We are indeed pursuing efforts for gene therapy of the brain in MPSIII and more specifically in MPSIIIB. We have produced some new data in the dog model of MPSI last year, as a proof of feasibility of AAV-mediated gene therapy to the brain. We showed that dogs could be efficiently treated provided that a strong immune response against the therapeutic enzyme was prevented. I have attached a pdf of the paper. More recently, we repeated very similar experiments in collaboration with the team of M. Ellinwood at Iowa State University (mellinwo@iastate.edu) and showed that we could obtain a reversion of the pathology in the entire brain of MPSIIIB dogs. We are currently in the process of defining manufacturing conditions for a clinical-grade bath of the AAV-NaGlu vector. Large scale production using baculovirus has been set up and validated. Toxicology and biodistribution studies will be started soon. This is performed in collaboration with the Dutch company Amsterdam Molecular Therapeutics (AMT). A retrospective epidemiological study aimed at producing a description of the natural history of all types of MPSIII is being performed using an exhaustive registry of the French patients diagnosed since 1990 that we have recently established. Data will be used to assess clinical benefit in treated children. An application for a phase I/II study is being prepared for submission to the French (AFFSAPS) and European (EMEA) regulatory agencies before next summer. Our work plan is to enroll patients at the end of 2007, though we already expect delay due to vector production.
The study is funded as a join program between the Institut Pasteur, the AFM (French Muscular Dystrophy patient association -Telethon) and the INSERM. The PI of the clinical study will be Pr. Marc Tardieu at the Hôpital Bicêtre in Paris (marc.tardieu@u-psud.fr). We anticipate patient recruitments in France, UK, Germany, Italy and Israel, since pediatricians in these countries participate to our clinical advisory board. However, we have not yet established a patient list. A RO5 application will be submitted by M. Ellinwood in collaboration with us; however this will not be intended to support the clinical study but more detailed investigations on the treatment of dogs and physiopathological issues.

I am willing to provide you with more information that might be useful to you, and again I strongly appreciate your interest for our work.

Sincerely,

Jean Michel Heard, MD, PhD

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