Neurocrine Reports Phase I Clinical Results With Indiplon In Elderly Subjects After Middle of the Night Dosing

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Indiplon Shows No Next Morning Residual Effects At 4, 6, and 8 Hours After Dosing Versus Placebo

SAN DIEGO, Nov. 10 /PRNewswire-FirstCall/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced results from the Company's indiplon immediate release Phase I clinical trial. The data showed that elderly subjects given indiplon 5 mg or 10 mg doses with middle of the night (MOTN) administration did not experience next morning residual effects as compared to placebo using standard measurements of psychomotor function and alertness. In the same study, patients given zopiclone 3.75 mg, the approved starting dose in Europe for the treatment of elderly patients with insomnia, experienced significant impairment the next morning as compared with placebo.

The study was a Phase I four-way crossover randomized, double-blind, placebo and active drug controlled, single center clinical trial designed to assess safety and tolerability of indiplon and zopiclone compared with placebo. The study was conducted in Europe on an in-patient basis with 36 healthy elderly subjects, aged 65 to 73 years. Subjects were awakened to an alert state four hours after they had fallen asleep at which time indiplon, zopiclone or placebo was administered. After falling back to sleep, subjects were awakened four hours post dose and psychomotor tests were conducted over the next four hours. Next day residual effects were assessed immediately after awakening at four hours, and also at six and eight hours post dosing the next morning using the three validated measurements of Digital Symbol Substitution Test (DSST), Symbol Copy Test (SCT), and Visual Analog Scale (VAS) of sleepiness.

Pharmacodynamic and safety results demonstrated that the 5 mg and 10 mg doses of the immediate release formulation of indiplon were well tolerated and there were no statistically significant differences in next day residual sedation as measured by DSST, SCT, and VAS as compared with placebo (p = not significant at all time points for both doses and with all three measurements). However, zopiclone 3.75 mg demonstrated statistically significant impairment the next morning as compared with placebo at 4 hours (p=0.001) and 8 hours (p=0.014) post dose using DSST, one of the three validated measurements used in this study. A trend toward impairment was also demonstrated for zopiclone at 4 hours (p=0.092) and 6 hours (p=0.086) post dose using SCT, another validated measure. There were no serious adverse events in the study. The incidence of AEs for the indiplon treatment groups was comparable to placebo.

"These results demonstrate that indiplon immediate release is safe and well tolerated when administered to elderly subjects after middle of the night administration. There was no evidence of next morning residual effects. These findings are consistent with an earlier study we did in the younger adult population," said Dr. Henry Pan, Executive Vice President and Chief Medical Officer for Neurocrine Biosciences

Neurocrine is also conducting a Phase II randomized, placebo controlled, double blind, parallel group, multi-center study to assess the efficacy and safety of MOTN administration of indiplon immediate release 10 mg and 20 mg doses as compared to placebo in 264 adult patients with chronic insomnia with frequent and prolonged MOTN awakenings. This study is being conducted on an outpatient basis over a four-week treatment period. The primary endpoint for this study is patient reported Latency to Sleep Onset (LSO) post dosing in the middle of the night at weeks two and four.

"This study represents a new area for the treatment of insomnia. Indiplon is the first insomnia treatment to evaluate efficacy, safety and next morning residual effects associated with treating extended awakenings in the middle of the night. We are planning to report the results of our Phase II clinical trial with indiplon immediate release after middle of the night administration in 264 patients by year-end 2003," added Pan.

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.

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) expected in the first half of 2004 for indiplon for multiple insomnia indications. The Phase III program alone will have data from approximately 5000 patients with different types of insomnia.

Insomnia is a prevalent condition in the United States, with more than 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% of the adult population reports that they have experienced insomnia every night or almost every night within the past year. Despite this widespread prevalence, insomnia remains a disorder with high unmet medical needs, including the ability to maintain sleep throughout the night without next-day residual effects.

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.

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