

# Tolerx Presents Preclinical Data on Novel Cancer Immunotherapeutic, TRX518, a First-in-Class Anti-GITR Antibody

*TRX518 Demonstrates Anti-Tumor Activity in Data Presented at Keystone Symposia*

**CAMBRIDGE, MA – February 9, 2011** – Tolerx, Inc., a biopharmaceutical company developing novel therapies to treat autoimmune diseases and cancer by normalizing the immune response, presented results from preclinical studies with TRX518, a first-in-class immunomodulatory agent for the treatment of cancer. TRX518 is a monoclonal antibody reactive with the glucocorticoid-induced tumor necrosis factor receptor (GITR) and is designed to enhance the immune system's anti-tumor response by enabling T cells to more effectively attack cancer cells. The preclinical data were presented as a poster and invited talk at the Keystone Symposia "Antibodies as Drugs" meeting held in Keystone, Colorado.

The presentation included a range of data from preclinical studies of TRX518 and details of the fully humanized TRX518 antibody. Results and data included:

- A murine analog of TRX518 showed anti-tumor activity as a monotherapy and, when used as a combination therapy with standard chemotherapeutics, prevented the establishment of tumors, induced complete and partial remission of established tumors, and prolonged survival in animal models of human cancer.
- The enhancement of the anti-tumor response afforded by anti-GITR combination therapy was shown to target specific immune responses, because these animal models were resistant to tumor re-challenge while other antigenically distinct tumors grew normally.
- TRX518 blocked the interaction of GITR with its ligand, enhanced the cytotoxicity of natural human killer cells, downmodulated GITR on peripheral blood lymphocytes, did not induce appreciable cytokine release, and was well tolerated and safe at high doses in non-human primates.
- Characterization of the TRX518 human clinical candidate, a fully humanized Fc-disabled anti-human GITR IgG1 mAb.

Based on these data, a Phase 1, first-in-human, open label, dose escalation safety study in adults with Stage III/IV metastatic melanoma was initiated in December 2010 and is currently underway.

"We are very excited about the anti-GITR program, notably the unique and multifaceted mechanism of action and its promising safety profile," said Tony deFougerolles, Tolerx Chief Scientific Officer. "The preclinical data indicate that TRX518 has tremendous potential for enhancing anti-tumor responses, regardless of tumor type, and for also improving the effectiveness of other cancer therapies including chemotherapeutics and cancer vaccines."

## **About TRX518**

TRX518 is an investigational immunotherapy designed to activate GITR (glucocorticoid-induced tumor necrosis factor receptor) found on multiple types of T cells and other immune cells. GITR plays a role in directing the anti-tumor immune response via a multifaceted mechanism of action that includes activating tumor antigen-specific T effector cells, abrogating the suppression induced by T regulatory cells, and activating NK cells. In preclinical studies, TRX518 achieved its effect without compromising normal immune function, and preclinical models suggest TRX518 to have a favorable safety profile. A Phase 1 clinical study of TRX518, a first-in-class anti-GITR monoclonal antibody, has been initiated to assess the safety, tolerability, pharmacokinetic, and pharmacodynamic profiles of ascending single doses of TRX518 in patients with malignant melanoma. TRX518 is designed to have activating and sustaining effects on T cells for enhancing the immune system's responses against cancer cells, including responses that may occur with TRX518 alone, as well as complementary responses in combination with other cancer therapies including vaccines.

## **About Tolerx**

Tolerx, Inc., a world leader in immunology for novel drug development, has a portfolio of innovative, first-in-class drug candidates to treat autoimmune diseases, diabetes, and cancer by normalizing the immune system. The company's pipeline

includes its lead candidate, otelexizumab, a targeted T cell immunomodulator in Phase 3 development for the treatment of type 1 diabetes that is partnered with GlaxoSmithKline. Tolerx's product candidate, TRX518, is a targeted T cell immunotherapy in Phase 1 development for the treatment of cancer. TRX1, a Phase 1 candidate, is a nonlytic anti-CD4 antibody that is being developed for the treatment of aberrant or untoward immune responses. The company also has two preclinical candidates, TRX585 and TRX385, which enhance immune responses and as such are being evaluated for potential benefit in the treatment of cancer and chronic infections. Tolerx is a privately held company headquartered in Cambridge, MA USA. For more information, please visit [www.tolerx.com](http://www.tolerx.com).

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