RESCUE: A Randomized, Blinded, Placebo-controlled, Parallel Group Design to Determine the Safety of RNS60 in Large Vessel Occlusion Stroke Patients Undergoing Endovascular Thrombectomy

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INTRODUCTION

Although reperfusion therapies have improved stroke prognosis profoundly, there remains a need for neuroprotective therapy to enhance the brain's resilience to and recovery from a stroke. RNS60 is an experimental neuroprotective therapy that has shown significant promise in preclinical rodent and primate models of stroke.

In addition to its effect in preclinical models of stroke, RNS60 has demonstrated significant neuroprotective effects in traumatic brain injury (TBI). RNS60 has also shown significant neuroprotection in models of multiple chronic neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), Alzheimer's disease and Parkinson's disease with no significant sign of toxicity in the preclinical toxicological studies.

Clinically, RNS60 has been generally safe and well tolerated in Phase I and Phase II studies, both after IV infusion, inhalation, and a combination of the two routes of administration. In addition to a Phase I safety trial involving continuous IV infusion in healthy participants, these studies also include a Phase IIa study in relapsing remitting MS as well as two studies with prolonged IV and inhalation administration in ALS (an open label pilot study in 16 subjects with ALS and a Phase II study in 147 subjects with ALS). Moreover, RNS60 is being used to treat people with ALS in an ongoing expanded access protocol at Massachusetts General Hospital, and as of this date, RNS60 has been generally safe and well tolerated in this patient population.

RNS60 is an electrokinetically altered aqueous fluid. Chemically, RNS60 is composed of saline and oxygen. The promising preclinical efficacy makes RNS60 a candidate to be tested in stroke for neuroprotection.

STUDY DESIGN

- Multicenter, Phase II, placebo controlled, double-blind/blinded assessor, two-dose study to test RNS60 treatment in 100 participants with a large vessel occlusion and acute ischemic stroke who are eligible for endovascular revascularization.
- Participants receive a 48-h infusion of either 0.5 mL/kg/h RNS60, 1 mL/kg/h RNS60, or 1 mL/kg/h placebo (normal saline) starting prior to arterial access closure and are followed up for 90 days. Randomization is 1:1:1 with block urn randomization to balance age, NIHSS, and Alberta stroke program early CT score (ASPECTS).
- Imaging post-EVT occurs at ≤2 hours, 48 hours and Day 90.

KEY ENROLLMENT CRITERIA

INCLUSION

- ✓ NIHSS >5
- ✓ ASPECTS >4
- ✓ mRS ≤2
- ✓ Stroke onset <24 hours
- ✓ Age >18 years
- ✓ Selected for EVT

EXCLUSION

- ✗ MI within 6 months
- ✗ History of CHF
- ✗ Intracranial hemorrhage or mass lesion
- ✗ Renal impairment requiring dialysis
- ✗ Seizure at stroke onset
- ✗ Ischemic stroke within 30 days
- ✗ QTcF > 460ms at Screening

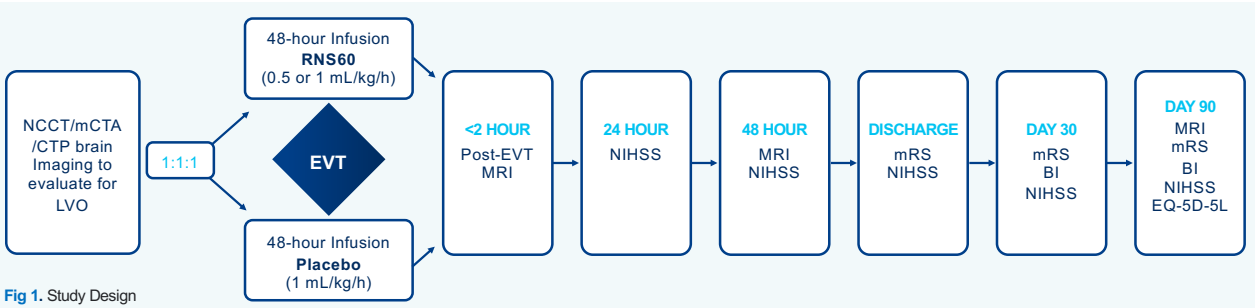

Fig 1. Study Design

OBJECTIVES

PRIMARY: Safety of RNS60 treatment in participants with a large vessel occlusion and acute ischemic stroke who are eligible for endovascular revascularization. Safety will be estimated by the proportion of participants with serious adverse events and the proportion of participants alive over 90 days.

SECONDARY: Changes in mean modified Rankin Scale (mRS) score, National Institutes of Health Stroke Scale (NIHSS), Barthel Index (BI), mortality rate, and the proportion of participants with a worsening of stroke over 90 days.

EXPLORATORY: Serial collection of imaging biomarkers (assessing changes in infarct size measured by MRI), plasma biomarkers, and assessment of quality of life measured by the EQ-5D-5L.

STUDY INFORMATION

- **LEAD INVESTIGATOR:** Ryan A. McTaggart, Rhode Island Hospital
- **SITE INVESTIGATORS:**
  Wayne Clark, Oregon Health Science University
  David Chiu, Houston Methodist
  Ruchir Shah, Chattanooga Center for Neurologic Research
  Christopher Favilla, Hospital at the University of Pennsylvania
  Tjoumakaris Stavropoula, Thomas Jefferson University
  Sameer Ansari, Northwestern University
  Sidney Starkman, University of California Los Angeles (pending activation)
- **PROTOCOL NUMBER:** 06.5.1.H1

STUDY STATUS

Enrollment is ongoing, the DSMB reviewed safety data twice and allowed continuing enrollment without any changes. The study aims to enroll a total of 100 participants by Q2 2023.

WANT TO LEARN MORE ABOUT RNS60?

Please email contact@revalesio.com for more information or visit www.revalesio.com.

STUDY WEBSITE: www.rescuestrokestudy.com