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**TARGETED GENE DELIVERY SIGNALS CANCER VACCINATION *IN VIVO*:  
Intravenous Infusions of Rexin-G followed by Reximmune-C induce tumor necrosis and  
recruitment of tumor infiltrating lymphocytes in cancerous lesions (ASCO 2008)**

May 27, 2008, San Marino, California—Epeius Biotechnologies ([www.epeiusbiotech.com](http://www.epeiusbiotech.com)) announced today that the results of a Phase I Feasibility Study of sequential targeted gene delivery—using Rexin-G followed by Reximmune-C—for cancer vaccination will be presented at the ASCO meetings in Chicago on June 1, 2008 (J Clin Oncol 26:3077, 2008). Rexin-G and Reximmune-C are pathotropic (disease-seeking) nanoparticles bearing a cytotoxic cyclin G1 gene and a granulocyte-macrophage colony stimulating factor (GM-CSF) gene, respectively. When injected intravenously, these targeted vectors seek out and accumulate in cancerous lesions, thus increasing the effective local concentrations of the therapeutic nanoparticles within the tumors.

The working hypothesis behind this two-stage approach to cancer management predicts that strategic and individualized vaccination of a patient against his/her own cancer can be achieved by combining (1) the targeted vector bearing a potent cytotoxic construct, Rexin-G, with (2) a targeted vector bearing an immune activating gene, Reximmune-C. Rexin-G is given first to kill the cancer cells and thus expose neoantigens within the tumors, followed by Reximmune-C to recruit the body's immune cells into the same tumor compartments, thereby prompting recognition of the tumor neoantigens *in situ* and inducing long-lasting anti-tumor immunity.

The purpose of the Phase I study was to evaluate the over-all safety/toxicity and therapeutic potential of this sequential regimen, in an effort to achieve a personalized cancer vaccination *in vivo*. Seven patients with chemo-resistant cancer, including carcinoma of breast, colon and pancreas, non-small cell lung cancer and leiomyosarcoma, received Rexin-G i.v. at a dose of  $4 \times 10^{10}$  cfu per day for 2 to 6 weeks (Cumulative Dose:  $4.0 \times 10^{11}$  to  $1.2 \times 10^{12}$  cfu) followed by Reximmune-C i.v. at  $2.5 \times 10^9$  cfu for 5 days or  $5 \times 10^9$  cfu for 2 days (Cumulative Dose:  $1.00 - 1.25 \times 10^{10}$  cfu).

Analysis of Safety showed that no dose-limiting toxicity was observed with this regimen, and immunoreactive GM-CSF protein was NOT detected in serum samples either during or after treatment with Reximmune-C. There was no significant alteration in hemodynamic function, bone marrow suppression, liver, kidney, or any other organ dysfunction related to the intervention. Immune-related reactions consisted of transient flu-like symptoms in two patients, redness and swelling of a tumor-infiltrated lymph node and one metastatic chest nodule, and acute flank pain in one patient with adrenal gland metastasis. Analysis of efficacy in biopsied tumor specimens revealed definitive expression of the GM-CSF transgene in cancer cells indicating effective gene delivery *in vivo*. Further, extensive tumor necrosis and tumor infiltrating lymphocytes (TILs) were observed within the tumors. Characterization of the recruited TILs showed CD35+ dendritic cells, CD8+ killer T cells, and CD138+ plasma B cells, with

lesser amounts of CD68+ macrophages and CD20+ B cells, suggesting a relatively mature or advanced immune response. Taken together, this landmark study demonstrates (1) that the functionality of the gene delivery platform is profound; (2) the genetic constructs employed are relatively safe; and (3) the potential for a personalized cancer vaccination using this sequential gene transfer approach is now a realistic goal.

For more information about Regin-G, Reginimmune-C, on-going clinical trials in the USA and abroad, and/or Epeius pathotropic (disease-seeking) gene delivery systems, please contact Dr. Erlinda M. Gordon at [egordon@epeiusbiotech.com](mailto:egordon@epeiusbiotech.com).