CARDIOVASCULAR TELEMETRY STUDY IN BEAGLE DOGS

**ANIMALS:** 4 Males, 4 Females

**STUDY DESIGN:**

<table>
<thead>
<tr>
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<th>Males</th>
<th>Females</th>
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<tbody>
<tr>
<td>Vehicle Control</td>
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<td>Low Dose</td>
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<td>Mid Dose</td>
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<td>High Dose</td>
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Animals will be treated and then allowed a one-week recovery period before the next dosing session. Each treatment will be conducted in the same eight animals.

**ANIMAL PREPARATION/SURGERY:** Animals will be acclimated to all experimental conditions prior to the initiation of testing. The dogs will be surgically implanted with a pressure transducer equipped telemetry transmitter. The transmitter assembly will be secured internally, the fluid-filled catheter will be placed into an appropriate artery, and ECG leads will be attached to the musculature to allow for collection of cardiovascular (hemodynamic and electrocardiographic) data.

**DOSing:** Test article will be administered by oral gavage. All animals will receive all doses of test article with a recovery period of approximately 1 week between each dosing session.

**CARDIOVASCULAR EVALUATIONS:** Cardiovascular evaluations at each dose of test article will be collected with animals allowed free movement in the home cage. The animals will be monitored continuously for 2 hours prior to, and 20 hours subsequent to, test article administration.

The following parameters will be monitored:
- Systolic, Diastolic and Mean Arterial Blood Pressures
- Heart Rate
- Electrocardiogram (RR, PR, QRS, QT, and QTc)
- Body Temperature

**ECG MORPHOLOGY:** Representative ECG tracings will be printed from the raw data record prior to dosing, at the expected or actual time of peak effect, and at the end of the cardiovascular monitoring period for each treatment. These traces will be reviewed by a board certified veterinary cardiologist who will perform a qualitative evaluation of the electrocardiograms.

**CARDIAC TROPONIN CONCENTRATIONS:** Blood samples will be collected within 2 hours of the end-of-monitoring period after the vehicle and high dose test article administrations for determination of cardiac troponin concentration. Concentrations of cardiac troponin I (cTpn I) will be measured.

**CLINICAL OBSERVATIONS:** Predose, at the expected or actual time of peak effect, and following the completion of the postdose monitoring period

**BODY WEIGHTS:** Prior to each dose

**ANALYTICAL CHEMISTRY:** Standard sample collections performed to support dose formulation analysis.

To receive information about this study, please contact Dr. Jill Dalton at Jill.Dalton@mpiresearch.com or call 1-269-668-3336, ext. 1461.
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STATISTICAL ANALYSIS: Descriptive statistics
FINAL REPORT: Standard GLP compliant report for regulatory submission

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