Neurocrine Biosciences Reports Positive Phase 2 Data for NBI-1117568 in Adults with Schizophrenia

August 28, 2024

- **The Once-Daily 20 mg Dose Met the Primary Endpoint, Demonstrating a Statistically Significant 7.5-Point Improvement (p=0.011, 0.61 Effect Size) in the PANSS Total Score Compared to Placebo at Week 6 with an 18.2-Point PANSS Total Score Improvement from Baseline**
- **The Once-Daily 20 mg Dose Met Additional Endpoints, Demonstrating Statistically Significant Improvements in Clinical Global Impression of Severity Scale and Marder Factor Score Positive Symptom Change and Negative Symptom Change**
- **NBI-'568 Was Generally Safe and Well Tolerated at All Doses Studied**
- **The Once-Daily 20 mg Dose Efficacy, Safety and Tolerability Phase 2 Results Support Advancement to Phase 3 in Schizophrenia in Early 2025**
- **Company to Host Conference Call with Management at 8 a.m. EDT**

SAN DIEGO, Aug. 28, 2024 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced positive top-line data for its Phase 2 clinical study of NBI-1117568 (NBI-'568) in adults with schizophrenia. NBI-'568 is the first investigational, oral, muscarinic M4 selective agonist in development for the treatment of schizophrenia.

The NBI-'568-SCZ2028 dose-finding study met its primary endpoint for the once-daily 20 mg dose. It demonstrated a clinically meaningful and statistically significant reduction from baseline in the Positive and Negative Syndrome Scale (PANSS) total score at Week 6 with a placebo-adjusted mean reduction of 7.5 points (p=0.011 and effect size of 0.61) and an 18.2-point reduction from baseline. The once-daily 20 mg dose also demonstrated a statistically significant improvement for additional endpoints, including improvement in the Clinical Global Impression of Severity (CGI-S) scale, Marder Factor Score – Positive Symptom Change, and Marder Factor Score – Negative Symptom Change.

"This Phase 2 dose-finding study delivered on our goal of identifying a once-daily, well tolerated dosing regimen with a compelling and competitive benefit-risk profile," said Eiry W. Roberts, M.D., Chief Medical Officer at Neurocrine Biosciences. "We recognize the significant need for new and innovative medicines to treat schizophrenia and look forward to advancing NBI-'568, the first M4 selective agonist, into Phase 3 development early next year."

"NBI-1117568 demonstrated a clinically meaningful and statistically significant reduction in PANSS scores and was well tolerated, importantly with minimal GI effects and no weight gain relative to placebo," said Dr. Maurizio Fava, Psychiatrist-in-Chief at Massachusetts General Hospital of Harvard University. "As a selective M4 orthosteric agonist, the potential of NBI-1117568 as an option that could reduce symptoms of schizophrenia with fewer side effects would be a welcome alternative to current treatments for patients and caregivers."

NBI-'568 was generally safe and well tolerated at all doses studied in the Phase 2 clinical trial. Treatment discontinuation rates due to adverse events were similar between NBI-'568 and placebo. Adverse events with the highest incidence were somnolence, dizziness, and headache. Gastrointestinal adverse events including nausea and constipation were low in frequency and similar to placebo. Cardiovascular-related events were also low in frequency and were not deemed to have clinical relevance at any dose tested. NBI-'568 was not associated with a greater increase in weight than placebo. Few extrapyramidal symptoms adverse events were reported.

Primary Endpoint Results Summary

Week 6 (Day 42)	Placebo (N=68)	20 mg QD (N=35)	40 mg QD (N=38)	60 mg QD (N=34)	30 mg BID (N=26)
PANSS Total Score LS Mean Change from Baseline*	-10.8	-18.2	-12.6	-13.7	-15.8

LS Mean Difference vs. Placebo*	-	-7.5 (p=0.011)	-1.9 (p=0.282)	-2.9 (p=0.189)	-5.0 (p=0.090)
Effect Size**	-	0.61	0.27	0.39	0.23

Least-squares (LS) means are from a MMRM which includes treatment group, visit, and study period as fixed effects; treatment group-by-visit interaction; baseline PANSS total score as a covariate; and subject as a random effect.
****Effect size (Cohen's D) is based on observed data.***

Next Steps for Neurocrine Biosciences' Muscarinic Portfolio
In addition to NBI-'568, Neurocrine Biosciences has a broad portfolio of assets in clinical development that selectively target muscarinic receptors. The company's muscarinic agonist portfolio also includes NBI-1117567, NBI-1117569, and NBI-1117570, which the company acquired the rights to develop and commercialize from Nxera Pharma (formerly Sosei Heptares). Neurocrine Biosciences is also developing NBI-1076986, a selective M4 antagonist that was discovered and is being developed internally at Neurocrine.

Compound	Primary Mechanism (M1-M4)	Phase	Therapeutic Areas	Potential Areas for Development
NBI-1117568	M4 agonist	2	Psychosis Cognition	Alzheimer's Disease Bipolar Disorder Lewy Body Dementia Parkinson's Disease Schizophrenia
NBI-1117567	M1 agonist	1		
NBI-1117569	M4 agonist	1		
NBI-1117570	M1/M4 dual agonist	1		
NBI-1076986	M4 antagonist	1	Movement Disorders	Dystonia Parkinson's Disease Tremor

Conference Call and Webcast Today at 8:00 AM Eastern Time
Neurocrine Biosciences will hold a live conference call and webcast today at 8:00 a.m. Eastern Time (5:00 a.m. Pacific Time). Participants can access the live conference call by dialing 800-579-2543 (U.S.) or 785-424-1789 (International) using the conference ID: NBIX. The live webcast and accompanying slides can be accessed on the investor relations section of Neurocrine Biosciences' website here. A replay of the webcast will be available on the website approximately one hour after the conclusion of the event and will be archived for approximately one month.

About NBI-1117568
NBI-'568 is the first and only M4 selective orthosteric agonist in clinical development. There are five muscarinic acetylcholine receptors involved in neurotransmission. Muscarinic receptors are central to brain function and validated as drug targets in psychosis and cognitive disorders. As an M4 selective orthosteric agonist, NBI-'568 offers the potential for a novel mechanism with an improved safety profile without the need of combination therapy to minimize off-target pharmacology-related side effects, while also not being dependent on the presence of acetylcholine for efficacy.

About the NBI-1117568-SCZ2028 Phase 2 Clinical Study
The Phase 2, multicenter, randomized, double-blind, placebo-controlled, multi-arm, multi-stage inpatient dose-finding study was designed to assess the efficacy, safety, tolerability, and pharmacokinetics (PK) of NBI-'568 compared with placebo in adult subjects with a primary diagnosis of schizophrenia who are experiencing an acute exacerbation or relapse of symptoms. The study enrolled 210 participants. For more information about this study, visit ClinicalTrials.gov.

About Schizophrenia
Schizophrenia is a serious and complex syndrome with heterogeneous symptoms. The World Health Organization estimates that the disorder impacts more than 20 million people worldwide. Annual associated costs for schizophrenia are estimated to be more than $150 billion in the United States. As one of the leading causes of disability worldwide, it often results in significant emotional and functional burden for those who experience symptoms, as well as their family and friends. This chronic and disabling mental health condition is thought to result from a complex interplay of genetic and environmental risk factors. Traditional treatment approaches for schizophrenia rely on the use of antipsychotic medications that can lead to considerable short- and long-term health impacts.

About Neurocrine Biosciences
Neurocrine Biosciences is a leading neuroscience-focused, biopharmaceutical company with a simple purpose: to relieve suffering for people with great needs, but few options. We are dedicated to discovering and developing life-changing treatments for patients with under-addressed neurological, neuroendocrine, and neuropsychiatric disorders. The company's diverse portfolio includes FDA-approved treatments for tardive dyskinesia, chorea associated with Huntington's disease, endometriosis* and uterine fibroids*, as well as a robust pipeline including multiple compounds in mid- to late-stage clinical development across our core therapeutic areas. For three decades, we have applied our unique insight into neuroscience and the interconnections between brain and body systems to treat complex conditions. We relentlessly pursue medicines to ease the burden of debilitating diseases

and disorders, because you deserve brave science. For more information, visit neurocrine.com, and follow the company on LinkedIn, X (formerly Twitter), and Facebook.
(**in collaboration with AbbVie*)

Forward-Looking Statements
In addition to historical facts, this press release contains forward-looking statements that involve a number of risks and uncertainties. These statements include, but are not limited to, statements regarding the clinical results from, and our future development plans with respect to, NBI-1117568, as well as the therapeutic potential and clinical benefits or safety profile of NBI-1117568. Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements are: top-line data that we report may change following a more comprehensive review of the data related to the clinical study and such data may not accurately reflect the complete results of the clinical study; risks that clinical development activities may not be initiated or completed on time or at all, or may be delayed for regulatory, manufacturing, or other reasons, may not be successful or replicate previous clinical trial results, may fail to demonstrate that our product candidates are safe and effective, or may not be predictive of real-world results or of results in subsequent clinical trials; risks that regulatory submissions for our product candidates may not occur or be submitted in a timely manner; our future financial and operating performance; risks associated with our dependence on third parties for development, manufacturing, and commercialization activities for our products and product candidates, and our ability to manage these third parties; risks that the FDA or other regulatory authorities may make adverse decisions regarding our products or product candidates; risks that the potential benefits of the agreements with our collaboration partners may never be realized; risks that our products, and/or our product candidates may be precluded from commercialization by the proprietary or regulatory rights of third parties, or have unintended side effects, adverse reactions or incidents of misuse; risks associated with U.S. federal or state legislative or regulatory and/or policy efforts which may result in, among other things, an adverse impact on our revenues or potential revenue; risks associated with potential generic entrants for our products; and other risks described in the Company's periodic reports filed with the Securities and Exchange Commission, including without limitation the Company's quarterly report on Form 10-Q for the quarter ended June 30, 2024. Neurocrine Biosciences disclaims any obligation to update the statements contained in this press release after the date hereof other than required by law.

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