developing anti-HGT-1110 antibodies. Secondary endpoints include:

Primary endpoints are safety of IT HGT-1110 and include: adverse
ambulatory at screening, and no history of stem cell transplantation.

Key entry criteria include: diagnosis of MLD, symptoms at or before
used for cerebrospinal (IDDD) every other week for 38 weeks (20 injections). The IDDD is
30, 100 mg) of HGT-1110. Dosing is via an IT drug delivery device

multicenter, open label, dose escalation study of HGT-1110 in up to

nonclinical studies were conducted to support IT administra-
tion of HGT-1110. The program currently has an ongoing phase I/II

Enzyme replacement therapy (ERT) for GD patients in Brazil. Because these drug interruption in 2010, adult and pediatric GD patients started the treatment of taliglucerase alpha. Since that time, at least 31 adult and 13 pediatric patients have been in treatment. The use on pediatric patients was short duration, except in 1 patient with type III GD that is using weekly infusion for 11 months. In accordance with the severity of each case, patients have received doses of 20 U/kg to 60 U/kg. During the use of taliglucerase alpha, hematologic responses (hemoglobin and ferritin concentrations, and platelet counts) were monitored and compared with the mean for these parameters in the previous 6 months. In the group of 18 patients that are using taliglucerase alpha between 18 and 23 months the mean of platelet count is 186 U/kg (54 U/kg–377 U/kg) and the mean of hemoglobin level for female is 12.5 g/dl and for males is 14.9 g/dl. Patients were monitored closely for adverse events. Reports of adverse reactions were consistent with those described in the literature. Not one of the patients had bone crisis or increase of spleen or liver which were clinically significant on physical exam. The data collected, and observations made to date, suggest that taliglucerase alpha is a potentially promising new ERT for GD patients in Brazil.

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Experience with taliglucerase alpha in Brazil at The State Institute of Hematology of Rio de Janeiro Arthur Siqueira Cavalcanti (HEMORIO)

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Taliglucerase alpha is a plant cell-expressed beta-glucocerebrosidase enzyme replacement therapy (ERT) used for the treatment of Gaucher disease (GD). In 2009, the Imiglucerase shortage led to treatment interruptions and dose reductions in some of the patients receiving ERT in Brazil. Because these drug interruption in 2010, adult and pediatric GD patients started the treatment of taliglucerase alpha. Since that time, at least 31 adult and 13 pediatric patients have been in treatment. The use on pediatric patients was short duration, except in 1 patient with type III GD that is using weekly infusion for 11 months. In accordance with the severity of each case, patients have received doses of 20 U/kg to 60 U/kg. During the use of taliglucerase alpha, hematologic responses (hemoglobin and ferritin concentrations, and platelet counts) were monitored and compared with the mean for these parameters in the previous 6 months. In the group of 18 patients that are using taliglucerase alpha between 18 and 23 months the mean of platelet count is 186 U/kg (54 U/kg–377 U/kg) and the mean of hemoglobin level for female is 12.5 g/dl and for males is 14.9 g/dl. Patients were monitored closely for adverse events. Reports of adverse reactions were consistent with those described in the literature. Not one of the patients had bone crisis or increase of spleen or liver which were clinically significant on physical exam. The data collected, and observations made to date, suggest that taliglucerase alpha is a potentially promising new ERT for GD patients in Brazil.

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Development program for an intrathecally (IT) administered recombinant human arylsulfatase A in children with metachromatic leukodystrophy (MLD)

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Recombinant human arylsulfatase A (HGT-1110) is under development by Shire HGT as enzyme replacement therapy (ERT) for MLD. Nonclinical studies were conducted to support IT administration of HGT-1110. The program currently has an ongoing phase I/II multicenter, open label, dose escalation study of HGT-1110 in up to 18 children with MLD designed to evaluate the safety of 3 doses (10, 30, 100 mg) of HGT-1110. Dosing is via an IT drug delivery device (IDDD) every other week for 38 weeks (20 injections). The IDDD is used for cerebrospinal fluid (CSF) sampling and HGT-1110 injections. Key entry criteria include: diagnosis of MLD, symptoms at or before 30 months of age, presence of neurological signs of disease, patient ambulatory at screening, and no history of stem cell transplantation. Primary endpoints are safety of IT HGT-1110 and include: adverse events, clinical and CSF laboratory testing, and proportion of patients developing anti-HGT-1110 antibodies. Secondary endpoints include:

change in motor function using the Gross Motor Function Measure-88 (GMFM-88) scale and serum pharmacokinetics. The primary clinical assessment is change in GMFM-88 score at week 40. Exploratory objectives include: effect of HGT-1110 on nerve conduction velocities, somatosensory evoked potentials, swallowing examination, and on biomarkers such as CSF serum and urinary sulfatide and lysosulfatide, and proton MR spectroscopy-detected N-acetylaspartate metabolite levels. With no treatments currently available for this progressive, ultimately fatal disease, a clear medical need exists for a novel approach such as ERT.
