Neurocrine Biosciences Presents Phase III Data at the American Psychiatric Association (APA) Meeting

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Results Demonstrate Both Formulations of Indiplon are Safe and Effective in Treating Patients With Chronic and Transient Insomnia

NEW YORK, May 6 /PRNewswire-FirstCall/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) announced today that four studies were presented this week at the 157th annual meeting of the American Psychiatric Association (APA) demonstrating the efficacy and safety of both formulations of indiplon, immediate release and modified release, in treating patients and subjects with chronic and transient insomnia. The results also show that indiplon is effective across different patient populations including the elderly who frequently suffer from insomnia.

"These data demonstrate that indiplon immediate release is effective in helping patients improve the quality and length of their sleep, importantly, without causing next day residual effects," said Dr. Marty Scharf, Director, Tri-State Sleep Disorders Center and Clinical Professor of Psychiatry at the Wright State University Department of Psychiatry. "The data presented with indiplon modified release demonstrated efficacy in treating patients with sleep maintenance insomnia, and confirmed that indiplon patients were able to sleep significantly longer than those taking placebo, with an effect that was sustained over the two-week treatment period."

Indiplon Immediate Release Demonstrates Efficacy and Safety in Adults with Chronic Insomnia

Results reported positive efficacy and safety data from a Phase III clinical trial with the immediate release formulation of indiplon, without evidence of tolerance or next day residual effects in 200 adult patients with Chronic Primary Insomnia over 35 days of treatment. In this study, indiplon immediate release demonstrated a statistically significant improvement in the primary endpoint of Latency to Persistent Sleep (LPS), a measure of the time it takes to fall asleep, as measured objectively by polysomnography. Results with the 10 mg dose reduced LPS to 28 minutes ($p<0.002$) and the 20 mg dose reduced LPS to 27 minutes ($p<0.05$) as compared to placebo (LPS of 37 minutes) and the effect was sustained over the course of the study. The 10 mg and 20 mg doses also demonstrated improvements in Sleep Quality. Both doses of the immediate release formulation of indiplon were well tolerated. In addition, side effects for the indiplon groups were no different from placebo and there were no statistically significant differences in next day residual sedation detected by any of the three validated measurements, Digital Symbol Substitution Test (DSST), Symbol Copy Test (SCT), and Visual Analogue Scale (VAS) for sleepiness.

Along with the reported efficacy and safety results, this study was also designed to evaluate the potential for rebound insomnia and withdrawal effects after discontinuation of indiplon immediate release after 35 consecutive nights of treatment. There was no evidence of withdrawal upon treatment discontinuation using the standard validated Benzodiazepine Withdrawal Symptom Questionnaire (BWSQ). In addition, no evidence of rebound insomnia was seen on any secondary measures comparing LPS measures during the treatment period to pretreatment visits. Rebound insomnia is an increase in the time it takes to fall asleep upon cessation of treatment as compared to the time to fall asleep prior to the initiation of treatment.

Indiplon Immediate Release Demonstrates Efficacy and Tolerability in Transient Insomnia

A second abstract presents results from the Company's Phase III clinical trial program with indiplon immediate release, achieving both primary and secondary endpoints of sleep initiation in 593 subjects with transient insomnia. Results demonstrated that both dose levels of indiplon immediate release (10 mg or 20 mg) were safe, well tolerated, and effective in inducing sleep, increasing sleep duration, and improving overall sleep quality without next day residual effects in subjects with transient insomnia.

The primary endpoint in this study was Latency to Persistent Sleep (LPS) as measured objectively by polysomnography (PSG) and the secondary endpoint was patient reported Latency to Sleep Onset (LSO). In this study indiplon immediate release demonstrated a statistically significant improvement in the primary endpoint of LPS at both dose levels relative to placebo ($p<0.0001$). Mean improvements over placebo were approximately 36% and 50% for the 10 and 20 mg dose group, respectively. The secondary efficacy endpoint of patient reported LSO also demonstrated statistically significant improvements in the drug treated groups as compared to the placebo group ($p<0.0001$). These results indicate that subjects on indiplon felt that they fell asleep more rapidly, supporting the results demonstrated through polysomnography. Total Sleep Time (TST) as measured objectively by PSG was significantly increased for both doses ($p<0.005$) as compared to placebo. Patient reported Sleep Quality was also significantly improved for both doses. There were no next day residual sedation effects detected by any of the three validated measurement tools, DSST, SCT or VAS when compared with placebo. Both doses of indiplon were well tolerated and the incidence of adverse events was comparable to placebo.

Indiplon Immediate Release Shows Efficacy and Safety in Elderly Patients with Chronic Insomnia

A third study demonstrates dose-related positive efficacy results with three doses (5 mg, 10 mg and 20 mg) of indiplon immediate release in a Phase II randomized, multi-center, double-blind, placebo-controlled, four-way crossover dose-response study in 42 elderly patients with chronic insomnia. The immediate release formulation demonstrated a statistically significant reduction in the primary endpoint of Latency to Persistent Sleep (LPS) as measured objectively by polysomnography (PSG) at all dose levels ($p<0.001$) with a time of 13.8 minutes to sleep initiation with 5 mg, 10.4 minutes with 10 mg, and 9.8 minutes with 20 mg compared with 25.2 minutes for placebo. Patient reported Latency to Sleep Onset (LSO), Total Sleep Time (TST) and Sleep Quality also improved significantly over placebo. TST was significantly increased on indiplon 10 mg and 20 mg. All dose levels of indiplon immediate release were found to be safe and well tolerated. There were no next day residual effects observed at any dose level relative to placebo using the three validated measurements, DSST, SCT or VAS for sleepiness.

"We are pleased to report on these important studies with indiplon immediate release in adult and elderly patients with chronic and transient insomnia. The combined results demonstrate indiplon immediate release has a significant impact on improving both the quantitative physiological measures through polysomnography as well as qualitative measures through patients' perception of sleep, without causing next day residual effects," said Dr. Murray Maytom, Senior Medical Director of Clinical Development for Neurocrine Biosciences.

Indiplon Modified Release Demonstrates Efficacy in Sleep Initiation and Sleep Maintenance in Chronic Patients

Data from a fourth study presents results from a Phase III clinical study with indiplon modified release, demonstrating that patients with chronic insomnia fell asleep more rapidly and stayed asleep longer. This study reported positive efficacy results in a randomized, double-blind, placebo-controlled, parallel group, multicenter, out-patient Phase III clinical trial with the modified release formulation of indiplon following nightly administration in 211 chronic patients with sleep maintenance difficulties. Results over a two-week period demonstrated a statistically significant improvement in the primary endpoint of patient reported Total Sleep Time (sTST) relative to placebo at both week 1 ($p<0.0001$) and week 2 ($p=0.0013$).

All secondary sleep maintenance measures also demonstrated significant improvement with indiplon modified release as compared to placebo. A key secondary efficacy endpoint of patient reported mean Latency to Sleep Onset (LSO) showed significant improvement in the indiplon treated group as compared to the placebo group ($p=0.0084$ at week 1, $p=0.0131$ at week 2). Patient reported Wake After Sleep Onset (sWASO), Sleep Quality and Patient reported Global Impression (PGI) were significantly improved for indiplon modified release ($p<0.005$) at both weeks of treatment as compared to placebo. PGI assessed the overall effect on sleep, time to sleep, amount of sleep, sleep quality, and strength of medication. Safety results demonstrated that the 30 mg dose of the modified release formulation of indiplon was well tolerated.

About Indiplon

Indiplon is a novel GABA-A receptor potentiator with high selectivity for the specific subtype of GABA-A receptors within the brain believed to be responsible for promoting sleep. Two formulations of indiplon, immediate release and modified release, are being developed to address different types of sleep problems. Indiplon was licensed from DOV Pharmaceutical in 1998.

Insomnia is a prevalent condition in the United States, with 58 percent 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 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 Neurocrine's business and finances and research programs in general including, but not limited to, risk and uncertainties associated with, or arising out of, drug discovery, pre-clinical and clinical development of products including risk that the Company's Urocortin and CRF research programs will not lead to clinical candidates, that the GnRH receptor antagonist, D2 receptor agonist and altered peptide ligand clinical candidates will not proceed to later stage clinical trials and risks and uncertainties associated with the Company's indiplon Phase III 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 including the risk that Phase III clinical trials may fail to demonstrate that indiplon is safe and effective in treating humans and the risk that additional clinical studies may be required to support filings for regulatory approval; risk that the Company may not complete indiplon Phase III clinical trials on the Company's projected timelines for various reasons, including the 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 report on Form 10-K for the year ended December 31, 2003. Neurocrine undertakes no obligation to update the statements contained in this press release after the date hereof.

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