Neurocrine Biosciences Initiates Phase 3 Registrational Program for NBI-1117568 as Potential Treatment for Adults with Schizophrenia

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SAN DIEGO, April 30, 2025 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced the initiation of a Phase 3 registrational program to evaluate the efficacy, safety and tolerability of NBI-1117568, the company's investigational oral muscarinic M4 selective orthosteric agonist, as a potential treatment for schizophrenia. Positive top-line data for the Phase 2 clinical study in adults with schizophrenia were reported in August 2024.

"There is a significant need for new and innovative medicines to treat schizophrenia, a disorder that impacts millions of people and their families," said Eiry W. Roberts, M.D., Chief Medical Officer, Neurocrine Biosciences. "With positive Phase 2 data in hand, we're excited to advance this investigational novel compound that works directly and selectively at the muscarinic M4 receptor."

The Phase 3 study is a global double-blind, placebo-controlled trial evaluating NBI-1117568 in adults with a primary diagnosis of schizophrenia who are experiencing an acute exacerbation or relapse of symptoms. The study is expected to enroll approximately 280 patients. The primary endpoint of the study is a reduction from baseline in the Positive and Negative Syndrome Scale (PANSS). The key secondary endpoint is improvement in the Clinical Global Impression of Severity (CGI-S) scale.

Neurocrine is initiating the Phase 3 study supported by positive top-line data from the Phase 2 clinical study, which met its primary endpoint for the once-daily 20 mg dose. The study found:

- A clinically meaningful and statistically significant reduction from baseline in the 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.
- A statistically significant improvement across several secondary endpoints, including the CGI-S scale, Marder Factor Score – Positive Symptom Change, and Marder Factor Score – Negative Symptom Change.
- NBI-1117568 was generally safe and well tolerated at all doses studied, with minimal gastrointestinal and cardiovascular adverse events.

About NBI-1117568
NBI-1117568 is the first and only investigational oral muscarinic M4 selective orthosteric agonist in clinical development for the treatment of schizophrenia. 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-1117568 offers the potential for a novel mechanism with an improved safety profile without the need for combination therapy to minimize off-target pharmacology-related side effects, while also not being dependent on the presence of acetylcholine for efficacy.

About Neurocrine Biosciences' Muscarinic Portfolio
In addition to NBI-1117568, Neurocrine 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. Neurocrine also is developing NBI-1076986, an investigational, 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	3	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

About Schizophrenia
Schizophrenia is a serious and complex syndrome with heterogeneous symptoms. The World Health Organization estimates that the disorder impacts approximately 24 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, Inc.
Neurocrine Biosciences is a leading neuroscience-focused, biopharmaceutical company with a simple purpose: to relieve suffering for people with great needs. 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, classic congenital adrenal hyperplasia, endometriosis* and uterine fibroids*, as well as a robust pipeline including multiple compounds in mid- to late-phase 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, 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. Factors that could cause actual results to differ materially from those stated or implied in the forward-looking statements include, but are not limited to, the following: 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 annual report on Form 10-K for the year ended December 31, 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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