IRS Form 1023: Application for Recognition of Exemption under Section 501(c)(3) of Internal Revenue Code

Attachment D: IRS Form 1023, Part IV
Narrative Description of Activities

The Disease

Lysosomal Storage Diseases (LSD's) are caused by inherited enzyme deficiencies and result in an accumulation of substrate in cellular lysosome organelles. The severity of these diseases generally varies with the degree of enzyme deficiency. The most severe deficiencies cause death in early childhood while less severe deficiencies may not present clinically until adulthood. The type and location of the cells affected and the rate of the substrate accumulation form the basis of the clinical abnormalities and the timing of initial onset. These diverse clinical manifestations, the infrequent occurrence of the individual diseases, and the variation in severity have made early diagnosis of these diseases difficult. The overall incidence of diagnosed LSD's has been estimated to be approximately one per 7700 births.

Of the more than 40 known lysosomal diseases, more than 60% have central nervous system (CNS) involvement. The inability of neuronal cells to regenerate makes LSD's with CNS involvement clinically significant and makes early treatment essential. Many of the systemic aspects of some LSD disorders are today being treated with clinically available, yet expensive, Enzyme Replacement Therapy (ERT). There is presently no proven clinical therapy available for the CNS aspects of any of the LSD's, and the CNS involvement remains a devastating and often fatal aspect of these diseases. Considering that many of the LSD's without CNS involvement are being addressed with ERT, additional advancements in treating LSD's will require that a treatment be found for the neurological aspects of these diseases. GM2 Gangliosidosis, more commonly called Tay Sachs Disease, was one of the first identified lysosomal storage diseases, and the dominant clinical presentation is neurological.

Perhaps the greatest opportunity for curing the neurological aspects of these diseases is through the use of gene therapy. The concept has already shown some success in multiple small animal models of lysosomal storage disease and is currently undergoing human clinical investigation for two lysosomal storage diseases. While there have been many exciting advances in the area of gene therapy for the LSD's, many challenges remain in proving the safety and efficacy of this therapeutic concept and in bringing this therapy to the individuals afflicted with the disease.

Because of the infrequent occurrence of the individual diseases, a specific therapeutic solution for one rare disease may be perceived as having relatively limited benefit. With this perspective, efforts to find cures for these individual diseases have been limited. Most research institutions and medical corporations have little financial incentive for investing in cures for these rather rare individual diseases or for cures that may not require periodic re-application of the therapy. With this perspective, alternative funding mechanisms are required to fund the research and clinical studies needed to help those with these diseases.

While it is indeed true that individual lysosomal storage diseases and other inborn errors of metabolism occur infrequently and are often individually classified as rare, taken as a whole, these diseases represent a large portion of chronic diseases around the world, especially those afflicting children. The opportunity is to understand the aspects of these diseases that are in common and to identify research or technology that can be leveraged across these diseases to make the individual therapeutic solutions economically achievable. The New Hope Research Foundation is dedicated to providing the support needed to find cures for these individual diseases that are not being supported by health care businesses and institutions.

For a more complete description of lysosomal storage diseases, please reference Attachment E: "GM2 Gangliosidosis: Clinical Presentation, Metabolic Basis, and Future Therapeutic Options."

The Mission and Charter

The New Hope Research Foundation is a non-profit organization dedicated to

- helping find a cure for gangliosidosis and other lysosomal storage diseases and
- providing hope to patients and their families currently facing the degenerative and debilitating aspects of these diseases.

New Hope Research Foundation will coordinate, direct, and financially support activities intended to find an effective genetic cure for patients born with enzyme deficiencies causing gangliosidosis and other lysosomal storage diseases that affect the central nervous system and to assist patients in economically accessing future cures. These activities include:

- Research on gene therapy and the means for infusing or delivering this therapy to correct lysosomal enzyme deficiencies of the central nervous system,
- Clinical studies and associated regulatory processes which are intended to show safety and efficacy of gene therapy for the central nervous system aspects of gangliosidosis, and if successful, related lysosomal storage diseases,
- Regulatory applications required to initiate investigations of clinical studies and the regulatory submissions required to allow patient access to proven therapies.
- Education and communication for patients and families on the clinical manifestations and molecular basis of gangliosidosis, and related diseases, on the mechanism of gene therapy, and on the status of related research and clinical studies, and

Past, Present, and Future Activities

The New Hope Research Foundation, Inc. was formed on December 22, 2006. It will be commonly referred to as the New Hope Research Foundation. The activities of the foundation will be focused on the coordination of research activities and funding of research grants. It is anticipated that this will consume greater than 80% of the expenses and volunteer support. All activities noted will be funded through the foundation's general fund.

Past: There are no prior activities to report.

Present: The present activities include:

- Web-site Communication: Site creation is in progress. A web-site designer is being found to create the site by October 2007. The site will be used to communicate the foundation mission, to invite research proposals, to communicate the current research status, and to request donations.
- Funding of Grants: A grant review board currently includes the Chair and Vice Chair. Additional members are currently being recruited. The board members will be composed of individuals knowledgeable in the science of gene therapy and lysosomal storage diseases. The members will not be financially associated with the organizations requesting the grants or benefit financially by specific grant selections. Research grants will not be provided to for-profit organizations. Academic institutions and research scientists are currently being contacted to announce the grant program and to communicate the grant process. Institutions and individuals being contacted who have conducted gene therapy research, have conducted pre-clinical studies in animal models of gangliosidosis, or have experience in conducting gene therapy clinical trials.

- Research Coordination: A meeting was organized to plan future research and clinical activities. The meeting was held in Boston on March 9, 2007. This scientific meeting focused on future research required to achieve the foundations goals. Scientists and researchers attending represented research activities at Harvard University, Auburn University, Boston College, and the University of Minnesota. The New Hope Research Foundation financially supported this scientific meeting with payment for transportation and lodging of participants, and meals during the meeting. The second meeting of the scientific group was conducted in Seattle on June 2, 2007. The New Hope Research Foundation organized and financially supported this meeting, coordinated discussion topics, and facilitated the meeting.

- Patient Outreach and Education: A $5,000 donation was made to the National Tay-Sachs & Allied Diseases association to support the Medical / Research Update at their annual conference held in Boston on April 19 – 22, 2007. The meeting included an overview presentation of the gene therapy initiative. A brochure was provided to the participants informing them of the gene therapy initiative, and for the scientists attending, requesting submission of grant proposals. Reference Attachment F.

Future: The anticipated future activities include:

- Web-site Communication: A web-site will be provide updated to include:
  - An overview of the New Hope Research Foundation mission and charter.
  - Background information on gangliosidosis disease. The information will be provided at a level relevant for patients, and it will also include more scientific oriented information to assist in the coordination of research scientists and researchers. Links to other relevant sites will also be included.
  - An explanation of the research master plan and the status of research activities.
  - Grant application process instructions and forms required to accompany the organization's proposal.
  - A request for donations including both mail-in and on-line instructions.

- Funding of Grants: Going forward, the New Hope Research Foundation will be primarily achieving its goals by making grants to other non-profit research organizations. The selection of grants will be made consistent with the mission and charter of the organization. A grant review board will be composed of individuals knowledgeable in the disease state, the research master plan, the current state of research, and the fair market value of the research funding being requested.

- Research Coordination: Periodic meetings, with a planned frequency of every six to nine months, will be conducted with research scientists and clinicians receiving grants or interested in making grants proposals. The objectives of these meetings will be to coordinate the ongoing research activities, and as necessary, update the master research plan. The location of these meeting will vary depending on the academic organizations attending.

- Patient Outreach and Education: In addition to the web-site activities, funding will be provided to communicate research progress in finding cures for gangliosidosis and associated lysosomal storage diseases. This program may be accomplished through other patient support group organizations, such as the National Tay-Sachs & Allied Diseases Association.