52. A Phase 1 Dose-Escalation Trial of Intravesical CG0070 for Superficial Transitional Cell Carcinoma (TCC) of the Bladder after Bacillus Calmette-Guerin (BCG) Failure

Neil Senzer,1,2 John Nemunaitis,1,2 Michael Goldstein,3 James Arsenneau,1 Don Lamm,1 Joe Stephenson,1 Harry Tsai,4 Kristina Neal,5 Junko Aimi,5 D. C. Yu,5 Daniel Maslyar,5 John Corman,6 James McKierman,7 James Burke,5

1Mary Crowley Medical Research Center, Texas Oncology PA, Dallas, TX; 2Baylor University Medical Center, Dallas, TX; 3BCG Oncology, Phoenix, AZ; 4Cancer Centers of the Carolinas, Greenville, SC; 5Cell Genesys, South San Francisco, CA; 6Virginia Mason Cancer Center, Seattle, WA; 7Columbia University, New York, NY.

Introduction and Objective: CG0070 is a replication competent adenovirus (AD) modified to express the cytokine granulocyte macrophage colony stimulatory factor (GM-CSF) and replicate preferentially in Retinoblastoma (RB) pathway defective cancers via replacement of the key wild-type AD promoter E1A with the human E2F-1 promoter. Preclinical studies show CG0070 to be a selective cytotoxic and immunostimulatant. BCG, which acts by generating an anti-tumor immune response, is the standard of care for patients with Superficial TCC. Given the limited treatment options following BCG therapy and the relevance of immunological therapy for TCC, this Phase 1 study was initiated. Methods: The primary goals for this study of intravesical (IVE) CG0070 in patients with existing TCC after BCG failure is the evaluation of safety and the identification of a maximum tolerated dose. Assessment of response rate and progression free survival is also planned. T1, Ta, or CIS patients with normal coagulation; and adequate kidney, liver, and bone marrow function are eligible. 3 patients at single IVE doses of 10^12, 3x10^12, 10^13, 3x10^13, and 10^14 viral particles (vp) will be evaluated. All patients receive dodecyl-maltoside, a mild detergent, prior to CG0070 to enhance penetration of the mucosal layer. Patients are assessed for adverse events (AE) and laboratory measures of toxicity. Results: 6 total patients have been treated to date at 10^12 and 3x10^12 vps. Treatment was tolerable with mild-moderate AE reported including dysuria, urgency, and malaise. No grade 3/4 AE or significant lab toxicity was reported. Cystoscopic examination of 3 patients day 8 after treatment with 10^12 vp revealed inflammation and tumor regression. A complete response (CR) at week 12+ after treatment was reported in a patient with Ta TCC treated with 10^12 vp. For all other patients efficacy assessment will be presented. Conclusions: Preliminary results of IVE CG0070 in patients with superficial TCC who have failed BCG suggest a good safety profile with limited local toxicity. Notably, initial evidence of anti-tumor activity is suggested by CR in 1 of 3 pts treated at the initial dose of only 10^12 vp. Conclusions regarding safety and efficacy will be updated at presentation.

K. Neal - Cell Genesys, Inc.
J. Aimi - Cell Genesys, Inc.
D. Yu - Cell Genesys, Inc.
J. Burke - Cell Genesys, Inc.

53. Preliminary Results of a Pilot Phase I Clinical Trial of Adoptive Immunotherapy for B Cell Lymphoma Using CD8+ T Cells Genetically Modified To Express a Chimeric T Cell Receptor Recognizing CD20

Oliver W. Press,1,2 Jinjuan Wang,1 Catherine G. Lindgren,2 Eric Y. Chen,1,2 Ajay K. Gopal,2 John M. Pagel,1,2 Xiaojun Qian,1 Stanley R. Riddell,1 Philip D. Greenberg,1,2 Andrew Raubitschek,3 Michael C. Jensen,1

1Clinical Research, Fred Hutchinson Cancer Research Center, Seattle, WA; 2Medicine, University of Washington, Seattle, WA; 3Cancer Immunotherapeutics & Tumor Immunology, City of Hope National Medical Center and Beckman Research Institute, Duarte, CA.

Follicular Lymphoma (FL) is the second most common type of Non-Hodgkin’s Lymphoma (NHL) in the United States, with over 120,000 Americans living with the disease. FL is considered incurable with conventional therapies and innovative new approaches are needed. We have initiated a pilot Phase I clinical trial to test the feasibility, safety, toxicity, and efficacy of treating patients with relapsed indolent B cell lymphomas with autologous CD8+ cytotoxic T lymphocytes (CTL) that have been genetically modified to express a chimeric T cell receptor (CTCR) recognizing the CD20 antigen present on B cell lymphomas. Five patients have been registered to the protocol to date. Peripheral blood mononuclear cells were obtained from patients by apheresis, activated with anti-CD3 monoclonal antibody and interleukin 2 and transfected by electroporation with a plasmid encoding a CD20-specific scFvFc-zeta...