REKLAIM, a novel Phase Ib Clinical Trial of FBX-101 (AAVrh10.GALC) Intravenously administered after UCBT for the treatment of Infantile Krabbe Disease

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REKLAIM is an intravenous AAVrh10.GALC gene therapy administered during myeloablation/ immune suppression after umbilical cord blood transplantation (UCBT) for infantile and Late Infantile Krabbe disease (IKD, LIKD). We report the results of the first 5 subjects with IKD treated with a low dose intravenous FBX-101 (1.6×10^{13} gc/kg). IKD is a fatal neurodegenerative disorder due to galactocerebrosidase (GALC) deficiency that results in psychosine toxicity to myelinating cells in the brain and peripheral nervous system. If untreated death occurs in average by 2 years.

Currently, pre-symptomatic neonates are treated with UCBT halting brain disease, but motor function declines due to progressive peripheral neuropathy. We hypothesized that FBX-101 administered during myeloablation for UCBT will override the antibody response to the vector's capsid and transgene. UCBT provides an immune system that does not recognize GALC as an antigen. REKLAIM is a Phase 1b dose-escalating intravenous gene therapy to evaluate safety and efficacy of FBX-101 administered IV >21 days after UCBT while the subject is myeloablated or later when immune suppressed. Each subject's immune suppression is approved by an independent committee including a Rituximab, Serolimus and Prednisolone regime adjusted to subject needs.

FBX-101 was well tolerated, with no treatment-related serious adverse events with follow up ranging from 4-24 months. No antibodies to the transgene developed. In the two subjects treated during myeloablation, there were no antibodies to AAV, plasma and CSF GALC significantly increased, psychosine dropped to normal and subjects achieved normal gross motor skills. The three subjects treated during immune suppression developed total and neutralizing antibodies to AAV with no signs of humoral or cellular toxicity and improved in gross motor skills.

In summary, FBX-101 after UCBT leverages the-myeloablation and immune suppression after UCBT, resulting in efficient AAV transduction and

providing increased GALC enzyme supporting brain myelination and gross motor development.

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