

### **How do you plan to treat aggressive cancers?**

Our target is a critical component of cancer cell metabolism. We are blocking the carnitine palmitoyl transferase (CPT1) that brings fatty acids into the mitochondria of the cancer cell, so these molecules can be broken down to make energy. With our first-in-class small-molecule drug, the cancer stem cells cannot make enough energy to support their malignant growth.

### **But can't cancer cells just use other fuels to make energy?**

For a long time, researchers thought cancer cells preferred to run on glucose. After all, normal healthy cells almost exclusively use glucose to make energy! But now we know that [aggressive cancer cells use glucose to make DNA and RNA](#), to support the growing tumor. Meanwhile, [fatty acids are the main fuel for energy production](#).

### **What is your primary disease indication? What are your secondary disease indications?**

Our primary disease indication is glioblastoma (GBM), the most common form of primary malignant brain tumor. This high-grade tumor carries a dire prognosis and few therapeutic options. Our secondary disease indications include triple-negative breast cancer, androgen-insensitive prostate cancer, and invasive bladder cancer, which also do not have good therapeutic options.

### **What is the market size for your product line?**

Our immediate market of glioblastoma patients in the US and EU represents \$2B in annual sales. With further pipeline development (and two already-filed patents!), we can reach a \$50B oncology market, by targeting the above-listed cancers with the same metabolic vulnerability.

### **What IP do you have to protect your lead asset?**

We have secured FDA orphan drug designation on our lead asset etomoxir, the first-in-class CPT1 inhibitor. This orphan designation provides seven years of post-approval market exclusivity, along with tax credits, regulatory fee waivers, and the ability to run accelerated clinical trials to reach approval.

### **What IP do you have to protect your follow-on assets?**

We have filed a patent on a follow-on combination product, to expand from the \$2B brain tumor market to the \$50B broader oncology market through a 505(b)2 regulatory pathway. In addition, we have filed for patent protection on diagnostic tools and the next generation of small molecule drugs to target this pathway.

### **Are big pharma companies interested?**

Yes, big pharma companies like the idea of a first-in-class orphan-designated lead asset for an urgent disease indication, followed by a pipeline of fresh patents to reach the broader oncology market. Any of the big pharma companies would be a good match for acquisition. Merck has already confirmed their interest in brain tumors. Other pharma companies are also keeping an eye on us, as we progress through clinical trials.

### **What stage is your company at?**

Our lead asset is clinic-ready. We already have Phase I safety data in 226 human subjects, showing this drug is safer than the current standard of care for glioblastoma patients. We have the full IND-enabling dataset, with extensive pharmacology and toxicology studies, and we have independently-replicated preclinical efficacy data, establishing the most likely therapeutic doses for the clinical trial. We have the regulatory paperwork prepared and a clinical protocol already designed. We also have a full supply chain in place, with clinical-grade product ready to be crystallized and formulated into soft-gel capsules.

### **How have you gotten this far when the company is only two years old?**

We were the first team to discover this key target, and now a number of research groups have independently replicated our findings. For a good while, we tracked the undervalued potential of this drug, with impressive safety data in human subjects and a scientific consensus around its therapeutic efficacy in cancer. So then we struck: We swept up the intellectual property, purchased the substantial datasets on this drug, and put together a plan to take it forward on \$365,000. We are now raising an equity financing round to support clinical development.

### **What makes you think your drug will be safe?**

In a previous Phase I/II trial for our drug etomoxir, every patient in the study had congestive heart failure. Fewer people actually died in the treatment group than in the control group (0.9% vs 3.3%) – but unfortunately the previous company never followed up these promising results, toggling instead to immunotherapies. The safety profile of the drug is excellent: 4 of 226 patients taking the drug (less than 2%) exhibited elevated liver enzyme levels – these effects were reversible, no liver damage was ever observed, and no other side effects were reported in the study. This safety profile appears to be a major improvement on standard-of-care chemotherapy, where severe hepatotoxicity is common.

### **What makes you think your drug will be effective?**

Five different laboratories have shown this drug, alone or in combination with other drugs, significantly slows tumor growth in state-of-the-art animal models of glioblastoma. Other labs have also shown this drug slows tumor growth in treatment-resistant breast cancer, treatment-resistant prostate cancer, and invasive bladder cancer. There is a very strong scientific consensus around this new oncology target.

### **A lot of new cancer drugs fail. What chances does this drug have to be successful?**

Approximately 25% of orphan designated drugs are approved, and the average time to market authorization is 5.3 years. A lot of de-risking has taken place to establish safety and efficacy already. So on average, once a drug reaches this stage, there is a 1 in 4 chance of success within the next five years.

### **What do key opinion leaders think?**

The First Director of the FDA Office of Orphan Products Development, Tim Cote, has written his support of our drug development program: “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.”

### **What is the competitive landscape like?**

A lot of other approaches have failed in the neuro oncology space – including immunotherapies, EGF inhibitors, PI3K inhibitors, and XPO1 inhibitors. The standard-of-care chemotherapy drug *temozolomide* only gives GBM patients 2-3 extra months, with terrible side effects. However, the recent approvals of *vorasidenib* for IDH-mutant low-grade glioma ([Agios](#)) and *dordaviprone* for H3K27M-mutant diffuse midline glioma ([Chimerix](#)) have shown that mitochondrial targets are a game-changer in the field. Over the past year, these drugs have significantly prolonged patient survival, received FDA approval, and led to billion-dollar corporate payouts. Yet these newly-approved drugs only serve a small subset of the neuro oncology patient population. With a far broader mitochondrial target, and FDA orphan designation for *all* malignant gliomas, we believe [our approach](#) will have a massive impact in this space.



**What is the next milestone, and how much money and time do you need to hit that milestone?**

Our next milestone is running an early-phase clinical trial, to find the optimal dose for our drug and an initial efficacy signal in our glioblastoma patient population. We will require \$10M and 3 years to do this work. We already have \$1.5M in written commitments and more in soft commitments for this equity financing round.

**What is the clinical trial design?**

Our clinical trial design benefits from existing Phase I safety data in 226 human subjects. Building on this momentum, we will run a dose escalation study to identify the optimal dose of our drug in our glioblastoma patient population. We will then run a window of opportunity surgical study to study the pharmacological effects of the drug in resected tumor tissue. Patients will continue taking the drug as we conduct the pharmacology work, so that we can begin looking for an efficacy signal.

**Who will run the clinical trial?**

Dr. Patrick Wen, Professor of Neurology at Harvard Medical School and Director of Neuro Oncology at Dana Farber Cancer Institute, has been at the forefront of designing and running clinical trials in neuro oncology for the past thirty years. Recently he sat on the five-person steering committee who set the global criteria for endpoint selection and trial design in neuro oncology. He also co-led the clinical trials that prompted the recent FDA approvals of [dordaviprone](#) and [vorasidenib](#). He has written a letter of support for our company, stating: “In 2016 as President of the Society For Neuro-Oncology I was proud to award Izi Stoll, the founder of Numiera Therapeutics, with the Society for Neuro Oncology’s Translational Research Award, when her team published this new target ... and I am proud to support her team now, as they work to move this promising new drug into the clinic.”

**What does an independent peer review panel have to say about this plan?**

The National Cancer Institute Study Section reviewed our proposed clinical trial and made the following summary statement: “The notable strengths of this project include the high significance of developing new targeted approaches to tackle deadly glioblastoma, the innovation of targeting fatty acid oxidation in this cancer, the outstanding team with strong record of accomplishments in drug development and glioblastoma, and the clinical trial outlined in excellence with appropriate statistical design.”

**What else do you need to do to reach market authorization?**

Once we conduct this trial, and identify a Phase II Recommended Dose (P2RD) for our patients, we will raise \$50M to run a combined Phase II/III clinical trial to evaluate the efficacy of this drug. One fantastic option is to work with the Global Coalition for Adaptive Research (GCAR) which has an existing clinical trial framework to evaluate new drugs in parallel for glioblastoma, with an established Phase II/III clinical protocol and a network of 100+ clinical sites who are prepared to run that larger trial.

**Who is on your team?**

Izi Stoll led the scientific team who originally discovered this new target to treat glioblastoma, then she put together a team to take the drug into clinical trials. Karl Nicholls was Director of Financial Planning and Analysis at Covidien for ten years leading up to their \$43B acquisition by Medtronic. He now supports the Colorado-based Numiera and Accure as fractional CFO. Gordon Beck served as Executive Director of Global Business Development at Roche, leading their Tamiflu initiative and conducting due diligence on therapeutic assets for potential acquisition. He is now working with Numiera Therapeutics to prepare the company for strategic partnerships and eventual acquisition.

