MANHATTAN PHARMACEUTICALS PRESENTS PRELIMINARY PHASE I RESULTS OF EXPERIMENTAL OBESITY DRUG

NEW YORK, NY October 17, 2005 - Manhattan Pharmaceuticals, Inc. (AMEX: MHA) announced preliminary results from two Phase I clinical trials of oleoyl-estrone (OE), an experimental, orally administered small molecule in development for the treatment of obesity. The data were presented in a poster yesterday at the 2005 Annual Scientific Meeting of NAASO, The Obesity Society, in Vancouver, BC.

The Phase I study, conducted in Switzerland, was done in two parts which consisted of a single dose study and a seven day repeat dose study. The primary purpose was to assess the safety, tolerability and pharmacokinetics of OE. Some efficacy parameters were included and measured in the repeat dose component of the study.

Highlights of the study included:

- OE was generally well tolerated at all doses investigated.
- OE demonstrated evidence of reduction in weight.
- OE demonstrated evidence of: reduction in desire to eat and hunger level, reduction in prospective food consumption, reduced fasting glucose, reduced LDL cholesterol and changes in other key measures.
- There were no clinically significant changes in the physical exams, vital signs, ECGs, coagulation or liver function tests.
- No serious adverse events were reported. Clinical laboratory findings included reversible, dose-dependent elevations in estrone and estradiol levels as well as reductions in testosterone levels.

Phase Ia was a dose-escalating study to measure OE's pharmacokinetic profile, safety and tolerability in 36 obese males and females ages 18-65, with a body mass index greater than 30.0 (a BMI of greater than 30.0 is classified as obese per guidelines from the U.S. Department of Health and Human Services). Twelve of the subjects received placebo and 24 received a single dose of OE in one of six doses ranging from 1mg to 150mg.

Phase Ib measured OE's safety and tolerability in 24 obese volunteers in four cohorts of six patients each who received either placebo or OE in doses ranging from 10mg to 150mg once daily for seven consecutive days. The protocol provided that subjects should maintain their normal diet and level of activity, but required that subjects abstain from consuming alcohol.

The OE-treated groups in the Phase Ib study demonstrated evidence of greater weight loss than the placebo group. Weights were assessed at baseline, Day 15, and Day 28. Weight loss appeared to be maintained for longer periods in the OE groups compared to placebo at Day 28, twenty-one days following cessation of treatment. This data may support the contention that the mechanism of action of OE involves a "resetting" of the ponderostat, or appetite "set point". It also provides a rationale for testing alternative regimens such as low or intermittent dosing.

Average change from baseline weight (in kilograms)

	Placebo	10mg	30mg	100mg	150mg
Day 15 (8 days following final dose)	-0.90 (n=8)	-0.75 (n=4)	-0.18 (n=4)	-1.95 (n=4)	-1.17 (n=4)
Day 28 (21 days following final dose)	0.00 (n=6)	not measured	-0.53 (n=4)	-1.35 (n=4)	-0.18 (n=4)

The OE-treated groups in the Phase Ib study also demonstrated evidence of a reduction in the feeling of desire to eat, hunger level and prospective food consumption as measured by changes in the visual analogue scales (VAS).

Average percent change in VAS scores as measured day 7 vs. baseline

	Placebo	10mg	30mg	100mg	150mg
1. How strong is your desire to eat right now?	+6.6%	+136%	-45.67%	-40.5%	-46.2%
2. How hungry do you feel right now?	-9.4%	+22%	-41.7%	-25.8%	-43.5%
3. How much food could you eat right now?	+2.9%	+61.2%	-42.1%	-39.7%	-37.5%
4. How full do you feel right now?*	+3.07%	-13.2%	+19.2%	-11.1%	+48.3%

* Note: In items 1, 2 and 3 increasing VAS scores indicate an increase in desire to eat. In item 4 an increase in VAS score indicates an increase in fullness.
')">Read a more detailed explanation of VAS here

OE was generally well tolerated. The most common side effects reported included headache, back pain, and diarrhea. No serious adverse events were reported.

Total mean cholesterol decreased at Day 7 at the 100mg and 150mg dose. Mean HDL-cholesterol increased and mean LDL-cholesterol decreased with a trend toward improvement in the LDL-to-HDL cholesterol ratio, even at the lower doses. Mean glucose concentration decreased in a reversible and dose dependent manner and remained decreased at Day 15. Mean estradiol and estrone levels were elevated, while mean testosterone levels were suppressed, all in a reversible and dose dependent manner. In addition, there were no clinically significant changes in the physical exams, vital signs, ECG's, coagulation or liver function tests.

The preliminary plasma concentration-time profiles show that the plasma concentration of OE did not increase with the administered dose level. There were no significantly elevated plasma concentrations of OE on Day 7 which may indicate that there is no clear accumulation in plasma after daily oral dosing for seven consecutive days. In this small sample study there were no clear differences between the sexes with respect to plasma concentration.

"Given the current crisis that we face with the growing prevalence of obesity, I am encouraged to see signs of efficacy in this study, though the metabolic and hormonal effects merit further study. Obesity and its complications, particularly type 2 diabetes, are rapidly becoming the number one health threat around the globe. Oleoyl-estrone may provide a new treatment option," said J. Larry Jameson, M.D., a leading endocrinologist who is Professor and Chairman of Medicine at Northwestern University Medical School.

"We are excited to have seen this much evidence of benefit in a phase I trial with only 7 days of exposure" said Doug Abel, President and CEO of Manhattan Pharmaceuticals. "We are working closely with our scientific and clinical advisors to interpret this data and finalize study designs. We plan to initiate a phase IIa trial early next year."

The full scientific poster of these results can be viewed on the company's website at www.manhattanpharma.com

ABOUT OLEOYL-ESTRONE
Oleoyl-estrone (OE) is an orally administered small molecule that has been shown to cause significant weight loss in extensive preclinical animal studies, without the need for dietary modifications. Developed by researchers at the University of Barcelona, OE has been tested in both obese and lean rats; treatment with OE resulted in significant weight loss even in the presence of abundant food and water. We believe that OE may prove to be a safe and effective treatment of obesity, potentially representing a significant advantage over currently available anti-obesity medications.

ABOUT OBESITY
Obesity is one of the most common metabolic disorders in the world. Nearly 61% of all Americans are considered to be overweight, and 26% percent are considered to be obese. The World Bank estimates that obesity alone accounts for more than 12% of the U.S. national health care budget. The National Institutes of Health estimated that direct costs for the treatment of obesity in 1988 were in excess of $45 billion and accounted for nearly 8% of the total national cost of health care; a decade later, annual direct costs for the treatment of obesity had risen to $102.2 billion dollars. As these statistics illustrate, obesity is a rapidly growing, costly disease, for which there is currently no effective treatment.

About Manhattan Pharmaceuticals, Inc.
Manhattan Pharmaceuticals, Inc. (AMEX: MHA), 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 weight loss. To meet the needs of other major, underserved medical markets while lowering development risks, Manhattan Pharmaceuticals is also developing PTH (1-34), a peptide believed to be a regulator of epidermal cell growth, for 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)

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