

# Cyberonics Press Release August 13, 2003

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## CYBERONICS ANNOUNCES MECHANISM OF ACTION ADVISORY BOARD

### Press Release

For Immediate Release Wednesday, August 13, 2003 Contacts: Cyberonics

Pamela Westbrook  
Vice President of Finance and CFO  
Cyberonics, Inc.  
100 Cyberonics Blvd.  
Houston, TX 77058  
Main: (281) 228-7200

Fax: (281) 218-9332  
pbw@cyberonics.com Other

Helen Shik  
Vice President  
Schwartz Communications

230 Third Avenue  
Waltham, MA 02154  
Main: (781) 684-0770 ext. 6587

Fax: (781) 684-6500

hshik@schwartz-pr.com CYBERONICS ANNOUNCES MECHANISM OF ACTION ADVISORY BOARD

HOUSTON, Texas, August 13, 2003 -- Cyberonics, Inc. (NASDAQ:CYBX) today announced the formation of a VNS Therapy™ Mechanism of Action Advisory Board to advise Cyberonics on research and studies to improve the knowledge and understanding of the biology of a variety of chronic, treatment resistant disorders and the mechanism of VNS Therapy. Charles Nemeroff, M.D., Ph.D., Reunette W. Harris Professor and Chairman, Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, Georgia, will chair the board, which consists of the following neuroscientists, researchers, epileptologists and psychiatrists:

§ Charles Nemeroff, M.D., Ph.D., Reunette W. Harris Professor and Chairman, Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, Georgia

§ Dennis Charney, M.D., Chief, Mood and Anxiety Disorder Research Program, NIMH Chief, Experimental Therapeutics and Pathophysiology Branch, NIMH

§ Alan Frazer, Ph.D., Chair, Department of Pharmacology, Associate Dean for Research Graduate School of Biomedical Sciences, Career VA Scientist, Audie L. Murphy VA Hospital (ALMVAH) University of Texas Health Science Center at San Antonio

§ Mark George, M.D., Director, Functional Neuroimaging Division, Psychiatry; Director, Brain Stimulation Laboratory; Professor of Psychiatry, Radiology and Neurology, Medical University of South Carolina

§ Thomas Henry, M.D., Director, Epilepsy Center, Associate Professor of Neurology, Department of Neurology, Emory University School of Medicine, Atlanta, Georgia

§ Scott Krahl, Ph.D., Assistant Professor, UCLA Division of Neurosurgery; Neurophysiologist, VA Greater Los Angeles Healthcare System, Los Angeles, California

§ Helen Mayberg, M.D., FRCP(C), Professor of Psychiatry and Medicine (Neurology), Sandra A. Rotman Chair in Neuropsychiatry, Rotman Research Institute, University of Toronto, Toronto, Ontario, Canada

§ James McNamara, M.D., Carl R. Deane Professor of Neuroscience in the Departments of Medicine (Neurology), Neurobiology and Pharmacology, Director, Center for Translational Neuroscience, Chairman, Department of Neurobiology, Duke University Medical Center, Durham, North Carolina

Robert P. (&ldquo;Skip&rdquo;) Cummins, Cyberonics&rsquo; Chairman of the Board and Chief Executive Officer, commented, &ldquo;Cyberonics&rsquo; mission is to improve the lives of people touched by chronic, treatment resistant disorders. Dr. Nemeroff and the other preeminent neuroscientists on the Mechanism of Action Advisory Board will accelerate the accomplishment of that mission by helping Cyberonics develop a comprehensive research program to better understand (a) the biology of pharmacoresistant epilepsy and treatment resistant depression, (b) the basic

mechanism of vagus nerve stimulation, (c) the acute and chronic mechanism of action of VNS Therapy as a treatment for epilepsy, depression and other chronic disorders currently under clinical study, and (d) the impact of stimulation parameters on patient outcomes.

The first meeting of the VNS Mechanism of Action Advisory Board occurred on August 7, 2003. None of the Advisory Board members have been granted stock options or issued shares by Cyberonics or were holding any Cyberonics stock as of August 7, 2003.

## ABOUT VNS THERAPY AND CYBERONICS

Cyberonics, Inc. (NASDAQ:CYBX) was founded in 1987 to design, develop and market medical devices for the long-term treatment of epilepsy and other chronic neurological disorders using a unique therapy, vagus nerve stimulation (VNS). Stimulation is delivered by the VNS Therapy System, an implantable generator similar to a cardiac pacemaker. The VNS Therapy System delivers preprogrammed intermittent mild electrical pulses to the vagus nerve 24 hours a day. The Company's initial market is epilepsy, which is characterized by recurrent seizures. Epilepsy is the second most prevalent neurological disorder. The Cyberonics VNS Therapy System was approved by the FDA on July 16, 1997 for use as an adjunctive therapy in reducing the frequency of seizures in adults and adolescents over 12 years of age with partial onset seizures that are refractory to antiepileptic medications. The VNS Therapy System is also approved for sale as a treatment for epilepsy in all the member countries of the European Economic Area, Canada, Australia and other markets. To date, more than 22,000 epilepsy patients in 24 countries have accumulated over 56,000 patient years of experience using VNS Therapy. The VNS Therapy System is approved for sale in the European Economic Area and in Canada as a treatment for depression in patients with treatment-resistant or treatment intolerant major depressive episodes including unipolar depression and bipolar disorder (manic depression).

VNS Therapy is at various levels of investigational clinical study as a potential treatment for depression, anxiety disorders, Alzheimer's disease, and chronic headache/migraine. Cyberonics' comprehensive VNS Therapy depression study program began with the first pilot study implant in July 1998. The depression study program includes the following studies: a 60-patient acute and long-term pilot study (D-01); a 235-patient double blind, randomized, placebo controlled 8-week fixed dose acute pivotal study with a long-term extension (D-02); a 127-patient long-term observational study of patients with chronic or recurrent treatment resistant depression treated only with treatment as usual (D-04); neuroimaging, neurochemical and sleep mechanism of action studies; and several healthcare utilization and cost effectiveness studies. The patients in these studies were suffering from chronic or recurrent treatment resistant depression. In the D-02 and D-04 studies, the average lifetime illness exceeded 25 years and the average duration of the current depressive episode exceeded 48 months.

Highly statistically and clinically significant acute and long-term response and remission rates were observed in the D-01 pilot study. The first implant in the D-02 pivotal study occurred in August 2000. In January 2002, Cyberonics announced that although clinically meaningful, the difference in the D-02 treatment and placebo group HRSD-24 response rates at the end of the 8-week fixed dose acute study was not statistically significant. In September 2002, after determining the likely contributors to the lack of statistical significance, Cyberonics submitted a revised, prospective long-term pivotal study analysis plan to FDA. In January 2003, Cyberonics announced that the one-year data from its D-02 depression pivotal study, analyzed pursuant to the D-02 analysis plan submitted to the FDA in September 2002, showed highly statistically significant (p-value < 0.001) and clinically significant improvements compared to baseline. In July 2003, Cyberonics reported that the preliminary one-year results from its D-02 VNS Therapy depression pivotal study and D-04 companion study of chronic and recurrent treatment resistant depression, analyzed pursuant to the D-02 analysis plan submitted to the U.S. Food and Drug Administration (FDA) in September 2002, showed a highly statistically significant causal relationship (p-value < 0.001) between VNS Therapy and the depression improvements from baseline observed in the D-02 VNS Therapy study. The causal relationship between VNS Therapy and the D-02 patients' one-year outcomes was determined using a repeated measures linear regression analysis to compare depression improvements as measured by the Inventory of Depressive Symptomatology-Self Report (IDS-SR) over one year in 205 D-02 patients receiving VNS Therapy and treatment as usual with the IDS-SR outcomes of 124 patients in a companion study, D-04, receiving only treatment as usual. In D-04, patients with chronic or recurrent treatment resistant depression who met the critical D-02 inclusion criteria were treated with standard medical management at 13 total study sites including 12 of the 21 D-02 study sites. Statistically and clinically significant differences in the physician and patient reported D-02 and D-04 patients' one-year response and remission rates were also observed. One-year response rates, defined as at least a 50% improvement in depression symptoms as measured by the IDS-SR and HRSD-24 (24 item clinician rated Hamilton Rating Scale for Depression) were 21% and 30%, respectively in D-02 and 12% and 13% respectively in D-04. One-year remission rates, defined as the percentage of patients free of depressive symptoms after one-year of treatment, were 16% and 17%, respectively in D-02 and 5% and 7%, respectively in D-04.

The Company is headquartered in Houston, Texas and has an office in Brussels, Belgium. For additional information please visit us at [www.cyberonics.com](http://www.cyberonics.com).

## FORWARD LOOKING STATEMENTS

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended and Section 21E of the Securities Exchange Act of 1934, as amended. These statements can be identified by the use of forward-looking terminology, including "may," "believe," "will," "expect," "anticipate," "estimate," "plan," "intend," and "forecast," or other similar words. Such forward-looking statements include statements concerning the timing and accomplishment of our corporate mission to improve the lives of patients touched by chronic, treatment resistant disorders. Statements contained in this press release are based upon information presently available to us and assumptions that we believe to be reasonable. We are not assuming any duty to update this information should those facts change or should we no longer believe the assumptions to be reasonable. Our actual results may differ materially. Important factors that may cause actual results to differ include, but are not limited to: continued market acceptance of VNS Therapy and sales of our product; the development and satisfactory completion of clinical trials and/or market test of VNS Therapy for the treatment of depression, Alzheimer's disease, anxiety, or other indications; adverse changes in coverage or reimbursement amounts by third-parties; intellectual property protection and potential infringement claims; maintaining compliance with government regulations and obtaining necessary government approvals for new applications; product liability claims and potential litigation; reliance on single suppliers and manufacturers for certain components; the accuracy of management's estimates of future expenses and sales; and other risks detailed in from time to time in the Company's filings with the SEC. ### Cyberonics, Inc.

The Cyberonics Building  
100 Cyberonics Blvd.  
Houston, TX 77058  
Main: (281) 228-7200  
Fax: (281) 218-9332