



Neurocrine Biosciences Announces Positive Phase I Results With Its Orally Active GnRH Receptor Antagonist

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Phase II Studies to Be Initiated in Second Quarter 2005

SAN DIEGO, March 2, 2005 /PRNewswire-FirstCall via COMTEX/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) announced positive results from the Company's Phase I clinical trial with its proprietary, orally active small molecule Gonadotropin- Releasing Hormone (GnRH) receptor antagonist. The trial was designed to evaluate the safety, pharmacokinetics (PK), and pharmacodynamics (PD) of two dose levels of NBI-56418 given once daily for 6 weeks in 60 healthy pre- menopausal women. The study demonstrated that NBI-56418 was safe and well tolerated. NBI-56418 demonstrated a dose-dependent suppression of estradiol that was observed throughout the duration of dosing.

The study was a double-blind, placebo-controlled trial involving 60 healthy pre-menopausal women randomized equally to one of three treatment groups: placebo, 50mg of NBI-56418, or 150mg of NBI-56418 each administered for 42 days. Dosing started on Day 2 to Day 7 following the onset of the menstrual cycle.

On day 42 of the study there were reductions of 40% and 79% in mean estradiol concentration in the 50mg and 150mg dose groups respectively compared with that in the placebo group. At times prior to day 42 of the study, the data showed early achievement of estradiol suppression. There was markedly less variability in estradiol concentration in treated subjects, particularly those in the 150 mg group. The estradiol concentrations achieved in this study are comparable with those associated with efficacy of other agents known to be effective in endometriosis. Additionally, because estradiol suppression is not complete, the data suggest that it may be possible to achieve efficacy and avoid the adverse impact of other hormonal treatments for the condition.

"As in our previous Phase I studies, we have once again shown that our GnRH antagonist can modulate estradiol levels. Since the effects of reduction in estradiol have been well correlated with a reduction of pain and other symptoms of endometriosis, we believe our GnRH antagonist will have significant therapeutic application in endometriosis," said Dr. Wendell Wierenga, Executive Vice President of Research and Development for Neurocrine Biosciences. "Based on these data, doses have been selected for a 3-month Phase II study evaluating NBI-56418 in patients with endometriosis, which is expected to be initiated in the 2nd Quarter of 2005," added Wierenga.

Background

GnRH is a neuroendocrine peptide which stimulates the secretion of the pituitary LH, which in turn stimulates the production of estrogen by the ovary or testosterone by the testes. The most widely prescribed drugs which modulate the GnRH receptor are peptide agonists, such as, Lupron(R) and Zoladex(R), with estimated combined sales in excess of \$2.5 billion worldwide (2003). These compounds are administered as injectable depots which act by first stimulating then eventually inhibiting the secretion of pituitary LH and consequently, estrogen or testosterone production. GnRH peptide agonists have proven clinically useful in the treatment hormone dependent diseases such as endometriosis, uterine fibroids, prostate cancer and breast cancer, as well as being used for assisted-reproductive therapy. Despite a multitude of potential applications, deleterious consequences of GnRH agonist therapy, especially permanent bone loss in women's health diseases, have limited the useful duration of treatment.

NBI-56418, discovered and developed within Neurocrine, is a specific highly potent non-peptide, orally active antagonist of the GnRH receptor. This compound inhibits pituitary LH secretion directly, potentially preventing the several week delay and flare associated with peptide agonist therapy. It is anticipated that an orally administered non-peptide small molecule GnRH antagonist would have distinct advantages over peptide agonists with respect to the degree of down-regulation of GnRH receptors that can be readily adjusted by dose. This level of flexibility should permit modest rather than profound down-regulation of the sex hormones. This, in turn, would allow for a moderate amount of circulating estrogen, e.g., in endometriosis, to mitigate long-term bone demineralization. Neurocrine believes that orally active, non-peptide GnRH antagonists should provide the potential to eliminate hormone add-back therapy, a rapid onset of action, an increased dosing flexibility, and a greater patient acceptability over currently available treatments.

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, 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 in general including the risks and uncertainties associated with, or arising out of, drug discovery, pre-clinical and clinical development of pharmaceutical products. Specifically, the Company faces risks and uncertainties arising out of its GnRH research and development program including risk that the GnRH receptor antagonist lead clinical candidate will not proceed to later stage clinical trials; risk that should the lead GnRH antagonist candidate prove unsuitable for continued development, the Company will not be successful in identifying alternative GnRH antagonist products that are safe and effective; risk relating to the Company's dependence on contract manufacturers for GnRH antagonist product clinical drug supply and compliance with regulatory requirements for marketing approval; risks that the Company may be dependent on corporate collaborators for commercial manufacturing and marketing and sales activities for its GnRH antagonist products; uncertainties relating to patent protection for the Company's GnRH antagonist products 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 GnRH antagonist products; risk that the Company will be unable to raise additional funding required to complete development of its GnRH antagonist product candidates; and the other risks described in the Company's report on Form 10-K for the year ended December 31, 2004. Neurocrine undertakes no obligation to update the statements contained in this press release after the date hereof.

SOURCE Neurocrine Biosciences, Inc.

Elizabeth Foster or Claudia Jones,
both of Neurocrine Biosciences, Inc.,
+1-858-617-7600