Novel NADPH Oxidase (NOX) Inhibitors

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OTT Breakfast Club
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Antioxidant Therapy Via NOX Inhibition

Candidate Indications
- Cancer
- Cardiovascular
- Metabolic
- Neurodegeneration
- Ophthalmologic
Dyeing to Prevent Tumorigenesis

Triaryl Dyes

Brilliant Green

Gentian Violet

Hemangioma Tumor Model

NOX Inhibition

Arbiser: Journal of Investigative Dermatology (2006) 126, 2316–2322
Gateway to Discovery, Innovation, and Products
Novel Triaryl NOX Inhibitor

Imipramine Blue

Inhibition of H$_2$O$_2$ in Nox4-expressing cells

<table>
<thead>
<tr>
<th>IB (µM)</th>
<th>Control</th>
<th>20</th>
<th>10</th>
<th>5</th>
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<tbody>
<tr>
<td>H$_2$O$_2$/hr/mg protein</td>
<td>30</td>
<td>20</td>
<td>10</td>
<td>5</td>
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</tbody>
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Gateway to Discovery, Innovation, and Products
Liposomal Nanoparticle Formulation for Brain Cancer Therapeutic

PEG Liposome

- Encapsulated IB

Plasma T½ increased (11 min. to 18 hrs.)

Glioblastoma Tumor Model

Survival increased (1 day)

CTL + IB
Intellectual Property

• “The Use of Imipramine Blue and Analogs Thereof in Treating Cancer”
  – Chemical compositions and methods of use

• “Nanocarrier Therapy for Treating Invasive Tumors”
  – PCT application pending (filed 4/2010)
  – Liposomal formulation and methods of use
Value Proposition

• Unique, anti-oxidative therapy
• Targets the source of reactive oxygen species (NOXes)
• Broad-based potential indications in several large markets
  – Invasive cancers (brain, melanoma, prostate)
  – Cardiovascular disease (atherosclerosis, cardiac hypertrophy)
  – Neurodegenerative diseases (Alzheimer's, ALS, Parkinson's, ischemic stroke)
  – Metabolic (diabetic neuropathy, chronic kidney disease)
• Target validation: Alimera Sciences license (dry AMD)
• Novel liposomal nanoparticle formulations
Future Plans

- Determine neuroblastoma MOA
- Animal studies in medulloblastoma model
- Test imipramine blue /doxorubicin co-formulated liposomes