

**A Double-Blind, Placebo-Controlled Study Evaluating the Pharmacodynamic Effects of Two Fixed Doses of XXXXX (XXmg bid and XXmg bid) on Hypothalamic-Pituitary-Adrenal Axis Function in Patients with Major Depressive Disorder**

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**Key Elements:**

- Inpatient
- Complex Infusion Study

**Indication:** Major Depressive Disorder

**Start Date:** May, 2007

**# of Subjects:** 18 Randomized; 16 completed; 40% of study total

**In-patient Period:** 8 days

**Objectives**

**Primary**

To evaluate the effects of two fixed doses of XXXXX (XXmg bid and XXmg bid) on hypothalamic-pituitary-adrenal axis function in patients with major depressive disorder

**Secondary**

Tolerability and safety

Efficacy of two fixed doses of XXXXX compared to placebo

To evaluate plasma concentrations of XXXXX

**Ratings**

HAM-D total, depressed mood, factor, and core items scores: Screen, D-1, D7, D14, D28, f/u

Clinical Global Impression (CGI) Severity and Improvement scores: Screen, D-1, D7, D14, D28, f/u

Diurnal symptoms questionnaire: D-1, D1, D7, D14, D25, D26, D27, D28

**Pharmacodynamics**

Plasma adrenocorticotrophic hormone (ACTH) and cortisol levels before and after corticotropin releasing factor (CRF) administration:

D-2 at 15:00, 15:30, 15:45, 16:00, 16:05, 16:15, 16:30, 17:00, 17:30, 18:00 and D27 at 15:00, 15:30, 15:45, 16:00, 16:05, 16:15, 16:30, 17:00, 17:30, 18:00

**Pharmacokinetics**

Blood samples for determination of plasma XXXXX concentrations:

- D7 and D28
- D-1, D7, D28: 5 minutes after ECG and at 8:00, 9:00, 10:00, and 12:00

**Safety**

**Physical examinations:** screen and D28

**Vital signs (including weight):** screen, D-4, D-3, D-2, D-1, D7, D14, D25, D27, D28, D35

**12-lead electrocardiograms (ECG):** screen, D-1, D7, D28 5 minutes prior to PK, and at 8:00, 9:00, 10:00, and 12:00

**24-hour Holter monitor:** from 8:00am on D-3 to 8:00am on D-2 and from 8:00am on D26 to 8:00am on D27

**24-hour urine collection:** from 4pm on D-4 to 4pm on D-3 and D-3 to D-2, D25 to D26, D26 to 27

**Clinical laboratories:** screen, D-7 D7, D28

**Hormone profiles:** D-3, D7, D26, D35

**Adrenal function checklist:** screen, D7, D14, D25, f/u

**Withdrawal symptoms questionnaire:** D28