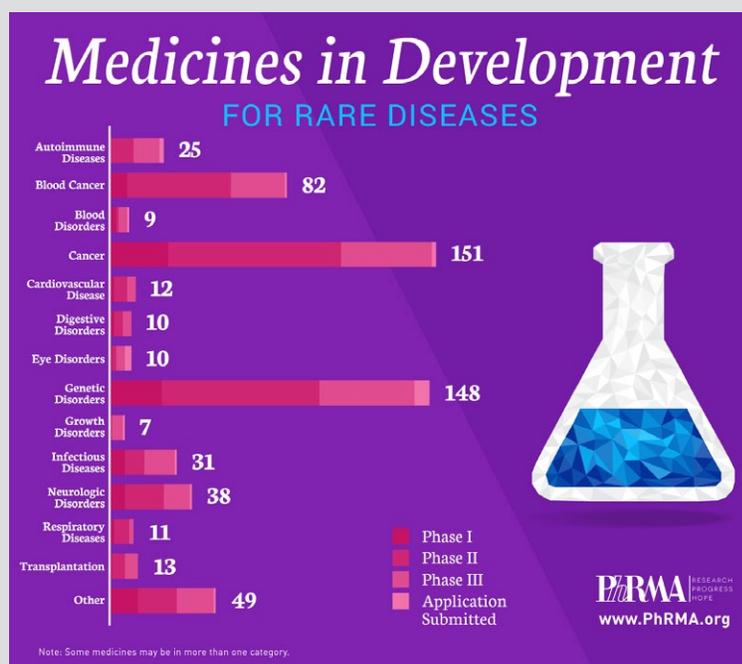
For a complete list of the 566 medicines in development, please visit: <http://phrma.org/sites/default/files/pdf/medicines-in-development-drug-list-rare-diseases.pdf>

## ORPHAN DRUGS IN DEVELOPMENT

# Medicines in the Pipeline for Rare Diseases

The 566 medicines in development for patients with rare diseases employ exciting new technologies and the growing scientific understanding of many rare diseases. Many of the medicines represent innovative new ways to target disease, including:

- Therapies in development for ALS include antisense technology against SOD1 (2 percent of ALS) currently in clinical trials and mutations in C9orf72 (10 percent of ALS) anticipated to be in clinical trials in 2017. Additional approaches include gene therapy and stem cell approaches for ALS with several new trials using stem cells about to be initiated in 2016 and 2017.
- An investigative fusion protein is in development to treat beta thalassemia, a blood disorder that reduces production of hemoglobin, the protein in red blood cells which carries oxygen to the body's cells. The investigational therapy regulates late-stage red blood cell production to increase hemoglobin levels and reduce transfusion burden.



## The ALS Association: Lorri's Story



**“I’M ONE OF THE LUCKY ONES. I WAS HOPING TO LIVE LONG ENOUGH TO SEE MY SONS GRADUATE FROM HIGH SCHOOL. AS IT TURNS OUT, I’VE BEEN BLESSED TO HAVE SEEN THEM GRADUATE FROM HIGH SCHOOL AND COLLEGE. WITH MY SONS AND HUSBAND, TOGETHER, WE’RE CHASING THE DREAM: A WORLD WITHOUT ALS.”**

“I was told I had ALS,” Lorri says today, 12 years later. “And when I walked outside, there were cars going by, people walking their dogs.”

In other words, everyday life would go on, even after her diagnosis with Amyotrophic Lateral Sclerosis (ALS), commonly known as Lou Gehrig’s Disease. “I was going to have to keep living and not give in,” Lorri says.

While there is no cure for ALS, patients like Lorri are fighting toward a brighter horizon. Collaborative efforts between patients, disease groups like The ALS Association, and researchers across the R&D ecosystem are driving big leaps in the science.

In the last year, The ALS Association alone has committed well over \$40 million since the Ice Bucket Challenge to find effective treatments and a cure for the disease. Together with their global research partners, the number of scientists working on ALS has increased dramatically, bringing new discoveries and potential treatments forward.

ALS Association-funded research has helped reveal important understandings about the molecular underpinnings of this devastating neurodegenerative disease, including the [discovery of a genetic abnormality](#) that is the most common known cause of ALS and a recent [finding in familial ALS](#) that shows how two proteins work together to help the survival of motor neurons.

These scientific steps forward are helping to unravel the long-standing mystery of ALS. The disease was first identified in 1869, but it wasn’t until 1939 that famed New York Yankee Lou Gehrig brought national and international attention to the disease.

Lorri was just one year older than Gehrig when she got her diagnosis. “I was only 37, but I had hallmark symptoms of the disease,” she says today. She knew there was work to do.

Lorri’s advocacy and that of thousands of others helped The ALS Association work with Congress to establish a nationwide ALS patient registry in 2010. That advocacy also led the FDA to agree to issue patient-focused drug development guidance designed to accelerate the development of therapies to slow or stop ALS.

These advances in both the understanding of the science underlying the disease and how we conduct clinical research are already driving major treatment advances in rare diseases. Since 2005, the FDA has approved more than 230 new medicines to treat rare diseases, and there are currently more than 560 orphan drugs in development. Treatment advances in rare diseases are driving the science forward, giving promise for the future and opening new doorways into the mystery of ALS.

When Lou Gehrig retired in 1939, he told the Yankee Stadium crowd, “I might have been given a bad break, but I’ve got an awful lot to live for.”

Lorri agrees, as cars go by and people walk their dogs today, twelve years after her diagnosis.

“I’m one of the lucky ones,” she says. “I was hoping to live long enough to see my sons graduate from high school. As it turns out, I’ve been blessed to have seen them graduate from high school *and* college. With my sons and husband, together, we’re chasing the dream: a world without ALS.”

## Orphan Drug Act of 1983

Recognizing the scarcity of medicines to treat diseases with small patient populations and the uncertain road researchers faced in pursuing such challenging disease areas, the Orphan Drug Act of 1983 introduced important incentives for companies to develop rare disease treatments. The Orphan Drug Act has been regarded as a tremendous success, with more than 500 medicines being approved to treat rare diseases since its passage, compared to fewer than 10 in the 1970s. As of April 2016, the FDA has granted orphan drug designation to more than 3,700 potential therapies.<sup>2</sup> Some of the medicines recently approved to treat a rare disease include:

- The first and only therapy for neonatal-onset multisystem inflammatory disease (NOMID). NOMID is one of three types of inherited auto-inflammatory diseases and is the most severe subtype. The disease presents itself during infancy or early childhood and causes fever, rash and disease of the joints and central nervous system.
- Two medicines were recently approved specifically to treat homozygous familial hypercholesterolemia (HoFH), an inherited genetic condition that biologically prevents patients from removing low density protein lipoprotein cholesterol from their blood, leading to abnormally high levels of the “bad cholesterol” in their blood.
- The first treatment for perinatal-, infantile-, and juvenile-onset hypophosphatasia was approved. This genetic metabolic disorder, in which patients experience devastating effects on multiple systems of the body, leads to severe disability and life-threatening complications.

## The Promise of Targeted Therapies for Rare Diseases

Advances in science and technology, such as tools and knowledge that will advance the development of targeted medicines, are creating new opportunities to improve and expand research into rare diseases and the development of potential new treatments. The Personalized Medicine Coalition estimates that available personalized medicines, treatments and diagnostic products increased from 13 in 2006 to 126 by the end of 2015. In 2015 alone more than a quarter of FDA’s novel new drug approvals were for personalized medicines, including several for rare diseases.<sup>6</sup>

Biopharmaceutical companies are committed to advancing the development of targeted therapies and other medicines

for the treatment of rare diseases. Researchers are increasingly able to pursue therapeutics aimed at precise molecular or genetic drivers of disease, allowing them to develop medicines for more targeted patient populations, which enables physicians to deliver more personalized care to patients. A recent analysis indicates that 42 percent of medicines in the pipeline have the potential to be personalized medicines, offering hope to patients with rare diseases.<sup>7</sup> Already researchers have found genes associated with rare diseases such as myotonic dystrophy, ALS, cystic fibrosis, progeria and neurofibromatosis. These breakthroughs are crucial steps toward developing new treatments.

### Sources:

1. Global Genes, *Rare Disease: Facts and Statistics*
2. U.S. Food and Drug Administration, Orphan Drug Designations and Approvals database.
3. PhRMA “A Decade of Innovation in Rare Diseases” Report, 2015
4. Upon request by a sponsor, the FDA can grant special status (“orphan status”) to a drug or biologic to treat a rare disease or condition. In order to receive an orphan designation, a qualifying drug or biologic must be intended for the treatment, diagnosis, or prevention of a rare disease or condition that affects fewer than 200,000 people in the United States, or affects more than 200,000 persons but is not expected to recover the cost of its development and marketing.
5. Number of medicines obtained through government and industry sources, and the Springer “Adis Insight” database. Current as of April 18, 2016.
6. Personalized Medicine Coalition, 2015 Progress Report “Personalized Medicine at FDA”
7. Personalized Medicine Coalition, “Biopharmaceutical Companies’ Personalized Medicine Research Yields Innovative Treatments for Patients”

