SERIOUS, POSSIBLY ASSOCIATED AND UNEXPECTED ADVERSE EVENTS
REPORTED FOR HUMAN GENE TRANSFER PROTOCOLS
REPORTING PERIOD: 05/01/02 -- 08/01/02
RECOMBINANT DNA ADVISORY COMMITTEE MEETING
September 2002

Event #	OBA Date	Event Date	Protocol #	Event Description
			9510-130	**Administration of Neomycin Resistance Gene Marked EBV Specific Cytotoxic T Lymphocytes to Patients with Relapsed EBV-Positive Hodgkin Disease.**
4446	05/24/2002	09/16/1997		Research participant had a Grade 3 cachexia. Deemed possibly related to gene transfer product by the investigator. No further details provided.
			9902-287	**Phase I Pilot Trial of Adenovirus p53 in Bronchioloalveolar Cell Lung Carcinoma (BAC) Administered by Bronchoalveolar Lavage. Sponsor: NCI-Cancer Therapy Evaluation Program (NCI-CTEP)**
4508	07/18/2002	10/26/2000		Research participant developed arrhythmia two days after receiving gene transfer agent. As per investigator, arrhythmia possibly related to gene transfer agent. Referred to cardiologist who treated research participant and problem resolved.

Event #	OBA Date	Event Date	Protocol #	Event Description
			9904-304	**Pediatric Phase I Study of AdV/RSV-TK Followed by Ganciclovir for Retinoblastoma**
4479	05/21/2002	04/12/2000		After receiving gene transfer agent by intraocular injection, research participant developed grade 1 irritation in the eye. Possibly related to injection, as per investigator.
4480	05/21/2002	04/20/2000		One week after event described in 4479, research participant developed a grade 2 irritation in the eye. Possibly related to the intraocular injection, as per the investigator.
4481	05/21/2002	04/20/2000		Concurrent with event 4480 research participant also developed a grade 1 conjunctival reaction. Possibly related to intraocular injection, as per the investigator.
4484	05/21/2002	08/24/2000		After receiving gene transfer agent by intraocular injection, research participant developed grade 1 irritation in the eye. Possibly related to injection, as per the investigator.
4485	05/21/2002	08/24/2000		Concurrent with event 4484 research participant also had a Grade 1 conjunctival response. Possibly related to injection, as per the investigator.
4486	05/21/2002	09/11/2000		Approximately 3 weeks after the events described in 4484 and 4485, research participant noted to have grade 2 irritation in the eye. Possibly related to intraocular injection, as per the investigator.
4487	05/21/2002	04/03/2001		After intraocular injection of the gene transfer product, research participant developed grade 1 lens opacity.
4488	05/21/2002	04/04/2001		Concurrent with event 4487, research participant also developed grade 1 eye irritation. Possibly related to intraocular gene transfer injection, as per investigator.
4495	05/21/2002	11/19/2001		Research participant had a Grade 1 corneal edema. Possibly related to intraocular gene transfer injection, as per the investigator.

Event #	OBA Date	Event Date	Protocol #	Event Description
			0002-388	**A Double-Blind, Randomized, Placebo-Controlled, Dose-Ranging, 26-Week Study to Assess the Safety and Efficacy of CI-1023 ($AD_{GV}VEGF_{121.10}$) in Peripheral Arterial Disease Patients with Severe, Disabling Intermittent Claudication. Sponsor: Parke-Davis Pharmaceutical Research**
4298	05/16/2002	05/01/2002		Follow-up from sponsor (for reports 4280, 4283, and 4291): As per sponsor, renal insufficiency most likely due to concomitant use of NSAIDs and ascites due to underlying malignancy.
4314	05/20/2002	05/01/2002		Follow-up report to 4280. 4283, 4291, and 4298: Repeat echocardiogram of heart showed near normal cardiac function and clot in ventricle no longer seen. Research participant underwent bypass graft surgery for correction of right lower leg ischemia. At this time, the subject's diagnoses are: acute cardiomyopathy, left ventricular clot, lower extremity ischemia necessitating bypass surgery, a stroke due to embolism originating from the left ventricular clot, ascites most likely due to ovarian cancer, and renal insufficiency due to NSAID use.
4318	05/23/2002	05/01/2002		Follow-up from sponsor (to reports 4280, 4283, 4291, 4298, and 4314). Following diagnoses not attributed to gene transfer agent by either the investigator or sponsor: renal insufficiency, left ventricular clot, acute cardiomyopathy, worsening ischemia of right leg, and ascites. In the investigator's opinion, possible association between study medication and ovarian cancer. In the sponsor's opinion, ovarian cancer probably related to other illnesses and not study drug.
4324	05/28/2002	05/01/2002		Follow-up from the investigator: Discharge summary containing summary of information already in reports 4280, 4283, 4291, 4298, 4314 and 4318. Etiology of adenocarcinoma cells in ascitic fluid still not identified but strongly suspected to be ovarian cancer.
			0005-396	**A Phase I, Open-Label, Dose-Escalating Study of the Safety, Tolerability, and Anti-Tumor Activity of a Single Intrahepatic Injection of a Genetically Modified Herpes Simplex Virus NV1020, in Subjects with Adenocarcinoma of the Colon with Metastasis to the Liver and the associated, long-term follow-up protocol: Long-Term Follow-Up of the Safety and Survival of subjects with Adenocarcinoma of the Colon with Metastasis to the Liver Who Enrolled in a Phase I Dose-Escalating Study Evaluating a Genetically Engineered Herpes Simplex Virus, NV 1020. Sponsor: NeuroVir Therapeutics, Inc.**
4380	06/19/2002	06/12/2002		Twelve hours after injection of the study agent the GGT level was elevated to 809 which was greater than 20 times the upper limit of normal. There was no baseline GGT level given. Pre-injection AST=30, ALT=21. Twelve hours post-injection AST=60, ALT=34. Conjugated bilirubin and LDH levels were elevated, but coagulation parameters were just at the upper limit of normal. By 24 hours post-injection, the GGT, AST, and ALT levels were normal. The research participant was asymptomatic.
4512	07/22/2002	06/12/2002		Follow-up to Event 4380 from the PI. After reviewing the laboratory information, the PI changed the causality of the elevation of G-GTP from possibly related to "most likely related to viral administration."

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			0006-402	**Phase I Study to Evaluate the Safety of Cellular Immunotherapy for Recurrent/Refractory Neuroblastoma Using Genetically-Modified Autologous CD8+ T Cell Clones.**
4322	05/28/2002	05/23/2002		Research participant developed fever 2 hours after receiving infusion of transduced T-cells. Positive blood cultures times two. Due to the timing of the fever and positive blood cultures, investigator suspected that gene transfer product contaminated. Results of further testing pending. (Follow-up Note [event 4360]: All tests on gene transfer product showed no contamination. Cause of positive blood cultures no longer suspected to be gene transfer product, as per investigator).
			0007-407	**A Phase I Double-blind, Placebo-Controlled, Escalating Dose, Multi-center Study of Ad2/Hypoxia Inducible Factor (HIF)-1-alpha/VP16 Gene Transfer Administration by Intramyocardial Injection During Coronary Artery Bypass Grafting (CABG) Surgery in Patients with Areas of Viable and Underperfused Myocardium not Amenable to Bypass Grafting or Percutaneous Intervention. Sponsor: Genzyme Corporation**
4502	07/12/2002	06/14/2002		The research participant was undergoing double coronary artery bypass surgery and receiving blinded study drug injections. Subsequent to injection number four, and the lifting of the heart to visualize the next injection site, the research participant went into spontaneous ventricular fibrillation. Following defibrillation and drug therapy, the participant converted into sinus rhythm and recovered. All remaining study injections were administered. The participant recovered without sequelae. The PI reported that the intensity of the event was moderate and that the event was unrelated to the study drug. The Sponsor determined that a relationship between the study drug and the event could not be excluded and changed the causality assessment to possibly related.
			0011-435	**Vaccination in Peripheral Stem Cell Transplant Setting for Multiple Myeloma: The Use of Autologous Tumor Cells with an Allogeneic GM-CSF Producing Bystander Cell Line. Sponsor: Cell Genesys, Inc.**
4323	05/24/2002	05/07/2002		Prior to receiving 6th cycle of vaccines, research participant admitted for 4 days of dry cough, fever, chills and slight dyspnea on exertion. CT scan showed ground glass infiltrates in both lung fields. Workup done to find cause of this event, but all results negative. Research participant improving. Investigator believes that events secondary to gene transfer product, while corporate sponsor believes that more likely due to self-limited viral infection.
			0105-472	**Phase I/II Study of Vaccination with Irradiated Autologous Lung Tumor Cells Mixed with a GM-CSF Secreting Bystander Cell Line (Lung Bystander GVAX®) in Advanced Non-Small Cell Lung Cancer. Sponsor: Cell Genesys, Inc.**
4313	05/20/2002	05/01/2002		Research participant with advanced lung cancer admitted to hospital due to increasing shortness of breath, leg swelling, and right sided chest pain. CT scan showed mass in lung field, two masses in liver, and multiple enlarged lymph nodes. As per investigator, these events most likely due to progression of disease but "possibly" related to gene transfer product (vaccines).

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			0107-481	**An Open-Label, Phase Ib/II Study of the Safety, Tolerability and Efficacy of G207, a Genetically Engineered Herpes Simplex Type-1 Virus, Administered Intracerebrally to Subjects with Recurrent Malignant Glioma. Sponsor: MediGene, Inc.**
4312	05/20/2002	04/27/2002		Follow-up for events 4278, 4279 and 4286: Clinical nurse coordinator spoke with research participant and presently doing well. Is due in for 28 day post-procedure visit in late May.
4371	06/18/2002	04/27/2002		Follow-up from the investigator: (see reports 4278, 4279, 4286): Final viral culture information: No growth on viral cultures. Cause of event probably related to gene transfer product, as per the investigator.