



## Neurocrine Reports Indiplon Effective in Treating Elderly Patients With Difficulties Maintaining Sleep

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Indiplon Modified Release Demonstrates Highly Statistically Significant Improvement in Sleep Maintenance

SAN DIEGO, March 2 /PRNewswire-FirstCall/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced positive results from its Phase III trial with the modified release formulation of indiplon, achieving highly statistically significant results in elderly patients with chronic insomnia who have sleep maintenance difficulties. Results demonstrated that with indiplon 20 mg modified release, patients achieved rapid sleep onset and maintained sleep. The primary endpoint for the study was patient reported Total Sleep Time (sTST). Efficacy results with indiplon modified release demonstrated a highly statistically significant improvement in sTST ( $p < 0.0001$  at both Weeks 1 and 2) as compared to placebo, adding more than one hour to total sleep time. Indiplon modified release also demonstrated a highly statistically significant improvement in patient reported Wake After Sleep Onset (sWASO) ( $p < 0.0001$  at both Weeks 1 and 2) as compared to placebo, a reduction of approximately one hour in time awake after sleep onset, a 40% improvement over placebo. Safety results demonstrated that the incidence of adverse events was similar to what had been observed in studies conducted previously.

Secondary sleep maintenance endpoints including patient reported Total Wake Time (sTWT), and Number of Awakenings After Sleep Onset (sNAASO) were also highly statistically significant compared to placebo. Additional secondary endpoints including Latency to Sleep Onset (LSO), or the amount of time it took patients to fall asleep and Sleep Quality (SQ) were also highly statistically significant compared to placebo. Evaluation of treatment response was also assessed by both patients and investigators. Patient reported Global Impression (PGI) assessed for overall effect of sleep, time to sleep, amount of sleep, sleep quality, and strength of medication was highly statistically significant and showed significant improvement over placebo. Investigator reported Global Rating for Severity of insomnia and Change as a result of treatment were both highly statistically significant over placebo and in favor of indiplon. Patients on indiplon also showed no symptoms of next day drowsiness compared to the placebo group.

"These data with indiplon modified release reflect some of the most robust efficacy results that we have seen yet in clinical trials with a sedative hypnotic. This new agent may offer improved clinical benefit to patients with chronic insomnia, particularly older adults who have increased difficulties with frequent and prolonged awakenings throughout the night," said Dr. James Walsh, Executive Director, Sleep Medicine and Research Center St. Luke's Hospital, St. Louis, Missouri.

"We are pleased to report these robust Phase III clinical results validating that indiplon modified release has significant clinical benefit in helping elderly patients maintain sleep as shown by adding over one hour to patient's overall time asleep with almost an hour less time awake during the night. These data suggest that indiplon significantly improves critical aspects of sleep maintenance," said Dr. Henry Pan, Executive Vice President and Chief Medical Officer for Neurocrine Biosciences.

### Study Design

The study was a randomized, double-blind, placebo-controlled, parallel- group, outpatient, multi-center Phase III clinical trial conducted over a two week period to assess the efficacy and safety of nightly administration of indiplon modified release (20 mg) relative to placebo in approximately 220 elderly chronic patients with sleep maintenance difficulties. Patients were given nightly administration of 20 mg of indiplon modified release over a two-week evaluation period. The study was conducted in 35 centers in the U.S.

### About Indiplon

Indiplon is a unique non-benzodiazapine agent that acts on a specific site of the GABA-A receptor. Indiplon has been shown to bind preferentially to the specific subtype of GABA-A receptors within the brain believed to be responsible for promoting sleep. There are two formulations of indiplon, immediate release and modified release are being studied in clinical trials to address different types of sleep problems.

### About Neurocrine Biosciences

Neurocrine is conducting one of the most comprehensive clinical programs in insomnia to address the multiple needs of younger and older adult patients with insomnia such as sleep initiation, sleep maintenance, and long-term administration. Neurocrine has initiated and is completing all of its Phase III safety and efficacy trials to support a New Drug Application (NDA) for the two formulations expected in the first half of 2004 for indiplon for multiple insomnia indications. The Phase III program alone will have data from approximately 5,000 patients with different types of insomnia. Indiplon was licensed from DOV Pharmaceutical in 1998.

Insomnia is a prevalent condition in the United States, with nearly one-half of the adult population reporting trouble sleeping a few nights per week or more, according to the National Sleep Foundation's (NSF) Sleep in America Poll 2002. Approximately 35 percent of the adult population reports that they have experienced insomnia every night or almost every night within the past year. Insomnia remains a disorder with high unmet medical needs, including prolonged awakenings during the night with difficulty falling back to sleep.

### Neurocrine Webcast at Lehman Brothers Conference

Neurocrine will present at the Lehman Brothers Seventh Annual Global Healthcare Conference at Loews Miami Beach Hotel on Thursday, March 4, 2004 at 2:00 PM Eastern Standard Time; 11:00 AM Pacific Standard Time. Gary Lyons, President and CEO of Neurocrine will highlight the Company's recent clinical data results. The presentation will be simultaneously webcast and can be accessed on the Company's website at <http://www.neurocrine.com>

Neurocrine Biosciences, Inc. is a product-based biopharmaceutical company focused on neurological and endocrine diseases and disorders. Our product candidates address some of the largest pharmaceutical markets in the world including insomnia, certain female and male disorders, anxiety,

depression, diabetes, multiple sclerosis, irritable bowel syndrome, eating disorders, pain, and autoimmunity. Neurocrine Biosciences, Inc. news releases are available through the Company's website via the Internet at <http://www.neurocrine.com>

In addition to historical facts, this press release may contain forward- looking statements that involve a number of risks and uncertainties. Among the factors that could cause actual results to differ materially from those indicated in the forward looking statements are risks and uncertainties associated with the Company's indiplon clinical development program and planned regulatory activities. Specifically, the risks and uncertainties the Company faces with respect to its indiplon program include, but are not limited to, risk that indiplon may not successfully proceed through Phase III clinical trials or Phase III clinical trials may fail to demonstrate that indiplon is safe and effective in treating humans; risk that the Company may not complete indiplon Phase III clinical trials on the Company's projected timelines for various reasons, including the possibility that patient recruitment may be slower than expected; risk that the clinical investigators and contract research organizations upon which the Company relies to conduct its clinical programs may not be diligent, careful or timely, and may make mistakes, in the conduct of the programs; risk relating to the Company's dependence on contract manufacturers for clinical drug supply and compliance with regulatory requirements for marketing approval; risk that the Company may not successfully co-ordinate the completion and submission of planned regulatory filings on the Company's projected timelines; risk that the Company may not receive regulatory approval for indiplon or approval may be delayed; risks associated with the Company's dependence on corporate collaborators for commercial manufacturing and marketing and sales activities; uncertainties relating to patent protection and intellectual property rights of third parties; risks and uncertainties relating to competitive products and technological changes that may limit demand for the Company's products; risk that the Company will be unable to raise additional funding required to complete development of all of its product candidates; and the other risks described in the Company's Form 10-K for the year ended December 31, 2002, the Company's most recent report on Form 10-Q and the Company's final prospectus supplement and accompanying prospectus relating to its recent offering. Neurocrine undertakes no obligation to update the statements contained in this press release after the date hereof.

SOURCE Neurocrine Biosciences, Inc.