PRELIMINARY RESULTS FROM A LONG-TERM REPEAT DOSAGE TOXICOLOGY AND TOXICOGENIC STUDY OF ANF-RHO™, A NOVEL ANTI-NEUTROPENIC FACTOR

Hemant Misra, PhD,1 Judith A Newmark, PhD,2 (1Prolong Pharmaceuticals, South Plainfield, NJ, 2Toxikon, Bedford, MA)

Methods: The study design used 288 rats, divided into 5 dosage groups: control, 100, 300, 1000 (high) and 1000 (positive) µg/kg. A total of 38 monkeys were also divided into 5 dosage groups: control, 75, 250, 750 (high dose) and 750 (positive) µg/kg of ANF-RHO™. Doses were administered by weekly subcutaneous injections on Day 1, 8, 15, 22, 29, 36, 43.

Results: Analysis, immunogenicity, gross necropsy, and histopathology. Genotoxicity assessments were evaluated using Salmonella typhimurium and Escherichia coli reverse mutation assay, rodent blood micronucleus assay, and chromosomal aberration assay. Toxicology assessment included clinical observations, body weight change, food consumption, ophthalmic examination, function observational battery (motor activity, behavioral changes, coordination and sensory/motor reflex response), organ weight, biophysical and biologic properties that produce a prolonged pharmacokinetic and pharmacodynamic profile as compared to pegfilgrastim. As such, it has potential applications in chemotherapy induced neutropenia and chronic idiopathic neutropenia. These disorders require prolonged administration of G-CSF agents to treat neutropenia. Therefore, long term toxicology, genotoxicity and Juvenile studies were conducted with ANF-RHO™.

Background: ANF-RHO™ is a novel polyethylene glycol-modified granulocyte colony stimulating factor that has biophysical and biological properties that produce a prolonged pharmacokinetic and pharmacodynamic profile as compared to pegfilgrastim (Neulasta®). As such, it has potential applications in chemotherapy induced neutropenia and chronic idiopathic neutropenia. These disorders require prolonged administration of G-CSF agents to treat neutropenia. Therefore, long term toxicology, genotoxicity and Juvenile studies were conducted with ANF-RHO™.

Aim: A 13-week study was conducted in Sprague Dawley rats and cynomolgus primates to assess various safety and pharmacokinetics of ANF-RHO™ as compared to Neulasta® (pegfilgrastim).

For More Information Please Contact: www.prolongpharma.com

Dosing Design for 3 Month Repeat Dose in Juvenile Rats

Results of 3 Month Repeat Dose in NHP

Immunogenicity for 3 Month Repeat Dose in NHP

Dosing Design for 3 Month Repeat Dose in Rats

Immunogenicity Analysis for 3 Month Repeat Dose in Rats

Dosing Design for 3 Month Repeat Dose in Juvenile Rats

Results of 3 Month Repeat Dose in Juvenile Rats

Genetic Toxikocity: Chromosomal Aberration

Conclusion

ANF-RHO™ is a granulocyte-stimulating factor that has a unique pharmacokinetic and pharmacodynamic profile as compared to pegfilgrastim. The current study was performed to provide support in indications which may require long term administration of ANF-RHO™. The results from this preliminary toxicology studies are unremarkable and consistent with those of an earlier 28-day study. Results from the 28-day rat neutropenia dosage model found that the blood pharmacodynamics parameters of ANF-RHO™ may be dosed at a significantly lower level as compared to pegfilgrastim, thereby potentially reducing side effects such as bone pain while mitigating severe neutropenia that follows chemotherapy. These long term 13-week toxicology studies provided evidence of safety sufficient to support advancement of ANF-RHO™ into Phase II clinical studies in chemotherapy-induced neutropenia and chronic idiopathic neutropenia in Europe, USA, and India.