DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Services
National Institutes of Health
National Cancer Institutes
Bethesda, MD 20892

April 3, 1995

S. R. Burzynski, M.D., Ph.D.
President
Burzynski Research Institute
12000 Richmond, Suite 260
Houston, Texas, 77082-2431

Dear Dr. Burzynski,

Dr. Friedman asked me to respond to your letter of 3/29/95 regarding the change we have been considering in eligibility criteria for the Memorial Sloan-Kettering and Mayo Clinic phase II studies of antineoplastons. At the investigators' request, the amendments to modify the eligibility restrictions for size of tumor, number of tumors, and leptomeningeal spread, and to allow entry of patients with KPS of 60, have been approved. These amendments were initiated by the investigators when it became apparent that many good candidates for the study were being excluded because of what were perceived to be overly stringent and unnecessary eligibility restrictions.

Approximately a year ago, we wrote to you asking for your concurrence to make similar changes to the protocol (see enclosed letter). We have documented that the revised eligibility criteria are consistent with those used in your very own protocols that employ identical or nearly identical treatment regimens. Furthermore, in a review of the 7 patients in the best case series presented to NCI, we have found that perhaps 4 of the 7 patients who apparently had tumor shrinkage would not have been eligible to enter the NCI phase II studies under the original stringent eligibility criteria (see attached). These types of patients will now be eligible for study using the revised eligibility criteria proposed by the investigators and recently approved by CTEP.

Despite the difficulties in accrual, we are committed to completing the phase II evaluation of the antineoplastons. Our goals remain unchanged, that is, we wish to determine whether the drugs used in the similar manner as you recommend, and in the similar population of patients, will yield results consistent with those in the best case series. As noted above, our careful evaluation of the materials you have provided indicate that the amendments to the eligibility criteria do not deviate from the eligibility criteria and methods you have employed in your experience. We would appreciate the opportunity to review your data, alluded to in your letter, that support the contention that inclusion of these patients requires a different treatment regimen or is unsafe. In the meantime, we will allow the amendments to stand, since all evidence you have provided to date indicates that these newly eligible patients may have a chance for benefit without undue risk of harm, and are appropriate candidates for evaluation of the drug.

We will forward the data on the first five patients in a separate mailing as you requested.

However, you have asked that we suspend accrual while you review the data. There is no medical or regulatory reason to suspend accrual at this time. Suspending accrual will likely further damage the efforts the investigators have made to increase accrual to the trial.

Sincerely,

Mario Sznol, M.D.

cc: Dottie Tisevich
Michael Friedman, M.D.
Mary McCabe
Office of Alternative Medicine

ANTINEOPLASTON CASES

1.	Histology	parietal lobe glioblastoma multiforme
	Size	2.3 cm largest diameter
	Response	CR possible
	prior Tx	RT, Surgery
2.	Histology	anaplastic astrocytoma stage IV grade 3
	Size	3.0 tumor 3.5 tumor & edema
	Response	CR possible
	prior Tx	RT
3.	Histology	infiltrating glioma (astrocytoma or mixed astrocytoma/oligodendroglioma)
	Size	4.4
	Response	good PR, possible CR
	prior Tx	RT & BUdR; Procarbazine, CCNU, VCR; B-Interferon; DFMO & MGBG
4.	Histology	well differentiated Stage IV astrocytoma, possibly juvenile pilocytic astrocytoma
	Size	5.5 X 3.3
	Response	40-50% decrease of solid component
	prior Tx	vitamins & laetrile
5.	Histology	glioblastoma multiforme
	Size	6.5 x 5.0
	Response	39% decrease
	prior Tx	RT
6.	Histology	glioma consistent with anaplastic astrocytoma, differential: anaplastic astrocytoma or spindle cell variant of oligodendroglioma
	Size	5.1 x 2.2
	Response	CR
	prior Tx	RT
7.	Histology	Infiltrating anaplastic astrocytoma
	Size	4.0 (L) 4.8 (bifrontal)
	Response	good response - possible CR
	prior Tx	RT