**BACKGROUND**

Anti-Neutropenia Factor - Rho (ANF-RHO) is a new longer acting granulocyte-colony stimulating factor (G-CSF) consisting of a novel pegylated version of recombinant human G-CSF protein. ANF-RHO has distinct biophysical and biological properties that produce an improved pharmacokinetic (PK) and pharmacodynamic (PD) profile as compared to either filgrastim (Neupogen®) or PEGfilgrastim (Neulasta®). ANF-RHO is not a biosimilar drug product.

**OBJECTIVES**

A Phase 1 clinical study was conducted in healthy volunteers to assess safety and tolerability of ANF-RHO as well as its PK and PD profile.

**MATERIALS & METHODS**

The ANF-RHO cohort dosage levels ranged from 5 to 50 µg/kg and were compared against both active (PEGfilgrastim) and placebo (saline) comparators. Subcutaneous, single dose treatment with ANF-RHO in ascending doses or PEGfilgrastim at the standard of care (saline) comparators. Subcutaneous, single dose treatment with ANF-RHO were compared against both active (PEGfilgrastim) and placebo comparators. The ANF-RHO profile assesses safety and tolerability of ANF-RHO as well as its PK and PD profile as compared to either filgrastim (Neupogen®) or PEGfilgrastim (Neulasta®). The ANF-RHO has distinct biophysical and biological properties that produce an improved pharmacokinetic (PK) and pharmacodynamic (PD) profile as compared to either filgrastim (Neupogen®) or PEGfilgrastim (Neulasta®). ANF-RHO is not a biosimilar drug product.

**RESULTS**

Phase 1 clinical safety results were unremarkable, with no severe adverse events in any cohorts. The ANF-RHO PK/PD results in this Phase 1 study were similar to preclinical findings. PK and PD results were markedly prolonged in the ANF-RHO treatment groups even at the lowest dose. Mean ANC counts for all ANF-RHO treated subjects showed a peak ANC spike 6-7 days, in contrast to 1-2 days for PEGfilgrastim treated subjects (Graph 1a). The peak blood levels of ANF-RHO were significantly lower than PEGfilgrastim at all levels tested (Table 1). Moreover, assessment of the ANC - AUC revealed that ANF-RHO at 10 µg/kg was equivalent to PEGfilgrastim at 100 µg/kg, demonstrating an approximately 10-fold potency improvement over PEGfilgrastim in healthy volunteers, with a longer duration of effect of almost two weeks (Graph 1b). Peripheral blood CD34+ levels also yielded similar results (Graph 2a and 2b). ANF-RHO-induced neutrophil counts increased in a stable and prolonged manner following treatment, followed by a slow gradual decline, in contrast to PEGfilgrastim that showed a rapid ANC spike (2 days) and decrease to baseline within 7 days following it’s administration.

**SUMMARY**

Phase 1 clinical safety results were unremarkable, with no severe adverse events in any cohorts. The ANF-RHO PK/PD results in this Phase 1 study were similar to preclinical findings. PK and PD results were markedly prolonged in the ANF-RHO treatment groups even at the lowest dose. Mean ANC counts for all ANF-RHO treated subjects showed a peak ANC spike 6-7 days, in contrast to 1-2 days for PEGfilgrastim treated subjects (Graph 1a). The peak blood levels of ANF-RHO were significantly lower than PEGfilgrastim at all levels tested (Table 1). Moreover, assessment of the ANC - AUC revealed that ANF-RHO at 10 µg/kg was equivalent to PEGfilgrastim at 100 µg/kg, demonstrating an approximately 10-fold potency improvement over PEGfilgrastim in healthy volunteers, with a longer duration of effect of almost two weeks (Graph 1b). Peripheral blood CD34+ levels also yielded similar results (Graph 2a and 2b). ANF-RHO-induced neutrophil counts increased in a stable and prolonged manner following treatment, followed by a slow gradual decline, in contrast to PEGfilgrastim that showed a rapid ANC spike (2 days) and decrease to baseline within 7 days following it’s administration.

**CONCLUSIONS**

The unique PK/PD of ANF-RHO suggests that a significantly lower dosage may achieve sustained neutrophil levels sufficient to mitigate neutropenia - specifically during the high-risk 7-day period following dose-dense myelosuppressive chemotherapy. Additionally, the sustained and elevated CD34+ counts suggest ANF-RHO may also have applications in stem cell mobilization. The lower effective dosages would be anticipated to reduce the incidence of leukocytosis. Collectively, the increased potency and prolonged pharmacodynamics of ANF-RHO should provide more effective management of hematological malignancies when treating patients at high risk for neutropenia and difficult to mobilize patients or when performing dose-intensification in advanced stage cancer patients.