BURZYNSKI
RESEARCH INSTITUTE, INC.

June 22, 1995

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Division of Cancer Treatment, NCI
National Institutes of Health
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Dear Dr. Friedman,

I have received your letter of June 6, 1995. Its rhetoric will not hide the simple fact that the FDA-approved and NCI-sponsored protocol for the treatment of brain tumors with antineoplastons has been violated by NCI-appointed investigators numerous times and that you condone these violations. Your letter brings additional new violations to the surface.

1) On the first page of your letter (attached) you stated: "This patient, however, had a brain scan 3 weeks prior to study entry." The protocol (page 7 attached) requires "scan, within one week of study entry." There is a good reason behind this requirement. This type of malignant brain tumor may double in three weeks, which means that the patient may have progressive disease (PD) even before beginning treatment. In addition, this patient should never have been admitted to the study, because this type of malignant brain tumor is excluded according to the protocol.

2) According to your own data (attached), patient 27-53-76-5 had the maximum tumor diameter of 6cm, which is substantially larger than admission criteria permits.

3) The responses of both patients were classified as PD. It took approximately two months and two letters from us, which documented violations of the protocol regarding these two patients for you to decide that "neither patient is counted in assessment of response."

4) Patient #196370 was classified as PD and removed from the study in violation of the criteria for therapeutic response of the protocol. According to the report from

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objective radiologist (attached), the MRI of the brain of this patient on May 2, 1994 showed "The amount of edema and mass effect is stable." Increased fluid retention in this patient observed by Dr. Malkin could have been easily treated by administration of diuretics. We strongly believe that this patient should not have been removed from the study and if he had continued the treatment, his life may have been saved.

5) Patients 4-166-190 and 4-336-656 clearly had multiple nodules according to the Theradex Report (attached). Their acceptance to the study was in violation of admission criteria. The statement of Dr. Buckner of May 2, 1995 that these patients had a single tumor should be confirmed by providing us with copies of the MRI films and submitting them for evaluation to objective radiologists.

6) Patient 4-336-656 had serious interruptions in the treatment program because of an infection associated with the catheter. I believe that the reason for infection was initial low white blood cell count (WBC). According to the Theradex Report (attached) her pretreatment WBC was 2800. This patient should not have been accepted to the study according to "contraindications" listed in the protocol (attached). Patients with WBC below 4000 should not be accepted. This patient was removed from the study after "The foci of abnormal enhancement had increased.... Subsequently, the patient underwent right frontal lobe resection, which confirmed the presence of recurrent glioblastoma multiforme with small scattered foci of radio-necrosis." There is reason to believe that the increasing foci corresponded to radiation necrosis and not tumor progression.

7) Patient 4-369-975 was removed from the study and classified as PD whereas subsequent tumor resection revealed no viable tumor. Only after our intervention was it promised that he won't be counted any longer as PD. In fact, it is entirely possible that this patient had rapid tumor regression and biopsy proven objective response. The Theradex Report (attached) does not provide any evidence that this patient received pretreatment radiation therapy, which could have resulted in the radiation necrosis claimed by Dr. Buckner.

8) Patient 4-429-449 was removed from the study because of a suspected skin reaction to Antineoplastons. According to the letter from Dr. Buckner of May 2, 1995, this patient "had received no other new drugs."

I trust Dr. Buckner that the patient did not receive any new drug, but he was receiving an old drug, DPH (Theradex Report attached), which is well known for causing skin reactions. Three days after discontinuation of Antineoplastons, the skin reaction was getting worse. It improved only after DPH was discontinued. I am sure that Dr. Buckner realized that it was DPH, not antineoplastons that caused the reaction.

9) Patient 4-429-449 received no more than 20 days of treatment, a substantial part of which was below effective dosage level. The follow-up MRI of the brain was done 17 days after the treatment was discontinued. These 17 days were sufficient for the tumor to grow The patient was classified PD.

Your letter of June 6, 1995 "conveys pessimism." My letter conveys outrage. The FDA protocol has been repeatedly violated. Patients were admitted against admission criteria. Their treatment was discontinued and their lives were jeopardized for frivolous reasons. In spite of your promise in the letter of April 3, 1995 that "We will forward the data on the first five patients in separate mailings as you requested," we never received any detailed data on these patients, except for sketchy Theradex Reports. There must be a reason why you are afraid to provide us with complete copies of medical records, including MRI films and pathology slides. Again, you promised to provide us with this documentation and we request that it be sent to us as soon as possible.

You are requesting that we provide you with additional data on the treatment of adult patients with primary brain tumors treated with antineoplastons. Somehow you do not realize that on October 17, 1991 we provided NCI with data on all adult patients who participated in our intramural trials in primary malignant brain tumors with antineoplastons. The data were audited and statistically analyzed by Clinical Multiphase Research, Inc. and submitted in quadruplicate to the FDA on September 10, 1992 and July 22, 1993. We supplied NCI and FDA with extensive data to allow approval of the existing protocol. It took two years to agree on the existing protocol. We do not have any reason to trust the investigators at Memorial Sloan-Kettering Cancer Center and Mayo Clinic and we will not allow them to reopen the studies. We request that you appoint investigators in different medical institutions who can conduct the studies strictly according to the FDA-approved protocol.

Sincerely,

S. R. Burzynski, M.D., Ph.D.