## WHY ENZYME REPLACEMENT THERAPY FOR GM1?

**SMALL MOLECULES** | **GENE THERAPY** | **ENZYME REPLACEMENT**

While there have been three AAV gene therapy clinical trials for GM1 and one small molecule clinical trial, enzyme replacement therapy has yet to reach clinical trials. Many of the small molecules require residual enzyme activity and therefore will not work for infantile GM1. The gene therapy presently requires very early treatment. We believe ERT is a critical tool and treatment modality for the majority of patients.

## PRIOR EXAMPLES OF SUCCESS IN LYSOSOMAL STORAGE DISEASES IN ENZYME REPLACEMENT THERAPY

There are many examples of successful protein / enzyme replacement therapies in lysosomal storage diseases like GM1. The lack of an enzyme replacement therapy for GM1 is simply due to a lack of financial resources, prioritization, and a team to execute. We believe that decades-long experiences with similar drugs such as Aldurazyme for MPS I and Brineura for CLN2 Batten disease serve as successful examples of ERT in rare lysosomal storage diseases.

## NEWBORN SCREENING READINESS

Cure GM1 funded the optimization of the first-ever newborn screening assay for GM1 gangliosidosis. The assay was developed by Dr. Michael Gelb at the University of Washington and led to the inclusion of GM1 in multiple newborn screening studies, including an international pilot study.

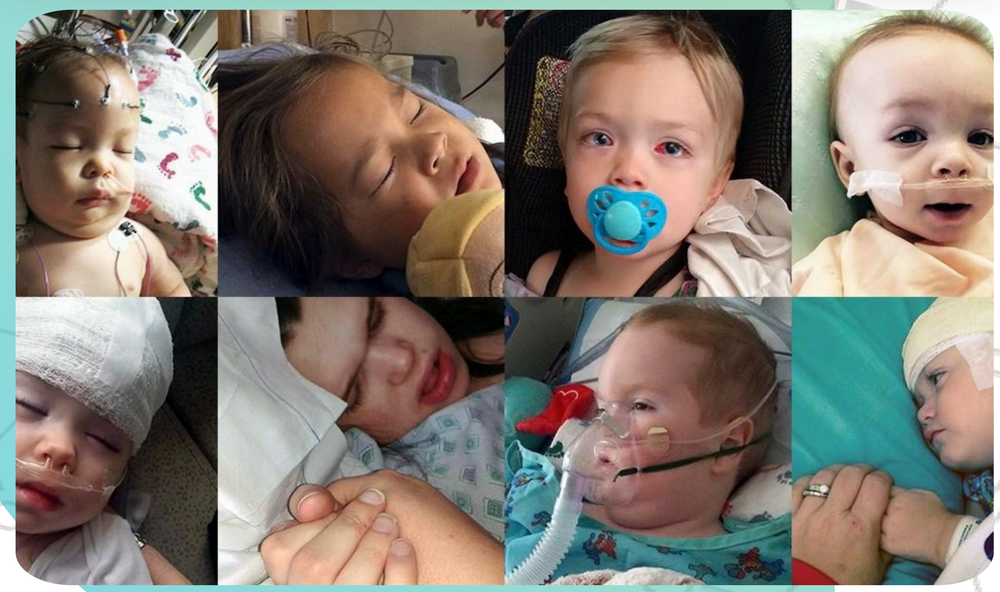
In addition, two babies have already been identified using this assay, which is one of the requirements for newborn screening to be expanded once there is an approved treatment available.

In the future, the best possible outcomes with ERT will be in babies identified at birth, avoiding the diagnostic odyssey and the development of severe symptoms of GM1.

**CUREGM1.ORG/DONATE**

CURE GM1™ FOUNDATION

## SAVE LIVES BY DONATING TO ENZYME REPLACEMENT THERAPY FOR GM1 GANGLIOSIDOSIS



# PILLARS OF DRUG DEVELOPMENT FOR GM1

Since the creation of Cure GM1 in 2015, we have been assembling building blocks to be able to support the drug development process and to improve the likelihood of success for GM1 research and clinical trials.

## COMMUNITY

To attract interest from biotech companies to invest in treatments, we as a community must show we exist. More importantly, we must support each other.

## ANIMAL MODELS


Cure GM1 partnered with the Jackson Laboratory to create the first publicly available mouse models in the history of GM1.

## REGULATORY INTERACTIONS

### EXTERNALLY-LED PATIENT-FOCUSED DRUG DEVELOPMENT MEETING

Cure GM1 organized the first-ever patient-focused drug development meeting with FDA and published the Voice of the Patient report published on the FDA website.


### ACCELERATED APPROVAL BASED ON BIOMARKERS

In partnership with other patient advocates and groups, Cure GM1 met with regulators to champion change for ultra-rare diseases to encourage accelerated approval based on biomarkers.


## BIOBANK AND NATURAL HISTORY

Cure GM1 established its own biobank.

Our real-world evidence and EHR natural history study.

The first-ever GM1 data sharing consortium.

# OUR INITIATIVES IN ENZYME REPLACEMENT THERAPY WILL CONTRIBUTE TO AN ARSENAL OF POSSIBLE TREATMENTS FOR GM1

Through the years since Cure GM1 was first founded, there have been clinical trials in both gene therapy and small molecules. However, there has yet to be a clinical trial for enzyme replacement therapy (ERT). We aim to change the landscape for GM1 and to contribute to creating an arsenal of possible approaches to treating GM1.

**$4M NEEDED TO MOVE FORWARD**

**IND stands for investigational new drug application.**

The reality of treating a disease as complex as GM1 is that combination therapies and multiple possible treatments may be required.

Some treatments work only when there is residual enzyme activity and some only work at certain times in the course of the disease.

**DONATE TO SUPPORT ENZYME REPLACEMENT**

## OUR ENZYME REPLACEMENT THERAPY TEAM

Cure GM1 has built a team of advisors and volunteers with decades of prior experience in protein / enzyme replacement therapies. Both Paul and Gouri have prior experience working on GM1 drug development and research.

**MARK DE SOUZA, PHD**

Business advisor

**GOURI YOGALINGAM, PHD**

R&D and Scientific Advisor

**PAUL FITZPATRICK, PHD**

CMC and Scientific Advisor

**CHRIS PHILLIPS, MS**

CMC Advisor