

**AMENDMENTS AND UPDATES TO
HUMAN GENE TRANSFER PROTOCOLS**

**RECOMBINANT DNA ADVISORY COMMITTEE MEETING
December 2001**

ID #	Letter	Protocol #	Amendment
		9303-040	Phase I Study of Non-Replicating Autologous Tumor Cell Injections Using Cells Prepared With or Without Granulocyte-Macrophage Colony Stimulating Factor Gene Transduction in Patients with Metastatic Renal Cell Carcinoma.
249	07/16/2001		<p data-bbox="558 500 1948 558"><i>Status Change:</i> Trial is closed. Study participants have been asked to enroll in long-term follow-up to monitor for replication competent retrovirus.</p> <p data-bbox="558 597 1948 656"><i>Annual Update:</i> Final annual reports for protocols 9303-40, 9411-093, and 9408-082 were submitted by the corporate sponsor, Cell Genesys, on July 16, 2001.</p> <p data-bbox="816 683 1990 862">Each study utilized a Moloney Murine Leukemia Virus (MMLV) vector with the functional gene being for human GM-CSF (granulocyte-macrophage-colony stimulating factor). The basic goal of each study was to take cancer cells, transduce them with the MMLV-GM-CSF vector, and reinject them into the subjects with the aim of stimulating a specific immune response against these malignant cells (with the GM-CSF being utilized for its pro-inflammatory capabilities). Thus, these studies were considered "cancer vaccine" studies.</p> <p data-bbox="816 889 1940 980">Each study was conducted under IND BB 5229, and focused on a different cancer. In study 040 metastatic renal cell carcinoma cells were transduced, in study 093 metastatic melanoma cells were transduced, and in study 082 metastatic prostate carcinoma cells were transduced.</p> <p data-bbox="816 1008 1976 1274">The number of subjects enrolled per study were: 18 in study 040 (8 receiving transduced cells and 10 receiving non-transduced cells), 27 in study 093 (with 19 of these completing all vaccinations at the assigned dose) and 8 in study 092 (with 5 of these completing all vaccinations at the assigned dose). In all three studies, analysis of draining lymph node cells (i.e., cells from the lymph nodes covering the area in which the vaccines were injected intramuscularly) showed initiation of a cascade of cytokine production, including IL-4 and IL-6 presence. Additionally, in some subjects in each study tumor-specific CD8+ cytotoxic T-lymphocytes could be derived from these draining lymph node cells. However, no significant clinical responses were seen, such as involution of a cancerous lesion.</p>

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			<p>Adverse events were common and nearly all were related to pain, induration and redness at the sites of injection of the vaccines. These were nearly all mild to moderate in severity. No serious adverse events "probably" related to the gene-transfer vaccines were noted, though one subject had a pleural effusion develop for which the relationship to the vaccine was deemed as "possible".</p> <p>No subjects had presence of replication competent retrovirus, with blood being obtained frequently.</p> <p>Overall, these studies showed some immunologic activity, with no significant clinical efficacy and predictable safety profiles.</p>
		9406-081	IL-12 Gene Therapy Using Direct Injection of Tumor with Genetically Engineered Autologous Fibroblasts.
232	10/10/2001	<i>Annual Update:</i>	# 81: IL-12 gene therapy using direct injection of tumors with genetically engineered autologous fibroblasts. This study is now completed (terminated on 1-18-2000) with 31 subjects enrolled in total. Of these, 2 subjects are still alive and these will be followed long-term under a new protocol (UPCI 01-027) whose sole reason is to follow for RCR in these subjects (of note, the fibroblasts were transduced with a retroviral vector). All SAEs and death reports were previously submitted to OBA and these were summarized in this annual report.

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9408-082	Phase I/II Study of Autologous Human GM-CSF Gene Transduced Prostate Cancer Vaccines in Patients with Metastatic Prostate Carcinoma.		
250	07/16/2001	<i>Protocol Change:</i>	Trial is closed. Study participants have been asked to enroll in long-term follow-up to monitor for replication competent retrovirus.
		<i>Annual Update:</i>	Final annual reports for protocols 9303-40, 9411-093, and 9408-082 were submitted by the corporate sponsor, Cell Genesys, on July 16, 2001.
			<p>Each study utilized a Moloney Murine Leukemia Virus (MMLV) vector with the functional gene being for human GM-CSF (granulocyte-macrophage-colony stimulating factor). The basic goal of each study was to take cancer cells, transduce them with the MMLV-GM-CSF vector, and reinject them into the subjects with the aim of stimulating a specific immune response against these malignant cells (with the GM-CSF being utilized for its pro-inflammatory capabilities). Thus, these studies were considered "cancer vaccine" studies.</p>
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			<p>The number of subjects enrolled per study were: 18 in study 040 (8 receiving transduced cells and 10 receiving non-transduced cells), 27 in study 093 (with 19 of these completing all vaccinations at the assigned dose) and 8 in study 092 (with 5 of these completing all vaccinations at the assigned dose). In all three studies, analysis of draining lymph node cells (i.e., cells from the lymph nodes covering the area in which the vaccines were injected intramuscularly) showed initiation of a cascade of cytokine production, including IL-4 and IL-6 presence. Additionally, in some subjects in each study tumor-specific CD8+ cytotoxic T-lymphocytes could be derived from these draining lymph node cells. However, no significant clinical responses were seen, such as involution of a cancerous lesion.</p>
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			<p>Overall, these studies showed some immunologic activity, with no significant clinical efficacy and predictable safety profiles.</p>

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9411-093	A Phase I Study of Vaccination with Autologous, Irradiated Melanoma Cells Engineered to Secrete Human Granulocyte-Macrophage Colony Stimulating Factor.		
251	07/16/2001	<i>Protocol Change:</i>	Trial is closed. Study participants have been asked to enroll in long-term follow-up to monitor for replication competent retrovirus.
		<i>Annual Update:</i>	Final annual reports for protocols 9303-40, 9411-093, and 9408-082 were submitted by the corporate sponsor, Cell Genesys, on July 16, 2001.
			<p>Each study utilized a Moloney Murine Leukemia Virus (MMLV) vector with the functional gene being for human GM-CSF (granulocyte-macrophage-colony stimulating factor). The basic goal of each study was to take cancer cells, transduce them with the MMLV-GM-CSF vector, and reinject them into the subjects with the aim of stimulating a specific immune response against these malignant cells (with the GM-CSF being utilized for its pro-inflammatory capabilities). Thus, these studies were considered "cancer vaccine" studies.</p>
			<p>Each study was conducted under IND BB5229, and focused on a different cancer. In study 040 metastatic renal cell carcinoma cells were transduced, in study 093 metastatic melanoma cells were transduced, and in study 082 metastatic prostate carcinoma cells were transduced.</p>
			<p>The number of subjects enrolled per study were: 18 in study 040 (8 receiving transduced cells and 10 receiving non-transduced cells), 27 in study 093 (with 19 of these completing all vaccinations at the assigned dose) and 8 in study 092 (with 5 of these completing all vaccinations at the assigned dose). In all three studies, analysis of draining lymph node cells (i.e., cells from the lymph nodes covering the area in which the vaccines were injected intramuscularly) showed initiation of a cascade of cytokine production, including IL-4 and IL-6 presence. Additionally, in some subjects in each study tumor-specific CD8+ cytotoxic T-lymphocytes could be derived from these draining lymph node cells. However, no significant clinical responses were seen, such as involution of a cancerous lesion.</p>
			<p>Adverse events were common and nearly all were related to pain, induration and redness at the sites of injection of the vaccines. These were nearly all mild to moderate in severity. No serious adverse events "probably" related to the gene-transfer vaccines were noted, though one subject had a pleural effusion develop for which the relationship to the vaccine was deemed as "possible". No subjects had presence of replication competent retrovirus, with blood being obtained frequently.</p>
			<p>Overall, these studies showed some immunologic activity, with no significant clinical efficacy and predictable safety profiles.</p>

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		9508-116	Gene Therapy of Malignant Gliomas: A Phase I Study of IL-4 Gene -Modified Autologous Tumor to Elicit an Immune Response.
269	11/06/2001		<i>Status Change:</i> This study has been re-reviewed following a reorganization of the University of Pittsburgh's IBC. Due to the IBC's request for modifications in both the clinical protocol and informed consent, the IRB has decided to suspend further enrollment. As of this date, no individuals have been enrolled or are undergoing screening.
		9508-118	Accelerated Re-endothelialization and Reduced Neointimal Thickening Following Catheter Transfer of
310	09/12/2001		<i>Protocol Change:</i> The following changes have been made: 1) Individuals will be evaluated at regular intervals for 12 (instead of 24) months following administration of the study agent; 2) Inclusion and exclusion criteria have been modified to indicate that individuals over 40 years of age are eligible. However, individuals who are capable of reproducing must be willing to use acceptable measures of birth control; 3) All individuals (20) still to participate in this study will receive 4 mg and no individual will receive more than one dose of study reagent; 4) Informed consent has been amended to reflect that 30 individuals have participated in this study to date and there has been one death.
		9701-175	Gene Therapy for Recurrent Glioblastoma Multiforme: Phase I Trial of Intraparenchymal Adenoviral Vector Delivery of the HSV-TK Gene and Intravenous Administration of Ganciclovir.
320	04/16/2001		<i>Protocol Change:</i> Changes have been made to state that women of childbearing age must undergo a pregnancy test due to the carcinogenicity and teratogenicity of ganciclovir in animal studies. Method of female contraceptive has been amended from oral to either barrier or oral (to be determined in consultation with the participant's OBGYN). Since adenoviral shedding has not been detected in this study, testing for shedding will be performed monthly for six months (instead of 12) after surgery. This change has been made to decrease the discomfort of participants.
			<i>Annual Update:</i> Received a copy of the annual report submitted to the FDA. During the reporting period, four additional individuals were enrolled in this study. To date, a total of 10 individuals have participated. Two individuals were enrolled in cohort III, three in cohort II, and five in cohort I.
321	08/30/2001		<i>Other:</i> A copy of the information presented to a Data Safety Monitoring Board has been provided.
284	10/04/2001		<i>Other:</i> Information regarding vector stability was submitted.

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		9703-179	A Phase I Study of Active Immunotherapy With Carcinoembryonic Antigen RNA-Pulsed Autologous Human Cultured Dendritic Cells In Patients with Metastatic Malignancies Expressing Carcinoembryonic Antigen.
307	09/18/2001	<i>Annual Update:</i>	As of this date, 32 individuals have been enrolled in this study. Of the 32, 23 have received all four immunizations and repeat leukapheresis and are considered evaluable. No toxicities associated with the immunizations have been observed.
		9707-199	IL-12 Gene Therapy Using Direct Injection of Tumors with Genetically Engineered Autologous Fibroblasts.
233	10/10/2001	<i>Annual Update:</i>	#199 (??) IL-12 gene therapy for head and neck cancer using direct injection of tumors with genetically engineered autologous fibroblasts. The exact title of this study does not match any in the OBA database, however the description of the study appears to match protocol 199. To date only 2 subjects have been enrolled (out of a proposed 30) and both have died from progression of disease. It appears that both have been reported to OBA but filed under protocol 81. The slow enrollment into protocol 199 is believed to be due, in large part, to changes in principal investigator. Dr. Agarwala has taken over this role from Dr. Michael Lotze, who is no longer with the University of Pittsburgh Medical Center.
		9707-204	Retrovirus-Mediated Transfer of the cDNA for Human CD18 into Peripheral Blood Repopulating Cells of Patients with Leukocyte Adherence Deficiency.
258	08/30/2001	<i>PI or Site Change:</i>	Notification that investigators have moved to the National Cancer Institute from the University of Washington, Seattle, WA.
		<i>Annual Update:</i>	Indication that the two individuals who were enrolled in this trial will continue to be followed at the NCI/NIH. The clinical protocol has been modified to reflect the fact that since it has been over two years post infusion for both individuals enrolled in this study, any possibly associated adverse events would be those with retroviral involvement.
		9709-210	Compassionate Use Protocol for Retreatment with Allovectin-7 Immunotherapy for Metastatic Cancer by Direct Gene Transfer. Sponsor: Vical, Inc.
262	06/09/2000	<i>PI or Site Change:</i>	Dr. Jon Richards, Lutheran General Hospital, Park Ridge, Illinois, has been added as an investigator.
315	08/30/2001	<i>PI or Site Change:</i>	Dr. John A. Thompson, University of Washington Medical Center, Seattle, Washington has been added as a new investigator.

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		9801-227	IL-12 Gene Therapy Using Direct Injection of Tumors with Genetically Engineered Autologous Fibroblasts (A Phase II Study).
234	10/10/2001	<i>Annual Update:</i>	# 227: IL-12 gene therapy for melanoma using direct injection of tumors with genetically engineered autologous fibroblasts. This study is still ongoing with the enrollment of 11 subjects to date (out of a proposed 30). Of the enrolled subjects, 5 have died due to disease progression (and have been previously reported to OBA) while the remainder have had progression of disease and no longer receiving therapy. The slow enrollment into protocol 227 is believed to be due, in large part, to changes in principal investigator. Dr. Agarwala has taken over this role from Dr. Michael Lotze, who is no longer with the University of Pittsburgh Medical Center.
259	11/01/2001	<i>Status Change:</i>	Notification that protocol is being terminated. The two individuals who were enrolled in this trial have passed away due to disease progression.
		9802-234	A Controlled, Randomized Phase III Trial Comparing the Response to Dacarbazine with and without Allovectin-7 in Patients with Metastatic Melanoma. Sponsor: Vical, Inc.
261	06/09/2000	<i>PI or Site Change:</i>	Dr. Jon Richards, Lutheran General Hospital, Park Ridge, Illinois, has been added as an investigator.
		9804-244	A Phase I Study Using Direct Combination DNA Injections for the Immunotherapy of Metastatic Melanoma.
306	09/05/2001	<i>Status Change:</i>	Notification that trial is closed to enrollment. Follow-up of those enrolled is continuing.
		9804-247	A Phase I Safety Study of Autologous Transfected Human Fibroblasts Producing Human Factor VIII in Patients with Severe Hemophilia A. Sponsor: Transkaryotic Therapies, Inc.
286	10/05/2001	<i>Annual Update:</i>	Received an annual report for this study. To date, 12 individuals have participated
		9809-265	Mutant MGMT Gene Transfer Into Human Hematopoietic Progenitors to Protect Hematopoiesis During O6-Benzylguanine (BG, NSC 637037) and BCNU Therapy of Advanced Solid Tumors. Sponsor: NCI-Cancer Therapy Evaluation Program (NCI-CTEP)
303	09/20/2001	<i>Protocol Change:</i>	Protocol has been changed in terms of the cytokines that are being employed during the ex vivo expansion of CD34 cells. The age limit for eligibility has been increased to age 70.

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		9901-280	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. Sponsor: Schering Corporation
298	08/24/2001	<i>PI or Site Change:</i>	Dr. Fredrick Ueland has replaced Dr. Gallion as the investigator at the University of Kentucky Medical Center, Lexington, KY.
265	10/29/2001	<i>PI or Site Change:</i>	The following investigators have been added: Dr. Sidney Scudder, University of California, Davis, Sacramento, California; Dr. Boniface Noubisi, University of Florida, Gainesville, Florida; and Dr. Paul Celano, Greater Baltimore Medical Center, Baltimore, Maryland.
		9902-285	A Phase I Trial of Intratumoral Antisense EGFR DNA and DC-Chol Liposomes in Advanced Oral Squamous Cell Carcinoma.
305	09/12/2001	<i>Other:</i>	Results from an independent audit conducted by the Vice Chancellor for Clinical Research at the University of Pittsburgh concluded that the deaths of the 13 individuals enrolled in this study was due to progression of the underlying disease. This conclusion agrees with the assessment of the PI that the deaths were not related to the research intervention, which employed a vector with an incorrect insert.
263	10/23/2001	<i>Status Change:</i>	Received a copy of the University of Pittsburgh's IRB's response to the Office of Human Research Protections. A copy of the response is included in the meeting material for the December 2001 RAC meeting.
		9902-289	Expression of an Exogenously Delivered Human Alpha-1 Antitrypsin Gene in Nasal Epithelium of Patients with Cystic Fibrosis.
277	10/24/2001	<i>Other:</i>	Notification of the intent to change the supplier of clinical grade vector material.
		9902-292	Immunization of Patients with Metastatic Melanoma Using a Recombinant Fowlpox Virus Encoding a GP 100 Peptide Preceded by an Endoplasmic Reticulum Insertion Signal Sequence. Sponsor: NCI-Cancer Therapy Evaluation Program (NCI-CTEP)
231	10/10/2001	<i>Protocol Change:</i>	The clinical protocol and informed consent have been amended to include the fact that transient hypotension (grade 2) has been observed in this and similar studies.

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		9904-308	Phase I Study of Adoptive Immunotherapy with Gene-Modified and Unmodified CD8+ Minor Histocompatibility (H) Antigen-Specific CTL Clones for Patients with Relapse of AML or ALL After Allogeneic Hematopoietic Stem Cell Transplant.
260	10/27/2001		<i>Annual Update:</i> Notification that individuals who are enrolled in this study will no longer receive gene modified cells. Only unmodified cells will be infused. Therefore as discussed with OBA staff, adverse events will no longer be reported, for those individuals who do not receive recombinant DNA, to the RAC for this trial. Adverse events will continue to be reported to the FDA and IRB.
		9905-315	A Phase I/II Study of a Prime-Boost Schedule of Human GM-CSF Gene Transduced Irradiated Prostate Allogeneic Cancer Vaccine (Allogeneic Prostate GVAX TM) in Hormone-Refractory Prostate Cancer (G9803) . Sponsor: Cell Genesys, Inc.
292	09/19/2001		<i>Annual Update:</i> Received a copy of the final report for this trial, which is now closed. All surviving individuals have been asked to enroll in long-term follow-up. Fifty-five individuals were ultimately enrolled in this study.
		9905-320	Pilot Study of CEA RNA-Loaded, FLT3 Ligand-Mobilized Peripheral Blood Antigen Presenting Cells for Patients with Metastatic Malignancies Expressing CEA.
308	09/18/2001		<i>Annual Update:</i> As of this date, no individuals have been enrolled in this study.
		9907-327	A Phase I Double-Blind, Placebo Controlled, Escalating Dose, Multi-Center Study of Ad2/Hypoxia Inducible Factor (HIF)-1-alpha/VP16 Gene Transfer Administered by Intramuscular Injection to Patients with Critical Limb Ischemia Who are Not Candidates for Surgical or Percutaneous Revascularization. Sponsor: Genzyme
283	10/03/2001		<i>Protocol Change:</i> This amendment is also for the related protocols: 9907-328/329. The stopping rule has been modified to be invoked for serious adverse events (SAE) in which there is a reasonable possibility that the event may have been caused by the study agent. Previously, the stopping rule was invoked for any unexpected SAE regardless of the relationship. Any study participant death within 30 days of study agent administration will continue to invoke the stopping

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		9907-332	A Multi-Center, Open-Label, Multiple Administration, Rising Dose Study of the Safety, Tolerability, and Efficacy of IL-12 Gene Medicine in Patients with Unresectable or Recurrent/Refractory Squamous Cell Carcinoma of the Head and Neck (SCCHN). Sponsor: Valentis, Inc.
241	09/28/2001		<p data-bbox="556 285 625 306"><i>Other:</i> Following review of their clinical trials, it was noted by the Dana-Farber Cancer Institute that a single subject amendment to this protocol was instituted in December, 1999. The subject received the gene transfer product (a plasmid vector/IL-12 gene for the treatment of subjects with unresectable or recurrent/refractory squamous cell carcinoma of the head and neck) on a weekly basis for a total of 8 weeks, while the protocol specified two injections in week one and then one injection per week for 6 weeks thereafter. While this change was small (same number of injections, but with a lower initial dose and prolongation of dosing) the investigator received approval from the corporate sponsor (Valentis), the FDA, as well as the IRB and IBC at Dana-Farber.</p> <p data-bbox="816 565 1976 651">Also included in this submission is a SAE report in which this subject's death is reported. The death occurred in February, 2001, was deemed unrelated to either the gene transfer product or change in dosing schedule and was seen as being due to progression of disease.</p>
		9908-336	Post-Transplant Infusion of Fibronectin-Assisted, Retroviral-Mediated Gene-Marked and Ex Vivo Expanded CD34+ Placental and Umbilical Cord Blood Cells
256	09/20/2001		<p data-bbox="556 816 751 837"><i>PI or Site Change:</i> Drs. Croop and Cornetta are now the investigators at Indiana University.</p>
		9910-346	A Phase II, Randomized, Multicenter, 26-Week Study to Assess the Efficacy and Safety of CI-1023 Delivered Through Minimally Invasive Surgery Versus Maximum Medical Treatment in Patients with Severe Angina, Advanced Coronary Artery Disease, and No Options for Revascularization. Sponsor: Parke-Davis
299	09/04/2001		<p data-bbox="556 1073 751 1094"><i>PI or Site Change:</i> Dr. James E. Lowe, Duke University Medical Center, Durham, North Carolina has been added as an investigator.</p>
		9910-350	A Phase I Dose Escalation Study of Intraperitoneal E1A-Lipid Complex (1:3) with Combination Chemotherapy in Women with Epithelial Ovarian Cancer. Sponsor: Targeted Genetics Corporation
280	11/01/2001		<p data-bbox="556 1287 751 1308"><i>Protocol Change:</i> Amendment to increase the total number of individuals enrolled to 27 (from 21) to more readily define the maximum tolerated dose (MTD). If a MTD is not reached, the highest dose being administered (12ug/ml) will be employed in the second portion of the trial. Currently individuals are being enrolled in the highest dose group. Only one individual experienced a dose limiting toxicity in the next lower (9ug/ml) dose. Therefore, the sponsor states that the MTD may not be reached.</p>

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		9912-360	Treatment of Patients with Metastatic Melanoma Using Cloned Lymphocytes Following the Administration of a Nonmyeloablative But Lymphocyte Depleting Regimen.
245	09/13/2001	<i>Protocol Change:</i>	<p>A proposed "compassionate exemption" for a subject enrolled into protocol #360 was sent on September 13, 2001 by the principal investigator, Dr. Steven Rosenberg at the National Cancer Institute, NIH.</p> <p>In this protocol, subjects with metastatic melanoma receive cloned activated lymphocytes, produced so as to be specifically active against their melanoma. In an attempt to maximize the activity of these cloned lymphocytes in vivo, subjects first undergo a non-myeloablative but lymphocyte depleting chemotherapy regimen.</p> <p>A particular subject enrolled into this protocol had their lymphocytes prepared for infusion. However, due to the clinical deterioration of the subject, Dr. Rosenberg believed that following through with the chemotherapy regimen would be detrimental. It was, thus, proposed that this subject receive their cloned activated lymphocytes without prior conditioning, potentially sacrificing efficacy so as to improve the safety for this subject. This was approved by NCI's IRB and by the FDA and Dr. Rosenberg submitted these approvals to OBA so as to include into the protocol files.</p>
266	10/30/2001	<i>Protocol Change:</i>	<p>Clinical protocol has been amended to no longer require that individuals must have "failed therapy on protocols involving immunization against the gp 100 antigen." Individuals are now eligible if they have disease that is refractory to standard therapy. The investigators' have improved in their ability to produce cells. The number of cells that an individual may receive has been amended to a maximum of 3×10^{11} (previously maximum was 10^9 to 10^{11}).</p>
		9912-366	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). Sponsor: Aventis Pharmaceuticals - Gencell Division (formerly Rhone-Poulenc Rorer)
318	08/21/2001	<i>PI or Site Change:</i>	Dr. Gary Clayman, University of Texas, MD Anderson Cancer Center, Houston, Texas has been added as an investigator.
300	09/11/2001	<i>PI or Site Change:</i>	Dr. William J. M. Hrushesky, Dorn Veterans Affairs Medical Center, Columbia, South Carolina has been added as an investigator.
236	10/18/2001	<i>PI or Site Change:</i>	Dr. Douglas Trask, at the University of Iowa Hospitals and Clinics, Iowa City, Iowa, is has been added as an investigator.
267	11/02/2001	<i>PI or Site Change:</i>	Dr. Robert Zitsch, University of Missouri Health Care, Columbia, Missouri has been added as an investigator.

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0001-370	Gene Therapy for Patients with Fanconi Anemia: A Pilot Study.		
235	10/15/2001	<i>Protocol Change:</i>	Method of stem cell collection has been changed from peripheral blood, after stem cell factor and G-CSF mobilization, to harvest from bone marrow. As of October 15, this study has not be opened to enrollment, due to developing the changes relating to stem cell collection.
0001-381	Gene Therapy of Canavan Disease using AAV for Brain Gene Transfer.		
242	09/12/2001	<i>Annual Update:</i>	<p data-bbox="816 427 1976 511">An interim report was submitted by Dr. Meryl Latsko of Thomas Jefferson University Medical College on September 12, 2001 for protocol 0001-381. This report documents the safety profile for the first three subjects enrolled into this protocol.</p> <p data-bbox="816 553 1976 699">In this protocol gene transfer product (AAV vector/gene for ASPA) is inserted via burr holes into the brain parenchyma. The subjects are kept as inpatients for a minimum of 24 hours and then return for a 2 week visit, a 4 week visit (at which point a repeat MRI is done) and multiple subsequent visits. This report documents results up to the 4 week visit for the three enrolled and treated subjects.</p> <p data-bbox="816 742 1976 888">All three subjects tolerated the procedure well, with average procedure time being circa 40 minutes. One subject developed a fever and emesis several hours after the procedure, which delayed discharge home. The subject's symptoms resolved by post-op day # 2. This SAE was previously reported to OBA (UEI # 3662) and was deemed as possibly related to the gene transfer product infusions. The other two subjects did not have SAEs.</p> <p data-bbox="816 930 1976 980">MRIs and safety laboratory results for these three subjects do not show any particular problems that could be associated with either the procedure or gene transfer product.</p>

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		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.
243	07/11/2001		<p><i>Annual Update:</i> An annual report was filed for protocol 0001-385 by the commercial sponsor, Cell Genesys, on July 11, 2001. This study is investigating the utility of using GM-CSF gene-modified autologous tumor vaccines in subjects with either early or late stage non-small-cell lung cancer, utilizing an adenoviral vector with which to modify the cells. To date 17 subjects have been enrolled, with all 17 treated with the vaccines. Three of these 17 are diagnosed with early stage (entered into Cohort A of the study) and the remaining are late stage (Cohort B of the study). There have been 7 serious adverse events (which have been submitted individually to OBA over the span of the last year) and none are associated with the vaccine product. Two subjects have died due to progression of their cancer.</p> <p>Of note, there have been three amendments to the initially proposed study (which was reviewed by RAC members but which did not go for public discussion). Details about the changes in each of these amendments and the presently used study protocol are included in this annual report.</p>
		0002-388	A Double-Blind, Randomized, Placebo-Controlled, Dose-Ranging, 26-Week Study to Assess the Safety and Efficacy of CI-1023 (ADGVVEGF121.10) in Peripheral Arterial Disease Patients with Severe, Disabling Intermittent Claudication. Sponsor: Parke-Davis Pharmaceutical Research
254	10/18/2001		<p><i>PI or Site Change:</i> Dr. Julie Miller at Johns Hopkins University, Baltimore, Maryland, has been added as an investigator.</p>
		0005-395	A Phase I/II Trial Investigating the Safety and Immunotherapy of Adenovirus Encoding the Melan-A/MART-1 and gp100 Melanoma Antigens Administered Intradermally to Patients with Stage II-IV Melanoma. Sponsor: Genzyme Corporation
288	09/27/2001		<p><i>PI or Site Change:</i> Dr. Marc Ernstoff, Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire has been added as an investigator.</p>
274	10/22/2001		<p><i>Other:</i> Notification that the risk section of the informed consent documents for both trial sites has been amended. This change incorporates language to describe retinal changes that have been observed in one individual in this study.</p>
		0005-399	An Open-Label, Phase I, Dose-Escalation Study of Tumor Necrosis Factor-alpha (TNFerade™ Biologic) Gene Therapy with Radiation Therapy for Locally Advanced, Recurrent, or Metastatic Solid Tumors. Sponsor: GenVec
252	07/19/2001		<p><i>PI or Site Change:</i> Dr. Nemunaitis at US Oncology, Dallas, Texas, has been added as an investigator.</p>

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		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
291	10/02/2001	<i>PI or Site Change:</i>	Dr. Gregory Fontana, Cedars-Sinai Medical Center, Beverly Hills, California has been added as an investigator.
282	10/03/2001	<i>Protocol Change:</i>	<p>Protocol has been amended to incorporate more detailed discussion between the PI and sponsor (Genzyme) regarding the screening of prospective participants. This dialogue is to aid in the decision as to whether to proceed with administration of the test article during surgery if it is determined that graft placement is not feasible. This modification has been discussed with and accepted by a data safety monitoring board.</p> <p>In addition the stopping rule has been modified to be invoked for serious adverse events (SAE) in which there is a reasonable possibility that the event may have been caused by the study agent. Previously, the stopping rule was invoked for any unexpected SAE regardless of the relationship. Any study participant death within 30 days of study agent administration will continue to invoke the stopping rule. Any SAEs that may be manifestations of coronary artery disease, regardless of the causal assessment, will invoke the stopping rule.</p>
		0009-412	A Phase III, Multi-Center, Open-Label, Randomized Study to Compare the Effectiveness and Safety of Intratumoral Administration of RPR/INGN 201 in Combination with Chemotherapy Versus Chemotherapy Alone in 288 Patients with Recurrent Squamous Cell Carcinoma of the Head and Neck (SCCHN). Sponsor: Aventis Pharmaceuticals - Gencell Division
319	08/21/2001	<i>PI or Site Change:</i>	Dr. Gary Clayman, University of Texas, MD Anderson Cancer Center, Houston, Texas has been added as an investigator.
301	09/11/2001	<i>PI or Site Change:</i>	Dr. William J. M. Hrushesky, Dorn Veterans Affairs Medical Center, Columbia, South Carolina has been added as an investigator.
237	10/18/2001	<i>PI or Site Change:</i>	Dr. Douglas Trask, at the University of Iowa Hospitals and Clinics, Iowa City, Iowa, is has been added as an investigator.
275	10/23/2001	<i>PI or Site Change:</i>	Dr. Kevin Cullen, Georgetown University Medical Center, Washington, D.C. has been added as an investigator.
268	11/02/2001	<i>PI or Site Change:</i>	Drs. Robert Zitsch, University of Missouri Health Care, Columbia, Missouri and Randall Breau, University of Arkansas for Medical Sciences, Little Rock, Arkansas have been added as an investigators.

ID #	Letter	Protocol #	Amendment
		0010-427	Effect of AdGVCFTTR.10 on the Cystic Fibrosis Phenotype.
238	10/12/2001		<i>Protocol Change:</i> Diluent for the vehicle has been changed from sucrose to trehalose.
		0011-431	A Phase II Study of High-Dose Allovectin-7 in Patients with Advanced Metastatic Melanoma. Sponsor: Vical
314	08/29/2001		<i>PI or Site Change:</i> Dr. Myo Thant, Maryland Hematology/Oncology Associates, Baltimore, Maryland has been added as an investigator.
313	09/05/2001		<i>PI or Site Change:</i> Dr. Ravi Patel, Comprehensive Blood and Cancer Center, Bakersfield, California is now an
290	09/14/2001		<i>PI or Site Change:</i> Dr. Paul Schwarzenberger, Louisiana State University Health Sciences Center Lions Clinic, and the Medical Center of Louisiana at New Orleans, New Orleans, Louisiana has been added as an investigator.
316	10/05/2001		<i>PI or Site Change:</i> Dr. John A. Thompson, University of Washington Medical Center and the Seattle Cancer Care Alliance, Seattle, Washington has been added as a new investigator.
271	10/11/2001		<i>PI or Site Change:</i> Dr. Laura Hutchins, University of Arkansas for Medical Sciences and Central Arkansas Veteran's Healthcare System, Little Rock, Arkansas has been added as an investigator.
		0011-432	A Phase II Study of Safety and Efficacy of Allovectin-7 Immunotherapy for the Treatment of Primary Resectable Squamous Cell Carcinoma of the Oral Cavity or Oropharynx. Sponsor: Vical Inc.
257	08/14/2001		<i>PI or Site Change:</i> Dr. Pierre Lavertu, Case Western University, University Hospitals of Cleveland, Cleveland, Ohio has been added as an investigator.
273	10/25/2001		<i>PI or Site Change:</i> Dr. Ehab Hanna, University of Arkansas for Medical Sciences, Little Rock, Arkansas has been added as an investigator.
270	11/07/2001		<i>PI or Site Change:</i> Dr. William Carroll at the University of Alabama-Birmingham, Birmingham, AL has been added as an investigator.
		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.
239	10/29/2001		<i>Protocol Change:</i> Changes have been made to the inclusion criteria to allow individuals with at least 30% (as opposed to at least 50%) bone marrow plasma cells to participate. Individuals are also permitted to have undergone a cycle of chemotherapy prior to enrollment.

ID #	Letter	Protocol #	Amendment
		0101-442	Phase I/II, Prospective Placebo Controlled, Randomized Assessment of Adenoviral Mediated VEGF121 cDNA Myocardial Angiogenesis Therapy as an Adjunct to Individuals with Diffuse Coronary Artery Disease Undergoing Off-Pump Coronary Artery Bypass Surgery.
244	08/20/2001		<p data-bbox="556 285 743 306"><i>Protocol Change:</i> Based upon suggestions by the FDA and IRB, the changes have been made to the clinical protocol. The following additions have been made to the exclusion criteria: 1) individuals with moderate or severe proliferative retinopathy or severe nonproliferative retinopathy; 2) individuals with unstable angina; 3) recent transmyocardial revascularization, coronary artery bypass grafting surgery or percutaneous transluminal coronary angioplasty; 4) history of malignancy, except fully resolved (for at least two years) basal cell skin carcinoma; and 5) any pre-study evaluation test/symptom, which in the investigators opinion could be the result of an underlying malignant condition.</p> <p data-bbox="816 532 1940 651">In addition the clinical protocol and informed consent have been modified to contain the findings from another VEGF study concerning the progression of a lung tumor in one individual. An eye exam will now be performed at baseline and 180 days post vector administration (exam to be performed by a board certified ophthalmologist).</p>
		0101-452	A Multicenter, Randomized, Double-Blind, Placebo Controlled, Dose-Response Study to Evaluate the Efficacy and Safety of Ad5.1FGF-4 in Patients with Stable Angina. Sponsor: Berlex Laboratories
264	10/11/2001		<p data-bbox="556 837 743 859"><i>PI or Site Change:</i> The following investigators have been added: Dr. Vasanth Bethala, Medical Research Institute, Slidell, LA; Dr. Norman Erenrich, Florida Cardiovascular Research, Atlantis, FL; Dr. Roger Gammon, Austin Heart, Austin, TX; Dr. Timothy Henry, Abbott Northwestern Hospital, Minneapolis, MN; Dr. Rudolph Licandro, Louisville Cardiology Medical Group, Louisville, KY; Dr. Jorge Saucedo, University of Arkansas for Medical Sciences, Little Rock, AR; Dr. Melvin Tonkon, Anaheim Heart and Research Institute, Santa Ana, CA; and Dr. Matthew Watkins, The University of Vermont, Burlington, VT</p>
279	09/24/2001		<p data-bbox="556 1114 743 1135"><i>PI or Site Change:</i> Dr. P. Michael Grossman, The University of Michigan Health System, Ann Arbor, MI has been added as an investigator.</p>

ID #	Letter	Protocol #	Amendment
		0101-457	An Open-Label, Phase I, Dose-Escalation Study of TNFerade™ Biologic with Radiation Therapy as an Adjunct to Surgery or for Palliation of Soft Tissue Sarcoma of the Extremities. Sponsor: GenVec.
253	07/19/2001	<i>PI or Site Change:</i>	Dr. Nemunaitis at US Oncology, Dallas, Texas, has been added as an investigator.
309	09/14/2001	<i>PI or Site Change:</i>	Dr. Arno Mundt, University of Chicago, Chicago, Illinois has been added as an investigator.
289	09/26/2001	<i>PI or Site Change:</i>	Drs. Srinivasan Vijayakumar and Michael Warso, University of Illinois at Chicago, Chicago, Illinois have been added as co-PIs.
276	10/25/2001	<i>PI or Site Change:</i>	Dr. Alan Sandler, Vanderbilt University, Nashville, Tennessee has been added as an investigator.
		0102-458	Pilot Phase II Study of Safety and Immunogenicity of a ALVAC-CEA/B7.1 Vaccine Administered with Chemotherapy, Alone or in Combination with Tetanus Toxoid or GM-CSF, as Compared to Chemotherapy Alone, in Patients with Metastatic Colorectal Adenocarcinoma. Sponsor: Aventis Pasteur Limited.
281	10/02/2001	<i>Protocol Change:</i>	The GM-CSF arm of this study has been removed due to toxicities observed in pre-clinical studies. The title of the study has been modified to reflect this.
		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 GVAXR) in Advanced Non-Small Cell Lung Cancer. Sponsor: Cell Genesys, Inc.
240	10/31/2001	<i>PI or Site Change:</i>	Drs. Aboulafia (at the Virginia Mason Medical Center, Seattle, Washington) and Sternman (at the University of Pennsylvania Medical Center, Philadelphia, Pennsylvania) have been added as investigators.