



Contact: Leonard Borrmann
President & CEO
Insert Therapeutics, Inc.
lbormann@insertt.com
626.683.7200

Marty Tullio
Investor Relation Resources
Marty@investorRR.com
949.566.9860

FOR IMMEDIATE RELEASE

**INSERT THERAPEUTICS, INC. REPORTS *IN VIVO* PERFORMANCE
OF CYCLOSERTM-CAMPTOTHECIN ANTI-CANCER FORMULATION**

Preclinical results demonstrate CyclosertTM formulation is more effective at preventing tumor progression than irinotecan

PASADENA, CA – April 1, 2003 – **Insert Therapeutics, Inc.**, a drug delivery and product-focused development company has reported preclinical data demonstrating that the company's patented CyclosertTM drug delivery technology can be used to systemically deliver camptothecin, a potent, anti-cancer agent, to tumors in a human tumor xenograft study in mice resulting in superior anti-tumor activity when compared to camptothecin alone, and to the marketed anti-cancer agent, irinotecan.

In a presentation by Insert's senior chemist, Dr. Jianjun Cheng, at the 11th International Symposium on Recent Advances in Drug Delivery Systems held March 3-6 in Salt Lake City, the company detailed *in vivo* data on the systemic delivery of camptothecin, a potent anti-cancer agent, using Cyclosert, Insert's proprietary cyclodextrin-based polymer drug delivery technology.

The recently completed study, conducted by a leading contract research laboratory, compared Insert's Cyclosert-camptothecin formulation against camptothecin alone; irinotecan, a camptothecin analogue currently marketed for cancer treatment; and placebo in athymic nude mice bearing a single subcutaneous LS-174t human colon carcinoma tumor. Animals were treated with Cyclosert-camptothecin, camptothecin alone or placebo every four days beginning on Day 1, for three doses or with irinotecan once weekly beginning on Day 1 for three doses.

Over the 114-day follow-up period, treatment with Cyclosert-camptothecin resulted in protracted anti-tumor activity and was substantially more effective at inhibiting tumor progression than all other treatment groups. Cyclosert-camptothecin produced lower median tumor size (256 mg vs. 1,568 mg), greater tumor growth delay (227% vs. 97%) and reduced median tumor burden in animals whose tumors had not reached the 1.5 gram endpoint by the end of the study (256 mg vs. 1,152 mg) than irinotecan treatment.

"Camptothecin is an ideal candidate for formulation with Cyclosert," said Insert's Founder Mark E. Davis, Ph.D. "Despite camptothecin's potent anticancer activity against a broad spectrum of tumor cell lines, the combination of its poor solubility, unfavorable pharmacokinetics, fast hydrolysis and high plasma protein binding prevented it from being successfully developed in the past. The results achieved in our animal studies provide clear evidence that the Cyclosert delivery technology has significant potential to improve the solubility, stability and pharmacokinetic properties of anticancer agents leading to improved therapeutic effects."

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Insert's Cyclosert delivery system is based on small cyclic repeating molecules of glucose called cyclodextrins. Using modified cyclodextrins as building blocks, Insert has developed an entirely new proprietary class of materials called linear cyclodextrin-containing polymers. Animal studies have confirmed that Cyclosert polymers are non-toxic and non-immunogenic, even after repeated administration. The polymers can be easily adapted to carry therapeutic agents of any size ranging from small molecule drugs to nucleic acids.

Cyclosert polymers have been synthesized at molecular weights ranging up to 100 kD and can be made biodegradable. The ability use high molecular weight (>50 kD) Cyclosert for systemic drug delivery has the potential to slow renal clearance, enhance circulation time and improve passive accumulation of active drug at the target tissue. Additionally, Cyclosert polymers can be tuned to be neutral, positively charged or negatively charged. This feature is unique to Cyclosert technology and provides great flexibility for formulation and delivery.

Insert has selected camptothecin as its initial drug delivery candidate. Camptothecin is a naturally occurring, water-insoluble alkaloid with established potent anti-tumor activity against a broad spectrum of tumor cell lines. The agent works by inhibiting the topoisomerase I enzyme that is essential for cell division. Analogues of camptothecin are currently marketed for treatment of various cancers, however, camptothecin itself has not been commercialized because its therapeutic potential was significantly reduced by its poor solubility, fast hydrolysis, unfavorable pharmacokinetics and high plasma protein binding. Conjugation of camptothecin with Cyclosert significantly increases the solubility of camptothecin more than 4000-fold allowing for systemic administration, reduces its *in vitro* cytotoxicity and stabilizes the molecule in its active lactone form.

"The results from our initial Cyclosert-camptothecin *in vivo* studies demonstrate that Cyclosert can address the diverse challenges of systemic drug delivery for small-molecule drugs with limited clinical effectiveness or unacceptable toxicity due to low solubility, unacceptable stability or poor pharmacokinetic profiles," said Insert CEO and President Leonard R. Borrmann. "On the strength of these results, we are moving aggressively forward with Cyclosert-camptothecin to complete necessary preclinical studies, file an IND and initiate human clinical trials. We also intend to leverage our Cyclosert delivery technology by building a pipeline of delivery-enhanced products and pursuing strategic collaborations with pharmaceutical and biotechnology companies whose marketed products or proprietary development compounds could benefit from Cyclosert."

INSERT THERAPEUTICS, INC.

Insert Therapeutics, Inc., a privately held biopharmaceutical delivery company, is pioneering the development of targeted, intracellular systemic delivery systems for small-molecule drugs and genes. Insert's technologies are designed to facilitate the efficient uptake and release of a broad range of therapeutics directly into cells. The company's proprietary delivery system, Cyclosert™, uses cyclodextrins as building blocks to create an entirely new class of drug delivery materials – linear cyclodextrin-containing polymers. Non-toxic and non-immunogenic at therapeutic doses, Cyclosert is designed for repeat and/or continuous administration. Insert is headquartered in Pasadena, CA. For more information, visit www.insertt.com.

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