ArmaGen expands treatments for the brain in lysosomal enzyme disorders

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ArmaGen has re-engineered the human lysosomal enzyme, iduronate 2-sulfatase (IDS), as an IgG fusion protein. The IDS is fused to a genetically engineered monoclonal antibody (MAb) against the human insulin receptor (HIR). The HIRMAb acts as a molecular Trojan horse to ferry the IDS across the human blood-brain barrier (BBB) for the treatment of the brain in the lysosomal storage disorder called Mucopolysaccharidosis (MPS) Type II, or Hunter's syndrome. Another lysosomal storage disorder that affects the brain is MPS Type I, Hurler's syndrome, which is caused by a deficiency of the lysosomal enzyme, iduronidase (IDUA). Patients with Hunter's or Hurler's syndromes have serious brain involvement, which is refractory to conventional enzyme replacement therapy, because the recombinant enzyme does not cross the BBB, and cannot penetrate the brain from blood. Following re-engineering of the lysosomal enzyme as a fusion protein with the BBB Trojan horse IgG, the enzyme penetrates the brain, and retains high lysosomal enzyme activity (Biotechnology & Bioengineering). The HIRMAb-IDUA fusion protein exhibited an excellent safety profile in a dose-ranging study in primates (Journal of Biotechnology). The most recent work describing the HIRMAb-IDS fusion protein for treatment of the brain in MPS Type II is published in Bioconjugate Chemistry.