A Neurobiology and Drug Development Company

2-deoxy-D-glucose (2DG) – a novel anticonvulsant exploiting metabolic regulation of neural plasticity

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2DG: a glucose analogue (a sugar) with novel anticonvulsant and antiepileptic actions

2DG is preferentially delivered to epileptic foci by neurovascular coupling and activity-dependent uptake, enabling “post-seizure” administration

Unique Anticonvulsant Mechanisms:
- Glycolytic inhibition is a novel anticonvulsant mechanism possibly related to the ketogenic diet
- 2DG regulates synaptic vesicle release by activity-dependent mechanisms
- 2DG prevents seizure-induced gene expression contributing to chronic epilepsy progression by metabolic regulation of NRSF and NADPH-CtBP dependent transcription

-glucose-6-phosphate → fructose-6-phosphate → pyruvate → TCA cycle

Glycolytic pathway

2DG is a PET imaging ligand concentrated at the site of seizure

18F-2DG is a PET imaging ligand concentrated at the site of seizure
### Completed Milestones - Preclinical Efficacy Studies

**In vivo animal models of acute & chronic epilepsy**

- Two-fold slowing of kindled seizure induction & progression evoked from different brain sites (UW Madison)
- Minimum dose of 37.5 mg/kg*
- Effective against seizure progression when administered up to 10 minutes after a seizure *
  * funded by NGX & Epilepsy Therapy Project
- Two-fold slowing of latency to status epilepticus onset by kainic acid and pilocarpine (Lian et al 2008)
- Protection by seizures evoked acutely by 6Hz stimulation (NIH ASP)
- Protection against audiogenic seizures in Fring's mice (NIH ASP)

  This pattern of efficacy is unlike ANY other marketed anticonvulsant

**In vitro models of seizure induction**

2DG reduces epileptic discharges evoked by

- potassium (7.5mM, ictal & interictal)
- bicuculline (GABA antagonist)
- 4AP (potassium channel antagonist)
- DHPG (metabotrophic glutamate agonist)

(Stafstrom et al, 2009, UW Madison)

Implies that actions of 2DG at the cellular level are potentially “broad-spectrum” against different mechanisms of network synchronization
Advantages of 2DG vs. Existing Drugs

- Novel pattern of effectiveness in pre-clinical models
- Lacks debilitating side effects of current therapies
- Slows long-term progression of the disease
- Novel acute and chronic anti-epilepsy mechanism of action in pre-clinical models
- 2DG concentrates to the areas of epileptic activity
- Intellectual Property licensed from WARF: 1 patent issued and 1 pending in US (has been issued in Australia)
- NGX has exclusive license from WARF for all human therapeutic use

Toxicology

- PET imaging agent for 30+ years
- Favorable toxicity history
- Completed Phase 1 in cancer
- More than 20 other investigator clinical studies with > 300 subjects
- Need to confirm safety in effective dose (ED) range – cardiac toxicity observed at high doses 10X > ED range, and very mild cardiac autophagy in ED range

Route of Administration

- Oral (liquid or capsule); IV; IM; SC
- Potentially novel methods of delivery through device therapies
Current Development Plan

Complete preclinical toxicity, formulation, CMC, and filing of IND
“IND-enabling preclinical studies of 2DG for treatment of epilepsy”
supported by NIH RAID, may be underway Q2 2010

Will complete preclinical studies including bioanalytical assay
development, pharmacokinetic, toxicological, toxicokinetic,
manufacturing, formulation, and clinical trial designs, and
regulatory documentation for submission of an IND.

Investigator-initiated first in humans Phase I/II clinical trial in patients
with intractable epilepsy
“A Preliminary Tolerability and Efficacy Study of 2DG in Intractable Epilepsy”
University of Virginia, Nathan Fountain, MD, supported by EpilepsyTherapy
Project-ERF, WARF, NGX, anticipated start in Q4 2010

This will be a preliminary study of 2DG that will seek to detect an
efficacy signal and assess tolerability in 10-15 intractable patients with
frequent seizures.

Development of delayed release formulations
Zeeh Experimental Pharmacy Station (University of Wisconsin)
E. Elder, PhD, supported by WARF

This program is developing delayed release formulations to
exploit the activity-dependent uptake and short $t_{1/2}$ (~ 40
min) enabling chronic administration at lower total doses.
NeuroGenomeX, Inc.

We are seeking funding for completion of additional Phase I/II studies

Efficient and prudent use of investor’s funds