Manhattan Pharmaceuticals Initiates Patient Dosing in Phase Ib Oleoyl Estrone Clinical Trial

Company concludes Phase Ia trial for obesity therapeutic candidate and begins results analysis

NEW YORK--(BUSINESS WIRE)- May 4, 2005-- Manhattan Pharmaceuticals, Inc. ("Manhattan" OTCBB: MHTT), has concluded its Phase Ia trial and begun patient dosing in the Phase Ib trial to evaluate the safety and tolerability of defined doses of orally administered Oleoyl estrone (OE) in obese adults. Like the Phase Ia trial, the Phase Ib trial will be conducted in Basel, Switzerland under Swiss Medic Approval.

The Phase Ia trial, conducted with the approval of the U.S. Food & Drug Administration (FDA) and SwissMedic, the Swiss regulatory authority, was a single-dose, dose-escalation trial that evaluated six cohorts of six patients, randomized 2:1 study drug to placebo. Manhattan is currently reviewing and analyzing the results of the trial, which will ultimately be used to obtain approval to move forward with Phase II studies.

The recently commenced Phase Ib trial is a repeat-dose, dose-escalation trial that will evaluate four cohorts of six patients each, randomized 2:1 study drug to placebo. Results from this study will also be used, in conjunction with extensive preclinical work, to establish the protocol and obtain approval from the US FDA to begin Phase II clinical trials.

"We are pleased that OE's clinical development is proceeding according to our anticipated timeline," said Douglas Abel, CEO of Manhattan Pharmaceuticals. "This Phase I trial will provide needed additional information about OE's tolerability and move us closer to securing the approvals necessary to bring this treatment to a patient population clearly in need of an alternative to the current therapeutics."

Oleoyl estrone - Targeting the Obesity Epidemic
Oleoyl estrone is believed to be a signaling molecule that acts on the hypothalamus to communicate satiety. It is hypothesized that, in healthy individuals, levels of naturally occurring OE are related to the size of the body's fat stores, while in obese individuals circulating OE levels are lower than would be expected for the level of body fat. Orally administered formulations of OE has demonstrated, in extensive preclinical animal studies, to cause significant weight loss and reduced caloric consumption without the need for dietary modifications. In such studies, OE appears to be safe and effective without side effects or evidence of rebound weight gain after treatment was stopped. The Company believes that OE may prove to be a safe and effective treatment for obesity, representing a significant advantage over currently available anti-obesity medications.

Manhattan believes OE could help address the obesity epidemic - one of the world's top health concerns. Nearly two-thirds of the U.S. adult population is estimated to be overweight and at least half of these are clinically obese. Though there are currently two FDA approved therapeutics on the market for the long-term treatment of obesity, market penetration remains low, possibly as a result of the modest efficacy (an average of 8-10% weight loss in the first year), and side effects reported with use of these treatment options.

Manhattan has reported favorable, peer-reviewed preclinical safety and pharmacokinetic data regarding OE at the 2004 annual meetings of the European Congress on Obesity, and the North American Association for the Study of Obesity.

About Manhattan Pharmaceuticals, Inc.
Manhattan Pharmaceuticals, Inc. (http://www.manhattanpharma.com/), 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 Oleoyl estrone, an orally administered novel therapeutic for weight loss. To meet the needs of other major, underserved medical markets while lowering development risks, Manhattan Pharmaceuticals also developing PTH (1-34), a peptide believed to be a regulator of epidermal cell growth, under development for psoriasis and other dermatological conditions and Propofol Lingual Spray, a convenient, proprietary lingual spray formulation of propofol, the world's best-selling general anaesthetic, as a sedative-hypnotic for use during diagnostic and therapeutic procedures.