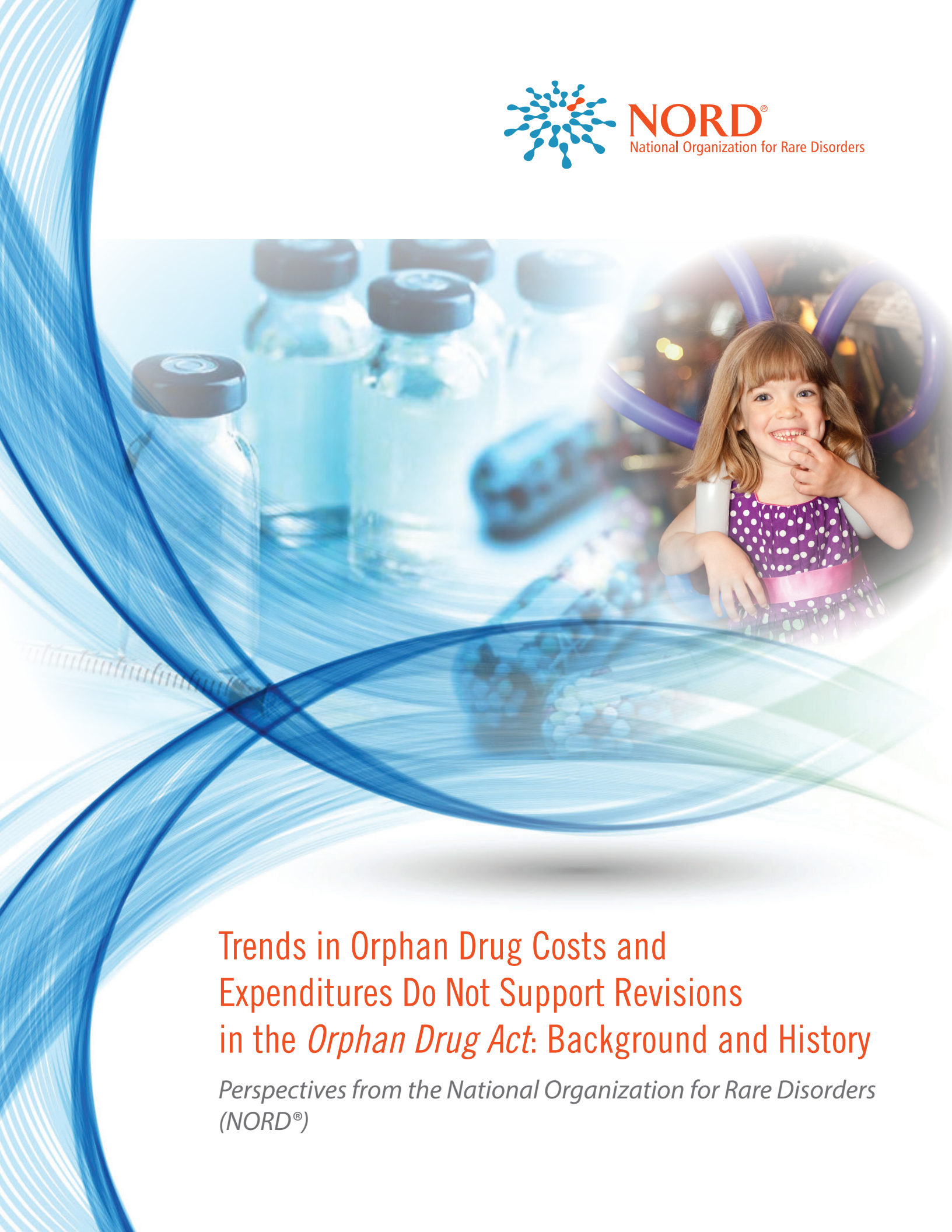




**NORD**<sup>®</sup>  
National Organization for Rare Disorders



Trends in Orphan Drug Costs and  
Expenditures Do Not Support Revisions  
in the *Orphan Drug Act*: Background and History

*Perspectives from the National Organization for Rare Disorders  
(NORD<sup>®</sup>)*

# Introduction

As the *Orphan Drug Act* (ODA) approaches its 35th anniversary in 2018, concerns have been raised as to whether orphan drugs are a significant contributing factor to rising healthcare costs in the U.S. NORD feels that discussion of this issue has been largely rhetorical and anecdotal, creating a debate more impassioned than informed.

As a result, NORD commissioned the QuintilesIMS Institute to conduct independent research on the use and cost of orphan drugs, as well as the current and future outlook for their impact on overall healthcare spending in the U.S. The Institute's analysis, ***"Orphan Drugs in the United States: Providing Context for Use and Cost"***,<sup>1</sup> provides relevant data and other information that support its primary finding: orphan drugs are not a major factor in healthcare spending.

Since NORD was established by leading advocates and continues to be the voice of the rare disease community, and NORD's history is so fundamentally intertwined with the history of the ODA, NORD takes very seriously any concerns related to the ODA and is committed to assuring that the original intent of the authors and supporters of the ODA is maintained.

NORD encourages an ongoing conversation between policymakers and stakeholders about the ODA. We hope this background document, along with the Institute's study, contribute to a dialogue that is well-informed about patient/family needs, medical innovation, and healthcare spending in the U.S.

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# What Problem Did the *Orphan Drug Act* Address?

In the late 1970s and early '80s, there was growing awareness that very few medical treatments were being developed for people who had diseases affecting small patient populations. The problem was that pharmaceutical companies couldn't expect to recover the investment required to develop treatments for diseases affecting a small number of people. Hence, these diseases came to be known as 'orphan' diseases.

From 1967 to 1983, only 34 drugs approved by the Food and Drug Administration (FDA) were for rare diseases, and only 10 of the products brought to market by the pharmaceutical industry in the decade before 1983 would have qualified under today's ODA as orphan drugs.<sup>2,3</sup>

One of the original voices speaking out about this issue was a task force whose members included staff of the FDA and National Institutes of Health (NIH) who considered individuals with rare diseases to be an underserved patient community and felt that the plight of these patients and their families was a public health issue. Chaired by Marion Finkel, M.D., of FDA, the task force submitted a report to the Secretary of Health, Education and Welfare in 1979 entitled *Significant Drugs of Limited Commercial Value* calling for this issue to be addressed.<sup>4</sup>

Members of the U.S. Congress also became focused on this issue, often after hearing from constituents who were affected by rare diseases such as Huntington's disease, cystic fibrosis, and ALS. Many members of Congress from both major parties became involved, with Representative Henry Waxman of California, Senator Orrin Hatch of Utah, and Senator Nancy Kassebaum of Kansas providing particular leadership.

Rare disease patient organization leaders also played a significant role and formed an ad hoc committee whose leaders, including Abbey Meyers who later served as NORD's president for its first 25 years, testified at hearings hosted by Rep. Waxman and the Subcommittee on Health and the Environment of the House Energy and Commerce Committee.

The combined efforts of patient advocates, rare disease medical experts, staff of NIH and FDA, and members of Congress ultimately led to the *Orphan Drug Act* of 1983. Shortly after the ODA was enacted, the leaders of patient organizations who had been most active in this effort formalized their ad hoc coalition as NORD.

The *Orphan Drug Act* provided pharmaceutical manufacturers with three primary incentives:

- Federal grants for orphan drug research
- A 50% tax credit to defray the cost of clinical trials and
- Seven years of marketing exclusivity for products approved as orphans

The legislation initially targeted drugs for which there was "no reasonable expectation" that sales in the U.S. could support development of the drug. It immediately became clear that there was no objective way to determine this. Thus, in a 1984 amendment, a rare disease was defined as a condition affecting fewer than 200,000 Americans. Subsequently, another incentive was added: Product application "user fees" were waived for orphan products, which has been particularly valuable for small, start-up companies but has also encouraged larger companies to sponsor orphan drugs.

# Most Rare Diseases Are Serious, Lifelong and Extremely Disabling

Approximately 7,000 rare diseases have been identified, all of which are listed on the NIH website. They are believed to affect 25 to 30 million Americans. While some of these diseases fall just below the upper threshold, many affect only a few hundred or even a few dozen individuals<sup>5</sup>

While these diseases can be found across the medical spectrum and each is unique, there are certain characteristics that are representative of rare diseases as a group. One is that they tend to be serious or even life-threatening with a significant impact on the lifespan and/or quality of life of those affected.

It is believed that more than 80% of rare diseases are genetic. While some may not present until later in life, many are apparent at birth or during childhood. Half of the patients with rare diseases are children. Many of these diseases are multi-system and many require extensive, lifelong medical care – often addressing just symptoms because there are no curative treatments for the underlying disease.

Delayed diagnosis is a reality of life for most people with rare diseases. On average, patients visit 7.3 physicians and experience symptoms for 4.8 years<sup>6</sup> before obtaining a diagnosis. Patients also experience difficulty finding medical experts knowledgeable about their diseases. In addition, individuals and families affected by rare diseases often must cope with financial burden, inability to attend school or work, social isolation, and other issues.<sup>7</sup>

## EXAMPLES OF RARE DISEASES

### **Friedreich's Ataxia (FA)**

*Symptoms of Friedreich's ataxia typically become apparent between the ages of 5 and 18 years. It is a debilitating, life-shortening, degenerative, neuromuscular disorder. About one in 50,000 people in the U.S. have this genetic condition.*

### **Lymphangiomyomatosis (LAM)**

*LAM is a rare lung disease that usually strikes women in the childbearing years without an apparent cause. It is estimated that, for every million women, 3 to 5 will have LAM. The average age at the time of diagnosis is 35 years. LAM is progressive and can become life-threatening.*

### **Mucopolysaccharidosis IV (MPS IV)**

*MPS IV is a rare metabolic condition that exists in two forms, one of which is rapidly progressive. The severe form becomes apparent between the ages of one and three. Symptoms may include growth retardation, various skeletal abnormalities, and hearing loss. This condition is genetic and is caused by an enzyme deficiency.*

### **Osteogenesis Imperfecta (OI)**

*OI is a genetic disorder characterized by brittle bones that break easily, often for little or no cause. It is believed that between 20,000 and 50,000 Americans are affected. There are different types of OI and a broad range of severity. Some of those affected may have only a few fractures in a lifetime while others may have hundreds.*

### **Pompe Disease**

*Pompe disease is an inherited disorder caused by the buildup of a complex sugar called glycogen in the body's cells. The accumulation of glycogen in certain organs and tissues, especially muscles, impairs their ability to function normally. There are different forms, including an infantile-onset form that typically results in death during the first year of life.*

# The *Orphan Drug Act* Has Been Considered Highly Successful for 35 Years

The success of the ODA in the U.S. has been widely recognized over the years and helped to encourage similar legislation in other parts of the world. Japan adopted orphan drug legislation in 1993, Australia in 1998, and the European Union in 2000.

As of January 2017, FDA had approved almost 600 orphan drugs and granted nearly 4,000 orphan drug designations since 1983. The orphan designation requests include new molecular entities, original biological products and new orphan uses of previously approved drugs and biologics.<sup>8</sup>

Over the years, the ODA has resulted in many treatments, such as zinc acetate for Wilson's disease, that have provided valuable treatment for patients but which had little prospect of commercial return.

It has also made possible treatments that have resulted in cost savings. For instance, a treatment for infant botulism developed by California Public Health officials and made possible by the ODA and the orphan grants program, used to date to treat more than 1,500 patients, has resulted in more than 90 years of avoided hospital stay and more than \$130 million of avoided hospital costs.<sup>9</sup>

The need for safe, effective treatments for children has been widely documented, and a 10-year analysis of the ODA concluded that from 2000 through 2009 pediatric products increased from 17.5% to 30.8% of total orphan approvals. These products were for diseases on the rare end of the spectrum, with a median prevalence of 8,972.<sup>10</sup>

The ODA has been credited with helping drive innovation in cancer treatment,<sup>11</sup> and it has resulted in life-saving enzyme replacement therapies for children and adults with metabolic diseases for which there was previously no treatment.

From the patient perspective, the Orphan Drug Act has been extremely successful, encouraging research and development of products for diseases that would otherwise have no treatment. While the vast majority of the 7,000 diseases do not yet have an FDA-approved treatment, many patients and caregivers feel that the ODA offers hope that even those with the rarest of diseases may someday have a treatment, thereby eliminating or reducing the need for a lifetime of medical care.

The three primary incentives of the ODA, along with waived user fees, have each contributed substantially to the success of the law. Credit is most often given to exclusivity, which has indeed proven a powerful incentive. However, a 2015 study underscored the substantial importance of the orphan drug tax credit (ODTC). According to that study, investment in orphan drugs would be reduced by one-third without the ODTC.<sup>12</sup>

Since 1983, the orphan products grant program has funded more than 600 clinical studies and provided support for more than 55 orphan products that were subsequently approved by FDA.<sup>13</sup> Also, as user fees have risen significantly, waivers have often been a key component of the ability of small companies to finance their research.

# Is the *Orphan Drug Act* responsible for rising healthcare costs?

While the issue of orphan drugs and rising healthcare costs is sometimes raised, NORD has always questioned whether the concern was speculative and headline-driven. New, just-released data from QuintilesIMS now document that the ODA has not been a significant driver of healthcare spending in the U.S. Specific to this conclusion:

- The volume of prescriptions for orphan drugs is relatively low because of the small patient populations. The orphan drug share of the total volume of pharmaceutical use in the U.S. was just 0.3% in 2016.
- Orphan drug spending represents a small percentage of total healthcare spending. Of the total drug sales of \$450 billion in the U.S. in 2016, almost 60% was for non-orphan traditional drugs, 32% was for non-orphan specialty drugs, and 7.9% was for orphan indications of approved drugs.

As QuintilesIMS emphasizes, there is widespread misunderstanding about the differences between orphan drugs (based on the size of the patient population) and specialty drugs (based on cost per month and conditions of delivery and use). While almost all orphan drugs are specialty drugs, only a modest proportion of specialty drugs are orphans.

Typically, specialty drugs cost more than \$600 per month or require special handling or administration by a healthcare professional, are distributed through non-traditional channels such as specialty pharmacies, are prescribed or maintained by a specialist physician, and/or have significant side-effects that require additional monitoring or counseling. Throughout this publication, when we speak of orphan drugs we are referring specifically to those that have been granted orphan designation by FDA.

Consistently, a study of healthcare payors released in September 2017 that focused on orphan drug spending concluded that “As long as orphan drugs fulfill a great unmet need, serve a small patient population, and have substantial efficacy, premium pricing and appropriate access appear sustainable, in our view.”<sup>14</sup>

Some recent media stories have questioned whether drug makers may be manipulating the ODA to benefit in ways that were not originally intended. NORD appreciates the important watchdog role of the press and supports ongoing vigilance against misuse of the ODA. Based on data available to date, NORD believes the ODA has generally been used appropriately – and to the benefit of patients – over the years.

# Is the *Orphan Drug Act* still needed?

The *Orphan Drug Act* is just as important today as it was in 1983. To reduce its ability to incentivize development of medical treatments for small patient populations would be tantamount to abandoning the 30 million Americans who have rare diseases and have either benefitted from the law or can reasonably hope to in the future.

This is particularly pertinent since scientific/medical momentum is spurring development of innovative, safe, and effective treatments for children and adults with very challenging medical conditions.

Today's emphasis on personalized medicine and focus on developing therapies with high patient outcomes value offer particular hope to the patients and families who have struggled for years with complex, little-understood rare diseases. The ODA is consistent with this.

## Moving Forward

We believe that the new QuintilesIMS study provides important insights that will be helpful to policymakers and regulatory officials. NORD engages regularly with policymakers, regulatory officials and others about the ODA, and we look forward to ensuring that these will be data-driven conversations.

FDA Commissioner Scott Gottlieb, M.D., has indicated that it will be one of his priorities to study this complex issue; determine whether, and the extent to which, the application of the ODA may need adjustment; and work to address any issues. We applaud his inquiry and look forward to playing a significant role.

We understand that, as medical science has progressed, it may be time to evaluate whether every aspect of the ODA is working exactly as it should, not only from a legislative perspective but on the regulatory level.

However, we also feel strongly that great care must be taken to preserve the original intent of the ODA. The name "orphan" was initially applied because rare disease patients and caregivers had been abandoned by our nation's healthcare system. Millions of Americans were suffering and few were paying attention. As a nation that professes to care equally for all its citizens, we have a responsibility to recognize and continue the major contributions of the ODA toward improving the lives of the children and adults living with rare diseases.

As the U.S. healthcare system continues to evolve, we must maintain the incentives for orphan drug development because the need for rare disease treatments remains very great; orphan drugs developed to date have helped significant numbers of patients cumulatively; and the ODA incentives are working to encourage the development of more orphan drugs.

The burden of healthcare costs in America is great and rising. It would be easy to say we can no longer afford to seek safe, effective treatments for those with diseases affecting only a few. However, the patient advocates and rare disease medical experts who led the charge for enactment of the ODA had a vision of a healthcare system based upon the premise that our entire nation benefits and is richer, both in spirit and materially, when the healthcare needs of all of our citizens are met to the best of our ability. NORD still subscribes to that vision today and will work tirelessly to assure that the essence of the ODA is maintained.



## THE PATIENT/CAREGIVER EXPERIENCE

While there is no such thing as a “typical” rare disease story, the following brief patient/caregiver stories illustrate the types of challenges experienced by patients and their families.

### **Living with Friedreich’s Ataxia (FA)**

At age 17, **Kyle Bryant** learned that he had the rare, debilitating, life-shortening disease known as Friedreich’s ataxia. As opposed to the active future this athletic young man had envisioned, he realized that his future held walkers, wheel chairs, vision and hearing loss, and an early death. However, Kyle took this bleak situation and turned it into an opportunity to provide hope to the FDA community and empower others, riding his incumbent bike thousands of miles and raising millions of dollars for FA research. His hope is that someday there will be a treatment for FA.



### **Living with MPS IVA**

In the first seven years of her life, **Annabelle Bozarth** endured several major and life-saving surgeries as a result of conditions associated with her rare genetic disease, MPS IVA. She has coped with severe skeletal dysplasia, hearing loss, corneal clouding, leaking heart valve, and chronic pain issues. As a young child, Annabelle participated in a clinical trial to replace the enzyme her body was missing. After that orphan product was approved, Annabelle’s mother said she was delighted that, at last, Annabelle could play on a playground without experiencing pain.



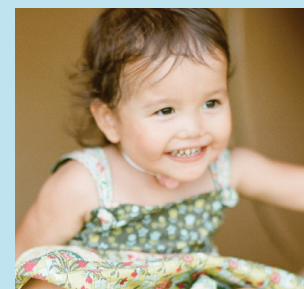
### **Living with New Onset Refractory Status Epilepticus (NORSE)**

**Daniel Wong** was just 22 years old and a recent graduate of Stanford University when he became suddenly ill on a Monday morning with incapacitating, out-of-the-blue seizures. Over the next 11 weeks, Daniel was kept in a drug-induced coma in a hospital ICU as doctors tried to control the seizures, which would not respond to available medication. Eventually, Daniel died and his parents now raise funds for research on NORSE.



### **Living with Congenital Central Hypoventilation Syndrome**

**Madilyn Yang** was born with a condition known as congenital central hypoventilation syndrome (CCHS) in which, as her mother describes it, her body “forgets to breathe.” People with CCHS take shallow breaths, especially during sleep, and must live with the reality that, without mechanical stimulation, they might simply stop breathing while asleep and die. Madi’s parents are medical researchers and her father is an MD. They work to promote awareness of this little-known condition and to support research toward treatment or, someday, a cure.



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## About NORD®

The National Organization for Rare Disorders is a unique federation of individuals, voluntary health agencies and other health related organizations ***dedicated to helping people with rare orphan diseases.***

NORD is committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and patient support services.