

Title: Phase 1/2 Study of the Safety, Pharmacokinetics, and Microvascular Effect Of Titrating Doses of Intravenous GMI-1070, a Pan-Selectin Inhibitor, in Adults with Sickle Cell Disease

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Synopsis:

The primary objectives are to evaluate the:

- Safety of multiple intravenous (IV) doses of GMI-1070 in adults with Sickle Cell Disease (SCD).
- Pharmacokinetics (PK) of multiple IV doses of GMI-1070 in adults with SCD.
- Microvascular perfusion and blood flow before and after treatment with IV GMI-1070 in adults with SCD.
- Biomarkers of adhesion, inflammation, and downstream selectin effect in the blood before and after treatment with IV GMI-1070 in adults with SCD

This will be an open-label, dose titration study of IV GMI-1070 in adults with SCD. Subjects will receive IV GMI-1070 at dose levels based on findings in earlier human studies.

Titration for this study may be done either up or down and not necessarily in a step-wise fashion. At the beginning of the study, 4 subjects will be enrolled at Dose Level A. Subjects in Dose Level A will receive a 20 mg/kg loading dose of IV GMI-1070 followed by a single 10 mg/kg dose of IV GMI-1070. Thus, subjects will receive a total of 2 doses: 1 loading dose (20 mg/kg) in the morning at 0 hours, and 1 single dose (10 mg/kg) in the evening at 10 ± 1 hours.

After these first 4 patients have been treated, safety, PK, and blood flow data from this first group will be reviewed by the Investigator and the Medical Monitor. After this review, a decision will be made to do 1 of the following:

- Enroll 4 more subjects at this dose level (continue at Dose Level A), OR
- Enroll 4 subjects at the higher dose level (Dose Level B, 40 mg/kg loading dose followed by 20 mg/kg for 1 dose), OR
- Enroll 4 subjects at any of the 2 lower dose levels (Dose Level C, 10 mg/kg loading dose followed by 5 mg/kg for 1 dose; or Dose Level D, 5 mg/kg loading dose followed by 2.5 mg/kg for 1 dose).

Safety, PK, and blood flow data will be reviewed after completion of each group of 4 subjects. At that time a decision will be made to do 1 of the following:

- Enroll 4 more subjects at the current dose level OR,
- Evaluate titration options and enroll 4 subjects at any other dose level.

This process will continue until a total of 20 subjects have been treated with GMI-1070.