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Clinical Trial for X-Linked Severe Combined Immunodeficiency in **Newly Diagnosed Infants**

Study Title: A Pilot Feasibility Study of Gene Transfer for X-Linked Severe Combined Immunodeficiency in Newly Diagnosed Infants Using a Self-Inactivating Lentiviral Vector to Transduce Autologous CD34+ Hematopoietic Cells

Brief Description: Children with X-SCID are born with severe immune defects that result in greatly increased susceptibility to opportunistic infections and that are fatal if left untreated. Patients treated with allogeneic transplant using a matched sibling donor have a very good prognosis; however, most patients lack a matched sibling donor and are transplanted with mismatched grafts that result in significantly poorer outcomes. This latter group of children will be eligible for this study, which will determine the safety and efficacy of using a lentiviral vector to insert a normal copy of the X-SCID gene into the subjects' own bone marrow cells. The LVXSCID lentiviral vector used in this study has been designed to avoid insertional oncogenesis and gene therapy-related leukemia. So far, eight subjects have been enrolled on this study, and their outcome is encouraging: all subjects are currently alive and doing well as outpatients with a median follow up of greater than one year. All subjects are growing with normal weight and height velocity, and no subject has developed a life-threatening infection or gene therapy-related leukemia since receiving gene therapy. These results have been presented at the 2017 ASH Meeting (Mamcarz et al; Blood, 2017:130 (Suppl 1), 523). The same vector was also shown to be both safe and efficacious in six older X-SCID children treated on a related protocol at the NIH Clinical Center (DeRavin et al, Science Translational Medicine, 2016).

What is involved: Bone marrow stem cells will be removed in the operating room, transduced with the vector, and then reinfused into the child following a low, subablative dose of busulfan. Participants will be followed closely for immune reconstitution of T, B, and NK cells as well as for any adverse events associated with the study procedure. Safety studies will focus on interactions of the vector with the host cell genome and monitor closely for any evidence of insertional activation of oncogenes.

Who can participate:

- A clinical diagnosis of SCID-X1 and a proven mutation in the common gamma chain gene (testing can be performed at St. Jude Children's Research Hospital)
- Age newborn to < 2 years old at time of enrollment
- No prior therapy with allogeneic stem cell transplantation
- Lack of an HLA-matched sibling donor for allogeneic hematopoietic stem cell transplant
- Less than 300 CD3+ T cells by flow cytometry or higher if evidence of maternal engraftment
- No evidence of HIV infection by genome PCR
- Lymphocyte proliferation to phytohemagglutinin (PHA) <10% of the lower limit of normal for the laboratory
- The absence of any medical condition suggesting that survival will be less than 16 weeks
- No medical contraindications to general anesthesia and bone marrow harvest

Participating Clinical Centers and Contacts:
Currently Enrolling

St. Jude Children's Research Hospital, Memphis, Tennessee, USA
University of California, San Francisco, California, USA
Seattle Children's Hospital, Seattle, Washington, USA

For eligibility or more information about the study, please contact Dr. Ewelina Mamcarz, Clinical Investigator at (901) 595-8343 Ewelina. *Mamcarz@stjude.org;* Jola Dowdy, Project Manager at (901) 595-6093, *Jola.Dowdy@stjude.org:* or the St. Jude Physician Referral line at 1-888-226-4343 (toll-free). *referralinfo@stjude.org*