NTSAD RESEARCH OVERVIEW

NTSAD launched its Research Initiative in 2002 to fund innovative research for neurodegenerative diseases that affect the central nervous system. NTSAD funds promising research that may lead to major grant support and programs with the potential to reach clinical trials. NTSAD's grants are sometimes made in collaboration with partners such as the NIH and other patient advocacy groups for related genetic diseases. Thirty-nine grants, totaling $2.5 million, have been awarded through the NTSAD Research Initiative program and another 13 grants through the Lysosomal Storage Disease Research Consortium. These grants have led to NIH grants of more than $10 million toward finding a cure. The Tay-Sachs Gene Therapy (TSGT) Consortium research project, which is the project closest to a human clinical trial, has received the majority of NTSAD grant awards in recent years. However, NTSAD continues to support a research program with a diverse set of technologies, diseases, and investigators.

2012 – 13 HIGHLIGHTS

Where is your money going and where is our time spent?

1. New Research Grants Awarded

The Tay-Sachs Gene Therapy Consortium has begun a new research proposal to address the unexpected adverse results that occurred as they were in the final stages of pre-clinical studies. Their approach is to generate a new panel of vectors, and over the next year, they will assess their safety and efficacy in a stepwise manner. Upon regulatory approvals of this plan and successful completion of three milestones, they will initiate human clinical studies. NTSAD and The Cure Tay-Sachs Foundation are sharing in the $545,000 cost for this next phase of the study.

The Jacob sheep have moved to a new pasture closer to the research conducted in Auburn, AL. Our many thanks to Joan and Fred Horak for shepherding them so lovingly over the years. To pay for this transition, NTSAD has made a grant to Auburn for $39,000, which includes the cost for the sheep to move and for their care in the next year. NTSAD paid for the flock's food and care for the years that they were bred and kept at St. Judes Farm.

A one year $50,000 Research Initiative grant award was made to Alessandra d'Azzo, PhD, of St. Jude Children's Research Hospital for her proposal, "Studies of the molecular and biochemical bases of neurodegeneration in sialidosis." The researcher and her group have a reputation for delivering high quality research in the field of lysosomal storage disorders (LSDs), including in GM-1. Data gained from this study could be important across many lysosomal diseases and may also apply to more common neurodegenerative diseases. Dr. d'Azzo submitted one of 16 grants that were received in NTSAD's annual Request for Proposal process.

2. Ongoing Research Grants

Doug Martin, PhD, Auburn University:

1. Sheep as a Model of Tay-Sachs Disease - Year 3
2. Supplemental Pre-Clinical Studies of AAV Gene Therapy in Feline Sandhoff Disease
3. Histological analysis of the central nervous system after intracranial injection of AAV vectors in normal cats

3. Research Grants Completed in fiscal year 2013 (July 1, 2012 – June 30, 2013) – reports are available in the Research section of the NTSAD web site library

Florian Eichler, MD, Massachusetts General Hospital

1. *A Biomarker for Disease Progression in GM2 and other Neurolipidoses*
2. *Clinical Outcome Measures for a Gene Therapy Trial in Infantile and Juvenile GM2*

Guangping Gao, PhD, University of Massachusetts Medical Center, *Optimization of Efficacious Gene Therapy for Canavan Disease*

Gustavo Maegawa, MD, PhD, Johns Hopkins University, *Developing a High Throughput Screening Assay to Identify Potential Drugs for MLD*; applicable to similar diseases

Jean-Pyo Lee, PhD, and Evan Snyder, MD, Tulane University, *The Therapeutic Potential of Human Induced Pluripotent Stem Cells in the Sandhoff Disease Mouse Model*

Fran Platt, PhD, University of Oxford, *Optimizing the Therapeutic Potential of Anti-Inflammatory Therapy in Tay-Sachs and Related Diseases*

Maria Traka, PhD, *Development of an In Vitro Approach to Identify Molecular Pathways of Canavan disease*

University of Florida, Grant for equipment used in toxicity studies for TSGT Consortium

4. **Orphan Drug Designation Approved**

NTSAD's orphan drug designation applications for Tay-Sachs and Sandhoff gene therapy treatment has been granted by the U.S. Food and Drug Administration (FDA). Receiving an orphan drug designation is a positive step toward our efforts to bring hope to families affected by these diseases. This designation supports drug development for rare diseases, and provides substantial benefits including the potential of funding for certain clinical studies and study-design assistance. These benefits can also be transferred to companies who may want to help make the therapy available. The applications were generously done *pro bono* for NTSAD .

5. Research Strategy Update in process

NTSAD is working on a refreshed research strategy to guide our research funding decisions and activities over the next five years. By interviews with SAC members and other leading researchers and other experts in the biotech and medical fields, we will have a strong understanding of existing and emerging treatment approaches for Tay Sachs, Sandhoff, GM1 and Canavan disease. A lot has changed since the 2009 strategy – e.g., new technologies for crossing the blood brain barrier; a number of companies working in these new technology approaches; gene therapy programs more diverse and evolved.

The plan, when complete, will be used to communicate with NTSAD's donors (current and prospective), scientists, venture capital, biotech, government funding agencies, and foundations with a goal to increase capacity, funding and partners to accelerate treatments.