Numiera Therapeutics

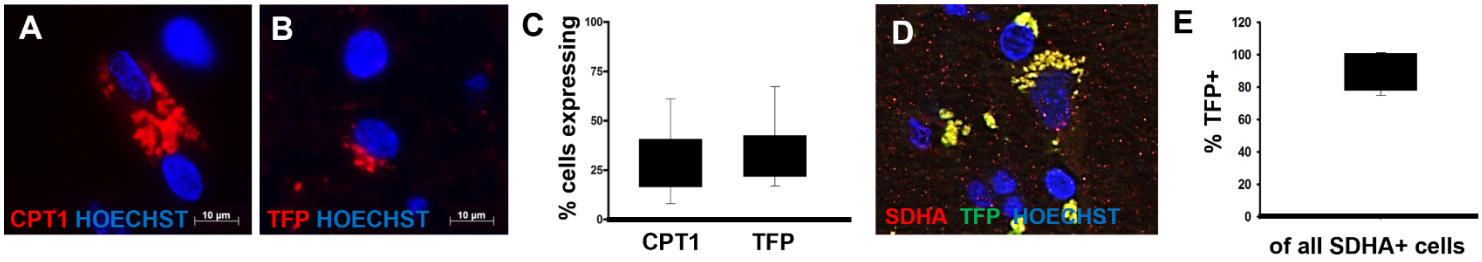
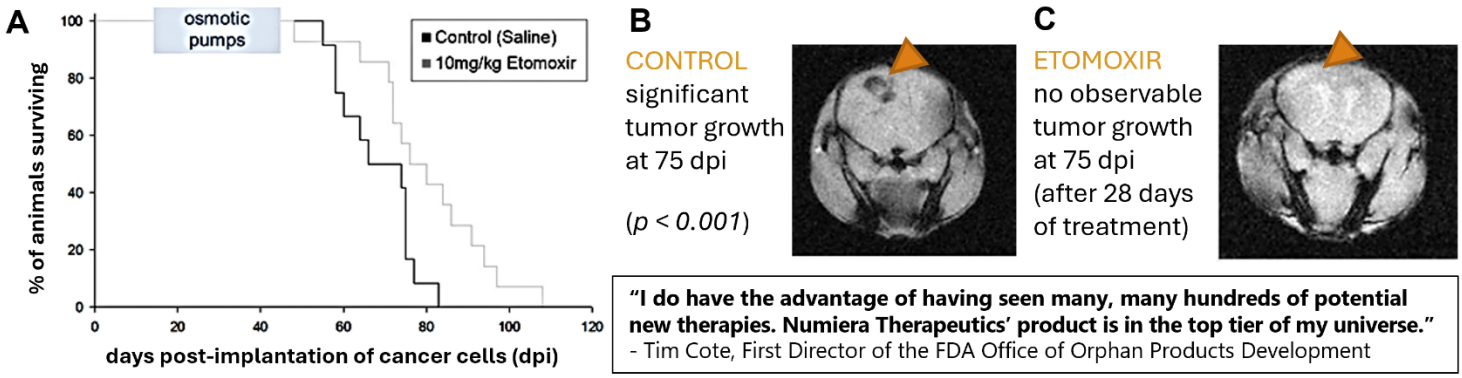


Figure 1. Fatty acid oxidation enzymes are present in all human glioblastoma tissues studied. The target enzyme carnitine palmitoyl transferase 1a (CPT1a, A), and other fatty acid oxidation enzymes, including trifunctional protein hydroxyacyl-CoA dehydrogenase/3-ketoacyl-CoA thiolase/enoyl-CoA hydratase (TFP, B) are expressed in *all* human glioblastoma samples studied. A third of cells on average exhibited expression (C). The pan-mitochondrial marker succinate dehydrogenase (SDHA) is typically co-labeled with TFP (D-E), indicating that any cells with mitochondria also have fatty acid oxidation capability. FAO enzymes are primarily found in the OLIG2+ cancer stem cells that drive tumor growth (data shown in Lin et al. *Neuro Oncology* 2016, Figure 1).



"I do have the advantage of having seen many, many hundreds of potential new therapies. Numiera Therapeutics' product is in the top tier of my universe."
- Tim Cote, First Director of the FDA Office of Orphan Products Development

Figure 2. Preclinical efficacy data has been independently replicated in five different laboratories. We demonstrated that etomoxir slows tumor growth in a syngeneic mouse model of glioblastoma (A-C, Lin *Neuro Oncology* 2016). Four other groups have now independently replicated these findings in their models of glioblastoma, demonstrating reliable single-agent efficacy in this indication (Kant *Cell Death Dis* 2020, Jiang *Nat Comms* 2022, Shim *Cancer Cell Int* 2022, Duman *Cell Death Dis* 2023).

Etomoxir †		**Temodar (Temozolomide) ***		**Avastin (Bevacizumab) #**	
Survival Benefit in Glioblastoma	?	Survival Benefit in Glioblastoma	2.5 months	Survival Benefit in Glioblastoma	2.2 months
Percentage of Patient Population Taking This Drug	?	Percentage of Patient Population Taking This Drug	80%	Percentage of Patient Population Taking This Drug	49%
Serious Side Effects		Serious Side Effects		Serious Side Effects	
High liver enzyme levels	<2%	High liver enzyme levels	12%	High blood pressure	18%
Moderate/Severe		Moderate/Severe		Moderate/Severe	
Cardiac arrhythmia or failure	<2%	Low platelet count	14%	Blood clots, stroke or heart attack	11%
Moderate/Severe		Moderate/Severe		Severe/Can Be Fatal	
		Bone marrow depletion	<10%	Kidney Problems	<7%
		Severe/Can Be Fatal		Severe/Can Be Fatal	
		Induction of other cancers	<2%	Fistula	<2%
		Severe/Can Be Fatal		Severe/Can Be Fatal	
Common Side Effects		Common Side Effects		Common Side Effects	
Increased exercise tolerance		Headache		Headache	
		Nausea		Back Pain	
		Vomiting		Watery Eyes	
		Hair Loss		Inflammation	
		Fatigue		Nosebleed	
Etomoxir †		**Temodar (Temozolomide) ***		**Avastin (Bevacizumab) #**	
Lower hepatotoxicity than standard of care Temodar or Avastin. Fewer deaths in treated group (0.9%) than placebo group (3.3%).		Serious adverse effects include liver toxicity, thrombocytopenia, bone marrow depletion and the induction of other cancers.		Serious adverse effects include heart attack, stroke, blood clots, kidney problems, and fistulas which are sometimes fatal.	

Table 1. Phase I clinical data in 226 human subjects shows a better safety profile than current standard-of-care. † Etomoxir was previously studied in human subjects. All participants in the Phase I clinical study for Etomoxir (ERGO1) were diagnosed with congestive heart disease. 4 patients (1.8%) exhibited high liver enzyme levels and three patients (1.3%) exhibited cardiac events after taking the drug. † Data was provided by Holubarsch et al. *Clin Sci* 2007. * Data on Temodar was provided by GoodRx.com and Stupp et al. *New Engl J Med* 2005. # Data on Avastin was provided by Avastin.com and Gramatzki et al. *Ann Oncol* 2018.