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## **TRANSFORM IDENTIFIES NEW FORMS OF THE ACTIVE MOLECULE IN ZOLOFT®**

*Significant industry implications for improving drug development and obtaining more comprehensive protection of intellectual property*

**Lexington, MA, November 3, 2003** – TransForm Pharmaceuticals, Inc. (TransForm) today announced important new findings about sertraline, the active molecule found in the blockbuster drug, Zoloft®. First, TransForm announced that it discovered 16 previously unreported salt forms of sertraline, 3 of which appear to be less prone to polymorphism than the currently marketed drug. In addition, TransForm discovered a new, pharmaceutically acceptable, crystalline form of the salt (sertraline hydrochloride) currently marketed in Zoloft®. These findings are significant given that many companies, along with the innovator, have studied sertraline extensively. Zoloft® is a world leader in the treatment of depression with annual sales in excess of \$2 billion.

TransForm conducted more than 6,200 total crystallization experiments on sertraline, in 3 separate studies, with each study completed in under 6 weeks, using less than 5 grams of material. TransForm's findings, reported in separate articles in Crystal Growth and Design and Organic Process Research and Development, suggest that early and thorough exploration of polymorphism in multiple salts, using high-throughput experimentation, should influence the choice of the salt form, and help to identify and advance better development candidates. Such studies also can enable the innovator to obtain more comprehensive intellectual property protection of its assets, and identify product extension opportunities.

“These studies demonstrate the power of high-throughput experimentation in identifying the various forms of the active pharmaceutical ingredient, which is crucial for comprehensive intellectual property to protect the investment of the innovator,” commented Colin R. Gardner, Ph.D., TransForm’s Chief Scientific Officer. “Zoloft® appears poised to go generic in 2006 despite a patent that covers the form in the marketed product and provides protection through 2012. With the benefit of hindsight and by using high-throughput physical form experimentation available today, the innovator might have been able to avoid this situation,” concluded Gardner.

Polymorphism refers to the propensity of a drug molecule to solidify in different crystalline arrangements, each of which may have different physico-chemical characteristics such as solubility and stability, and which may translate into different levels of bioavailability or shelf-stability of the drug product. Over half of all currently marketed drugs involve the use of salt forms of the active moiety. Finding and developing less polymorphic salt forms of a compound, enables more predictable performance and results in more efficient and better understood drug development and manufacturing processes.

“The unexpected appearance of a more stable crystal form is a challenging aspect of drug development, which can result in a host of problems for the developer,” noted Christopher Walsh, Ph.D., a TransForm Board Member and the Hamilton Kuhn Professor in Biological Chemistry and Molecular Pharmacology at Harvard Medical School. “Early and comprehensive exploration of the crystalline forms of a compound can lower the risk of encountering unpredictable forms that create unforeseen challenges later in the development process, or even with marketed products. These findings may also have profound implications for how the industry thinks about protecting its assets in the future,” continued Walsh.

The research titled “*High Throughput Survey of Crystal Form Diversity of Highly Polymorphic Pharmaceutical Compounds*”, will appear in Crystal Growth and Design in November/December 2003 and “*Salt Selection and Simultaneous Polymorphism Assessment via High-Throughput Crystallization: The Case of Sertraline*”, appears in the November 2003 issue of Organic Process Research and Development. In addition, the findings were presented in two posters at the 2003 American Association of Pharmaceutical Sciences meeting held in October.

## **About TransForm**

TransForm Pharmaceuticals is reinventing the pharmaceutical industry's approach to form and formulation, with a novel set of high-throughput, automated platform technologies, powered by state-of-the-art informatics and a scientific and managerial team with deep experience in pharmaceuticals. It uses these capabilities to optimize drug form and/or formulations, and increase the clinical and commercial value of pharmaceutical products, across the entire pharmaceutical value chain. In research and development, TransForm is working with partners such as Alza Corporation and Lilly, to help them make better candidate selection decisions, and reduce attrition and development time and cost. For later stage and marketed products, TransForm can help partners enhance product life cycle management by rapidly discovering novel forms and/or formulations to potentially improve bioavailability, broaden intellectual property protection and enable new dosage forms and/or combination products.

TransForm is also using these capabilities to develop its own proprietary product portfolio. TransForm is a privately held company located in Lexington, MA. For more information visit our website at [www.transformpharma.com](http://www.transformpharma.com).

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