A PROPOSAL FOR

INFANTILE NEUROAXONAL DYSTROPHY (INAD)

RESEARCH SUPPORT

Presented to

Jasper Valentijn Foundation

June 2015

Department of Neurology
Movement Disorders Section

Washington University School of Medicine has demonstrated unwavering commitment to the discovery of knowledge, the advancement of medical research, and the training of future physician scientists. Our overarching vision is to use our resources as a top-tier research institution to make significant and lasting contributions to improving world health. The solutions are complex, and yet for Washington University School of Medicine the action is straightforward: martial our extraordinary scientific resources to make discoveries and create knowledge that improve and prolong lives.

The Movement Disorders Section within the Department of Neurology at Washington University School of Medicine represents one of the finest examples of an academic program committed to researching and treating movement disorders in adults and children. The balance of outstanding faculty, exemplary facilities, and a cohesive philosophy ensure consistent excellence across the missions of maintaining national prominence in research, teaching and patient care.

Dr. Paul Kotzbauer is one of the School of Medicine's most outstanding examples of a doctor who takes care of patients and also does important research. We want to thank you for your commitment to supporting Infantile Neuroaxonal Dystrophy (INAD) research in Dr. Kotzbauer's laboratory along with Kristin Phillips, Mary and Kyle Herschelman, Leslie LeMaire, Kim "Rooster" Rossiter with Ainsley's Angels, Jennifer Thompson, Jean loup Vasseur with AIDNAI Patient Association, and many others.

Dr. Kotzbauer began research work on INAD about nine years ago when genetic researchers first identified PLA2G6 gene mutations as the underlying cause of INAD. The gene mutations interfere with the ability of the PLA2G6 enzyme to function properly. Over the past nine years, Dr. Kotzbauer has been inspired by the children and families whom he has had the opportunity to know.

The current focus of research in Dr. Kotzbauer's laboratory is to understand how INAD specific treatments can be developed. To eventually develop a treatment for INAD, his laboratory has outlined a research plan for an initial two year project.

The two year project focuses on identifying ways to develop treatments for impaired PLA2G6 enzyme function. Initial support has allowed Dr. Kotzbauer to purchase important lab supplies and to hire a full-time scientist. Dr. Kotzbauer's laboratory is developing approaches to screen chemical compounds for their ability to either directly improve the function of the PLA2G6 enzyme or to stimulate other enzymes to compensate for impaired PLA2G6 function. The objective is to develop efficient and sensitive screening approaches and then to perform initial screens to identify compounds with the desired properties. The initial screening effort could identify molecules that are suitable for further optimization and testing as therapeutic agents. The research will also provide important information about the best strategies for further screening efforts to develop treatments for INAD.

Further funding of the two year project will enable Dr. Kotzbauer to pursue the development of two different screening strategies in parallel. In addition to developing a screening strategy to identify compounds that directly improve the function of the PLA2G6 enzyme, he would be able to focus more resources on identifying ways to stimulate other enzymes to compensate for impaired PLA2G6 function. Pursuing the development of two complementary approaches and testing them in an initial screen of chemical compounds will provide more information about best strategies and will improve the chance of developing a treatment for INAD.

Additional support will afford Dr. Kotzbauer the ability to devote more time to the project and to purchase essential lab supplies critical to the project. Additional funds will also allow us to enlist help from the High Throughput Screening Core facility, which will provide the automated equipment, expertise, and chemical compound collections needed to conduct initial pilot screens of up to 2000 compounds, using the two screening strategies developed in the project.

Once again, thank you for partnering to advance our knowledge of INAD. Many devastating diseases are not well understood because of the limited funding for research. It is well known that the National Institutes of Health (NIH) has scaled back their granting significantly. One critical element of our success is the ability to partner with individuals through private philanthropy. Philanthropy plays a critical role in advancing our knowledge to improve treatment and care. Respectfully, we are asking you to consider an additional $100,000 to propel discovery. Through your gift you will participate in invaluable research to advance the care of patients and improve their outcomes for generations to come.

We look forward to providing informal progress updates throughout the two year project. In addition, we commit to providing an annual written update on progress in Dr. Kotzbauer's laboratory.

Thank you for your consideration of this leadership gift