Neurocrine Announces 12-Week Safety Results From Initial Phase IIB Study Of VMAT2 Inhibitor NBI-98854

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OPEN-LABEL EXTENSION SHOWS A FAVORABLE SAFETY PROFILE AND DYSKINESIA REDUCTION THROUGH 12 WEEKS OF DOSING

SAN DIEGO, Jan. 9, 2014 /PRNewswire/ -- Neurocrine Biosciences, Inc. (NASDAQ: NBIX) announced today that NBI-98854, a small molecule VMAT2 inhibitor, in development for tardive dyskinesia, showed an excellent safety profile and a clinically meaningful reduction in tardive dyskinesia symptoms in up to twelve weeks of continuous dosing. This is the second study reporting out this week that demonstrates the potential of NBI-98854 as a safe and highly effective therapy for tardive dyskinesia sufferers. Both of these studies will serve as the foundation for an End of Phase II meeting later this year.

The Kinect study was a randomized, parallel, double-blind, placebo-controlled, Phase IIb clinical trial utilizing the capsule formulation of NBI-98854 in moderate to severe tardive dyskinesia patients with underlying schizophrenia or schizoaffective disorder. The study assessed NBI-98854 over a six-week placebo-controlled dosing period. The top-line results from the placebo-controlled portion were previously reported by the Company in September 2013. Subsequent to the placebo-controlled dosing period, all subjects were eligible to enter a six-week open-label safety extension of 50 mg of NBI-98854 administered once daily, followed by a four-week washout period.

NBI-98854 was generally safe and well tolerated in the Kinect study. During the twelve-week treatment period the frequency of treatment-emergent adverse events was 40% for NBI-98854, similar to previous clinical trials. There were no drug related serious adverse events. The most common treatment-emergent adverse event during the entire twelve-week period was urinary tract infection in six subjects (5.9%) on NBI-98854, which were assessed as not related to study drug by the investigators. All other adverse events occurred at less than a 3% frequency.

Participants were assessed utilizing the Barnes Akathisia Ratings Scale (BARS) for akathisia and the Simpson-Angus Scale (SAS) for parkinsonism. Both of these scales documented minimal symptoms at baseline and were stable to improved during the twelve weeks of treatment. Subjects were also assessed using various safety scales including the Positive and Negative Syndrome Scale (PANSS) for Schizophrenia, the Calgary Depression Scale for Schizophrenia and the Columbia-Suicide Severity Rating Scale (C-SSRS); all of these scores were stable to improved from baseline. Clinical hematology, chemistry and ECG monitoring indicated no emergent safety signals.

There were no drug-drug interactions identified in subjects who were utilizing a range of psychotropic and other concomitant medications.

"We are very pleased with the safety profile of NBI-98854 over twelve weeks of continuous dosing. The drug was generally well tolerated and there were no obvious safety signals," said Christopher F. O'Brien, Chief Medical Officer of Neurocrine Biosciences. "Although this phase of the Kinect study was not placebo-controlled, we are further encouraged by the reduction in tardive dyskinesia through Week 12."

Efficacy Profile

At Week 12, there was a marked reduction from baseline in the Abnormal Involuntary Movement Scale (AIMS) scores for both groups of subjects; those who were initially randomized to NBI-98854 with 12 weeks of continuous dosing and those who were originally randomized to placebo for 6 weeks, then entered the 6-week open-label extension of NBI-98854. The Week 12 responder rate (defined as a 50% or greater reduction in AIMS from baseline) was 54%.

The Week 12 improvement in tardive dyskinesia symptoms was also corroborated by the Clinical Global Impression–Tardive Dyskinesia (CGI-TD). Treating clinicians determined at Week 12 that approximately 61% of the subjects taking NBI-98854 were "much improved" or "very much improved" at Week 12. The twelve-week treatment period was followed by a four-week washout period. At the end of this washout period, only 29% of these same subjects were evaluated by the treating physicians as "much improved" or "very much improved" utilizing the CGI-TD.

"This twelve-week safety and related efficacy data is another important component for our End of Phase II FDA meeting that we plan to request during the first half of 2014," said Kevin C. Gorman, Chief Executive Officer of Neurocrine Biosciences.

Subject Profile

The Kinect study randomized 109 subjects; 81 subjects completed Week 12, of which 42 subjects were originally randomized to placebo and 39 were originally randomized to NBI-98854. Similar to the Company's other studies, the average age of the trial participants was 55 years with an average age at onset of tardive dyskinesia of 47 years. Approximately two-thirds of the subjects were male.

Kinect Study Design

The Kinect study was a randomized, parallel, double-blind, placebo-controlled, Phase IIb clinical trial utilizing the capsule formulation of NBI-98854 in moderate to severe tardive dyskinesia patients with underlying schizophrenia or schizoaffective disorder. The study assessed two doses of once-daily NBI-98854 over a six-week placebo-controlled dosing period. Half of the randomized subjects received placebo and half received one of two doses of NBI-98854. The two NBI-98854 dosing groups consisted of a 50mg group for six weeks and a group that began at 100mg for the initial two weeks then converted to 50mg for the final four weeks of the placebo-controlled dosing period. Subsequent to the placebo-controlled dosing, all subjects were eligible to enter a six-week open-label safety extension of 50mg of NBI-98854 administered once daily with additional AIMS assessments. The primary efficacy endpoint of the study was a comparison of placebo and active scores as determined by the on-site AIMS raters at the end of Week 6.

Next Steps for NBI-98854

This Kinect twelve-week data, along with the initial six-week data from the Kinect study will be integrated with the Kinect 2 study data to inform the ultimate design of the next study. The Company will work with its consultants and scientific advisors to expand and refine the pharmacokinetic/pharmacodynamic models as well as to complete the remaining safety and efficacy analyses from both Kinect and Kinect 2. These data will form the basis for an End of Phase II briefing package along with the proposed Phase III protocol.

About Tardive Dyskinesia

Tardive dyskinesia is characterized by involuntary, repetitive movements of the extremities: lip smacking, grimacing, tongue protrusion, facial movements or blinking, puckering and pursing of the lips, or involuntary movements of the limbs. These symptoms are rarely reversible and there is currently no approved treatment.

About NBI-98854

VMAT2 is a protein concentrated in the human brain that is primarily responsible for re-packaging and transporting monoamines (dopamine, norepinephrine, serotonin, and histamine) in pre-synaptic neurons. NBI-98854, developed in the Neurocrine laboratories, is a novel, highly-selective VMAT2 inhibitor that modulates dopamine release during nerve communication, while at the same time having minimal impact on the other monoamines, thereby reducing the likelihood of "off target" side effects. NBI-98854 is designed to provide low, sustained, plasma and brain concentrations of active drug to minimize side effects associated with excessive monoamine depletion. The Company has completed nine-month in-vivo toxicology studies to support longer dosing regimens in humans.

NBI-98854 may also be useful in other disorders such as Huntington's chorea, schizophrenia, Tourette's syndrome, and tardive dystonia.

About Neurocrine Biosciences

Neurocrine Biosciences, Inc. is a clinical stage drug discovery company primarily focused on neurological and endocrine based diseases and disorders. The Company discovers and develops innovative pharmaceuticals, in diseases with high unmet medical needs or where the existing drug classes are inadequate, through a disciplined yet entrepreneurial process. Utilizing a portfolio approach to drug discovery, Neurocrine has multiple small molecule drug candidates at various stages of pharmaceutical development. Neurocrine's two lead late stage clinical programs are elagolix, a GnRH antagonist for women's health that is partnered with AbbVie Inc., and a wholly owned VMAT2 inhibitor for the treatment of movement disorders. 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, as well as risks and uncertainties associated with the Company's VMAT2 program and Company overall. Specifically, the risks and uncertainties the Company faces with respect to the Company's VMAT2 program include, but are not limited to; risk that NBI-98854 will not proceed to later stage clinical trials and risk that the Company's clinical trials will fail to demonstrate that NBI-98854 is safe and effective. With respect to its pipeline overall, the Company faces risk that it will be unable to raise additional funding required to complete development of all of its product candidates; risk relating to the Company's dependence on contract manufacturers for clinical drug supply; risks associated with the Company's dependence on corporate partners for development, commercial manufacturing and marketing and sales activities for the Company's partnered programs; 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; and the other risks described in the Company's report on Form 10-K for the year ended December 31, 2012 and on Form 10-Q for the quarter ended September 30, 2013. Neurocrine undertakes no obligation to update the statements contained in this press release after the date hereof.

SOURCE Neurocrine Biosciences, Inc.

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