



Neurocrine Announces Advancement of NBI-3001 for Malignant Brain Tumors: Phase I Results Presented/Initiation of Multi-Center, International Phase I/II Clinical Trial

November 25, 1998

Also Announces Manufacturing and Drug Delivery Agreements
For Advanced Clinical and Commercial Requirements

SAN DIEGO, Nov. 25 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX)) today announced results of a Phase I study with IL-4 Fusion Toxin (NBI-3001) which were presented last week at The Society for Neuro-Oncology Meeting in San Francisco, CA. In this study, NBI-3001 was infused directly into brain tumors and surrounding parenchyma via convection catheter delivery in nine patients with recurrent malignant gliomas (brain tumors). In the abstract presented at the meeting it was concluded that the infusion of IL-4 Fusion Toxin (NBI-3001) produced no evident systemic or neurological toxicities as documented by laboratory and neurological examinations. The abstract also stated that of nine patients treated, five patients showed evidence of necrosis (tumor cell death) in major sections of tumor by MRI, PET and MR-SPEC scanning. The IL-4 Fusion Toxin (NBI-3001) binds with high affinity to IL-4 receptors, which are numerous on malignant glioblastoma cells, and are not found on normal brain cells. NBI-3001 was designed to bind and destroy malignant cells without having an effect on normal brain cells.

The Phase I study was conducted by Dr. Robert Rand at the John Wayne Cancer Institute in collaboration with the inventors, Dr. Raj Puri, from the Center for Biologics Evaluation and Research (CBER) of the Food and Drug Administration (FDA) and Dr. Ira Pastan of the Laboratory of Molecular Biology, National Institutes of Health (NIH). Neurocrine licensed exclusive worldwide rights to NBI-3001 from the NIH in May, 1998.

Expanded Clinical Development Program

Neurocrine also announced today that it has initiated a multi-center, multi-national Phase I/II clinical trial in 30 patients with recurrent glioblastoma. The Phase I/II study is an open-label, dose-escalating safety and efficacy trial. The primary endpoints of the Phase I/II trial are safety, tumor regression and progression free survival. The drug will be administered by infusion via a special catheter, which will permit diffusion of NBI-3001 into the tumor and surrounding parenchyma of the brain.

"Neurocrine is undertaking an aggressive clinical program to confirm the Phase I findings in major neurosurgical centers in the United States and Germany. This compound has the potential to translate into a significant advance in the treatment of this life threatening form of cancer," said Stephen G. Marcus M.D., Senior Vice President Clinical and Regulatory Affairs and Chief Medical Officer of Neurocrine Biosciences, Inc.

New Drug Delivery and Manufacturing Agreements; Joint Drug and Delivery

System Clinical Program Planned

Neurocrine recently announced a collaborative agreement with Medtronic, Inc. (NYSE: MDT) to clinically evaluate NBI-3001 and a delivery system for treating malignant brain tumors. Under the terms of the agreement, the two companies will collaborate to clinically evaluate the drug for direct delivery to the brain using Medtronic's SynchroMed(R) Infusion System. This system consists of a programmable, implantable drug pump and catheter that delivers medication directly to the site where the drug can be most effective. Current plans are for joint clinical studies to begin in the later half of 1999.

In addition, Neurocrine announced today that it has signed an agreement with Covance Biotechnology Services Inc. to manufacture GMP drug supplies of NBI-3001. NBI-3001 is a recombinant protein molecule produced in bacterial expression systems. Covance, will be responsible for scale-up manufacturing and quality control.

"The expansion of the clinical program for NBI-3001 is an important milestone in the development of this investigational compound for the treatment of malignant brain cancer. The multinational trial which is now in progress may help establish the therapeutic potential of this compound, which can then be extended to the joint clinical studies with NBI-3001 and the Medtronic drug delivery system," said Gary A. Lyons, President and Chief Executive Officer of Neurocrine Biosciences. "

"Our new collaborative partners in drug delivery and manufacturing will enhance the advancement of NBI-3001. Medtronic is the world's leading medical technology company specializing in implantable and interventional therapies. Covance is a leader in

recombinant molecule process development and manufacturing," added Lyons

Neurocrine currently has five compounds in clinical development for CNS related disorders. In addition to NBI-3001, 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 a second Phase II clinical trial with Neurocrine's APL compound in patients with multiple sclerosis. Neurocrine is also conducting a Phase I trial with NBI-34060 for insomnia. In addition, Neurocrine's affiliate, Neuroscience Pharma, Inc. (NPI), recently announced completion of a Phase III clinical trial with its neurosteroid compound in Alzheimer's disease. Neurocrine also plans to file an IND equivalent in Europe for a second APL compound for diabetes by year-end 1998.

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, Parkinson's disease, stroke, traumatic brain injury, multiple sclerosis, obesity and diabetes.

Neurocrine Biosciences, Inc. news releases are available free of charge through PR Newswire's Company News On-Call fax service. For a menu of Neurocrine's previous releases, or to receive a specific release via fax call: (800) 758-5804, ext. 604138, or use the Internet via <http://www.prnewswire.com>.

The statements in the press release that relate to the development of potential products, including the expected date of entry into and the completion of clinical trials, are forward looking statements. Such forward looking statements involve risks and uncertainties, including, without limitation, that compounds which demonstrate efficacy in pre-clinical studies may not prove to be effective for treatment in humans, that development candidates which have successfully progressed through pre-clinical and early state clinical trials will not successfully proceed through later stage large scale clinical trials, that the regulatory clearances required for clinical testing, manufacturing, and marketing of products may not be received in a timely manner (or at all), potential difficulties in manufacturing products in sufficient quantities on a timely and cost-effective basis, and the potential adverse impact of competitive technologies, products, and intellectual property rights of third parties as well as the risk that Neurocrine's collaborative partners may elect not to proceed with the development of a potential product. For a discussion of the other risks and uncertainties potentially impacting the Company's business, see the Company's Form 10-K for the year ending December 31, 1997. Actual results and timing of certain risks could differ materially from those indicated in the forward looking statements as a result of these and other factors

SynchroMed is a registered trademark of Medtronic, Inc.

A CIRCULARLY PERMUTED INTERLEUKIN-4-PSEUDOMONAS EXOTOXIN FOR
TREATMENT OF MALIGNANT GLIOMAS

Robert W. Rand, PhD, MD, Santa Monica, CA, Robert Kreitman, MD, Bethesda, MD,

Ira Pastan, MD, Bethesda, MD, Raj Puri, MD, PhD, Bethesda, MD

An effective means of treatment is lacking for malignant glioblastoma and astrocytoma. In an escalating Phase I FDA approved clinical trial, we have investigated the safety of directly injecting IL4(38-37)-PE38KDEL, a chimeric protein composed of circularly permuted Interleukin-4 (IL-4) and truncated form of Pseudomonas exotoxin, into recurrent malignant gliomas. As we have shown in preclinical tissue culture and efficacy testing, this toxin binds with high affinity to malignant cells with IL-4 receptors, which are numerous on glioblastoma cells, and nonexistent in normal brain cells. The nine subjects underwent stereotactic frame placement followed by a pre-infusion MRI to determine the volume and coordinates of the tumor and then IL4-toxin infusion. The amount of infusate at a predetermined concentration was calculated based on the volume of the tumor plus a 2cm margin surrounding the tumor area to account for new and undetectable malignant cells. All procedure followed the same infusion rates: 0.3ml/hr for the first six hours and then 0.6ml/hr for the remaining volume calculated. The infusion of IL-4-toxin and the procedure have produced no evident systemic or neurotoxicities, as documented by serum chemistry, hematology screen including liver panels and neurological examinations. Five patients at two dose levels (two and six microgram/ml) have shown evidence of necrosis in major sections of tumor by MRI, PET and MR-SPEC scanning; Four patients at past infusion craniotomy had extensive tumor necrosis. We conclude that direct injection of IL4(38-37)-PE38KDEL is thus far safe and merits further clinical study. Our trial is ongoing to determine efficacy of this novel glioma-targeted cytotoxin.

SOURCE Neurocrine Biosciences, Inc.

Web site: <http://www.neurocrine.com>

Company News On-Call: <http://www.prnewswire.com/comp/604138.html> or fax, 800-758-5804, ext. 604138

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