Neurocrine Announces Phase IIb Results Of VMAT2 Inhibitor NBI-98854 For Treatment Of Tardive Dyskinesia

September 9, 2013

Company To Host Conference Call And Webcast Monday, September 9th At 5:00PM ET / 2:00PM PT

SAN DIEGO, Sept. 9, 2013 /PRNewswire/ -- Neurocrine Biosciences, Inc. (NASDAQ: NBIX) announced today that the 50mg dose of NBI-98854, a small molecule VMAT2 inhibitor in development for tardive dyskinesia, did not meet the primary endpoint in the Phase IIb Kinect study while the 100mg dose showed a statistical and clinically significant improvement. The pre-specified primary endpoint was the change-from-baseline in the Abnormal Involuntary Movement Scale (AIMS) at Week 6 in the intent-to-treat (ITT) population.

Although the 50mg dose of NBI-98854 did not reach statistical significance for the primary endpoint at Week 6, the 100mg dose, utilizing the blinded central video AIMS assessment, showed a statistically significant and clinically meaningful reduction in tardive dyskinesia symptoms at Week 2 (the end of the 100mg dose interval). AIMS scores were reduced by 5.5 points in the 100mg per-protocol (PP) group compared to a reduction of 2.7 points in placebo (p=0.008), and the responder rate (>= 50% improvement from baseline) was 48% in the 100mg group compared to 23% in placebo (p=0.034). The 100mg dose was expected to be a maximum tolerated dose based on earlier data; however in this patient population, 100mg was well tolerated. The pre-specified statistical analysis plan included three data sets: safety set (all subjects with at least one dose), ITT set (all randomized subjects with at least one AIMS assessment) and the PP set (all subjects except those with no detectable drug levels at the evaluation time point).

"Although this was not the result we anticipated in the 50mg dose based on the data set from the earlier clinical studies, we were pleased to see a clear dose related response at the end of Week 2, with the 100mg dose, " said Kevin C. Gorman, President and Chief Executive Officer of Neurocrine. "The 100mg dose was statistically superior to placebo as well as providing a clinically significant improvement in tardive dyskinesia symptoms and importantly a very good safety profile. We will now perform an additional Phase II study utilizing 100mg and higher doses."

The improvement in Week 2 AIMS for 100mg was also corroborated via another validated assessment tool, the Clinical Global Impression–Tardive Dyskinesia (CGI-TD). Treating clinicians determined that 36% of the subjects taking 100mg of NBI-98854 were "much improved" or "very much improved" at Week 2 compared to only 8% of the placebo subjects (p=0.002) in this pre-specified key secondary efficacy endpoint.

"It is clear that the 100mg dose resulted in a substantial improvement in tardive dyskinesia symptoms," said Christopher F. O'Brien, Chief Medical Officer of Neurocrine. "Future clinical trials of NBI-98854 will utilize a central video assessment of AIMS as it appears that the AIMS assessments have greater sensitivity to change when administered by a blinded central rater rather than multiple raters."

The tables below summarize the primary endpoint, LS Mean change-from-baseline AIMS, for both the ITT population and the PP population at Weeks 2 and 6, as well as the responder analyses, for both the on-site and the blinded central rater AIMS ratings.

	Week 2				
	PBO	**50mg**	**p-value**	**100mg**	**p-value**
AIMS Change from Baseline (on-site assessment)					
LS Mean AIMS ANCOVA (ITT)	-1.2	-2.1	ns	-2.1	ns
LS Mean AIMS ANCOVA (PP)	-1.3	-2.4	ns	-2.5	ns
Responder Rate (ITT)*	7%	7%	ns	12%	ns
Responder Rate (PP)*	7%	8%	ns	14%	ns
AIMS Change from Baseline (video assessment)					
LS Mean AIMS ANCOVA (ITT)	-2.7	-3.9	ns	-4.8	0.034
LS Mean AIMS ANCOVA (PP)	-2.7	-3.9	ns	-5.5	0.008
Responder Rate (ITT)*	23%	30%	ns	40%	ns
Responder Rate (PP)*	23%	31%	ns	48%	0.034

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

	Week 6		
	PBO	50mg	p-value
AIMS Change from Baseline (on-site assessment)			
LS Mean AIMS ANCOVA (ITT)	-2.5	-3.3	ns
LS Mean AIMS ANCOVA (PP)	-2.4	-3.0	ns
Responder Rate (ITT)*	11%	24%	ns
Responder Rate (PP)*	10%	21%	ns
AIMS Change from Baseline (video assessment)			
LS Mean AIMS ANCOVA (ITT)	-2.2	-3.5	ns
LS Mean AIMS ANCOVA (PP)	-1.9	-3.3	ns
Responder Rate (ITT)*	21%	29%	ns
Responder Rate (PP)*	18%	28%	ns

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

The tables below summarize the key secondary endpoint, CGI-TD, for the per-protocol population at Weeks 2 and 6.

	Week 2				
CGI-TD	**PBO**	**50mg**	**p-value**	**100mg**	**p-value**
LS Mean Score	3.6	3.2	ns	3.0	0.007
Responder Rate*	8%	15%	ns	36%	0.002

**a responder is defined as "much improved" or "very much improved"*

	Week 6		
CGI-TD	**PBO**	**50mg**	**p-value**
LS Mean Score	3.2	3.3	ns
Responder Rate*	22%	23%	ns

**a responder is defined as "much improved" or "very much improved"*

Subject Profile

The Kinect study randomized 109 subjects. At Week 2, the ITT population included 54 placebo subjects, and 27 and 26 subjects who were randomized to the 50mg and 100mg of NBI-98854, respectively. At Week 6 the ITT population consisted of 50 placebo subjects and 49 subjects randomized to 50mg of NBI-98854. The PP population excluded four subjects whose plasma concentrations of NBI-98854 were below the lower limit of quantitation (i.e., not detectable), one randomized to 50mg and three randomized to 100mg. Given the timing of serum sample collections and the pharmacokinetic profile of NBI-98854, it was determined that these subjects were not taking the study drug. The subjects in the Kinect study had moderate to severe tardive dyskinesia with a mean baseline AIMS score of 14.9. 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 and all subjects were on stable doses of antipsychotic medication.

Safety Profile

NBI-98854 was generally safe and well tolerated; the frequency of treatment-emergent adverse events during the initial two-week period was 17%, 18% and 15% in the placebo, 50mg and 100mg groups, respectively. During the six-week treatment period the frequency of treatment-emergent adverse events was 37% for placebo and 26% for NBI-98854. There were no drug related serious adverse events. The most common treatment emergent adverse event was mild and transient somnolence that occurred in two subjects initially randomized to the 50mg group and one subject initially randomized to the 100mg group.

"The frequency and severity of treatment related adverse events were significantly lower than we expected," said Dr. O'Brien. "There were no signals of an over-suppression of dopamine such as parkinsonism or akathisia; this observation coupled with our recent long-term preclinical toxicology work supports the evaluation of a daily dose range above 100mg."

The underlying psychiatric state of subjects was monitored using the Positive and Negative Syndrome Scale (PANSS) and subjects were shown to be stable or improved across all study groups at Week 6 of the study. Study participants were also 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.

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

The ongoing Kinect 2 study is assessing moderate to severe tardive dyskinesia sufferers with underlying mood disorders, schizophrenia and schizoaffective disorder and gastrointestinal disorders and is expected to report top-line results in the fourth quarter of 2013. This study is a randomized, parallel, placebo-controlled, double-blind, Phase IIb study assessing six-weeks of NBI-98854 against placebo in daily doses up to 75mg. The primary endpoint in this study is a mean change from baseline in AIMS at Week 6. The Kinect 2 study protocol is being amended such that the primary endpoint will be assessed via a blinded central AIMS video rater.

Planning for an additional Phase II study of NBI-98854 at daily doses of 100mg and above has begun and the Company's timeline to an end-of-phase II meeting is delayed by approximately one year.

Kinect Study Design

The Kinect Study is 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. This 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 entered a six-week open label safety extension of 50mg of NBI-98854 administered once daily with additional AIMS assessments. The primary endpoint of the study was a comparison of placebo and active scores to baseline scores utilizing the AIMS at the end of Week 6.

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 Study is the AIMS total dyskinesia score, items one through seven which rate facial, extremity and trunk movement severity.

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 September 9, 2013 at 5:00 p.m. Eastern Time (2:00 p.m. Pacific Time). Participants can access the live conference call by dialing 1-866-952-1906 (US) or 785-424-1825 (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 1-800-757-4770 (US) or 402-220-7228 (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 June 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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