Neurocrine Announces Positive Results of VMAT2 Inhibitor NBI-98854 in Kinect 2 Study

January 6, 2014

Plans to submit end of phase II meeting request to FDA
Company to host conference call and webcast Monday, January 6th at 5:00pm ET / 2:00pm PT

SAN DIEGO, Jan. 6, 2014 /PRNewswire/ -- Neurocrine Biosciences, Inc. (NASDAQ: NBIX) announced today that NBI-98854, a small molecule VMAT2 inhibitor, showed a statistically significant and clinically meaningful reduction in tardive dyskinesia symptoms in the Phase IIb Kinect 2 study. The pre-specified primary endpoint was the change-from-baseline in the Abnormal Involuntary Movement Scale (AIMS) at Week 6 as assessed by central blinded video raters.

At Week 6, AIMS scores were reduced by 2.6 points in the NBI-98854 intention-to-treat (ITT) group compared to a reduction of 0.2 points in the placebo arm (p<0.001). Additionally, the responder rate (>= 50% improvement from baseline) was 49% in the NBI-98854 ITT group compared to 18% in placebo (p=0.002). In the per-protocol (PP) group AIMS scores were reduced by 3.3 points for those subjects taking NBI-98854 (p<0.001), with a corresponding responder rate of 59% (p<0.001).

"The profound response in this Kinect 2 study demonstrates the potential of NBI-98854 as both a safe and highly effective treatment for patients suffering from tardive dyskinesia," said Christopher F. O'Brien, Chief Medical Officer of Neurocrine Biosciences. "It is clear from these results that the use of blinded central AIMS raters coupled with the ability to titrate up to 75 mg of NBI-98854 were both critical to the success of this trial."

The improvement in Week 6 AIMS was also corroborated by the Clinical Global Impression–Tardive Dyskinesia (CGI-TD). Treating clinicians determined that approximately 67% of the subjects taking NBI-98854 were "much improved" or "very much improved" at Week 6 compared to only 16% of the placebo subjects (p<0.001) in this pre-specified key secondary efficacy endpoint.

"The data from this Kinect 2 study allows us to submit an End of Phase II meeting request as well as finalize the initial draft of a Phase III protocol, both of which we anticipate filing with the FDA in the first half of 2014," said Kevin C. Gorman, President and Chief Executive Officer of Neurocrine. "Our Phase II studies of NBI-98854 have served to define the study population, elucidate the primary endpoint, refine our dosing regimen and provide the necessary efficacy and safety data to enable pivotal studies."

The pre-specified statistical analysis plan included three data sets: a safety set (all subjects with at least one dose), an ITT set (all subjects who had an AIMS assessment at Week 6) and a PP set (all ITT subjects except those with no detectable drug levels at the evaluation time point). The table below summarizes the primary endpoint, LS Mean change-from-baseline AIMS, for both the ITT and PP populations at Week 6, as well as the responder analyses.

	Week 6		
	Placebo	**NBI-98854**	**p-value**
AIMS Change from Baseline			
Baseline AIMS	7.9	8.0	-
LS Mean AIMS ANCOVA (ITT)	-0.2	-2.6	<0.001
LS Mean AIMS ANCOVA (PP)	-0.3	-3.3	<0.001
Responder Rate (ITT)*	18%	49%	0.002
Responder Rate (PP)*	18%	59%	<0.001

** a responder is defined as 50% or greater reduction in AIMS*

The table below summarizes the key secondary endpoint, CGI-TD, for both the ITT and PP populations at Week 6.

	Week 6		
CGI-TD	**Placebo**	**NBI-98854**	**p-value**
LS Mean Score (ITT)	3.1	2.2	<0.001
LS Mean Score (PP)	3.1	2.2	<0.001
Responder Rate (ITT)*	16%	67%	<0.001
Responder Rate (PP)*	16%	68%	<0.001

**a responder is defined as "much improved" or "very much improved" (a "2" or "1", respectively) on the CGI-TD. A "4" on the CGI-TD indicates "no change"*

Subject Profile

The Kinect 2 study randomized 102 subjects. At Week 6, the ITT population included 44 placebo subjects and 45 subjects who were randomized to NBI-98854. By Week 6, approximately 70% of the ITT population, randomized to NBI-98854, were titrated to the 75 mg dose, approximately 20% were titrated to the 50mg dose and the remaining subjects received 25 mg of NBI-98854. At Week 6 the PP population consisted of 44 placebo subjects and 34 subjects randomized to NBI-98854. The PP Week 6 final titrated dose level of NBI-98854 was similar to that of the ITT population. The PP population excluded eleven subjects whose plasma concentrations of NBI-98854 were below the lower limit of quantitation (i.e., not detectable). Given the timing of serum samples collections and the pharmacokinetic profile of NBI-98854, it was determined that these subjects had not ingested the study drug. The subjects in the Kinect 2 study had moderate to severe tardive dyskinesia with a mean baseline video AIMS score of 8.0. Similar to previous studies, the average age of the trial participants was 56 years with an average age at onset of tardive dyskinesia of 49 years. Approximately 60% of the subjects were male.

Safety Profile

In this study NBI-98854 was generally safe and well tolerated. During the six-week treatment period the frequency of treatment-emergent adverse events was 33% for placebo and 43% for NBI-98854. There were no drug related serious adverse events. The most common treatment emergent adverse events were fatigue in five subjects (9.8%) randomized to NBI-98854 vs. two subjects (4.1%) in the placebo group, and headache reported by four subjects (7.8%) on NBI-98854 vs. two subjects (4.1%) on placebo. Discontinuation rates were similar in both the NBI-98854 and placebo treatment groups with five per study arm (none of which were study drug related).

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 there was no worsening during the six weeks of treatment. 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.

Next Steps for NBI-98854

Data from the Kinect 2 study will be integrated with the Kinect study data to inform the ultimate design of the next study, Kinect 3. 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.

Kinect 2 Study Design

The Kinect 2 Study was a randomized, parallel, double-blind, placebo-controlled, dose titration Phase IIb clinical trial utilizing the capsule formulation of NBI-98854 in moderate to severe tardive dyskinesia patients with an underlying mood disorder (e.g., bipolar disorder), schizophrenia or schizoaffective disorder, or a gastrointestinal disorder with exposure to metoclopramide. This 100 subject study assessed once-daily NBI-98854 over a six-week placebo-controlled dosing period. Half of the randomized subjects received placebo and half received NBI-98854. The NBI-98854 dosing regimen began with a once-daily dose of 25 mg for the initial two weeks. At the completion of the initial two weeks of dosing, based on certain efficacy and safety criteria, patients were titrated to a once-daily 50 mg dose, or continued on the once-daily 25 mg dose for the following two-week period. At the completion of the second two weeks of treatment another efficacy and safety assessment was performed and patients were eligible to be titrated to a once-daily 75 mg, 50 mg or 25 mg dose for the final two weeks of treatment. The primary endpoint of the study was a comparison of placebo vs. active scores utilizing the AIMS at the end of Week 6 by blinded central raters.

About the Abnormal Involuntary Movement Scale (AIMS)

The AIMS is a structured neurological examination that was developed in 1976 and has been used extensively in movement disorder assessments. It consists of ten distinct ratings of regional involuntary body movements that are scored on a zero to four scale with zero being rated as none and four being rated as severe. The primary endpoint of the Kinect 2 Study is the video AIMS total dyskinesia score, items one through seven which rate facial, extremity and trunk movement severity as assessed by blinded central raters. The raters were movement disorder neurologists with expertise in dyskinesia assessment.

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.

Conference Call and Webcast Information

The Company will host a live conference call and webcast to provide additional details of this study on, Monday January 6, 2014 at 5:00 p.m. Eastern Time (2:00 p.m. Pacific Time). Participants can access the live conference call by dialing 800-894-5910 (US) or 785-424-1051 (International) using the conference ID: NBIX. The call can also be accessed via the webcast through the Company's website at http://www.neurocrine.com. Slides will also be made available through www.neurocrine.com for the conference call and webcast. If you are unable to attend the webcast and would like further information on this announcement please contact the Investor Relations Department at Neurocrine Biosciences at (858) 617-7600. A replay of the Conference Call will be available approximately one hour after the conclusion of the call by dialing 800-688-4915 (US) or 402-220-1319 (International) using the conference ID: NBIX. The call will be archived for three weeks.

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.

Neurocrine Biosciences, Investor Relations, +1-858-617-7600