Current enzyme replacement therapies for LSDs and the potential for CNS treatment

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Lysosomal storage disorders (LSDs) are a family of diseases that originate from disease-specific gene mutations and lead to accumulation of undigested substrate within the lysosomes of cells. Replacement of these enzymes via intravenous administration is a successful strategy in the treatment of LSDs with peripheral symptoms such as Hunter syndrome, Gaucher disease and Fabry disease. However, current intravenous approaches have not been proven successful in ameliorating the CNS symptoms of these and other LSDs. Shire Human Genetic Therapies is developing new technologies to help address the CNS symptoms associated with LSDs including Hunter syndrome with CNS involvement, Metachromatic Leukodystrophy, and Sanfilippo A syndrome. These three diseases feature a deficiency in a class of enzymes known as lysosomal sulfatases. Through the development of proprietary technology in which the gene for formylglycine generating enzyme (FGE) is co-expressed with the sulfatase of interest in a human cell line, the enzyme can be produced in its most active form. This technology allows for the potential to produce lysosomal enzymes in large scale for development of ERTs for the treatment of LSDs that affect the CNS.