



Metabolex, Inc.
3876 Bay Center Place
Hayward, CA 94545 USA
Tel 510 293-8800
Fax 510 293.9090

Contact:

Mark Bagnall
Chief Business Officer
(510) 293-8800

For Media:

Joan Kureczka (415) 821-2413
Kureczka/Martin Associates
Jkureczka@aol.com

FOR IMMEDIATE RELEASE

**Metabolex Announces Start of Phase 2 Trial of its
Novel Insulin Sensitizer, MBX-102**

Drug Well-tolerated in Phase 1 Study; G.I. Toxicity of Halofenate Not Seen

HAYWARD, CA (March 2, 2004): Metabolex, Inc. today announced the start of its Phase 2 study of its investigational insulin sensitizer, MBX-102. The double-blind, placebo-controlled study will enroll approximately 200 patients with type 2 diabetes who are currently on insulin, but whose fasting blood-glucose levels are not well controlled. Researchers at 29 centers throughout the United States and Mexico will participate in the study, which is expected to complete in early 2005.

Sherwyn Schwartz, MD, a noted diabetes researcher and the Director of the Diabetes & Glandular Disease Clinic in San Antonio, Texas enrolled the first patient in the study. "I am very excited about participating in the MBX-102 clinical development program," commented Dr. Schwartz. "Insulin sensitizers are an extraordinarily important addition to the management of Type 2 diabetes, as they get right to the root of the problem in these patients, namely insulin resistance."

MBX-102 is a potential best-in-class insulin sensitizer for the treatment of type 2 diabetes, and is a single optical form (enantiomer) of halofenate, a compound studied in the 1970's as a lipid-lowering agent. "In Phase 3 studies, MBX-102's parent compound, halofenate, serendipitously demonstrated significant glucose-lowering activity in people with type 2 diabetes," said Harold Van Wart, Ph.D., president and chief executive officer of Metabolex. "Importantly, halofenate did not cause the troublesome weight gain and edema observed with currently marketed insulin sensitizers."

Dr. Schwartz added, "The currently marketed insulin sensitizers, while very effective, are unfortunately associated with a few notable side-effects, such as weight gain, which bothers the patients the most, and edema that can precipitate congestive heart failure, which is of most concern to us physicians. Having a sensitizer that lowers blood glucose and lipids but which causes little-or-no weight gain and edema would be a very substantial advance in our management of the rising diabetes epidemic."

Dr. Van Wart continued, "Halofenate's sponsor at the time dropped further development of this drug because it exhibited gastrointestinal (GI) side effects. Metabolex scientists discovered that halofenate is an inhibitor of cyclooxygenase-1 (Cox-1), similar to common NSAIDs like Motrin™ or Naprosyn™, accounting for its GI side effects. MBX-102 is a single enantiomer of halofenate that retains the desirable glucose and lipid-lowering activity of the parent drug, while lacking the Cox-1 inhibition, which was contributed by the other enantiomer. Our Phase 1 study was designed to demonstrate that by removing one of the enantiomers of halofenate, we could eliminate the GI side effects. We used upper GI endoscopy to confirm that MBX-102 does not cause GI toxicity in humans, which was the major hurdle to MBX-102's successful clinical development."

Dr. Van Wart noted that over the next 12 –15 months, Metabolex hopes to confirm with MBX-102 the excellent glucose and lipid lowering and lack of edema and weight gain seen in the earlier studies of halofenate. If successful, the company plans to partner MBX-102 for Phase 3 development and commercialization.

Results of the Phase 1 MBX-102 Study

Investigators conducted a 10-day, multiple ascending dose study of MBX-102 in 71 patients using doses of up to 1000 mg/day compared to both a placebo-control (24 patients) and a positive-control (Naproxen) (23 patients) group. Trial participants underwent upper GI endoscopies at the 400, 600, 800 and 1000 mg dose levels to study the effects of MBX-102 treatment on the GI mucosa. Results of the study showed good, dose-proportional pharmacokinetics for MBX-102, and study subjects tolerated the drug well. Moreover, there was no significant GI toxicity observed in MBX-102-treated individuals or in patients on placebo, while signs of such toxicity were significant in those subjects receiving the positive control drug.

The study investigator, Dr. Frank Lanza, Clinical Professor of Medicine, Section of Gastroenterology, Baylor College of Medicine and Director of the Houston Institute for Clinical Research concluded, "MBX-102 appears to be a very safe product with respect to upper gastrointestinal mucosal injury."

About Insulin Sensitizers

Insulin sensitizers, the newest class of drugs to treat type 2 diabetes, work to reverse insulin resistance – a defect in which the glucose-utilizing tissues fail to take up that sugar appropriately. As such, insulin sensitizers work to help the body make better use of its own insulin. While the first two insulin sensitizers to achieve commercialization command sales of over \$1 billion per year each, they have two serious side effects. The first is an increase in fat cell mass, leading to weight gain – itself a major risk factor for diabetes. The second is fluid retention, leading to edema and an increased risk of congestive heart failure.

Clinical trials of MBX-102's parent compound produced no reports of edema and only modest weight gain in patients treated with the drug, as well as comparable glucose lowering activity and superior lipid lowering activity compared to marketed insulin sensitizers. Moreover, preclinical studies support a superior side effect and similar activity profile for MBX-102, suggesting MBX-102's potential as a best-in-class insulin sensitizer.

About Metabolex

Metabolex, Inc. is a privately held pharmaceutical company dedicated to the discovery and development of drugs to treat diabetes and related metabolic disorders. The company's lead compound, MBX-102, is a novel insulin sensitizer in Phase 2 clinical development. Metabolex has also built a portfolio of other potential diabetes therapeutics, which includes a product candidate in preclinical development plus several programs optimizing lead drug candidates. Additionally, Metabolex has two target discovery programs that have produced one of the world's largest databases of diabetes-expressed genes. One of these programs, in insulin secretion, is partnered with Pfizer. The other, in insulin resistance, is partnered with Yamanouchi Pharmaceuticals Co. Ltd.

###