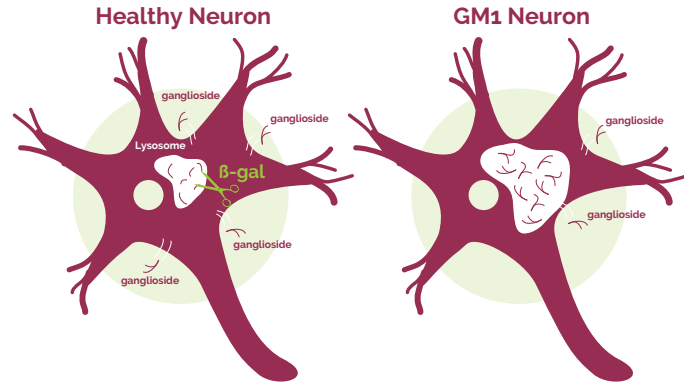


# What is Gene Therapy for GM1 Gangliosidosis?



## GM1 gangliosidosis (GM1) is a rare genetic disease

GM1 is one of a group of diseases called "lysosomal storage diseases". There are about 50 known lysosomal storage diseases, all of which are genetic and result from defects in the lysosomes of cells. In the case of GM1, genetic mutations lower the level of  $\beta$ galactosidase ( $\beta$ -gal) activity in the body - an enzyme needed to break down GM1 ganglioside and keratan sulfate within the lysosomes. Low levels of  $\beta$ -gal cause waste products to accumulate. Neurons, or cells that transmit information within the nervous system, are particularly affected



## RESIDUAL $\beta$ -gal ACTIVITY CORRELATES WITH DISEASE SEVERITY



**Type 1 GM1 Gangliosidosis**



**Type 2 GM1 Gangliosidosis**



**Type 3 GM1 Gangliosidosis**



**MPS IVB**

Neurologic Symptoms & Seizures

Bone & Joint Problems

## CURRENTLY THERE IS NO TREATMENT

## HOW CAN GENE THERAPY HELP?

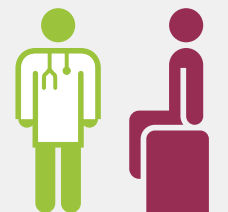
Gene therapy represents a promising new therapy with the potential to significantly slow or stop progression of neurological and other deficits and to improve quality of life. While several approaches to GM1 gene therapy are being developed, intrathecal gene therapy strives to deliver a functional copy of the  $\beta$ gal gene to the brain via the cerebrospinal fluid.

### Safety First



Safety is being evaluated in animal models

### What's next?

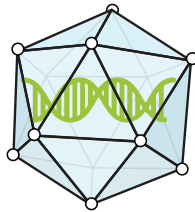


early clinical trials for GM1 evaluating safety in human subjects are on the horizon

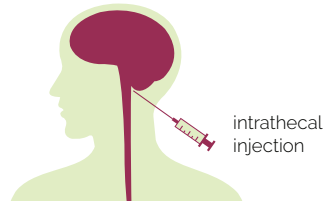
1. a normal, healthy copy of the  $\beta$ -gal gene is produced



2. gene is inserted into a harmless Adeno-Associated Virus (AAV) to create a viral vector



3. AAV vector is injected into the cerebrospinal fluid (CSF) that flows around the brain and spinal cord



4. some cells take up AAV vector and begin to make functional  $\beta$ -gal, which is released into the CSF



5. secreted  $\beta$ -gal can be used by other cells throughout the brain and spinal cord which may improve cognitive function

