

## Study Provides New Information on Efficacy of Manhattan Pharmaceuticals' Obesity Treatment Candidate

### European Journal of Pharmacology Publishes Results of Animal Studies Showing OE Induces Significant Weight Loss Alone and in Combination Treatments

New York NY, May 25, 2005 -Oleoyl-estrone (OE), the lead product candidate of Manhattan Pharmaceuticals, Inc. (OTC BB: MHTT, "Manhattan"), demonstrated efficacy in inducing significant weight loss in a preclinical pharmacology study when administered alone and in combination with other obesity treatments. Findings of the study, conducted by Professor Maria Alemany from the University of Barcelona and lead research scientists on OE were published in a paper entitled, "Effects of Oleoyl-estrone with Dexfenfluramine, Sibutramine or Phentermine on Overweight Rats," in the April 2005 issue of the European Journal of Pharmacology.

For the study, 8 groups of 6 male wistar rats were dosed with Oleoyl-estrone, dexfenfluramine, sibutramine, or phentermine alone; Oleoyl-estrone in combination with dexfenfluramine, sibutramine, or phentermine; or a placebo, for 10 days. Food intake, weight loss, levels of insulin, cholesterol and triacylglycerol were measured on a daily basis.

Key findings of the study include:

- Rats dosed with Oleoyl-estrone showed lower levels of triacylglycerol, cholesterol, and insulin together with a lower homeostasis model assessment (HOMA) score.
- Weight loss was maximal when Oleoyl-estrone was combined with sibutramine and dexfenfluramine, with losses of 1% and 1.1% per day respectively.
- Oleoyl-estrone combined with sibutramine resulted in the highest lipid loss of all the groups - 29% over 10 days, without dietary constraints.
- Food intake decreased across all groups, except those animals treated with phentermine.

"The results of this study are an important contribution to the already robust collection of preclinical data on OE," said Douglas Abel, CEO of Manhattan Pharmaceuticals. "It reinforces OE's viability as a potential alternative to currently approved obesity treatments and suggests a role for OE in the treatment of The Metabolic Syndrome, the cluster of metabolic abnormalities associated with an increased risk of diabetes and cardiovascular disease in adults."

#### 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 have demonstrated, in extensive preclinical animal studies, to cause significant weight loss and reduce 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 treatments 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 anesthetic, as a sedative-hypnotic for use during diagnostic and therapeutic procedures.

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