Safety and Tolerability Study of ST-503 for Refractory Pain Due to Peripheral Neuropathy (Small Fiber Predominant, SFN)

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria 1. Signed and dated informed consent document indicating that the subject (or a legal representative) has been informed of all pertinent aspects of the study. 2. ≥ 18 years of age. 3. Diagnostic characterization of peripheral neuropathy (small fiber predominant) according to the Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities and Networks (ACTTION) criteria. a. Minimal large fiber polyneuropathy by clinical examination and by nerve conduction studies (NCS) during screening. NCS results may be based on unilateral assessment. However, bilateral SNAP responses must be within normal range for age and gender in the ulnar, radial, and sural nerves to enhance sensitivity of monitoring for DRG ganglionopathy post ST-503 dosing or sham procedure treatment. Only persons with normal SNAP responses may be enrolled. 4. An IENFD punch skin biopsy demonstrating reduction below the 5th percentile of sex and age-adjusted normal values must be performed and sent for IENFD evaluation at the Cutaneous Nerve Lab at University of Utah. 5. Medical record documentation that pain is refractory to 2 o 3 categories of first line medical therapy for at ≥ 6 months prior to screening. a. "Refractory to first line medical therapy" is defined as failure to have an average weekly pain score \< 5 after an adequate trial of two of three categories of first line medication treatments for neuropathic pain (tricyclic antidepressants, SNRI, or gabapentinoids). 6. Average PI-NRS score ≥ 5 over seven-day pain assessment interval. 1. Minimum acceptable PI-NRS reporting requirement for eligibility: Four of seven days with two daily PI-NRS scores (morning and afternoon) must be recorded with a single PI-NRS score (morning or afternoon) for the remaining three days. 2. Subjects will not be told at any time that the eligibility requirement is an average PI-NRS ≥ 5, to avoid biasing the pain intensity scoring during the screening and baseline periods. 7. Body mass index (BMI) ≥ 18.5 kg/m2 and ≤ 40 kg/m2 8. Agreement to limit alcohol consumption to not more than one 12 oz beer, 5 oz glass of wine, or 2 oz of liquor daily for a minimum of two months after the procedure. 9. Negative screening test for mycobacterium tuberculosis (MTB) within 1 year prior to consent. 10. Willing and able to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures. Exclusion Criteria 1. Serum sample positive for pre-existing anti-AAV9 antibodies per predefined cut point based on assay sensitivity. 2. Drug- and alcohol-related: 1. Persons using opioid analgesics for under 3 months or persons who are not on a stable dose of opioids; if on a stable dose, the dose may decrease over the course of the study but should not be increased. 2. History of known alcohol abuse, opioid analgesic abuse, or illicit drug abuse within 2 years of Screening. 3. Positive urine test for drugs of abuse (including opiates, benzodiazepines, amphetamines, cocaine, barbiturates, and phencyclidine) without prescription and investigator approval, at Screening and Day -1. 4. Use of cannabinoids is not permitted. 3. Persons with Fabry disease, fibromyalgia, peripheral neuropathies due to alcohol or drug toxicity, or diagnosed channelopathies (congenital insensitivity to pain, inherited erythromelalgia). 4. Corticosteroid-related: 1. Use of glucocorticoids except for topical or ophthalmic preparations within 6 weeks prior to screening visit 2. Hypersensitivity or contraindications to corticosteroid use including but not limited to clinically significant osteoporosis, uncontrolled hypertension, poorly controlled diabetes, uncontrolled hyperlipidemia, or hypercholesterolemia 5. Neurologic-related: 1. Subjects with severe pain conditions other than SFN which would interfere with clinical study assessments 2. Documented stroke or transient ischemic attack within 1 year prior to consent 3. History of poorly controlled epilepsy or recurrent unexplained blackouts 6. Procedure-related: 1. Contraindications to LP, general anesthesia or sedation 2. Any medical disorders that, in the opinion of the Investigator, could interfere with LP including but not limited to evidence for a pressure gradient between supratentorial and infratentorial compartments, Arnold-Chiari malformation, bleeding diathesis, clinically significant coagulopathy, thrombocytopenia, increased intracranial pressure, or spine disease or past surgical procedures involving the spine 7. Infectious disease-related: a. Active viral infection or bacterial infection including but not limited to the following: i. Active Hepatitis A, B, or C infection * Patients with previous, adequately resolved hepatitis A, B or C are eligible for the study * Patients with chronic hepatitis B or C are not eligible for the study b. A severe infection (e.g., pneumonia, septicemia, central nervous system infections \[e.g., meningitis, encephalitis\]) within 12 weeks prior to Screening c. Patients who receive COVID-19 vaccine or booster will have a waiting period of 4 weeks or more before they may be dosed with ST-503, so that the vaccine response does not interfere with the gene therapy and vice versa. They should not receive a COVID-19 vaccine or booster within 4 weeks after subjects have been dosed with ST-503. Subjects should not receive any live-attenuated vaccine, for any disease, 2 weeks before and 20 weeks after the ST-503 or sham procedure administration. 8. Endocrine-related: a. History or evidence of impaired glucose metabolism based on hemoglobin A1C level of ≥ 6.5% 9. Cardiac- and circulatory system-related: 1. History of unstable angina, myocardial infarction, or chronic heart failure within 1 year prior to consent 2. Clinically significant primary valvular heart disease and/or prosthetic cardiac valve 3. 12-lead ECG demonstrating QTcF (Fridericia's correction) \> 450 msec i. If QTcF exceeds 450 msec, the ECG should be repeated two more times and the average of the three QTcF values should be used to determine the subject's eligibility. The ECG can be repeated after the subject is supine for 10 minutes. A third ECG can be obtained after an additional 10 minutes while remaining supine. d. Presence of uncontrolled hypertension 10. Hepatic disease- and hepatotoxic medication-related: 1. Presence of clinically relevant liver disease 2. Hepatic dysfunction as indicated by one or more of the following: i. Albumin ≤ 3.5 g/dL ii. Total bilirubin \> 1.5 x ULN and direct bilirubin ≥ 0.5 mg/dL iii. ALP \> 2 x ULN iv. ALT or AST \> 1.5 x ULN c. Hepatotoxic medications should be avoided during the study period including acetaminophen exceeding 4 gm/day unless essential to patient's treatment, approved by investigator, and hepatic dysfunction is not identified d. Hepatotoxic supplement use during the study period 11. Hematologic-related: 1. Personal or family history of coagulopathy 2. Presence of condition or treatment associated with increased bleeding risk associated with LP 3. Hematocrit \< 35% (assigned male at birth) or \< 32% (assigned female at birth) 4. Absolute neutrophil count \< 2000 cells/µL 5. International normalized rate (INR) above normal range for lab at study site 6. Platelet count below laboratory lower limits of normal (LLN) 12. Renal-related: a. History of chronic renal disease or creatinine ≥ 1.5 mg/dL 13. Cancer-related: a. History of cancer, including B-cell cancers, within 5 years of Screening i. Exceptions to this exclusion are fully excised non-melanoma skin cancers, non-metastatic prostate cancer, and fully treated ductal carcinoma in situ of the breast, provided subject has been stable for at least 6 months 14. Allergy- and immunology-related: 1. History of severe allergic or anaphylactic reactions 2. History of hypersensitivity to any inactive ingredient of the IP or to corticosteroids 3. Chronic autoimmune disease that is being treated with immunosuppressants, including but not limited to corticosteroids 4. Previous autologous or allogeneic bone marrow transplant, peripheral stem cell transplant or solid organ transplantation 15. Previously received gene or cellular therapy 16. Participation in other interventional studies during the period of current study participation 17. Planned surgery within three months prior to consent or during the study 18. Any active legal action related to pain disorder 19. Any other reason that, in the opinion of the Site Investigator or the Study Medical Monitor, would render the subject unsuitable for participation in the study. A suicide risk of imminent risk of self-harm according to the C-SSRS is an exclusion criterion for the clinical study.

Conditions & Interventions

Interventions:

GENETIC: ST-503, PROCEDURE: Sham (No Treatment)

Conditions:

Chronic Neuropathic Pain

Keywords:

Small Fiber Neuropathy

More Information

Contact(s): Patient Advocacy - clinicaltrials@sangamo.com

Principal Investigator:
IRB
Number:
System ID: NCT06980948

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