



Nature Medicine Publication Demonstrates IL-4 Fusion Toxin is Effective In Treating Systemic Form of Cancer in Preclinical Models

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SAN DIEGO, June 29 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced that a research team from the Center for Biologics Evaluation and Research (CBER) of the Food and Drug Administration (FDA) and the National Institutes of Health (NIH) reported preclinical data with IL-4 Fusion Toxin in the July 1, 1999 issue of *Nature Medicine*. The publication reports that in preclinical models of Kaposi's sarcoma (KS), treatment with IL-4 Fusion Toxin resulted in eradication of KS tumors and prevented disease-related symptoms, such as cachexia (weight loss) and lymphopenia. IL-4 Fusion Toxin was discovered and developed by Dr. Raj Puri and his colleagues from the laboratory of molecular tumor biology of CBER of the FDA in collaboration with scientists from the National Cancer Institute of the NIH. Neurocrine Biosciences licensed the rights to IL-4 Fusion Toxin in May 1998 and is currently conducting Phase I/II clinical trials with IL-4 Fusion Toxin (NBI-3001) in the lead indication, glioblastoma (malignant brain tumors). Neurocrine expects to report on the results of the Phase I/II trial for glioblastoma at the end of 1999.

The research team from the FDA and NIH have previously published results with IL-4 Fusion Toxin, demonstrating a high level of binding and destruction of malignant tumor cells obtained from patients with colon cancer, breast cancer, gastric cancer, prostate cancer, kidney cancer, lymphoma, melanoma, and malignant brain tumors.

"These results are significant in further demonstrating that IL-4 Fusion Toxin has the potential to treat not only glioblastoma, which is localized in brain tissue, but may also treat systemic forms of cancer. Neurocrine is conducting an advanced clinical program for glioblastoma and may consider developing this compound for other cancer indications in the future," said Stephen G. Marcus, M.D. Senior Vice President of Clinical and Regulatory Affairs and Chief Medical Officer of Neurocrine Biosciences.

Previously reported preclinical data from Dr. Puri's group suggest that when infused directly into the glioblastoma, IL-4 Fusion Toxin kills the tumor cells but not healthy cells. IL-4 Fusion Toxin is a protein in which a blood cell derived growth factor (IL-4) has been joined with a *Pseudomonas* exotoxin, a potent toxin that can destroy cancer cells. IL-4 has very high affinity for IL-4 receptors, which are highly localized on malignant brain tumors, but not on normal brain cells. IL-4 binds tightly to the IL-4 receptors on the surface of the glioblastoma cells and delivers the exotoxin directly into the cell, resulting in cell death. IL-4 Fusion Toxin is administered via a special catheter that permits delivery directly into the brain tumor.

Including NBI-3001 which is in Phase I/II for glioblastoma, Neurocrine has now advanced five programs into development. The Company's CRF receptor antagonist is currently in Phase II clinical development with its partner, Janssen Pharmaceutica, for anxiety/depression. Neurocrine and its partner, Novartis Pharmaceuticals, are conducting their second Phase II clinical trial with Neurocrine's APL compound in patients with multiple sclerosis. Neurocrine is also conducting a Phase II trial with NBI-34060 for insomnia. In addition, Neurocrine commenced a Phase I trial with a second APL compound (NBI-6024) for diabetes in the first quarter of 1999.

Neurocrine Biosciences is a leading neuroscience company focused on the discovery and development of novel therapeutics for neuropsychiatric, neuroinflammatory and neurodegenerative diseases and disorders. The Company's neuroscience, endocrine and immunology disciplines provide a unique biological understanding of the molecular interaction between central nervous, immune and endocrine systems for the development of therapeutic interventions for anxiety, depression, Alzheimer's disease, insomnia, stroke, malignant brain tumors, multiple sclerosis, obesity and diabetes.

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In addition to historical facts, this press release contains 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 research and development programs and business and finances including, but not limited to, risks and uncertainties associated with, or arising out of, drug discovery, pre-clinical and clinical development of products including risk that research may not generate development candidates, development candidates will not successfully proceed through early clinical trials or that in later stage clinical trials will not show that they are effective in treating humans; determinations by regulatory and governmental authorities; changes in relationships with strategic partners and dependence upon strategic partners for performance of clinical and commercialization activities under collaborative agreements including potential for any collaboration agreement to be terminated without any product success; uncertainties relating to patent

protection and intellectual property rights of third parties; impact of competitive products and technological changes; availability of capital and cost of capital; and other material risks. A more complete description of these risks can be found in the Company's Form 10K for the year ended December 31, 1998 and the current form 10Q each of which should be read before making any investment in Neurocrine common stock. Neurocrine undertakes no obligation to update the statements contained in this press release after the date hereof.

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CONTACT: Elizabeth Foster or Paul Hawran of Neurocrine Biosciences, Inc., 619-658-7600