

Company Spotlight: BrainCells Inc.

840 Memorial Drive, Cambridge, MA 02139 617.374.9009
Key Contacts: Jim Schoeneck CEO

Privately held

Funding Raised: \$77.7 million

Investors: Oxford Bioscience, New Enterprise Associates, Bay City Capital, NeuroVentures, AM Pappas, Technology Partners, MedImmune Ventures, Alexandria Real Estate Partners

Platform/Programs

Neurogenesis Screening: This company combines technologies devised by Fred Gage at the Salk Institute, and Eric Kandel via the acquired **NeuroGenix**. BrainCells screens compound libraries to find molecules which are either repurposed or had failed in previous indications, that spur generation of hNSCs. BrainCells has shifted its focus from single compounds to combinations of compounds, having looked at combinations covering a total of sixty mechanisms, some of which are synergistic in their neurogenic effects. Interestingly, about 10% result of combinations actually decrease neurogenesis, which has implications well beyond BrainCells itself: Any pharma company addressing a neurogenic target will need to become aware of these previously unknown negative effects of polypharmacy, including non-CNS components.

BCI-540/Depression: This is a repurposed compound licensed from **Mitsubishi**, who had tried it in Alzheimer's. It has two direct mechanisms, choline uptake enhancement and a second, which has not been disclosed. It does not act at any of the usual monoamine targets. After 4 weeks, it produces a 20% increase in NSCs in vivo. BrainCells has begun a 90pt Phase II clinical trial with BCI-540 in depression with anxiety features, since it has been strongly anxiolytic in animal models. There is no evidence of sexual or GI AEs. Results are expected in late 2009, a PTSD trial will begin in 2009 as well.

BCI-838: BrainCells licensed this program from **Taisho** and vetted it in their neurogenesis model. BCI-838 is the prodrug of BCI-632, which is active in cognition models. Taisho retains rights in China and Japan. Depression, anxiety, and cognition are potential indications.

BCI-952/Synergistic Combinations: BrainCells has identified a number of combinations of currently marketed drugs which together, increase neurogenesis 2-3 fold compared to either of the constituent drugs on its own. The first pairing tested is BCI-952, which consists of buspirone and melatonin. In an investigator IND trial done at MGH, for Major Depression. BCI-952 produced a clinical response rate of 58%, better than buspirone (38%) or placebo. BCI-956 is another combination which is in preclinical testing.

Partnerships

Taisho, Lundbeck, Mitsubishi, Organon

Outlook

The pedigree of the science is impressive, and BrainCells has been very successful in their fundraising, particularly given the cutting-edge nature of the basic neurogenic premise. There is data that supports the neurogenesis approach to depression, but it has not yet had its principle proven. Using clinical-stage compounds does assure BBB access and some degree of safety, which reduces risk somewhat. One underlying concern that will accompany any program which significantly accelerates neurogenesis will be whether that also incurs an increased risk of tumorigenicity, but thus far, there has been no evidence of this.

BrainCells continues to look for potentially neurogenic compounds for inlicensing. They have had screening relationships with **Lundbeck** and **Organon**. The unexpected complexity of the combination compound issue should make BrainCells an even more compelling screening partner. If the depression program succeeds, the ramifications of the neurogenesis approach could extend across a range of cognitive and neurodegenerative disorders, as well as mood and anxiety disorders.