AAN 70th ANNUAL MEETING ABSTRACT

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Abstract Title: RG7916 significantly increases SMN Protein in SMA Type 1 Babies

Press Release Title: Preliminary Study Suggests Drug May Help Babies with Spinal Muscular Atrophy

Objective: Interim SMN protein data from FIREFISH Part 1 are presented for the first time. FIREFISH (NCT02913482) is a multi-center, open-label, seamless study of RG7916 (RO7034067) in babies aged 1–7 months with Type 1 spinal muscular atrophy (SMA) and two SMN2 gene copies.

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Background: SMA is a severe, progressive, inherited disease that leads to loss of motor function and is the leading genetic cause of mortality in infants and toddlers. SMA is caused by reduced levels of SMN protein due to deletions or mutations of the survival of motor neuron 1 (SMN1) gene and alternative splicing of a related SMN2 gene. The published median time to death or permanent ventilation in Type 1 patients with two SMN2 gene copies is 10.5 months of age (Finkel, Neurology 2014). RG7916 is an orally administered, centrally and peripherally distributed small molecule that modulates SMN2 pre-mRNA splicing to increase SMN protein.

Design/Methods: The exploratory Part 1 (n=8–24) of the FIREFISH study assesses safety, tolerability, pharmacokinetics and pharmacodynamics of RG7916 at different dose levels. The confirmatory Part 2 (n=40) will assess safety and efficacy of RG7916.

Results: A dose-dependent increase in SMN protein levels in blood was observed, with an up to 6.5 -fold increase versus baseline after 4 weeks of treatment at the highest dose of RG7916 (range 2.0 – 6.5). To date, no safety-related stopping rules have been met, and while follow up was limited, no patient lost the ability to swallow, required tracheostomy, or reached permanent ventilation. Updated survival data will be presented.

Conclusions: The up to 6.5-fold increase in SMN protein observed in FIREFISH Part 1 compares favorably with the approximately 2-fold difference in SMN protein levels between SMA severity types (e.g., Type 2 vs. Type 1). All doses explored so far have been well tolerated. FIREFISH is currently recruiting globally.

Study Supported By: F. Hoffmann-La Roche