Cerliponase Alfa for CLN2 Disease

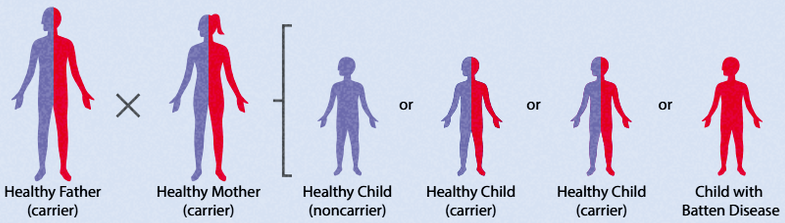
BIOMARIN®

CLN2 Disease, a Form of Batten Disease

Batten disease is the **umbrella term** for a group of rare disorders that are also referred to as neuronal ceroid lipofuscinoses, or **NCLs**[1]

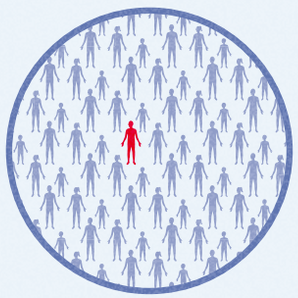
Named after British pediatrician, **Frederick Batten**, who first described it in 1903[2]

When **both parents** carry one defective gene, each of their children faces a **1 in 4 chance** of inheriting an NCL[1]



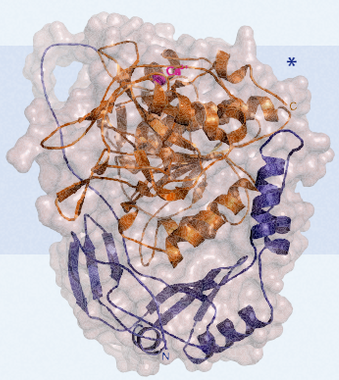
CLN2 Disease

CLN2 disease is **rare**, occurring in **less than one** in 100,000 people[3]



CLN2 disease is a form of Batten disease that primarily affects the central nervous systems of young children

Potential risk: Studies in animals have indicated that cerliponase alfa may be beneficial for the neurological symptoms of CLN2 disease. Although these data are encouraging, it is important to understand that it is an experimental therapy in an early stage of clinical development. The safety and efficacy of cerliponase alfa needs to be evaluated in patients. In animals, the most common side effects were inflammation associated with the drug delivery device and allergic reactions to cerliponase alfa.



Caused by a **deficiency** in a critical enzyme, **TPP-1**[2]

Cerliponase alfa is a specially engineered recombinant human TPP-1 enzyme designed to replace the enzyme that children with CLN2 disease are lacking

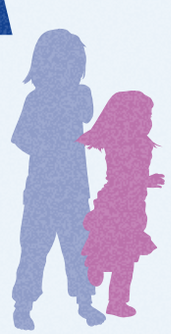
CLN2 disease typically presents when a child is about **three years old**[4]

Seizures, language delay, and/or loss of acquired language are the most common **first signs**[2]

Cerliponase Alfa Clinical Trial Process

48 weeks
minimum length of study duration

8 -10
estimated size of the specialized medical support team required



About **24 study participants** between the ages of **3 and 16**

Subjects relocate to one of **five designated clinical sites** in **four countries** in order to participate

4,854 miles/7,811 kilometers
Distance between the lab where cerliponase alfa is made and the furthest clinical trial site

Infusion of medicine to the fluid in the brain is an established delivery technique; however, it is a novel **method of** delivering an **enzyme replacement therapy** such as cerliponase alfa

Intracerebroventricular (ICV) Infusion Procedure

Prior to receiving infusions, **surgery is required** to implant a special delivery device in the brain through which cerliponase alfa will be administered

4 hours
average length of each infusion/treatment

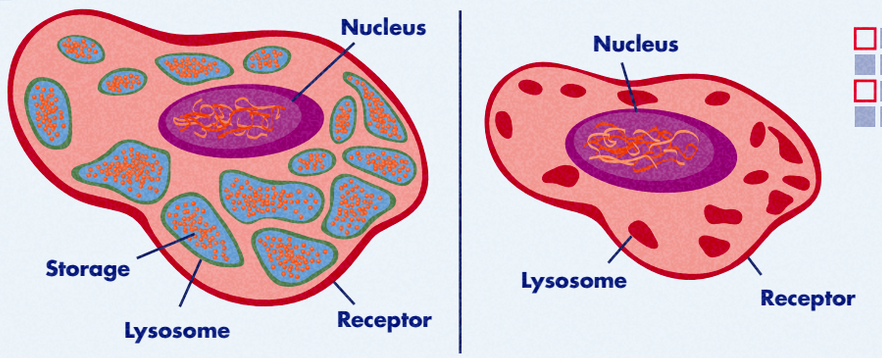
Every 2 weeks
frequency with which study patients receive cerliponase alfa infusions

One experimental therapy:
cerliponase alfa

Enzyme Replacement Therapy for Lysosomal Storage Diseases (LSD)

Healthy Cell | **Unhealthy Cell**

The difference in appearance between a normal and LSD cell is readily visible under light microscopy, as depicted here



*Attribution PDB ID: 3EDY, Guhaniyogi J. et al. J Biol Chem. 2009. 284:3985

1 "Batten Disease Fact Sheet." National Institute of Neurological Disorders and Stroke. Last accessed on March 26, 2015. Available here: http://www.ninds.nih.gov/disorders/batten/detail_batten.htm.
2 "What is Batten Disease?" Batten Disease Support and Research Association. Last accessed on March 26, 2015. Available here: http://bdsra.org/what-is-batten-disease/.
3 From BioMarin Corporate Presentation dated 5/14/14, slide 24.
4 Clinical Trials: CLN2 (Batten Disease). BioMarin. Last accessed on March 26, 2015. Available here: http://www.bmrn.com/pipeline/clinical-trials/cln2.php.