Digital Neurotherapy (DNT): A New Class of CNS Therapy

Focus: Treatment and Diagnosis of Depression
Major Depressive Disorder – High Prevalence and Poor Response to Current Treatments

Depressive disorders are the most common cause of disability globally\(^1\)

- >300 million global prevalence
- 18 million US prevalence
- >$200B economic burden in the US

Depression reduces quality and duration of life in many chronic diseases

- 20-39% decrease in survival time in cancer\(^2,3\)
- 3.4 X increase in CVD mortality\(^4\)
- 5X increase in dementia in diabetes\(^5\)

Treatment for depression is of limited efficacy

- Anti-depressant drug Rx: 50% response rate\(^6\) >50% relapse rate\(^7\)

Annual health care costs/cancer patient with depression $235,337 vs. without depression $110,650\(^8\)
What is Digital Neurotherapy (DNT) and How Does It Work?

The brain is hierarchically organized with cognition and emotion existing only in neurosystems.

Depression is a neurosystems disorder.
REJUVENATE™ DNT Looks Like a Computer Game

6 of 9 modules in REJUVENATE™

- Carefully crafted perceptual and cognitive tasks stimulate the brain’s own repair processes to restore neurosystem function.
- NIH Director’s Award for “paradigm-changing medical research”
- “Easily the most sophisticated brain training program ever conceived"
Mechanism of Action Demonstrated with fMRI

C8 Digital Neurotherapy

Brain Activation
Schizophrenia

Depression
Brain Connectivity

Wexler et al Am J Psychiatry 2000

Increases in the number/efficiency of neurosystem connections measured by fMRI that support cognition, mood and emotion

- **# of rich club connections**
  - p < .001

- **Small World efficiency**
  - p < .001

- **Global efficiency**
  - p < .001

REJUVENATE™ Control
The Highest Efficacy Intervention for Treatment Resistant Depression Across Multiple Therapy Classes

Three trials with C8 augmentation. **All patients Rx-refractory**

- CBT augmentation of drug in TRD (STAR*D Trial)
- 2nd Drug augmentation of drug in TRD (STAR*D Trial)
- TMS augmentation of drug (meta-analysis)
- Composite results of drug studies submitted to the FDA
- Placebo response rate in drug studies submitted to the FDA
- Click Therapeutics EMFM training. **Any patient who had failed to respond to drug was excluded**
- Akili Interactive AKL-T03
- Active digital controls from C8, Click and Akili trials

C8 is the only therapy that also significantly improves multiple areas of cognition
Superior Clinical Outcomes from Superior Intervention Design and Patented Algorithms

More Breadth
Nine Treatment Modules Target Neurocognitive Systems

More Precision
• Incremental Variations of Perceptual and Cognitive Processing Demands
• >60 Levels within Each Module

More Content
One Year of Therapy Content vs. One Month of Competitor Programs

U.S. Patent 10,424,212 B2
Depression includes patients with different types of neuropathology requiring different treatments.

Micro-Cognition Biomarkers
1,000's of responses from each patient on training and probe trials that differ incrementally in perceptual and cognitive processing demands.

Subgroups of patients with the same neuropathology.

Clinical Treatment
Development and prescription of treatment for individual patients appropriate for their illness.
Development of a DNT from Neuroscience to Revenue

Identify Disorder-Related Neurosystem Target
Spec, Program, Pilot and Revise DNT
Gamify
Full Clinical Trial (Regulatory Approvals)
Distribution Marketing, Sales
Support, Maintenance & Data

C8 Stays Lean
• We only do what we do best
• Design and create new DNTs and biomarkers for specific disorders and populations

Out Licensee
• Pharmas, Insurers, Provider Organizations, Digital Health and Wellness Companies
• Regulatory, distribution, marketing, sales and customer support functions

We seek
• Out license partners
• $15 million in venture funding
Highly Experienced Science and Business Leadership

Tim Kish, CEO, VP/CFO Biogen, VP/CFO Illumina

Bruce E. Wexler, MD
Professor
Yale School of Medicine
Take-Aways

• NIH Director’s Award for “paradigm-changing medical research”
  • “Easily the most sophisticated brain training program ever conceived”

• Comprehensive and versatile platform technology
  • Modular plug-and-play architecture enables rapid product differentiation for different disorders
  • Patented algorithms shape treatment to the deficits of each patient in real time

• Two high-value propositions
  • Differentiated digital therapies for multiple specific disorders and populations
  • Novel biomarkers to refine diagnosis and individualize treatment

• Industry-leading treatment for depression in market now
  • Higher response and remission rates than drugs, CBT, TMS or other digital therapies
  • Mechanism of action confirmed by both fMRI and the reversal of cognitive deficits

• Business plan
  • Stay lean
  • Do only what we do best
  • Out license from a library of DNTs for specific indications and populations