



## **Manhattan Pharmaceuticals Expanding Oral Oleoyl-Estrone Clinical Program To Include Morbidly Obese**

NEW YORK, NY OCT 12, 2006 - Manhattan Pharmaceuticals, Inc. (AMEX: MHA) today announced expansion of its oral Oleoyl-estrone (OE) clinical obesity program to include the morbidly obese. A new US Phase 2a clinical trial evaluating oral OE in morbidly obese male subjects will be initiated in October 2006. The morbidly obese population in the US is estimated to be 14 million people. OE is the Company's orally administered product candidate in development for the treatment of obesity.

This single-center, Phase 2a randomized, double-blind, placebo-controlled, parallel group study will be conducted at St. Luke's-Roosevelt Hospital Center, University Hospital of Columbia University College of Physicians and Surgeons. F. Xavier Pi-Sunyer, MD, will serve as Principal Investigator. Approximately 24 morbidly obese male subjects with a body mass index (BMI) of 40-55 will be randomized into three treatment groups to evaluate the safety and efficacy of 10mg or 30mg of oral OE compared to placebo given once daily for 30 days. Subjects will be evaluated at Days 1, 15, and 30. A final follow-up visit will also occur at Day 60, 30 days after the final dose.

Morbidly obese males are considered to be the most at risk segment of the obese population. Published studies have indicated that morbidly obese males have a mortality rate higher than the general, non-obese population and a higher mortality rate than morbidly obese women. Morbidly obese males are also at significantly higher risk for other life threatening conditions including cardiovascular disease, coronary heart disease, and unexplained cardiac arrest.

This new clinical study will be conducted in parallel with Manhattan Pharmaceuticals' currently ongoing, Swiss Phase 2a study, designed to evaluate the safety, preliminary efficacy and pharmacokinetics of two, 14-day cycles of escalating oral doses of OE in both male and female obese adult subjects with BMIs of less than 40. "This new study marks significant progress in the clinical advancement of OE for the treatment of obesity, and allows us to gather meaningful data in another distinct, high risk, patient population, the morbidly obese" said Alan G. Harris, MD, PhD, Manhattan's chief medical officer.

OE is an orally administered, synthetic form of oleoyl-estrone, a molecule that exists naturally in the body. As shown in animal studies, it is believed to work by a dual mechanism of action. Centrally, OE appears to act at the hypothalamus, resetting the body's ponderostat, the "food control center" in the brain that detects and integrates signals that control both appetite and metabolic behavior. Peripherally, OE also causes reduced storage of fat in "white fat" tissue and allows skeletal muscle to use fat as an alternate energy source.

### **About Morbid Obesity**

Morbid obesity (also referred to as clinically severe obesity or extreme obesity) is defined as having a BMI of 40 or more. According to the American Obesity Association, the morbidity and mortality risk from being overweight is proportional to its degree. Individuals with morbid obesity, therefore, have the highest risk for developing numerous illnesses that often reduce mobility and quality of life due to their excess weight. In particular, cardiovascular disease, type 2 diabetes, gallbladder disease, osteoarthritis and sleep apnea have been found to increase concurrently with higher BMI. Premature death has also been found in individuals with morbid obesity. The last published figures from the US Centers for Disease Control and Prevention indicate the morbid obese population in the US is estimated to be 14 million people (or 4.7% of the US population).

### **About F. Xavier Pi-Sunyer, MD**

F. Xavier Pi-Sunyer, MD, MPH is Professor of Medicine at Columbia University College of Physicians and Surgeons and Professor of Applied Physiology at Columbia Teachers College, both in New York City. At St. Luke's-Roosevelt Hospital Center he serves as Chief of Endocrinology, Diabetes, and Nutrition, and is Director of the New York Obesity Research Center. Dr. Pi-Sunyer is also a Senior Attending Physician at St. Luke's-Roosevelt Hospital and New York-Presbyterian Hospital.

### **About Manhattan Pharmaceuticals, Inc.**

Manhattan Pharmaceuticals, Inc., a development-stage pharmaceutical company, acquires and develops proprietary prescription drugs for large, underserved patient populations. In view of the worldwide obesity epidemic, the company is developing OE, an orally administered novel therapeutic for the treatment of obesity. To meet the needs of other major, underserved medical markets Manhattan Pharmaceuticals is also developing PTH (1-34), a peptide believed to be a regulator of epidermal cell growth, for the treatment of psoriasis, and Propofol Lingual Spray, a convenient, proprietary lingual spray formulation of propofol, the world's best-selling general anesthetic, as a sedative-hypnotic for use during diagnostic and therapeutic procedures. (<http://www.manhattanpharma.com>)