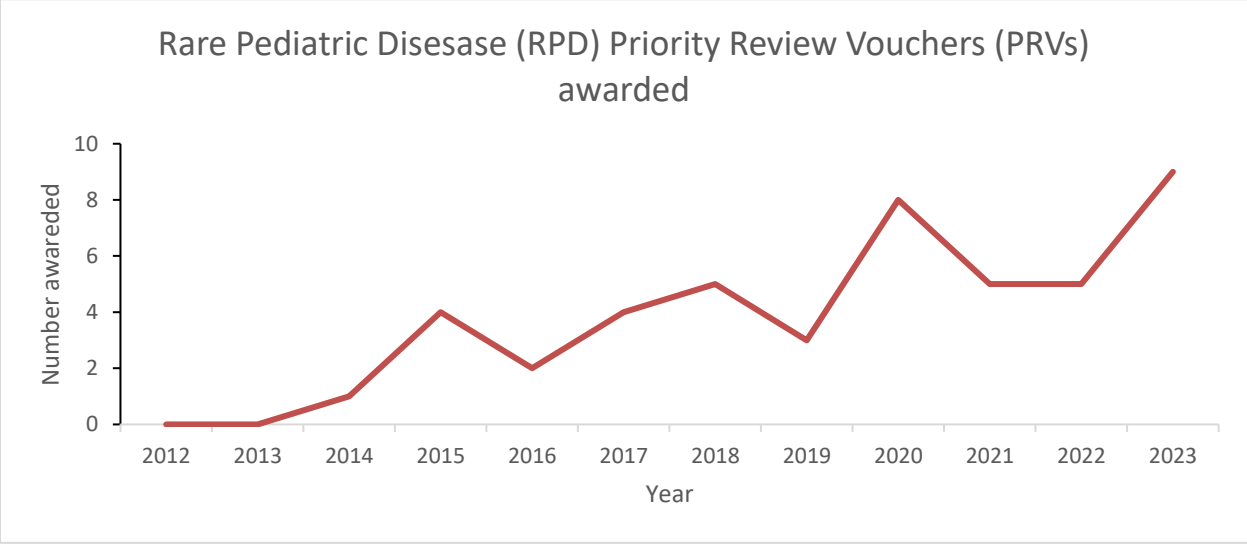
February 9, 2024

Reauthorize the Rare Pediatric Disease Priority Review Voucher Program

As many as half of those living with a rare disease are children, and rare pediatric disease priority review vouchers (PRVs) offer a crucial incentive for companies to develop therapies for particularly challenging patient populations. Reauthorizing this vital program before the September 30, 2024, deadline would maintain an important tool in ongoing efforts to address the significant unmet treatment needs that exist in the pediatric rare disease population.

Background on PRVs

The Rare Pediatric Disease PRV has helped to spur rare disease drug development in pediatric populations and brought almost four dozen therapies to market with critical safety and dosing data specific to children. The PRV program began in 2006 to address the unmet need of developing drugs for tropical diseases and was ultimately expanded in 2012 to include rare pediatric diseases. Under this program, companies that develop novel therapies for rare pediatric diseases can be awarded a PRV. The PRV allows a sponsor to obtain priority review for a new drug application (NDA) or biologic license application (BLA) that would otherwise not qualify for priority review or it can be sold to another manufacturer to obtain a priority review for their product. The program's authorization ends on September 30, 2024, and without a timely reauthorization, FDA will no longer be allowed to initiate the process necessary to issue new rare pediatric disease PRVs.



Timely reauthorization is needed to support rare disease drug development

To date, 46 PRVs have been awarded for 35 different rare pediatric diseases (see Table below). More than half of these PRVs were awarded after 2019, the year prior to when the most recent

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Government Accountability Office (GAO) analysis ended.[1] It is important to note that at the time of the prior analysis, the program had only been in place for 7 years; on average, it takes 10+ years to bring a new rare disease therapy to market.[2]

The significant uptake in pediatric rare disease approvals in recent years demonstrates the value of the program to the rare disease patient community, where more than 95% of rare diseases lack an FDA approved treatment. NORD urges Congress to reauthorize the Rare Pediatric Disease PRV program before the September 30, 2024, deadline.

Table: Pediatric Rare Disease Priority Review Vouchers Awarded Since the Program's Inception

Disease	Description	Individuals Diagnosed	PRVs Awarded	Years Awarded
Duchenne muscular dystrophy	Genetic disorder characterized by progressive muscle degeneration and weakness; premature death often around **ages 16 to early 20s**.	20,000 children diagnosed globally each year	6	2016;2017; 2020;2020; 2021;2023
Neuroblastoma/neurofibromatosis type 1	The most common pediatric solid tumor outside the brain, and the most common cancer in infants; about 90% occurs in **children younger than 5**.	700 to 800 children diagnosed in the US per year	3	2015; 2020;2020
Spinal muscular atrophy	Disorder affecting the motor neurons. Children with the most severe form **usually die before their 2nd birthday**.	Impacts 1 out of every 10,000 births	3	2017;2019; 2020
Hypophosphatasia	Rare genetic disorder that affects the development of bones and teeth. Patients with the perinatal or infantile form **often die in the first 5 years of life**.	~ 1 in 100,000 people	2	2015; 2018
Cystic fibrosis	Genetic disease that damages lungs, digestive tract and other organs. **Median age of death before treatment was 34**	30,000 individuals in	2	2019; 2020

[1] U.S. Government Accountability Office. (2020, January 31). *Drug development: FDA's Priority Review Voucher Programs*. Drug Development: FDA's Priority Review Voucher Programs | U.S. GAO. https://www.gao.gov/products/gao-20-251

[2] Orphanet: About orphan drugs. (n.d.). https://www.orpha.net/consor/cgi-bin/Education_AboutOrphanDrugs.php?lng=EN

	years; thanks to treatments now predicted at 56 years.	the United States		
Morquio A syndrome	Rare congenital lysosomal storage disease, leading to problems with bone development, growth, and movement. **Mean age at death is 25 years.**	Between 1 in 71,000 and 1 in 500,000 individuals	1	2014
Bile acid synthesis disorders	Inborn errors of bile acid synthesis, leading to a failure to produce normal bile acids. **Severe forms lead to death in the first 2 years of life.**	1 in 50,000	1	2015
Hereditary orotic aciduria	Rare inborn error of metabolism; generally causes anemia and/or other hematological issues, excessive urinary excretion of orotic acid, failure to thrive, and developmental delay and cognitive impairment.	Fewer than 30 known cases	1	2015
CLN2 disease (Batten disease)	Rare and rapidly progressing pediatric brain disorder; leading to progressive decline in language, cognitive, and motor skills, epileptic seizures, vision loss and **premature death, typically between the ages of 8 and 12.**	0.6 to 0.7 per million people	1	2017
Acute lymphoblastic leukemia	Cancer of the blood and bone marrow; survival rare has increased drastically thanks to therapies.	Less than 10,000 per year	1	2017
Mucopolysaccharidosis Type VII	Progressive inborn error of metabolism that affects many parts of the body; **severe forms typically lead to death in early childhood.**	1 in 250,000 live births	1	2017
Biallelic RPE65 mutation	Inherited ocular neurodegenerative disorder that leads to gradual vision loss and may cause complete blindness in young adulthood.	1 in 50,000-100,000 cases	1	2018
Dravet Syndrome or Lennox-Gastaut Syndrome	Group of largely genetic epilepsies often leading to long-term seizures, cognitive decline, and mobility impairment; for **severe forms, seizures typically occur between the ages of 3 – 5.**	1 in 15,700 and 0.1 to 0.28 per 100,000 people respectively	1	2018

Adenosine Deaminase-Severe Combined Immunodeficiency	Inherited disorder that damages the immune system and causes severe combined immunodeficiency (SCID) and related frequent severe infections, behavioral and psychological problems, and occasionally deafness; **untreated it is typically fatal within the first 2 years of life.**	1 in 500,000 live births	1	2018
Hemophagocytic/lymphohistiocytosis	Aggressive and life-threatening syndrome of excessive immune activation leading to multi-organ failure; **most frequently affects infants from birth to 18 months of age; without treatment it is often fatal within 2 – 6 months of onset.**	1.5 per million live births	1	
Lysosomal Acid Lipase deficiency	Inherited lysosomal storage disorder, which typically causes liver disease, developmental delays, and other health issues including cardiovascular issues and secondary blood disorders; left untreated, **children with the severe forms of the disease usually do not survive past the age of 5.**	1 in 40,000 or more	1	2019
Proopiomelanocortin (POMC)	POMC deficiency affects the way the body stores and uses energy. The main symptoms include constant hunger and excessive feeding, known as hyperphagia. Hyperphagia leads to obesity by one year of age and without treatment people with POMC deficiency remain obese throughout life.	approximately 50 cases reported	1	2020
Progeria	A rare, fatal, genetic condition of childhood with striking features resembling premature aging. At approximately nine to 24 months of age, affected children begin to experience profound growth delays, **and without treatment, children rarely survive past their 15th birthday.**	approximately 400 children	1	2020

Primary hyperoxaluria type 1	Group of rare genetic and progressive metabolic disorders characterized by the accumulation oxalate in the kidneys and other organs, ultimately leading to end-stage renal disease and death from renal failure; **most cases manifest before age 10 and become progressively worse.**	1 to 3 per million people	1	2021
Molybdenum Cofactor Deficiency	A rare condition characterized by progressive brain dysfunction. Babies with this condition appear normal at birth, but within a week they have difficulty feeding and develop intractable seizures; **median age at death is before 3 years of age.**	1 in 100,000 to 200,000 births	1	2021
Hypoplasminogenemia	A rare multi-system disease leading to thick growths on mucous membranes (e.g., in the eyes and mouth, ear, respiratory tract, kidneys etc.); **without adequate treatment it is associated with significant disability and can be life-threatening.**	1.6 people per million people	1	2021
Congenital athymia	Infants are born without a functioning thymus, **and without treatment, typically die by age two or three.**	17 to 24 live births per year	1	2021
ß-thalassemia	Inherited blood disorder characterized by reduced levels of functional hemoglobin; **the more severe form typically manifests within the first year of life and without treatment is deadly in childhood or adolescence.**	1 in 100,000 people	1	2022
Cyclin-dependent kinase-like 5	Rare developmental epileptic encephalopathy; onset of seizures usually at a very early age and **severe neurodevelopmental delay impacting cognitive, motor, speech, and visual function.**	1 in 40,000 to 60,000 live births	1	2022
Achondroplasia	Most common skeletal dysplasia, characterized by an unusually large head (macrocephaly), short upper arms (rhizomelic dwarfism), elbow flexion	1 in 20,000 to 30,000 people	1	2022

	contractures, trident hands, leg bowing and short stature (adult height of approximately 4 feet).			
Familial intrahepatic cholestasis	Progressive liver disease, which typically leads to liver failure and an increased risk of hepatocellular carcinoma; **severe forms lead to liver failure in first years of life.**	1 in 18,000 live births	1	2022
Cerebral adrenoleukodystrophy	Progressive peroxisomal disease, characterized by endocrine dysfunction (adrenal failure and sometimes testicular insufficiency), progressive myelopathy and peripheral neuropathy, and leukodystrophy; **age of onset is often in the first decade of life, and premature death typically occurs within 2-4 years of symptom onset.**	1 in 5,000 to 17,000 live births	1	2022
Alpha-mannosidosis	Rare lysosomal storage disorder characterized by a deficiency of the enzyme alpha-D-mannosidase, leading to progressive mental and cognitive impairment, hearing loss, facial dysmorphism and skeletal abnormalities, behavioral problems, among other symptoms; leading to premature death.	1 in 300,000 to 1,000,000 live births	1	2023
Friedreich's ataxia	Progressive, neurodegenerative movement disorder, leading to frequent falling, fatigue and progressive difficulty walking due to impaired ability to coordinate voluntary movements (ataxia); **typical age of onset between 10 and 15 years leading to premature death.**	1 in 40,000 people	1	2023
Rett Syndrome	Progressive neurodevelopmental disorder that almost exclusively affects females; infants with Rett syndrome generally develop normally for about 7 to 18 months after birth, when they lose previously acquired skills (developmental regression) such as	1 in 23,000 live female births	1	2023

	purposeful hand movements and the ability to communicate, and leading to premature death.			
Activated PI3K delta syndrome	Rare inborn error of immunity characterized by frequent infections, autoimmune disease, and lymphoproliferation; **age of onset tends to be in early childhood (before the 5th birthday); the disease was first described in 2013 and due to large diagnostic delays prevalence and life expectancy are not well understood.**	unknown	1	2023
Epidermolysis bullosa	A rare condition that causes fragile, blistering skin in response to minor injury, even from heat, rubbing or scratching; in severe cases, the blisters may occur inside the body, such as the lining of the mouth or stomach; **morbidity can be significant, and patients with the most severe form are at major risk of death during the first few years of life.**	500,000 people worldwide	1	2023
fibrodysplasia ossificans progressiva	Rare genetic connective tissue disorder characterized by the abnormal development of bone in areas of the body where bone is not normally present (heterotopic ossification), such as the ligaments, tendons, and skeletal muscles; **leads to shortened life expectancy and most patients require help with walking by age 30.**	1 in 2,000,000 people	1	2023
CHAPLE Disease	Inherited immune disease leading to severe gastro-intestinal problems, severe lung infections, and severe blood clots, among other systems. **Severe thrombotic vascular occlusions (blockage of blood vessels) can occur which can be life-threatening.**	fewer than 100 worldwide	1	2023

Acid sphingomyelinase deficiency	Rare, progressive, and often fatal lysosomal storage disease often associated with developmental delays, regression, and learning disability; **the most severe infantile forms are typically fatal by 3 years of age.**	1 in 250,000 people	1	2023

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