

SMA Research Update – Providing Hope!

Currently, there are (7) active studies within Columbia University Medical Center:

A Two Part Seamless, Open-label, Multicenter Study to Investigate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics and Efficacy of RO7034067 in Infants With Type 1 Spinal Muscular Atrophy (Firefish)

Open-label, multi-center clinical study is to assess the safety, tolerability, pharmacokinetic, pharmacodynamics, and efficacy of RO7034067 in infants with Type 1 spinal muscular atrophy (SMA). The study consists of two parts, an exploratory dose finding part (Part 1) and a confirmatory part (Part 2) which will investigate RO7034067 for 24-months at the dose selected in Part 1.

Ages Eligible for Study:	1 Month to 7 Months (Child)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Inclusion Criteria:

- Clinical history, signs or symptoms attributable to Type 1 SMA with onset after 28 days but prior to the age of 3 months
- Gestational age of 37 to 42 weeks
- Confirmed diagnosis of 5q-autosomal recessive SMA
- Participant has two survival motor neuron 2 (SMN2) gene copies, as confirmed by central testing
- Body weight greater than or equal to (\geq) third percentile for age, using appropriate country-specific guidelines
- Receiving adequate nutrition and hydration (with or without gastrostomy) at the time of screening, in the opinion of the Investigator
- Adequately recovered from any acute illness at the time of screening and considered well-enough to participate in the opinion of the Investigator

Exclusion Criteria:

- Concomitant or previous participation in any investigational drug or device study within 90 days prior to screening or 5 half-lives, whichever is longer
- Concomitant or previous participation in a SMN2 targeting antisense oligonucleotide or SMN2 splicing modifier or gene therapy study
- Any history of cell therapy
- Hospitalization for pulmonary event within the last 2 months, or planned at the time of screening
- Presence of clinically relevant electrocardiogram (ECG) abnormalities before study drug administration
- Unstable gastrointestinal, renal, hepatic, endocrine or cardiovascular system diseases

- Participants requiring invasive ventilation or tracheostomy
- Participants requiring awake non-invasive ventilation or with awake hypoxemia (arterial oxygen saturation less than [$<$] 95 percent [%]) with or without ventilator support
- Participants with a history of respiratory failure or severe pneumonia, and have not fully recovered their pulmonary function at the time of screening
- Multiple or fixed contractures and/or hip subluxation or dislocation at birth
- Presence of non-SMA related concurrent syndromes or diseases
- Any major illness within one month before the screening examination or any febrile illness within one week prior to screening and up to first dose administration
- Any inhibitor of cytochrome P450 (CYP) 3A4 and/or any Organic Cation Transporter 2 (OCT-2) and multidrug and toxin extrusion (MATE) substrates taken within 2 weeks and/or any inducer of CYP3A4 taken within 4 weeks (or within 5-times the elimination half-life, whichever is longer) prior to dosing or participants (and the mother, if breastfeeding the infant) taking any nutrients known to modulate CYP3A activity and any known flavin containing monooxygenase (FMO) 1 or FMO3 inhibitors or substrates
- Prior use, anticipated need for hydroxychloroquine, vigabatrin, retigabine, or any other drug known to cause retinal toxicity during the study
- Recent history (less than 6 months) of ophthalmic disease that would interfere with the conduct of the study as assessed by an ophthalmologist

Estimated Enrollment: 48

Actual Study Start Date: December 23, 2016

Estimated Study Completion Date: July 7, 2020

Additional participating locations:

Domestic: Stanford University Medical Center (California)

International: UZ Gent (Belgium), UZ Leuven Gasthuisberg (Belgium), Hospital Arman Trousseau (France), Policlinico Agostino Gemelli; Dipartimento di Neurosichiatria Infantile (Italy), Fondazione IRCCS Istituto Neurologico "Carla Besta"; UO di Neurologia dello Sviluppo (Italy), Universitäts-Kinderspitalbeider Basel_Abteilung für Neuro-und Entwicklungspadiatrie (Switzerland), Hacettepe University (Turkey)

If you would like more information about this study please contact Claudia Chiriboga, MD, MPH or Luz Sanabria at ls2328@cumc.columbia.org

