RESPONSES TO APPENDIX M-I-C-1
HUMAN GENE TRANSFER PROTOCOLS

RECOMBINANT DNA ADVISORY COMMITTEE MEETING
June 2002

ID #	Letter	Protocol #	Response
		0001-386	**Phase II Study of a B-7.1 Gene Modified Autologous Tumor Cell Vaccine and Systemic IL-2 for Patients with Stage IV Renal Cell Carcinoma.**
401	03/14/2002		*Response to M-I-C-1:* Received a copy of the latest IBC and IRB approvals and other documentation indicating that study may proceed. First individual was enrolled on February 7, 2002.
		0101-440	**Phase I Study of gp75 DNA Vaccine in Patients with AJCC Stage III and IV Melanoma. Sponsor: ImClone Systems, Inc.**
400	04/02/2002		*Response to M-I-C-1:* Received a copy of the IRB and IBC approvals, IRB-approved informed consent, and approved clinical protocol submitted to the FDA. IND was authorized and enrollment was initiated on March 13, 2002
		0101-455	**Phase II, Single Arm, Single Institution Clinical Trial of Docetaxel and Doxorubicin in Combination with Local Administration of Ad5CMV-p53 (RPR/INGN-201) in Locally Advanced Breast Cancer (LABC). Sponsor: Introgen Therapeutics, Inc.**
422	04/23/2002		*Response to M-I-C-1:* Received copies of the final clinical protocol, IBC approval, IRB approval, and informed consent. Date trial initiated not given.

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		0104-462	**A Phase I Trial of Genetically Modified Salmonella typhimurium Expressing Cytosine Deaminase (TAPET-CD, VNP20029) Administered by Intra-Tumoral Injection in Combination with 5-fluorocytosine for Patients with Advanced or Metastatic Cancer. Sponsor: Vion Pharmaceuticals, Inc.**
440	02/26/2002		*Response to M-I-C-1:* This submission includes the required materials following the enrollment of the first research participant on January 29, 2002 at the Mary Crowley Medical Research Center. The packet includes the following: 1.) A copy of the IRB-approved consent form 2.) A copy of the protocol as approved by the IBC 3.) A copy of the final IBC approval from the clinical trial site 4.) A copy of the final IRB approval 5.) Notification that there is no applicable NIH grant number 6.) Notification of the FDA IND number 7.) Notification that the date of initiation of this trial was 29 January 2002 8.) Brief written report describing how the investigator's responded to the recommendations by the RAC on the protocol (discussed at the June 15, 2001 RAC meeting), and any modifications to the protocol as required by the FDA. The RAC made three recommendations which are shown below in brackets. The response in this submission follows in quotes. [Consideration should be given to developing a method for assessing the possible long-term consequences of Salmonella infection such as a surrogate marker for detection of persistent colonization.] "Vion has given substantial consideration to this recommendation. To date, we have been unable to devise a more accurate marker for persistent colonization with live organisms than routine cultures. A long antibiotic course is administered to all patients going off study. That, in the view of our infectious disease consultants, should be sufficient to clear all of the Salmonella organisms, which are highly attenuated and extremely sensitive to antibiotics. At the end of the antibiotic course, blood, urine and stool cultures are checked for the presence of TAPET-CD organisms." [The sponsor agreed to conduct and assess the outcomes in a study wherein animals receive a direct intracranial injection of TAPET-CD followed by antibiotic therapy.] "Vion is currently working on the design of the experimental study, and hopes to complete the study during the second half of 2002."

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			[The sponsor and investigator agreed to make clarifying changes in the language of the consent form document in the section on "relinquishment of property rights." It was also agreed that the consent form document would include investigator financial disclosure information. Finally, to the extent possible there would be clarification of any monetary costs to the research subject.] "The changes to the Informed Consent document were made as requested, and a copy of that document is included in this submission (ATTACHMENT II)." (N.B. In reviewing the Informed Consent document submitted in Attachment II, the OBA Medical Officer did not note any information on Investigator financial disclosure.) With respect to protocol modifications required by the FDA, the sponsor noted that all FDA-required modifications were incorporated into the current version of the CLI-017 protocol which was included in this submission (ATTACHMENT III), and was previously submitted as part of Vion's submission to NIH/OBA dated 13 April 2001.
		0106-475	**A Safety and Efficacy Trial of Lethally Irradiated Allogeneic Pancreatic Tumor Cells Transfected with the GM-CSF Gene in Combination with Adjuvant Chemotherapy for the Treatment of Adenocarcinoma of the**
456	02/21/2002		*Response to M-I-C-1:* Received a copy of the IBC approval, IRB approval, and informed consent. A copy of the amended clinical protocol was received which modified the procedure used to process autologous tumor cells that are used for immune monitoring delayed type hypersensitivity studies. The first participant was enrolled (consented) on January 30, 2002 and received the first dose of the study agent on February 13, 2002.
		0107-484	**A Phase I Open-Label Study of the Safety and Feasibility of Vaccinating Cancer Patients with Repeated Doses of ZYC300. Sponsor: ZYCOS, Inc.**
392	04/11/2002		*Response to M-I-C-1:* Received information in response to Appendix M-I-C-1. Changes to the clinical protocol in response to review by the FDA: 1) A 12 month follow-up visit has been added 2) Grade 2 allergic toxicity and autoimmune toxicity were added as potential reason for discontinuation until the toxicity is reviewed by the FDA 3) Many of the adult cancers must have a second line of treatment for metastatic disease prior to study inclusion

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			4) Additional tumor staging and tumor marker assessment have been added to visit 16 5) Addition of the following sentence in the informed consent (in the section: "Are There Benefits to Taking Part in the Study?"): "There is no proven benefit of this vaccination therapy."
		0107-490	**A Pilot Phase I/II Study of Intranodal Delivery of a Plasmid DNA (Synchrotope MA2M) in Stage IV Melanoma Patients. Sponsor: CTL ImmunoTherapies Corp.**
460	02/12/2002		*Response to M-I-C-1:* Received a copy of the IBC approval, IRB approval, and informed consent. Changes to the revised clinical protocol that was received include indication that individuals with tumor type known to be Melan-A/Mart-1 positive do not need to have their tumor material re-tested to be eligible. Chang in immunological evaluations so that the tetramer, instead of the dimer XI assay, will now be performed to assess antigen-specific CTL response. The first individual was enrolled in this study on February 11, 2002.
		0108-496	**Pilot Feasibility and Safety Study of Cellular Immunotherapy for Recurrent/Refractory Malignant Glioma using Genetically Modified Autologous CD8+ T Cell Clones.**
426	03/18/2002		*Response to M-I-C-1:* Received a copy of the final IBC and IRB approvals, informed consent, and clinical protocol. The investigator states that no changes were required by the FDA; however a response to suggestions made by the FDA is being developed. To date, no participants have been enrolled.
		0109-497	**Randomized Multicenter Phase II Study Evaluating Two Dosing Schedules ofTG4010 (MVA-MUC1-IL2) in Patients with Adenocarcinoma of the Prostate. Sponsor: Transgene, Inc.**
421	04/16/2002		*Response to M-I-C-1:* Received copies of the final clinical protocol, IBC approval, IRB approval, and informed consent. Date trial was initiated not provided.
		0110-503	**Single Dose Escalation Study to Evaluate Safety of Nasal Administration of CFTR001 Gene Transfer Vector to Subjects with Cystic Fibrosis.**
438	04/08/2002		*Response to M-I-C-1:* Received a copy of the IBC approval, IRB approval, informed consent, and clinical protocol. The first individual was enrolled on March 26, 2002 and trial was initiated on April 2, 2002. Changes made to the clinical protocol based upon recommendations from the FDA were (i) an additional pulmonary function test will be performed at 4 hours plus/minus 30 minutes after dosing and (ii) individuals to be eligible must weigh at least 40kg.