Introduction
There is convincing evidence from the preclinical realm that the pharmacologic agent riluzole attenuates certain aspects of the secondary injury cascade leading to diminished neurological tissue destruction in animal SCI models. The safety and pharmacokinetic profile of riluzole have been studied in a multicenter pilot study in 36 patients. Efficacy of riluzole in acute human SCI has not been established.

Phase I/IIa Riluzole Trial
Primary Aim: To develop acute care safety and pharmacokinetic profiles of riluzole in patients who have sustained a traumatic spinal cord injury
Secondary Objectives: To conduct exploratory analyses of neurological outcomes for purposes of planning a subsequent Phase II b –Phase III randomized study of the efficiency of riluzole for the treatment of acute spinal cord injury

Phase III RCT
Subjects: A total of 351 patients with acute traumatic SCI will be randomized in a prospective doubleblind placebo-controlled trial involving up to 35 sites internationally.
Randomization will be 1:1 to riluzole 2 × 100mg daily for 24 hours followed by 2 × 50mg daily for the following 13 days after injury, or to the same regimen of placebo. Key inclusion criteria include: able to receive study drug within 12 hours of injury; ISNCSCI Impairment Scale Grade A, B or C; level of injury C4-C8 Key exclusion criteria include: injury from penetrating mechanism, significant concomitant head injury

Study Design
Primary outcome measure is change in ISNCSCI Total Motor Score between baseline and 180 days following enrollment.
Secondary outcome measures include ISNCSCI grade, ISNCSCI Sensory Scores, SCIM, SF-36v2, EQ-5D, GRASSP, Pain NRS.

Statistical Design
Sample size of 316 evaluable subjects will have 90% power to detect .37 Cohen’s d effect size (i.e. 9 difference in ISNCSCIMS). There is no published minimally significant difference for ISNCSCIMS.
The current effect estimate of 9 is arbitrarily set. Study uses adaptive sequential design that allows sample size change during the interim analysis.

Results
Demographics
Outcome Measures
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Conclusions
This is a Phase III study of riluzole in acute SCI.