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 well tolerated in Phase I and Phase II studies, both after (intravenous) 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 shown excellent safety and tolerability.

RNS60 is an electrokinetically altered aqueous fluid. Chemically, RNS60 is composed of saline and oxygen. It is available for IV and inhalation (nebulization) administration. The exceptional safety and promising preclinical efficacy makes RNS60 an ideal candidate to be tested in stroke for neuroprotection.

STUDY DESIGN

RESCUE is a multicenter, Phase II, blinded assessor, two-dose study to test RNS60 treatment in 100 participants with a large vessel occlusion and acute ischemic stroke, NIHSS score > 5 and pre-stroke mRS score ≤ 2, who are eligible for endovascular revascularization. Randomized 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 done 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 > 450 ms at Screening

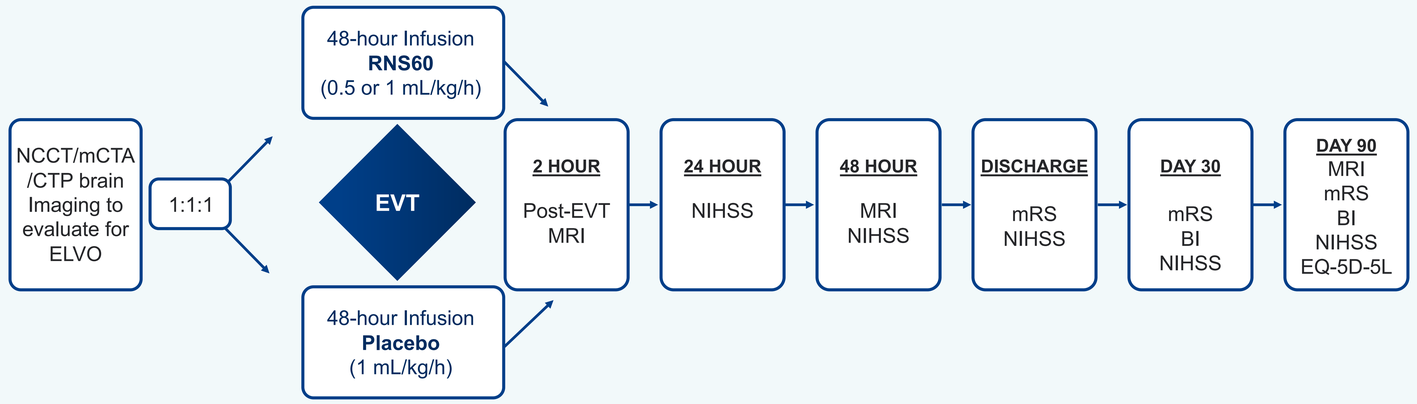

Fig 1. Study Design

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:** Dr. Ryan A. McTaggart, Rhode Island Hospital
- **PROTOCOL NUMBER:** 06.5.1.H1
- **STUDY WEBSITE:** www.rescuestrokestudy.com
- ClinicalTrials.gov **IDENTIFIER:** NCT04693715

STUDY STATUS

A total of six participants have been enrolled at Rhode Island Hospital, with other US sites expected to begin enrolling in February 2022. Selection of sites is ongoing. The study aims to enroll a total of 100 participants by the end of Q1 2023.

INTERESTED IN ENROLLING FOR RESCUE?

To be considered for selection as an enrolling investigator or site for the RESCUE study, please email contact@revalesio.com for more information.