SERIOUS, POSSIBLY ASSOCIATED AND UNEXPECTED ADVERSE EVENTS
REPORTED FOR HUMAN GENE TRANSFER PROTOCOLS
REPORTING PERIOD: 11/1/00 -- 02/1/01
RECOMBINANT DNA ADVISORY COMMITTEE MEETING
March 2001

Event #	OBA Date	Event Date	Protocol #	Event Description
			9510-128	**Phase I Study of Recombinant CEA Vaccinia Virus Vaccine with Post Vaccination CEA Peptide Challenge.**
3228	01/02/2001	10/15/1998		Initial; Hospitalization for blood glucose of 16 occurring 3 days post injection. After 48 hrs of heavy glucose infusion, glucose level returned to normal. This patient had a history of non-insulin dependent diabetes mellitus and reportedly had been on an oral hypoglycemic agent but no other details were available. Event was considered possibly related to study drug.
3280	01/19/2001	10/15/1998		Follow Up1 to ID #3228. Submission of event by sponsor.
			9512-137	**Phase I Study of E1A Gene Therapy for Patients with Metastatic Breast or Ovarian Cancer that Overexpresses Her-2/neu. Sponsor: Targeted Genetics Corporation**
3198	08/25/2000	11/13/1997		Follow Up1; Subject was hospitalized and treated for obstipation, nausea and vomiting. The intensity of the event was considered severe and the condition resolved. The event was considered as "unlikely related" to the study drug.
			9603-149	**Ovarian Cancer Gene Therapy with BRCA-1.**
3116	05/31/2000	12/16/1997		Initial; Sterile peritonitis deemed related to study drug administration. Event occurred 29 days after intraperitoneal injection of study drug.

Event #	OBA Date	Event Date	Protocol #	Event Description
			9706-193	**A Pilot Study of Sequential Vaccinations with ALVAC-CEA and Vaccinia-CEA with the addition of IL-2 and GM-CSF in Patients with CEA Expressing Tumors. Sponsor: National Cancer Institute-Cancer Therapy Evaluation Program (NCI-CTEP)**
3176	12/13/2000	12/04/2000		Initial; Subject diagnosed with small bowel cancer was undergoing experimental intervention requiring subcutaneous delivery of recombinant avian pox virus on a repeating 28 day cycle. Subject informed PI that his spouse was six weeks pregnant and inquired whether the experimental procedure may have caused any potential harm to the fetus. The attending obstetrician has been contacted by the PI. As of 3/5/01 the wife of the patient was reportedly being closely followed and doing well with her pregnancy.
			9707-198	**A Phase I/II Study of Autologous CC49-Zeta Gene-Modified T Cells and alpha-Interferon in Patients with Advanced Colorectal Carcinomas Expressing the Tumor-Associated Antigen, TAG-72. Sponsor: Cell Genesys, Inc.**
3237	11/14/2000	02/21/1998		Initial; Subject developed a spontaneous left central retinal artery thrombosis with acute loss of vision in left eye. The erythrocyte sedimentation rate was 119; temporal artery biopsy negative. Subject treated with brief course of high dose prednisone without improvement in vision or decrease in erythrocyte sedimentation rate. Event believed to be possibly associated to study drug.
			9709-214	**A Phase II Multi-Center, Open Label, Randomized Study to Evaluate Effectiveness and Safety of Two Treatment Regimens of Ad5CMV-p53 Administered by Intra-Tumoral Injections in 78 Patients with Recurrent Squamous Cell Carcinoma of the Head and Neck (SCCHN). Sponsor: Aventis (formerly Gencell)**
3124	11/29/2000	09/18/1998		Follow Up1 to ID #1016; Wound culture positive for Pseudomonas spp. and Staphylococcus aureus.
3130	11/30/2000	09/18/1998		Follow Up2 to ID #1016; Cover letter from sponsor was changed to indicate that the submission was a follow-up, not an initial report.

Event #	OBA Date	Event Date	Protocol #	Event Description
			9802-238	**Phase 1/2 Study of the Effects of Ascending Doses of Adenovirus Mediated Human FGF-4 Gene Transfer in Patients with Stable Exertional Angina. Sponsor: Berlex Laboratories, Inc.**
3117	11/27/2000	10/12/2000		Follow Up2 to ID #3001 (from sponsor). Biopsy confirmed diagnosis of glioblastoma multiforme. Several expert opinions regarding causality accompany the report. Current belief is that study drug did not cause the neoplasm, but contribution to its growth cannot be excluded.
3118	11/28/2000	10/12/2000		Follow Up3 to ID #3001 (from PI). Same information as ID #3117.
3146	12/06/2000	01/24/2000		Follow Up2 to ID #438. Comments from Dr. David P. Kelson, Chief, GI Oncology Service Memorial Sloan Kettering. Believes subject had a genetic predisposition to colon cancer. Unable to make firm statement regarding study drug contributing to rapid tumor growth.
3159	12/11/2000	12/05/2000		Initial; Hospitalization for exacerbation of dysphagia and confusion. Symptoms improved with IV steroids. Event deemed possibly related to IND agent.
3301	01/29/2001	10/12/2000		Follow Up4 to ID #3001. The brain tumor biopsy sample was negative for viral DNA by PCR (polymerase chain reaction) analysis and FGF-4 RNA by RT-PCR analysis.

Event #	OBA Date	Event Date	Protocol #	Event Description
			9802-239	**A Phase I/II Study of Hepatic Infusion of Autologous CC49-Zeta Gene-Modified T Cells in Patients with Hepatic Metastasis from Colorectal Cancer. Sponsor: Cell Genesys, Inc.**
3248	11/14/2000	06/30/1998		Initial; Following second infusion of study drug, subject developed grade 2 fevers, grade 3 bilirubin, increased LDH, decreased hematocrit and increased WBC count. Subject complained of fatigue, right shoulder and right flank pain. Treated with antibiotics without improvement in fevers. All cultures negative, no evidence of infection, bleeding or hemolysis. All symptoms resolved spontaneously. Event considered possibly related to study drug.
3253	11/14/2000	10/28/1998		Initial; 25 minutes post cell infusion, subject developed rigors and slight decrease in O2 saturation. Treated with IV Demerol; condition resolved rapidly. Four hours after infusion of the agent, the patient spiked a fever to 38.7degrees C. He was admitted for observation and evaluation. Blood cultures were drawn and he was given IV antibiotics. He was discharged the next morning. The blood cultures were negative. The investigator noted other patients treated with IV or intrahepatic infusions of CC49-Zeta T cells have developed culture-negative fevers following infusion and considered this (i.e. the fever) an expected AE.
3252	11/14/2000	11/24/1998		Initial; Subject with history of chronic atrial fibrillation developed rigors, fever, more rapid atrial fibrillation and hypotension two hours post study drug injection. Treated with IV fluids, prophylactic antibiotics, digoxin and metoprolol. WBC increased, hematocrit and platelet count decreased. Work-up for hemolysis, bleeding and disseminated intravascular coagulation (DIC); all negative. Cultures negative. Developed shortness of breath and hypoxia believed to be related to fluid overload and mild congestive heart failure due to atrial fibrillation. Event considered definitely associated with study drug administration.
			9806-255	**Phase I Trial of Intraperitoneal Adenoviral p53 Gene Therapy in Patients with Advanced Recurrent or Persistent Ovarian Cancer. Sponsor: National Cancer Institute - Cancer Therapy Evaluation Program (NCI-CTEP)**
3139	12/04/2000	11/28/2000		Follow Up3 to ID #3129. Preliminary autopsy showed severe fibrinopurulent peritonitis, although subject showed no signs of clinical peritonitis at time of death. Event now considered possibly related to study drug.
3260	01/11/2001	11/28/2000		Follow Up4 to ID #3129. NCI-CTEP response that the event "peritonitis" was unlikely related to the study drug. The event is considered possibly related to subject's disease and peritoneal catheter. A final autopsy report is due in 6-8 weeks. Final autopsy results to be faxed 3/6/01. The final autopsy report showed extensive metastatic disease with involvement of the following: lungs, diaphragm, urinary bladder, gallbladder, liver, large intestine, multiple abdominal and thoracic lymph nodes, esophageal adventitia, and the peritoneum. Additionally, there was a large organizing right atrioventricular thrombus (without evidence of neoplastic tissue), bilateral atelectasis and pleural effusions, and organized pulmonary thromboembolus. The cause of death was: "Metastatic clear cell carcinoma of the ovary complicated by peritonitis and respiratory failure."

Event #	OBA Date	Event Date	Protocol #	Event Description
			9806-256	**Autologous, Irradiated, Melanoma Cells Transduced Ex Vivo with an Adenovirus Vector (Adv/GM-CSF) Expressing Granulocyte-Macrophage Colony Stimulating Factor Gene.**
3103	11/17/2000	09/19/2000		Initial; Subject was admitted with grade 3 neurological toxicity: grand mal seizures. Previously, subject had been prescribed Tegretol for previously observed petit mal seizures. Seizures are suspected to be due to brain metastases. Possible association with study drug administration cannot be ruled out.
3111	11/22/2000	09/19/2000		Follow Up1 to ID #3103. The subject had no adverse effects following second vaccination and no further seizures.
			9812-274	**A Phase I, Multi-Center, Open Label, Safety and Tolerability Study of Increasing Single Dose of NV1FGF Administered by Intra-Muscular Injection in Patients with Severe Peripheral Artery Occlusive Disease. Sponsor: Aventis (formerly Gencell).**
3076	11/13/2000	08/10/2000		Follow Up1 to ID #2880. Subject underwent GI evaluation for abnormal liver CTscan. Utrasound and MRI of liver were performed. Abnormality was diagnosed as hepatic cysts. No intervention was required and no neoplastic progression is contemplated.
3075	11/13/2000	10/15/2000		Initial; Subject hospitalized for severe exacerbation of chronic renal dysfunction. Admitted for hemodialysis and cardiac monitoring. Believed to be possibly associated with study drug administration. Event occurred on day 10 following last dosing.
3106	11/20/2000	10/15/2000		Follow UP1 to ID #3075. Submission by sponsor. Creatinine: 4.6; Blood Urea Nitrogen:128. No baseline labs given but subject described as having history of "borderline renal dysfunction", "tenuous fluid balance" and congestive heart failure.

Event #	OBA Date	Event Date	Protocol #	Event Description
			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)**
3079	11/14/2000	10/12/2000		Initial; Reported as: "Increase in subject's LDH and CO2 levels that were considered to be possibly associated with IND agent."
3108	11/21/2000	10/12/2000		Initial; Additional information on ID #3079. Subject had a history of prior chemo- and radio- therapies for another malignancy and was on concomitant medications during this study. At baseline, the subject's LDH was at the upper limit of normal and his CO2 was just below the lower limit of normal. Prior to cycle #6, his LDH showed grade 1 elevation, but CO2 level was unchanged. These lab values were not considered clinically significant and cycle #6 was administered. The investigator considered these events to be possibly associated with the study agent.
3210	12/20/2000	12/07/2000		Initial; Subject undergoing Ad-p53 experimental therapy for bronchioalveolar lung cancer was diagnosed on day 3 post-administration as having a progressive right lung mass adenopathy suggestive of a superimposed pneumonia. Subject was afebrile and the white blood cell count was not elevated. The grade 1 inflammation seen in the right lung was considered probably associated with the administration of the IND agent. Repeat chest X-ray seven days later indicated a worsening condition described as a "patchy and linear density" in the right suprahilar region. The scheduled day 14 treatment was postponed.
3261	01/11/2001	12/07/2000		Follow Up1 to ID #3210. Report from NCI-CTEP.
			9903-302	**A Open-Label, Rescue-Therapy Study of Intramuscular Vascular Endothelial Growth Factor-2 (VEGF-2) Gene Therapy in Patients with Moderate-Risk or High-Risk Critical Limb Ischemia. Sponsor: Vascular Genetics, Inc.**
1244	05/11/2000	04/25/2000		Initial; Four months after last dose and after lifting heavy boxes, subject noticed blood tinged urine associated with mild lower abdominal pain and mild discomfort in both testicles. Subject was referred to a urologist. Cystoscopy reveled papillary transitional cell carcinoma of the bladder (Grade 1). Suspected cause of event was concurrent illness. Event is considered possibly associated with study drug.
3142	12/05/2000	04/25/2000		Follow Up1 to ID #1244; Cystoscopy performed four months after the original diagnosis, revealed no evidence of tumor recurrence. Event considered possibly related to study drug.

Event #	OBA Date	Event Date	Protocol #	Event Description
			9911-354	**A Placebo-Controlled, Dose-Escalating Study of Intramyocardial Vascular Endothelial Growth Factor 2 (VEGF2) Gene Therapy Administered Using Percutaneous Cardiac Catheterization in Patients with Class III or IV Angina. Sponsor: Vascular Genetics, Inc.**
3175	12/12/2000	11/29/2000		Initial; Subject with history of coronary artery disease, diabetes, CABG and angioplasty received experimental new drug (VEGF) or placebo via percutaneous cardiac catheterization. On follow up exam, subject was diagnosed with proliferative diabetic retinopathy (PDR) of the right eye. This condition was not noted prior to enrollment in the experimental study, but review of an exam performed 4 years earlier indicated pre-existence of PDR in the right eye. PI suspects the cause of the event to be due to pre-existing disease but the association with the study drug is unknown.
			0001-385	**Phase I/II Study of GM-CSF Gene-Modified Autologous Tumor Vaccines in Early and Advanced Stage Non-Small Cell Lung Cancer (NSCLC). Sponsor: Cell Genesys, Inc.**
3278	01/19/2001	12/27/2000		Initial; Subject underwent restaging evaluation. The CT scan of chest showed evidence for a large pericardial effusion. The pericardial effusion was present prior to the experimental study treatment, but increased in size following the intervention. Investigator believes the increase in effusion as possibly associated with the experimental study treatment.
3279	01/19/2001	01/02/2001		Initial; Subject in event ID #3278 was admitted for echocardiogram to rule out a pericardial tamponade and possible pericardial window placement. No tamponade, but pericardial window done to obtain fluid for diagnostic purposes. Fluid cytology and pericardial biopsy were negative for malignancy and bacteria.
			0001-387	**A Randomized, Double-Blind, Placebo-Controlled, Multicenter, 12-Week Follow-up, Pilot Study of the Tolerability and Feasibility of Administering ADGVVEGF121.10 (CI-1023) Via the Biosense Intramyocardial Injection Device to Patients with Advanced Coronary Artery Disease. Sponsor: Parke-Davis Pharmaceutical Research**
3072	11/07/2000	10/30/2000		Initial; Patient developed recurrent vomiting with persistent nausea post procedure. Pt was treated with antiemetics and vomiting subsided the next day. The event was considered possibly related to study drug.
3144	12/06/2000	11/29/2000		Initial; About 13 hrs post study drug injection or placebo, subject developed high-grade fever with chills. The condition was treated with a single dose antibiotic and antipyretics. Fever subsided the next evening. Subject was observed for 24 hours and remained afebrile. She was discharged the next day.
3218	12/21/2000	11/29/2000		Follow up1 to ID #3144. Sponsor submission of same event.

Event #	OBA Date	Event Date	Protocol #	Event Description
			0002-391	**Phase II Study of Leuvectin in Patients with Metastatic Renal Cell Carcinoma. Sponsor: Vical Inc.**
3179	12/14/2000	10/20/2000		Initial; Hospitalization for dehydration. Subject was treated with IV fluids; recovered and was released two days later. Event believed to be due to Interleukin-2, expressed by the plasmid DNA in the experimental drug substance, Leuvectin .
			0006-403	**A Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Effect of Ad5FGF-4 on Myocardial Perfusion Defect Size and Safety in Patients with Stable Angina. Sponsor: Berlex Laboratories**
3096	11/17/2000	11/15/2000		Initial; On study day 3, following administration of experimental agent, subject awoke with fever (102.6 ºF), chills, general body aches and low back pain. Subject self-medicated with acetaminophen and fever broke in five hours. Subject went to the ER and was admitted for "fever of unknown origin". Discharged the following day (day 4 post-administration) with continued back pain. Subject scheduled to return for repeat labs and exam in 5 days. The cultures done at admission were all negative. The patient returned for follow-up as instructed and the bilirubin was back to normal.
3299	01/30/2001	01/10/2001		Initial; At Week 12 the patient was found to have an asymptomatic elevation of his liver function test (LFT) values: Alk Phos 441, ALT 477, AST 363, LDH 390. Lipitor was discontinued and the patient was referred to a gastroenterologist. The patient was found to be Hepatitis C positive by PCR methodology. He is negative for Hepatitis A and B. Relationship to the experimental study drug is unknown.
3381	02/23/2001	01/10/2001		Follow-up1 to ID #3299; Baseline serum samples were negative for Hepatitis C RNA by rtPCR followed by PCR analysis. The patient remains asymptomatic and his LFTs are declining. The patient had received active product so the following were tested and found negative for Hepatitis C RNA by rtPCR followed by PCR analysis: Samples of the final product used in the clinical study Reserve samples of the bulk used to produce the final product Reserve samples of the harvest used to produce the final product Master Cell Bank used to produce the final product.