

# NEWS

For Immediate Release  
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## Tranzyme Pharma Receives IND Clearance for its Novel Ghrelin Agonist, TZP-101

*Company to Initiate Phase I Trial for Post-Operative Ileus*

**RESEARCH TRIANGLE PARK, N.C.** and **SHERBROOKE, Québec** (January 10, 2006) - Tranzyme Pharma, a leading biopharmaceutical company developing novel mechanism-based therapeutics for the treatment of gastrointestinal (GI) and metabolic disorders, today announced that the U.S. Food and Drug Administration has cleared its Investigational New Drug (IND) application for TZP-101, a new chemical entity originating from Tranzyme Pharma's proprietary small molecule macrocyclic chemistry. TZP-101 is a selective ghrelin receptor agonist with potent gastroprokinetic properties that represents the first in its class to enter into a clinical trial. Tranzyme Pharma is developing TZP-101 as a mechanism-based therapy for post-operative ileus (POI) and other GI motility disorders.

Ghrelin is a peptide hormone secreted by the stomach and small intestine and plays a physiological role in the stimulation of GI motility. Animal data suggest that ghrelin accelerates gastric emptying, enhances small bowel transit, and reverses delayed GI transit stemming from surgery or opioid therapy. Clinical studies have shown that exogenous administration of ghrelin peptide accelerates gastric emptying and stimulates interdigestive motility in healthy volunteers and gastroparesis patients.

In preclinical studies, TZP-101 has shown exceptional *in vivo* efficacy. The gastroprokinetic activity of TZP-101 has been demonstrated in animal models measuring gastric emptying in naïve rats, and in the treatment of rats with delayed GI transit caused by high caloric intake (i.e. a model of gastroparesis), abdominal surgery (i.e. a model of POI), and pharmacological means (i.e. morphine). Importantly, concurrent studies in rats have demonstrated that TZP-101 does not elicit growth hormone release at gastroprokinetic doses, in contrast to other ghrelin agonists.

The Phase I trial will be a single-center, randomized, double-blind, placebo-controlled, dose-escalation study designed to evaluate safety, tolerability, pharmacokinetic, and pharmacodynamic parameters of TZP-101.

"The initiation of Phase I studies is a significant step in the development of a mechanism-based therapeutic for the management of delayed gastric emptying," said Gordana Kosutic, M.D., Vice President of Clinical and Regulatory Affairs for Tranzyme Pharma. "Disorders of delayed gastric emptying, such as POI and gastroparesis, currently have limited therapeutic options. We anticipate having data available from first-in-man study by 3Q2006."

"This announcement marks Tranzyme's transition to a clinical-stage company and is a major milestone in our continued growth," said Vipin K. Garg, Ph.D., President and Chief Executive Officer. "It also validates our chemistry technology in the successful development of a small molecule macrocyclic compound as a clinical candidate. Tranzyme's ghrelin agonist represents a considerable therapeutic and commercial opportunity as we continue to develop it for other unmet GI indications such as diabetic gastroparesis."

*About post-operative ileus (POI)*

POI is the impairment of GI motility that routinely occurs after major surgeries and contributes significantly to post-operative morbidity, prolonged hospitalization and increased health care costs. The pathophysiology of POI is multifactorial and its duration correlates with the degree of surgical trauma. The morbidity related to POI includes increased post-operative pain, increased nausea and vomiting, delayed resumption of food intake, poor wound healing, delayed post-operative mobilization, and increased risk of other post-operative complications (e.g., pneumonia and pulmonary embolism). Annually, over 2 million surgeries in the U.S., in particular colonic surgeries, are at high risk for the development of POI.

*Tranzyme Pharma is a leading biopharmaceutical company developing novel orally bioavailable, small molecule therapeutics for the treatment of gastrointestinal (GI) and metabolic diseases. The Company's candidate drugs originate from its own discovery pipeline of proprietary compounds with high affinity for validated and druggable targets. Tranzyme is developing mechanism-based therapeutics for post-operative ileus (POI), diabetic gastroparesis, irritable bowel syndrome (diarrhea-type) and functional dyspepsia. The Company is initiating a Phase I clinical trial of its lead product, TZP-101, for the treatment of POI in the first quarter of 2006. Tranzyme is leveraging its small molecule chemistry through internal programs and partnerships to drive the discovery and development of new therapeutics. For more information, please visit: [www.tranzyme.com](http://www.tranzyme.com).*

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