



A Novel Human Growth Hormone XTEN Construct (VRS-317) for Monthly Administration

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A recombinant human growth hormone [rhGH; somatotropin for injection] product with a monthly dosing interval, comparable efficacy and safety to daily rhGH, minimal injection site reactions, and room temperature stability may provide significant benefit to patients. The second generation extended half-life (XTEN) hGH product, VRS-317, consisting of rhGH with XTEN amino acid sequences genetically fused to the N terminus and the C terminus were produced in *E. coli*. The XTEN domain of VRS-317 is a non-immunogenic and biodegradable amino acid sequence. In rats, the new VRS-317 construct had an absorption phase after subcutaneous dosing of approximately 48 hr and the terminal half-life after intravenous dosing of 15 hr. In monkeys, the new VRS-317 construct had a slow absorption phase over several days and a 110 hr terminal half-life. A three-fold reduction in clearance was achieved for the new VRS-317 construct compared to the original VRS-317 construct, which should allow for monthly dosing. The new VRS-317 construct had equal or better potency compared to daily injections of rhGH, as measured by body weight gain in hypophysectomized rats. Studies are currently underway to determine whether there will be any injection site lipoatrophy in pigs and repeat dose immunogenicity in monkeys. VRS-317 may also be formulated to enable room temperature stability. VRS-317 may be dosed monthly and have a liquid room temperature stable formulation to provide optimal convenience, safety and efficacy for growth hormone deficient patients. Further development of this promising, long-acting rhGH product is planned.

International Congress of Endocrinology 2010

Session P13-1-5: Pediatric Endocrinology

13:10 – 14:20 Monday, March 29, 2010