BURZYNSKI
RESEARCH INSTITUTE, INC.

April 20, 1995

Mario Sznol, M.D.
Department of Health &
Human Services
National Institutes of Health
Bldg. EPN Room 715
Bethesda, MD 20892

Dear Dr. Sznol,

Your letter of April 3, 1995 (copy attached) does not provide adequate justification for the changes in the protocol for "Phase II Study of Antineoplastons A10 and AS2-1 in Patients with Advanced Recurrent Astrocytomas."

Let me make perfectly clear that, as the discoverer and developer of antineoplastons and the individual with nearly 20 years clinical experience using them, it is my professional opinion that the drugs will not produce substantial benefit in such advanced patients. The current protocol has had success only in patients who have tumors not exceeding 5cm in diameter and who do not have multiple tumors or leptomeningeal or systemic metastases. As the Senior Investigator of NCI requested, patients should have Karnofsky Performance Status of not lower than 70% (letter attached).

As I have repeatedly informed you, it is exactly because of the current protocol's failure to benefit advanced patients that we developed new and more aggressive protocols for such patients. The protocol that we are currently using for such advanced tumors, for example, provides antineoplaston A10 in doses three times greater than that specified in the protocol currently being used. In order to make such dosing possible, we are using a much higher concentration of A10 -- 300mg/mL instead of 80mg/mL.

The dosing schedule being used for such advanced tumors is also quite different. Instead of injections of each antineoplaston every 30 minutes, patients receive a much greater amount every four hours.

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The acceptance of very advanced brain tumor patients to the current protocol would be highly unethical because there is no realistic chance they will have a meaningful response. The list attached to your letter of April 3, 1995 (enclosed), proves my observation that patients who had tumors substantially larger than 5cm do not respond well under the current protocol. There were only two such patients, with the largest tumor diameter corresponding to 5.5 and 6.5cm. Both had less than 50% decrease in the size of their tumors. According to the existing protocol, patients should have more than a 50% decrease in tumor size to be classified as responders.

Please bear in mind that the point of this trial is not to prove once again that this protocol does not work in patients with very large tumors, multifocal tumors, and low Karnofsky scores. We have already established this fact.

Moreover, the informed consent form as currently written falsely implies that the discoverer of antineoplastons believes such advanced patients may benefit substantially from the current protocol. In fact, I have specifically informed you on several occasions that I do not believe advanced patients will obtain substantial benefit. Please be forewarned that you may face legal liability resulting from these unethical misrepresentations.

We are anxiously awaiting the complete data on the first five patients as promised in your letter of April 3, 1995. Based on the limited information received from Theradex on the first seven cases, we have reason to believe that the protocol has been violated in every case. Five cases have been accepted in violation of Inclusion Criteria. Due to interruptions in the treatment schedule and the time necessary to escalate the dosage, one of these patients received less than three weeks of full dose treatment. Such duration of treatment was not sufficient to show the effectiveness of the therapy. Finally, two additional patients were removed from the study and said to have progression of disease when in fact no progression was documented. One of these patients, #4369975, underwent tumor resection three weeks after discontinuation of the treatment with antineoplastons. Microscopic examination of the tumor specimen confirmed absence of viable tumor cells. It is clear that what was classified as tumor progression corresponded to extensive necrosis or tumor death. What I thought was especially inexcusable and unethical is that the 30 year old patient #196370, who clearly did not have progression of the tumor, was removed from the study against the criteria for removal listed in the protocol. This patient died a few months later. I strongly believe that if this patient had continued the treatment under the protocol,
his life would have been saved.

Attached to this letter, you will find a list of

violations of the protocol. Based on these violations, it is clear that the current investigators are unable to conduct this study under the current protocol. I hereby request that:

1) The National Cancer Institute immediately terminate the current investigators and appoint new investigators at different medical institutions acceptable to Burzynski Research Institute.

2) Patient accrual must cease until such investigators and institutions are appointed.

Until you appoint the new investigators, I will provide free treatment and medical care under my supervision as long as necessary to the patients currently being treated under the protocol.

Sincerely,

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

SRB/cf
Enclosure

cc: Senator Joseph Biden
Senator Barbara Boxer
Senator Dianne Feinstein
Senator Tom Harkin
Senator Barbara Mikulski
Congressman Berkly Bedell
Congresswoman Nancy Pelosi
Dr. Jan Buckner
Dr. Daniel Eskinazi
Dr. Michael Friedman
Dr. Jay Greenblatt
Mr. Richard Jaffe
Dr. Mark Malkin
Ms. Mary McCabe
Dr. Ralph Moss
Dr. David Parkinson
Ms. Dorothy Tisevich
Mr. Frank Wiewel