

SMA Research Update – Providing Hope!

Ongoing Clinical Trials

ISIS 396443 - CS2: An Open-Label, Dose Escalation Study to Assess the Safety, Tolerability and Dose-Range Finding of Multiple Doses of ISIS 396443 Delivered Intrathecally to Patients with Spinal Muscular Atrophy.

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Isis Pharmaceuticals, Inc. is conducting a Phase 1/2a clinical study of ISIS-396443 (ISIS-SMNRx) in patients with Spinal Muscular Atrophy (SMA). ISIS-SMNRx is a drug that is designed to modulate the splicing of the SMN2 gene to significantly increase the production of functional SMN protein. In previously published results, researchers showed that ISIS-SMNRx produced sustained activity in mouse models of SMA and that adequate drug tissue concentrations were achieved in the spinal cord of non-human primates. The Phase 1/2a study of ISIS-SMNRx is a dose-escalation study designed to assess the safety, tolerability and pharmacokinetic profile (drug levels) of ISIS-SMNRx in patients with SMA. Approximately 24 children will be enrolled in the study - the study consists of 3 groups of patients with 8 patients in each group. In this study, ISIS-SMNRx will be administered by intrathecal delivery 2 or 3 times (into the cerebral spinal fluid) through an injection in the lower back into the fluid-filled space below the bottom of the spinal cord. The study will last for approximately 9 months.

To be considered for eligibility in the study, patients must:

- be between 2 and 15 years of age
- have genetic documentation of 5q SMA (homozygous gene deletion or mutation) and symptoms of SMA
- not be required to use ventilator support
- not be required to have a gastric feeding tube (where the majority of feeds are given by this route)
- not have been hospitalized for surgery or a pulmonary event within the past 2 months or planned during the study
- meet additional study-specific criteria

The study is being conducted in multiple centers within the United States. The Columbia University Medical Center is participating in the study to provide this opportunity to patients with SMA in the United States. If you would like more information about this study please contact Claudia Chiriboga, MD, MPH or Nicole Holuba LaMarca, DNP, MSN at **(212) 304-5205**.