Tragara Initiates Clinical Study of TG02 in Combination with Carfilzomib in Multiple Myeloma

TG02 synergizes with carfilzomib in multiple myeloma models; data to be presented at ASH 2013 Annual Meeting

San Diego – December 3, 2013 – Tragara Pharmaceuticals, Inc. today announced the initiation of a phase 1b clinical trial of TG02, in combination with the poteosome inhibitor carfilzomib (Kyprolis®), in patients with relapsed or refractory multiple myeloma. TG02 is a potent oral inhibitor of CDK9, which leads to the depletion of key survival proteins, such as Mcl-1, resulting in p53-independent apoptosis across a wide range of tumor cells. The study is being led by Craig C. Hofmeister, M.D., at The Ohio State University Comprehensive Cancer Center, and is open for enrollment at multiple centers in the U.S.

This study is an open-label dose-escalation phase 1b trial in which TG02 is combined with carfilzomib in patients with relapsed or refractory multiple myeloma. The trial will include patients who have one or more cytogenetic abnormalities that predict poor prognosis and reduced responsiveness to current standard-of-care therapies, including deletion of chromosomes 17p or 1p, amplification of chromosome 1q, or the chromosomal translocation t(4:14). Patients who have received at least two prior therapies, including a proteasome inhibitor and an immunomodulatory agent, will also qualify for enrollment. The primary objective of the trial is to determine the dose-limiting toxicity, maximum-tolerated dose, and recommended phase II dose of TG02 in combination with carfilzomib. The secondary objectives include the assessment of safety, tolerability, pharmacokinetics, and the evaluation of exploratory biomarkers, in addition to evidence of anti-tumor activity.
“A meaningful percentage of patients with multiple myeloma have disease characterized by cytogenetic abnormalities, and the prognosis for these cases is typically poor,” said Craig C. Hofmeister, M.D., Assistant Professor at The Ohio State University, College of Medicine, and principal investigator. “The treatment options for this subset of patients are limited, so we are very interested in exploring the potential of TG02, in combination with carfilzomib, in this clinical trial.”

Rationale for the Combination
Multiple myeloma cells are dependent upon the anti-apoptotic protein Mcl-1 for survival. The rationale for the combination of TG02 and carfilzomib is based on the ability of both agents to target Mcl-1 via independent mechanisms. Carfilzomib upregulates the protein NOXA, which inhibits Mcl-1 in the cell. TG02 inhibits CDK9, which downregulates the production of Mcl-1, reducing the level of Mcl-1 in the cell by blocking its replenishment. The combination of these treatments has been shown to have synergistic effects in human myeloma cell lines.

Preclinical data describing TG02 in combination with carfilzomib will be shown during a poster presentation at the American Society of Hematology Annual Meeting in New Orleans. The poster, “Dual Inhibition Of Mcl-1 By The Combination Of Carfilzomib and TG02 In Multiple Myeloma”, presents the results of work conducted by the Winship Cancer Institute of Emory University. The poster (#3171) will be shown on Sunday, December 8, at 6:30pm CST in Hall G of the Morial Convention Center.

About TG02
TG02 is a unique, oral multi-kinase inhibitor which combines the benefits of inhibiting important cyclin dependent kinases equipotently with JAK2, FLT3, and ERK5 inhibition. TG02 exerts its antitumor activity primarily via its potent CDK9 inhibition, which leads to the depletion of key survival proteins, such as Mcl-1, resulting in p53-independent apoptosis of a wide range of tumor cells. TG02 development will initially focus on the treatment of hematologic malignancies, including multiple myeloma (MM) and chronic lymphocytic leukemia (CLL), based on the consistent anti-tumor activity that has been observed across a broad spectrum of hematologic cancer models, including those resistant to currently available therapies. In these models, TG02 demonstrated both single agent activity and synergy when administered with current standard of care therapies. Subsequent development will focus on an important group of solid tumors with unmet medical need, such as small cell lung cancer, triple negative breast cancer, and melanoma, which will also benefit from this mechanism of action, complemented with the benefits of inhibiting both JAK2 and ERK5. These pathways affect disease progression and survival in hematologic malignancies and solid tumors.
TG02 is currently being evaluated in two separate phase I clinical trials in patients with MM and CLL in the United States.

In early 2010, TG02 was selected by the Multiple Myeloma Research Foundation as a winner of its Biotech Investment Award, which represents a multi-year research grant commitment to fund the early-stage drug development of novel compounds that show potential in treating MM.

About Tragara
Tragara Pharmaceuticals, Inc. is a privately held pharmaceutical company based in San Diego, Calif. The company is focused on the clinical and commercial development of proprietary medicines for the treatment of cancer. TG02 is a unique, oral multi-kinase inhibitor which combines the benefits of inhibiting important cyclin dependent kinases equipotently with JAK2, FLT3, and ERK5 inhibition. TG02 exerts its antitumor activity via its potent CDK9 inhibition, which leads to the depletion of key survival proteins, such as Mcl-1, resulting in p53-independent apoptosis of a wide range of tumor cells. Tragara is managed by a team of entrepreneurs with both Big Pharma and Biotech experience in the development and commercialization of oncology therapeutics. Its investors include: Domain Associates, Mitsubishi International Corporation, Morgenthaler Ventures, ProQuest Investments and RusnanoMedInvest.

Tragara strives to provide much-needed therapies that will contribute to patient health through better survival and an increase in the quality of life. For more information, visit www.tragarapharma.com.