# STATISTICAL ANALYSIS PLAN

**Official title: iSTAND: IVIG (Gamunex-C) Study of Treatment for Autoimmune Neuropathic Dysautonomia/Postural Tachycardia (POTS)**

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This study was powered to determine a difference between treatment groups for the COMPASS-31 change from baseline assuming the IVIG group would have a 15-point decrease and the Albumin group would have a 4-point decrease with a pooled standard deviation of 10.0. These estimates were based on reported changes in POTS patients treated with IVIG and accounted for an estimated 7% dropout rate. Based on these, sample sizes of 14 per group achieved 80% power to detect this difference (effect size of 1.1) using a two-sided two-sample t-test and assuming a significance level of 0.05.

After a six-week washout, subjects who completed the protocol were allowed to continue into a second treatment phase to receive the other treatment using an identical infusion schedule, with both participants and investigators remaining blinded to treatment assignment. This second phase treatment option was included in the protocol to improve recruitment but was not part of the primary study outcome. Data for phase 2 (which included 23 of 30 participants) was analyzed separately.

Data from all participants who began treatment were analyzed in an intention-to-treat analysis using Kruskal-Wallis test for COMPASS-31 score change (primary) and other non-parametric ordinal variables. Fisher exact tests were used for dichotomous variables such as symptomatic outcome (COMPASS-31 score improved/worsened by 20%). Summary statistics for continuous variables were reported with means and standard deviations if normally distributed, medians and interquartile range if non-normally distributed. Summary statistics for categorical variables were reported as counts and column percentages. Outcomes were evaluated both as “intention-to-treat” (ITT, including 28 evaluable participants) and “per-protocol” (including only the 27 who completed > 85% of study treatments per protocol).