Neurocrine Biosciences Announces Pre-Clinical Efficacy of CRF1 Receptor Antagonists for: Irritable Bowel Syndrome;

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SAN DIEGO, May 20 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) announced today that compounds from the company's proprietary small molecule CRF1 receptor antagonist programs have demonstrated robust efficacy in pre-clinical models of irritable bowel syndrome (IBS), a third stress-related indication for CRF1 receptor antagonists. Neurocrine is currently in Phase I clinical studies with a CRF1 receptor antagonist for anxiety and depression. Results of CRF1 receptor antagonists in IBS will be presented this week at the Digestive Diseases Week (DDW) meeting, the largest international gathering of physicians, researchers and academics in the field of gastrointestinal research, medicine and technology. IBS is a disturbance of function of the lower intestine and colon, affecting 15-20% of the population, mainly women. Numerous studies have shown a close relationship between stress resulting from life events or psychiatric disturbance and the onset and severity of IBS symptoms. Recent studies have suggested that CRF, which is believed to be a primary mediator of stress, plays an important role in the control or modulation of the gastrointestinal system. These new data suggest that CRF1 receptor antagonists may provide a new therapeutic intervention for IBS, a very large and underserved market. A single dose Phase I safety study has been successfully completed with Neurocrine's lead clinical compound. Multi-dose Phase I trials are scheduled to begin shortly and once completed will lead to Phase II efficacy based trials.

Two presentations at the Digestive Diseases Week meeting will report efficacy of Neurocrine's proprietary small molecule CRF1 receptor antagonists in pre-clinical models. IBS is characterized by three primary symptoms, altered gastrointestinal function, visceral pain or discomfort and bloating. The two studies presented demonstrate that Neurocrine's CRF1 receptor antagonist compounds address multiple aspects of IBS. In one study using Neurocrine's CRF1 receptor antagonist, Dr. Yvette Tache, Professor of Medicine, CURE/Digestive Diseases Research Center, Division of Digestive Diseases, UCLA, demonstrated efficacy by restoring normal function in a model that reflects stress-induced gastrointestinal function disturbances suffered by IBS patients. In the study, an increase in colonic transit was induced by intravenous administration of CRF, an experimental condition that mimics stress-induced exacerbation of this IBS symptom. Treatment with a single oral dose of the CRF1 receptor antagonist produced a 12-fold reduction in colonic transit, restoring it to normal.

"Several years of research in my laboratory have substantiated the hypothesis that the activation of CRF receptors is intimately involved in the regulation of gastrointestinal motor function under stressful conditions," said Dr. Tache. "These data with highly selective small molecule CRF1 receptor antagonists, confirm and extend this work and provide enthusiasm to test this hypothesis in clinical trials with IBS patients."

In a second independent study, conducted in the laboratory of Dr. Beverley Greenwood-Van Meerveld at the Oklahoma Foundation for Digestive Research - Basic Science Labs, administration of a Neurocrine CRF1 receptor antagonist was highly effective in a model of the pain and discomfort that is experienced by IBS patients. In the study, oral administration of the compound produced a dose-dependent relief of experimentally induced visceral discomfort, with a significant effect at 0.1 mg/kg (50% response), and at higher doses responses were restored to baseline (100% response).

Dr. Greenwood-Van Meerveld commented, "The effects of Neurocrine's CRF1 receptor antagonist in our visceral hypersensitivity model were most impressive. CRF1 receptor antagonists represent an entirely new approach to the treatment of IBS, a disease which is in desperate need of effective therapies."

"We are very excited by these data that suggest that our proprietary CRF1 receptor antagonists may have utility in irritable bowel syndrome in addition to their potential activity in anxiety and depression," said Dr. Paul Conlon, Vice President of Drug Discovery for Neurocrine Biosciences. "While existing therapies for IBS such as fiber, antidiarrheal or antispasmodics either are poorly active or the newer serotonergic agents may have safety issues, a completely new therapy, such as the CRF receptor antagonists, that act on both the central emotional component and on the peripheral gut motility, may prove to be the most effective way forward to treat the disease."

Conlon added "It is a high priority for us to advance our small molecule CRF1 receptor antagonist into clinical development for IBS."

Background

According to the International Foundation for Gastrointestinal Disorders (IFFGD), IBS is the most common GI disorder affecting an estimated 15-20% of adults. A substantial proportion of patient visits to primary care physicians for gastrointestinal complaints and referrals to gastroenterologists are for IBS. It is a disorder that affects the nerves and muscles of the bowel, and causes abdominal pain, irregular bowel movements, and can cause deep personal distress. Painful attacks can last from a matter of days to several months. In many cases, the cause is unknown, but stress, diet and infection can bring on or aggravate symptoms. The social and economic costs of functional GI disorders are enormous and represent an important health care burden.

The symptoms of IBS heavily impact patients' lifestyles. IBS is a leading cause of worker absenteeism, second only to the common cold, with an average of 13.4 missed workdays a year among IBS patients. The disease has been estimated to result in $10.5 billion in excess direct medical expenses compared to control subjects annually in the US. Approximately 70% of IBS cases are reported in women, making this a major women's health issue and in addition is becoming one of the most common diseases in the elderly. Data has revealed that women with IBS have an increased risk of unnecessary surgery; hysterectomy or ovarian surgery and these are performed more often in IBS patients than in other comparative groups. IBS does not show any evidence of an organic or physical disease, and the cause of a functional GI disorder does not show up in traditional laboratory examinations such as blood tests or x-rays. For this reason, IBS is an under diagnosed disorder, and was formerly a "diagnosis of exclusion", meaning that it was observed only after diagnostic tests had excluded other causes. But over the past two decades, medical opinion has changed with regard to the diagnosis of IBS and an evaluation known as the "Rome II" criteria has become increasingly used by physicians to diagnose this debilitating disease.

Neurocrine Biosciences, Inc. is a product-based biopharmaceutical company focused on neurologic and endocrine diseases and disorders. Our product candidates address some of the largest pharmaceutical markets in the world including insomnia, anxiety, depression, cancer, diabetes and irritable bowel syndrome.

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 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 CRF receptor antagonist research and development program 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 CRF receptor antagonists will not successfully proceed through development or that clinical trials will not show that it is effective in treating IBS; determinations by regulatory and governmental authorities; dependence upon strategic partners for performance of clinical and commercialization activities under collaborative arrangements that have not been entered into and may not be entered into advantageous terms, if at all; 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, 2000 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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Web site: http: //www.neurocrine.com
CONTACT: Paul Conlon, PhD, or Claudia Jones, 858-658-7600, or at DDW, Alan Foster, PhD, 858-349-2666, all of Neurocrine Biosciences