SAFETY REPORTS AND ADVERSE EVENTS FOR
HUMAN GENE TRANSFER PROTOCOLS
RECOMBINANT DNA ADVISORY COMMITTEE MEETING
September 25-26, 2000

ID #	OBA Date	Protocol	Description
2439	6/1/00	9303-037 Sponsor: GTI/Novartis	Gene Therapy for the Treatment of Recurrent Glioblastoma Multiforme with In Vivo Tumor Transduction with the Herpes Simplex Thymidine Kinase Gene/Ganciclovir System. Initial; Event: Pt found to be pancytopenic, believed possibly related to study drug. Treated by transfusion.
2443	6/1/00	037	Initial; Event: Neurological deterioration and cerebral edema deemed probably due to study drug. Cerebral edema occurred soon after ganciclovir and responded to glucocorticoid therapy .
2444	6/1/00	037	Initial; Event: Headache, hemiparesis, reduced responsiveness, aphasia, cerebral edema and mass effect on MR scan deemed probably due to study drug. Event occurred 2 days post injection.
2449	6/1/00	037	Initial; Event: Ommaya reservoir infection deemed definitely related to study drug. Resolved with antibiotic therapy.
2450	6/1/00	037	Initial; Event: Severe headache, lethargy, nuchal sensitivity, and pain associated with Ommaya reservoir infection believed definitely related to study drug. Resolved with antibiotic therapy.
2455	6/1/00	037	Initial; Event: Mild rigors & fever followed by nausea & vomiting the next day believed to be possibly related to study drug. Spontaneously resolved within 24 hrs.
2465	6/1/00	037	Initial; Event: Post-operative hemiplegia deemed possibly related to study drug. Resolved within 1 week.
2469	6/1/00	037	Initial; Event: Fever and headache probably due to study drug.
2471	6/1/00	037	Initial; Event: Intracranial hypertension possibly related to study drug. Resolved after therapy with mannitol and glucocortioids.
2482	6/1/00	037	Initial; Event: Cerebral edema deemed probably related to study drug. Resolved after craniotomy with evacuation of necrotic tissue.
2485	6/1/00	037	Initial; Event: Increased cerebral edema with left side neglect, dysarthria and confusion believed to be possibly related to study drug.
2486	6/1/00	037 Roth	Initial; Event: Somnolence (probable cerebral edema) believed possibly related to study drug.

2491	6/1/00	037	Initial; Event: Convulsion soon after study drug. Convulsion believed possibly related to study drug. Phenytoin level sub-therapeutic.
2495	6/1/00	037	Initial; Event: Cerebral edema, lethargy, dysphagia and hemiparesis occurred soon after injection of study drug. Event believed to be possibly related to study drug.
2504	6/1/00	037	Initial; Event: Increased confusion, hemianopsia and unsteadiness deemed possibly related to study drug
2510	6/1/00	037	Initial; Event: Cerebral edema, lethargy, hemiparesis, headache and nausea, vomiting with peri-cavity edema seen on CT scan. Event probably caused by study drug. Improvement with increased glucocorticoids.
2430	6/1/00	9306-050 Sponsor: GTI/Novartis	Gene Therapy for the Treatment of Recurrent Pediatric Malignant Astrocytomas with In Vivo Tumor Transduction with the Herpes Simplex Thymidine Kinase Gene. Initial; Event: Focal seizures with cerebral edema deemed to be probably related to study drug. Resolved with corticoids.
2432	6/1/00	050	Initial; Event: Cerebral edema, focal seizures, headache, fever deemed possibly related to study drug. Resolved post resection.
223	1/20/00	9403-069 Sponsor: NIH/Cell Genesys, Inc.	A Phase I/II Pilot Study of the Safety of the Adoptive Transfer of Syngeneic Gene-Modified Cytotoxic T-Lymphocytes in HIV-Infected Identical Twins. Initial; Event: Hospitalized with 12 hr history of fever, chills, productive cough and dyspnea, O2 saturation level in low 70s, basilar rales, DX with pneumonia.
1715	6/12/00	9409-083 Sponsor: Targeted Genetics Corp.	Initial; Event: Pt admitted for subacute pulmonary exacerbation of CF lung disease with increased cough and sputum and decreased FEV1 from 76%(predicted) at screening to 60.6% just prior to vecto delivery to 49.2% 2 weeks post infusion. Pulmonary exacerbation believed to be possibly related to study medication.
1825	6/27/00	083	F1 to ID #1715: 15 yo pt received vector 5/26/00. On 6/2/00, pt experienced symptoms of subacute pulmonary exacerbation of CF lung disease. Pt admitted 6/12/00 for IV antibiotics. Exacerbation resolved, pt discharged 6/23/00. Investigator believes event possibly related to study drug.
2645	6/21/00	9412-098 Grossman & Woo	Phase I Study of Adenoviral Vector Delivery of the HSV-TK Gene and the Intravenous Administration of Ganciclovir in Adults with Malignant Tumors of the Central Nervous System. Initial; Event: Pt experienced severe headache immediately post vector injection. CT showed air within the ventricular system raising the possibility of vector entry into the CSF. Twelve hrs post injection pt became obtunded and had fever 38.9C. Pt subsequently returned to baseline neurological status.
2646	6/21/00	098	Initial; Event: Three days post vector injection, pt developed

			hyponatremia and obtundation. Initially showed improvement after correction of hyponatremia, but later deteriorated. CT showed hydrocephalus, VP shunt placed. CSF protein increased. Pt gradually improved until tumor progression supervened.
2648	6/21/00	098	Initial; Event: Six day post vector injection, pt had generalized seizure. Ct showed right frontalhematoma. Pt improved, but did not return to baseline neurological status.
2649	6/21/00	098	Initial; Event: Pt experienced alteration in mental status 24 hours po vector injection; subsequently improved.
2580	5/30/00	9503-100 Link & Morrman	A Phase I Trial of In Vivo Gene Therapy with Herpes Simplex Thymidine Kinase/Ganciclovir System for the Treatment of Refractory or Recurrent Ovarian Cancer. Initial; Event: Pt complained of abdominal pain and distention after receiving study drug. Pt admitted for pain control and observation. Discharged next am.
2365	8/8/00	9503-103 Morgan & Tavel	Gene Therapy for AIDS using Retroviral Mediated Gene Transfer to Deliver HIV-1 Antisense TAR and Transdominant Rev Protein Genes to Syngeneic Lymphocytes in HIV Infected Identical Twins. Initial; Event: Pt began experiencing significant weight loss. Ileal mass identified. Biopsy positive for lymphoma (diffuse, high-grade B-cell). Documentation has conflicting causality - "research team" states event unlikely to be related to study drug / treatment; investigator states "possible association".
627	1/31/00	9506-109 Hwu	Treatment of Patients with Advanced Epithelial Ovarian Cancer using Anti-CD3 Stimulated Peripheral Blood Lymphocytes Transduced with a Gene Encoding a Chimeric T-cell Receptor Reactive with Folate Binding Protein. Initial; Event: Several hours after delivery, pt complained of dyspnea; pulmonary infiltrates were noted. Pt recovered fully after several days of treatment.
2548	8/25/00	9512-137 Sponsor: Targeted Genetics Corp.	Phase I Study of E1A Gene Therapy for Patients with Metastatic Breast or Ovarian Cancer that Overexpresses Her-2/neu. Initial; Event: Pt hospitalized with fever, chest pain, pleural effusion and dyspnea. Fever believed to be probably related to study drug. Pleural effusion believed to be possibly related to study drug. Ches pain and dyspnea believed to be related to study drug.
1504	6/1/00	9512-138 Black & Fakhrai	A Phase I Study of the Safety of Injecting Malignant Glioma Patients with Irradiated TGF- $ 2 Antisense Gene Modified Autologous Tumor Cells. Initial; Event: Pt received contaminated vector (aspergillus). No adverse effects. Pt subsequently received 4 more injections.
2604	5/30/00	9602-146	Adoptive Immunotherapy for Leukemia: Donor Lymphocytes

		Link, Burt & Traynor	Transduced with the Herpes Simplex Thymidine Kinase Gene for Remission Induction Initial; Event: Several hrs after pt received study drug, complained c chills and low-grade fever. Pt went to ER, was monitored and later released. Fever and chills resolved.
2661	6/20/00	9605-154 Harsh et.al.	Phase I Study of Retroviral-Mediated Incorporation of the HSV Thymidine Kinase Gene and Ganciclovir in Malignant Gliomas Initial; Event: Pt developed intracranial infection approximately 2 weeks post-injection of study drug.
1849	5/26/00	9908-157 Sponsor: GTI/Novartis	Prospective, Open-Label, Parallel-Group, Randomized Multicenter Trial Comparing the Efficacy of Surgery, Radiation, and Injection o Murine Cells Producing Herpes Simplex Thymidine Kinase Vector Followed by Intravenous Ganciclovir Against the Efficacy of Surgery and Radiation in the Treatment of Newly Diagnosed, Previously Untreated Glioblastoma. Initial; Event: Cerebral edema deemed possibly associated with treatment. Steroid dosage was increased
1876	5/26/00	157	Initial; Event: Poor appetite, depression, nausea, vomiting increased left-side weakness. Considered by PI as not related to study drug or treatment; considered by sponsor to be possibly related to treatment.
1892	5/26/00	157	Initial; Event: Tumor necrosis. MRI (9/29/97) indicated tumor progression by increased enhancement. Craniotomy revealed only necrosis.
1904	5/26/00	157	Initial; Event: Atrial flutter with heart block. Event deemed not related to study drug / treatment by PI. Sponsor indicates possible association. Event occurred day after surgery. Potential precipitating factors: Surgery, peri-operative anesthesia, vector producer cell injections. Pt treated with medication and cardioversion.
1917	5/26/00	157	Initial; Event: Post-operative epidural hematoma, intra-tumoral hematoma, cerebral edema, increased intracranial pressure, herniation. Events deemed unlikely to be associated with study drug by PI; sponsor offers a possible association. Pre-operative mild prolongation of PT/PTT -- treated with Vitamin K. History of polycythemia vera. Treatment: postop evacuation of epidural hematoma effected 2X plus anti-edema treatment including intraventricular drain. Narrative provided.
1918	5/26/00	157	Initial; Event: Pt developed pneumonia, sepsis, and neutropenia. Events were considered possibly associated with study medication / treatment by PI; sponsor indicates probable association Neutropenia and myelosuppression are the suspected consequence of Gancyclovir therapy, complicated by sepsis. Narrative not found
1919	5/26/00	157	Initial; Event: (see ID #1918). Pt. Expired.
1938	5/26/00	157	Initial; Event: Suspected tumor recurrence and post-op intracerebral hematoma. Considered possibly associated with study drug /

			intervention. MRI (1/23/98) indicated increased enhancement but below progression threshold. Pathology analysis following craniotomy indicated presence of necrosis and recurring glioblastoma multiforme
1949	5/26/00	157	Initial; Event: Pt. experienced aphasia, R-side hemiparesis with evidence of L-brain edema. Event considered possibly associated and resolved. Event was contemporary with radiotherapy; though edema is not usually seen with radiotherapy alone. Pt recovered fully without sequelae and was prescribed steroids.
1952	5/26/00	157	Initial; Event: Pt. suffered acute worsening of pre-existing hemiparesis resulting in R-side hemiplegia. Event deemed possibly associated to drug / intervention. Condition improved. Steroids were prescribed .
1985	5/26/00	157	Initial; Event: Pt. experienced high fever and hypertension. Radiation therapy was interrupted. Pt was administered Paracetamol & Indomethacin. Condition resolved. Event was deemed possibly associated.
1993	5/26/00	157	Initial; Event: Cystic encapsulation of the resection cavity with surrounding edema. Pt developed worsening R-side hemiparesis and persisting dysphasia. Event is considered possibly associated with study drug / treatment and is believed to be a possible inflammatory response to vector producer cells. Pt was treated by implantation of an intra-cystic reservoir and aspiration.
1996	5/26/00	157	Initial; Event: Cerebral edema w/ headache, vomiting and L-side hemiparesis. MRI results (5/20/ 97) indicated progression by increased enhancement. Radionecrosis is suspected. Event is deemed possibly associated.
1997	5/26/00	157	Initial; Event: (see #1996). Pt developed cerebral edema w/ associated hemiparesis and drowsiness. Pt steroid dose was increased. Condition resolved; event was deemed possibly associated.
2037	5/26/00	157	Initial; Event: Pt exhibited moderate L-side hemiparesis appearing 4 days after start of ganciclovir treatment and after reducing prednisone dosage (25 mg to 10 mg per day). Event was considered possibly associated with drug / treatment and condition resolved.
2557	8/25/00	9610-162 Sponsor: Targeted Genetics Corp.	A Phase I Multicenter Study of Intratumoral E1A Gene Therapy for Patients with Unresectable or Metastatic Solid Tumors that Overexpress HER-2/neu. Initial; Event: Pt experienced a mental status change of moderate severity, but requiring hospitalization. Condition resolved and event was deemed possibly associated with study drug / treatment.
2185	6/27/00	9701-175 Lieberman, Germano	Gene Therapy for Recurrent Glioblastoma Multiforme: Phase I Trial of Intraparenchymal Adenoviral Vector Delivery of the HSV-TK Gene and Intravenous Administration of Ganciclovir.

		& Woo	Initial; Event: Pt woke up from surgery able to move all extremities and follow commands. Later in the day suffered status epilepticus. Continued to have seizures for more than 20 days. Investigator ruled seizures to be possibly related.
287	12/13/99	9706-191 Sponsor: Vical, Inc.	Phase II Study of Immunotherapy by Direct Gene Transfer with Allovectin-7 for the Treatment of Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck. Initial; Event: Severe abdominal pain and ascites, fever (100.2 F)
566	2/3/00	9708-205 Simons	Phase I/II Study of Allogeneic Human GM-CSF Gene Transduced Irradiated Prostate Cancer Cell Vaccines in Patients with Prostate Cancer. Initial; Event: 3 days post delivery pt developed right arm swelling and pruritis, hospitalized for IV antibiotics
177	2/8/00	9708-207 Sponsor: NCI-CTEP	Phase I Clinical Trial of a Recombinant ALVAC-CEA-B7 Vaccine in the Treatment of Advanced Colorectal Carcinoma Initial; Event: Grade 1 fever (100.2 F) 1 day post vaccination. Lab analyses within normal levels; discharged 6/13/98
2122	7/3/00	9709-214 Sponsor: Aventis Pharmaceuticals	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). FU to ID #2123: Treatment with paracetamol at the time of the event then prophylactically prior to injection
2123	7/3/00	214	Initial; Event: Six hours post injection pt developed fever and chills. Events considered probably related to study drug.
2139	7/3/00	214	Initial; Event: Five days post injection pt developed nausea, generalized weakness and fever. Admitted and treated. Fever considered probably related to study medication.
2144	7/3/00	214	Initial; Event: Bleeding from oral cavity ulcer 14 days post injection. Admitted for evaluation. Electrocautery treatment successful. Hemorrhage considered possibly related to study medication.
2155	7/3/00	214	FU to ID #2157: Clarification of dates of treatment and event. Fever considered possibly related to study medication.
2157	7/3/00	214	Initial; Event: Post injection pt complained of fatigue, chills, temp 103.5, minimal bleeding. Admitted and treated with Advil, Surgi-Cell. Discharged 2 days later, afebrile, no bleeding
2340	8/3/00	214	F1, no initial report found. Pt admitted for progressive weakness and

			inability to ambulate. Diagnosis indicates Guillain-Barre Syndrome. Investigator deems G-B syndrome to be possibly associated with study medication.
2094	7/3/00	9712-226 Sponsor: Aventis Pharmaceuticals	A Phase II, Multi-Center, Open Label, Study to Evaluate Effectiveness and Safety of Ad5CMV-p53 Administered by Intra-Tumoral Injections in 39 Patients with Recurrent Squamous Cell Carcinoma of the Head and Neck (SCCHN). Initial; Event: After beginning treatment, pt required opiate-class analgesics to control tumor pain. Event considered possibly related to study medication.
567	2/3/00	9802-238 Sponsor: Berlex Laboratories, Inc.	Phase I/II Study of the Effects of Ascending Doses of Adenovirus Mediated Human FGF-4 Gene Transfer in Patients with Stable Exertional Angina. Initial; Event: 1 day post delivery, fever to 40.1C, complete blood count within normal limits, blood cultures negative, chest X-ray indicates no change, treated with Tylenol
1615	6/6/00	238	Initial; Event: Pt hospitalized for worsening chest pain. Pt exhibited history of chest pain w/ atypical features before and after administration of study drug via single intracoronary injection. No evidence of myocardial infarction was noted. Pt was discharged the day after hospitalization and remains stable with occasional episodes of pain. Pt's cardiac markers are all within normal limits. Event was considered possibly associated with study drug / treatment.
1642	6/7/00	238	F1 to ID #1615: Correction to previous report: IBC reporting date provided.
1826	6/27/00	238	Initial; Event: Pt had accelerating angina over 3-month duration. Pt elected to undergo coronary artery by-pass graft surgery.
1833	6/27/00	238	Initial; Event: Pt suffered acute myocardial infarction post coronary artery by-pass graft surgery (see #1826).
1787	6/12/00	9803-241 Sponsor: Chiron Corp.	A Phase I/II Outpatient, Multicenter, Intrapatient, Multiple Dose Escalation Study of Herpes Simplex Virus Thymidine Kinase (HSV-TK) Transduced Mononuclear Cells in Subjects with Persistent or Relapsed Chronic Myleogenous Leukemia, Chronic Lymphocytic Leukemia, Multiple Myeloma, and Non-Hodgkin's Lymphoma after HLA-Matched Sibling Allogeneic Stem Cell Transplant. Initial; Event: Subject is male undergoing treatment for chronic myelogenous leukemia (CML) that recurred following partial-match stem cell transplantation. Subject received a TK-DLI infusion on 12/22/98 w/o complications. Pt developed severe abdominal pain with ileus and intestinal obstruction. Laparotomy and appendectomy were performed. Colonic biopsies were initially read as Graft-Versus-Host-Disease (grade II). The diagnosis was subsequently reversed as the clinical syndrome was not consistent

			with GVHD. Pt was removed from study and subsequently discharged. Pt was noted subsequently to have episodes of pancytopenia, a condition typical for the disease pattern. The subject eventually succumbed to progressive CML. Events: Appendicitis, intestinal obstruction, were considered possibly associated with the study drug or treatment.
1801	6/12/00	241	Initial; Event: Subject is male with diagnosis of CML (1/22/93) that recurred following matched bone marrow transplantation in Nov. 1994. The subject received four administrations of study drug (TK-DLI) over the period of one year. Following the 4th dose, pt was hospitalized for fever and chills, treated with analgesics and antihistamines and discharged w/o sequelae. The pt completed the protocol in Feb. 1999. He subsequently died of progressive CML. Events: Chills and fever were considered possibly related to study drug.
2523	6/1/00	9803-242 Kipps	A Phase I Study of CD 154 Gene-Transduced Leukemia Cells in Patients with Chronic Lymphocytic Leukemia. Initial; Event: After receiving 3rd dose, pt experienced cholecystitis, hypoxia and hypotension requiring admission to ICU. Due to the temporal relation, investigator cannot rule out event is related to study drug. Pt recovered completely.
2524	6/1/00	242	Initial; Event: After 1st dose pt experienced flu-like symptoms, abdominal pain, dyspnea, fatigue, transient thrombocytopenia, prolonged PT, edema, elevated serum creatinine and elevated total bilirubin. Because of the severity of the symptoms, the pt's hospitalization was prolonged. The pt recovered completely.
2525	6/1/00	242	Initial; Event: After 2nd dose pt experienced severe flu-like symptoms requiring an extended hospitalization. Flu-like symptom deemed related to study drug. Pt recovered completely.
2526	6/1/00	242	Initial; Event: After 2nd dose pt experienced elevated transaminases deemed related.
2527	6/1/00	242	Initial; Event: After 3d dose pt experienced fever, nausea, worsening of fatigue and anemia. Given 2 units packed red blood cells. Pt taken off study 1 week later due to disease progression.
2532	6/1/00	242	Initial; Event: After 1st dose pt experienced moderate to severe flu-like symptoms, postural hypotension, prolonged PT, decreased serum albumin, elevated hepatic transaminases and thrombocytopenia. Postural hypotension rated severe and probably related to therapy. Pt recovered completely.
2533	6/1/00	242	Initial; Event: After 1st dose pt experienced flu-like symptoms, insomnia, worsening fatigue, and worsened thrombocytopenia related to therapy requiring an extended hospitalization. Symptoms resolved within one week.
503	1/28/00	9804-243	Phase I Study of Direct Administration of a Replication Deficient Adenovirus vector (Ad_{GV}VEGF121.10) Containing the VEGF121

		Sponsor: GenVec, Inc.	cDNA to the Ischemic Lower Limb of Individuals with Peripheral Vascular Disease. Initial; Event: Pt hadcystoscopy to remove bladder tumor. Initial diagnosis: Papillary transitional cell carcinoma, Grade I/III.
75	11/11/99	9804-244 Walsh	A Phase I Study Using Direct Combination DNA Injections for the Immunotherapy of Metastatic Melanoma. Initial; Event: Grade 4lymphopenia, consent form changed as a result
2404	8/16/00	2804-245 Sponsor: Targeted Genetics Corp.	A Phase I Study of Aerosolized tgAAVCF for the Treatment of Cystic Fibrosis Patients with Mild Lung Disease. Initial; Event: Pulmonary exacerbation requiring hospitalization deemed possibly related to study drug.
2405	8/16/00	245	Initial; Event: Pneumonia requiring hospitalization deemed possibly related to study drug.
2397	8/16/00	9804-246 Sponsor: Targeted Genetics Corp.	A Multicenter Phase II Study of E1A Lipid Complex for the Intratumoral Treatment of Patients with Recurrent Head and Neck Squamous Cell Carcinoma. Initial; Event: Vomiting, severe, requiring intervention to prevent permanent impairment, believed to be possibly related to study drug
1501	6/1/00	9804-250 Sponsor: Aventis Pharmaceuticals	An Efficacy Study of Adenoviral Vector Expressing Wildtype p53 (Ad5CMV-p53) Administered Intralesionally as an Adjunct to Radiation Therapy in Patients with Non-Small Cell Lung Cancer. Initial; Event: Pt presented to ER complaining of chest pain within few hrs of receiving vector. Admitted to CCU for recovery from myocardial infarction.
1823	6/26/00	250	Initial; Event: 70yo pt with NSCLC two days post intratumoral injection, pt had increase in sputum with temperature of 37C Levofloxacin started 6/16/00, CRP increased, CXR WNL. Started on cefozopan 6/19/00, CXR 6/20/00 showed obstructive pneumonia. Event considered remotely related to study drug.
2341	8/3/00	250	F1, but no initial report found. Pt admitted for hydration. Pt complained of esophagitis, inability to swallow. Initially considered by investigator as related to radiotherapy, not study drug. Investigator changed causality to "possibly associated" with study drug.
2348	8/7/00	250	Initial; Event: Subject is female with diagnosed lung cancer (tumor in right upper lung lobe). Pt was treated for a third time with AdCMV-p53 on Feb. 16 1999. In January 1999, pt complained of

			dyspnea and was hospitalized for pneumonia. Event was considered by the PI to be "possibly associated" with study drug.
1810	6/21/00	9806-255 Sponsor: NCI-CTEP	Phase I Trial of Intraperitoneal Adenoviral p53 Gene Therapy in Patients with Advanced Recurrent or Persistent Ovarian Cancer. Initial; Event: Pt presented for cycle II, course XII gene transfer treatment. Pre treatment exam showed white blood cell count of 2.8. Treatment was delayed 1 week pending WBC recovery >3.0. Pt is asymptomatic.
1828	6/22/00	255	Initial; Event: Patient is female with diagnosis of papillary serous ovarian cancer (see #1810). Pt presented for for 12th course of intraperitoneal administration of Ad-p53. Pt presented with grade II leukopenia and anemia. Treatment was delayed pending recovery of WBC counts. Pt was asymptomatic Event was considered possibly related to treatment and has been noted previously in the same patient on 10/12/99. At that time, pt recovered spontaneously as well.
749	12/16/99	9806-259 Sponsor: Vical, Inc.	Phase II Study of Direct Gene Transfer of IL-2 Plasmid DNA/DMRIE/DOPE Lipid Complex (Leuvectin) as an Immunotherapeutic Regimen in Patients with Metastatic Renal Cell Carcinoma. Initial; Event: Admitted for suspected pancreatitis.
788	11/11/99	9808-263 Sponsor: NCI-CTEP	Phase I Trial of Adenovirus-Mediated Wild Type p53 Gene Therapy for Malignant Gliomas. Initial; Event: Post-op bleed - with mild left sided weakness, probably related to injection technique, but possibly related to IND drug.
2314	7/28/00	263	Initial; Event: Patient has diagnosis of glioblastoma multiforme of the L frontal lobe. Pt experienced grade 3 aphasia and grade 3 MRI enhancement. IV glucocorticoid administered. Repeat MRI showed significant decrease in enhancement size. Pt's clinical symptoms have improved
254	12/13/99	9901-280 Sponsor: Schering Corp.	A Phase II/III Trial of Chemotherapy Alone Versus Chemotherapy Plus SCH 58500 in Newly Diagnosed Stage III Ovarian and Primary Peritoneal Cancer Patients with ≥0.5 cm and ≤2 cm Residual Disease Following Surgery. Initial; Event: During infusion, pt experienced facial flushing and abdominal pain. Infusion interrupted, events resolved and infusion restarted. Later, after infusing 70 cc of 100 cc total, pt experienced chest pain, pressure and nausea, infusion stopped, events resolved, ECG's negative, later that evening pt experienced rigors, sweating, slurred speech, nausea, vomiting, diagnosis - possible central nervous system bleed.

255	12/13/99	280	Initial; Event: Fever (38.5 C), severe nausea, vomiting, neutropenia. Ileus noted on x-ray
256	12/13/99	280	F2 to ID #255: Copy of 836 submitted by B. Ndubisi.
824	11/2/99	280	Initial; Event: Nausea, vomiting, diarrhea, neutropenia
836	11/2/99	280	F1 to ID #1051: Neutropenia probably related to IND drug
1050	12/15/99	280	Initial; Event: Pt developed a fistula along intraperitoneal catheter.
1051	10/20/99	280	Initial; Event: Pt hospitalized with fever and neutropenia. Also had nausea, vomiting, abdominal pain - diagnosed with ileus.
1129	2/2/00	280	F2 to ID #13: Additional pt history provided.
2242	7/21/00	280	Initial; Event: After approx 50% of infusion, green, purulent, foul smelling drainage noted from abdominal catheter site. Infusion immediately discontinued. Several hrs later drainage changed to light black. Pt diagnosed with enterocutaneous fistula. Exp lap with extensive adhesiolysis. Sponsor considers adhesions possibly related to study drug.
2255	7/19/00	280	Initial; Event: Pt complained of bowel obstruction - CT showed new cystic tumor and peritoneal carcinosis. X-ray 6/23/00 showed small bowel obstruction. Stomach tube placed, TPN initiated. Fever 6/26/00 - cultures (+) anaerobic bacteria. Abdominal surgery 6/30/00 - adhesions and abscess removed. Adhesions considered probably related to study drug.
2258	7/19/00	280	F1 to ID #2255. Blood cultures (-) for bacteroides, one peritoneal abscess (+) for E.coli; others sterile.
2279	7/2500	280	Initial; Event: (See 2280, 2281, 2282) Pt admitted for peritonitis and febrile neutropenia - surgery to remove intraperitoneal catheter 6/27/00. Pt had several episodes nausea and vomiting, SBFT showed partial small bowel obstruction. Pt to surgery 7/1/00 - exp lap with lysis of adhesions, resection of ileum and placement of dual lumen Stamm gastrostomy tube. Event considered probably related to study drug.
2280	7/25/00	280	Initial; Event: (See 2279, 2281, 2282) Pt admitted for after nausea, vomiting, abdominal pain, and thick yellow drainage from the intraperitoneal site. Started on IV antibiotics, IV hydration, pain and nausea control. Event believed to be probably related to study drug.
2281	7/25/00	280	Initial; Event: (See 2279, 2280, 2282) Pt to ER complaining of weakness. Pt found to have orthostatic changes. Hydrated with IV fluids. Event considered probably related to study drug.
2282	7/25/00	280	Initial: Event: (See 2279, 2280, 2281) Pt to ER complaining of nausea, vomiting, diarrhea, intermittent sharp stabbing abdominal pains, pain and aching in arms, legs and shoulders. Admitted and given and IV fluids and pain control. Causality assessment not completed.
2335	8/2/00	280	Initial; Event: 5 days post infusion, pt experienced intermittent paresis of the left leg, diarrhea, disorientation and somnolence.

			Admitted with subfebrile temperatures and elevated CRP. Grade 2 fever began one day into admission. Pt complained of constipation and abdominal pain. IV antibiotics and pain control initiated. Blood cultures neg. MRI showed colon ileus. TPN started. CXRs showed increasing pleural effusions. Intraperitoneal port removed 7/19 - culture neg. Blood culture from subclavian catheter (+) for Candida Albicans. Peripheral blood cultures neg. On 7/22, pt experienced increased respiratory insufficiency and transferred to ICU and intubated. Colonoscopy showed stenosis of descending colon 30 cm from anus. Pt's condition continued to worsen and patient expired 7/24.
2336	8/2/00	280	Initial; Event: Death of pt described in 2335. Autopsy (abdominal only) - no abdominal tumor noted, colon stenosis not seen. Investigator felt the study medication may have impacted the pt's immune system thus contributing to the fatal Candida sepsis and considered the death as possibly related to the study medication.
2337	8/2/00	280	F1 to ID #2335. Pt was severely neutropenic and study may have contributed to pt's lack of response to cytokines. The sponsor believes the candida sepsis was caused by a subclavian catheter infection and pneumonia in a pt immunocompromised from chemotherapy and believes the event is unlikely to be related to study medication.
2338	8/2/00	280	F1 to ID #2336. Investigator believes fatal sepsis was possibly caused by study medication. Sponsor believes unlikely related to study medication.
2342	8/3/00	280	F2 to ID #2256. Additional pt history provided. Causality remains possibly related.
2343	8/3/00	280	F2 to ID #2257. Additional pt history provided. Causality remains possibly related
2344	8/3/00	280	F2 to ID #2255. Additional pt history provided. Causality remains possibly related.
2364	8/8/00	280	F1 to ID #2242: Event resolved 4/26/00. Investigator believes event probably related to study drug.
753	12/23/99	9902-285 Grandis	A Phase I Trial of Intratumoral Antisense EGFR DNA and DC-Chol Liposomes in Advanced Oral Squamous Cell Carcinoma. Initial; Event: Pt admitted with cellulitis of the face.
2231	7/18/00	285	Initial; Event: Pt had increased oozing from old biopsy site and new injection site (6/14/00). Cultures showed streptococci. Started on antibiotics. Fever and oozing considered as possibly related to the study medication.
2232	7/18/00	285	F1 to ID #2231: Pt's condition continued to worsen. Tumor nodules visible on outside on pt's neck.
2250	7/19/00	9903-298 Link & Morrman	A Phase II Trial of In Vivo Gene Therapy with the Herpes Simplex Thymidine Kinase for the Treatment of Ovarian Cancer.

			Initial; Event: Pt admitted due to myalgia and arthralgia. Dx as probable RA. Treated with prednisone and Celebrex with relief. Determined to be possibly related to study drug.
2590	5/30/00	298	Initial; Event: Immediately post infusion of study drug, pt complained of light-headedness and acute abdominal pain. Temp 100.4F, HR 42 R 16 BP 66/33. 15 minutes later BP 122/60. Admitted for pain control and observation. Discharged next day.
80	2/2/00	9903-301 Sponsor: Vascular Genetics, Inc.	A Randomized, Double-Blind, Placebo-Controlled, Dose-Escalating Study of Intramuscular Vascular Endothelial Growth Factor-2 (VEGF-2) Gene Therapy in Patients with High-Risk Critical Limb Ischemia. Initial; Event: Hospitalized with severe bilateral lower extremity edema and shortness of breath, discharged 12/23/99
94	1/6/00	301	Initial; Event: Hospitalized due to increased toe necrosis, pain and edema. Treated for pain management, diuretics, re-evaluated for potential amputation.
1824	6/26/00	9905-314 Sponsor: NCI-CTEP	A Phase I Trial of Intralesional RV-B7.1 Vaccine in the Treatment of Malignant Melanoma. Initial; Event: 20 days post injection, 57yo complained of severe pain in spleen area following physical exertion. Admitted for observation and treatment. Pain significantly decreased within 24 hrs. Discharged.
1054	10/22/99	9905-318 Sponsor: Schering Corp.	A Phase II Study of SCH 58500 in Combination with Chemotherapy Alone in Patients with Colorectal Cancer Metastatic to the Liver. Initial; Event: Decreased liver function tests and hemoglobin, urine and blood cultures (+). Hospitalization prolonged due to leukocytosis, fever and anemia. Investigator considers the leukocytosis probably due to IND drug.
2345	8/4/00	9906-323 Sponsor: Valentis, Inc.	A Multi-Center, Open-Label, Randomized Study of the Safety and Efficacy of Multiple Intratumoral Injections of hIl-2 Plasmid (1.8 mg) Formulated with DOTMA/Cholesterol [Ratio 1:0.5 (-/+)] Liposomes in Patients with Unresectable or Recurrent/Refractory Squamous Cell Carcinoma of the Head and Neck. Initial; Event: Pt experienced a "seizure episode" with alteration of consciousness while on study medication. Event considered possibly related to study medication.
1784	6/1/00	9906-324 Butler & Aguilar-Cordova	Phase I-II Study Evaluating HSV-tk + Valacyclovir Gene Therapy in Combination with Radiotherapy for Prostate Cancer. Initial; Event: Pt was admitted for chills, rigors and fever (103 F) hours after receiving injection of gene transfer product. Pt improved within hours after treatment with analgesics. Pt was discharged after one day (7/29/99). All vital signs are within normal limits. No

			specific causality was attributed to the event by the PI; it is considered by default, serious, possibly associated, and unexpected.
624	1/4/00	9908-335 Dranoff	A Phase I Study of Vaccination with Lethally Irradiated, Autologous Ovarian Carcinoma Cells Engineered by Adenoviral Mediated Gene Transfer to Secrete Human Granulocyte-Macrophage Colony Stimulating Factor. Initial; Event: Syncope with postural hypotension, tender, erythematous injection site, abdominal tenderness, white blood cell count: 22,100. Treated by IV hydration, hypertension resolved, abdominal tenderness decreased
2319	7/31/00	9909-339 Holt	Ovarian Cancer Gene Therapy with BRCA1. Initial; Event: During first infusion, pt had intractable pain 10/10. Infusion stopped, pain subsided. After total infusion of 72 ml and multiple recurrent episodes of pain, infusion discontinued and pt withdrew from study. Pain completely resolved.
760	12/29/99	9911-353 Sponsor: Vascular Genetics, Inc.	An Open Label Study of Intramuscular Vascular Endothelial Growth Factor-2 (VEGF-2) Gene Therapy in Patients with Critical Limb Ischemia. Initial; Event: Pt admitted with severe bilateral lower extremity edema and shortness of breath. Discharged 12/23/99.
2536	8/25/00	9912-355 Sponsor: Valentis Pharmaceuticals	A Phase III Multi-Center, Open-Label, Randomized Study to Compare the Overall Survival and Safety off Bi-Weekly Intratumoral Administration of RPR/INGN 201 Versus Weekly Methotrexate in 240 Patients with Refractory Squamous Cell Carcinoma of the Head and Neck (SCCHN). Initial; Event: Pt hospitalized with pneumonia, investigator assessed the event to be related to study drug.