December 5, 2017

NEURALSTEM INC.

# Neuralstem Presents Positive Updated Data from Phase 2 Study of NSI-189 in Major Depressive Disorder at the 56th American College of Neuropsychopharmacology (ACNP) Annual Meeting

***40 mg dose showed statistically significant improvement on Cogscreen objective cognitive measures of attention and memory***

***Two additional self-rated secondary endpoints (CPFQ and QIDS) showed statistically significant improvements in depressive symptoms with procognitive benefits, reinforcing the benefit with SDQ endpoint reported previously***

***NSI-189 appeared to be safe and well tolerated with no serious adverse events***

***The Company will be hosting a conference call today, Tuesday, December 5th at 8:30 a.m. ET***

GERMANTOWN, Md., Dec. 05, 2017 (GLOBE NEWSWIRE) -- Neuralstem, Inc. (Nasdaq:CUR), a biopharmaceutical company developing novel treatments for nervous system diseases, today announced that additional safety, efficacy and tolerability data from its exploratory Phase 2 clinical trial examining the efficacy of NSI-189 at 40 mg once daily (QD) and 40 mg twice daily (BID) compared to placebo for the treatment of major depressive disorder (MDD) were presented at the 56th American College of Neuropsychopharmacology (ACNP) Annual Meeting in a poster entitled, “A Phase 2, Double-Blind, Placebo-Controlled Study of NSI-189 Phosphate, a Neurogenic Compound, Among Out-Patients with Major Depressive Disorder.” These additional results suggest that NSI-189 has antidepressant effects with cognitive benefits shown on both objective and subjective measures.

“NSI-189 appears to be a broad-acting antidepressant, with effects in both core symptoms of depression and in aspects of cognition where standard antidepressants typically show very modest effects. These results warrant the continued study of this compound among MDD patients who are inadequately managed by current antidepressant therapies,” said Maurizio Fava, MD, Director of the Division of Clinical Research of the MGH Research Institute and Executive Vice Chair, Department of Psychiatry at Massachusetts General Hospital, and the principal investigator of the trial.

In the Phase 2 trial, 220 subjects were randomized to: NSI-189 40mg daily (n=44), NSI-189 80mg daily (n=44), or placebo (n=132) for 6 weeks (Stage 1). At the end of 6 weeks, placebo-treated subjects who were non-responders (defined as less than 50% reduction in Montgomery-Asberg Depression Rating Scale (MADRS)) with a MADRS score greater than 15 were re-randomized to 6 weeks treatment with NSI-189 40 mg daily (n=22), NSI-189 80 mg daily (n=22), or placebo (n=22) (Stage 2). Patients on NSI-189 who completed Stage 1 continued the same dose for another 6 weeks. The primary outcome measure was the MADRS. Secondary outcome measures included the 17-item Hamilton Depression Rating (HAMD-17), the Symptoms of Depression Questionnaire (SDQ), the Cognitive and Physical Functioning Scale (CPFQ), the patient-rated version of the Quick Inventory of Depressive Symptomatology Scale (QIDS-SR), and CogScreen and CogState objective cognitive tests. Efficacy results concerning all patients randomized in Stage 1 were pooled (50:50 weighted average) with the Stage 2 results of all re-randomized patients who had been non-responders to placebo in Stage 1.

Using the Sequential Parallel Comparison Design (SPCD) pooled analysis approach, MADRS score reduction from baseline with 40mg or 80mg NSI-189 versus placebo did not reach statistical significance (mean difference -1.8, p=0.22, mean difference -1.4, p=0.34, respectively). However, the 40 mg dose resulted in a statistically significant reduction in SDQ (mean difference -8.2, p=0.04), and CPFQ scores (mean difference -1.9, p=0.03) versus placebo in the pooled SPCD analyses. There was also a statistically greater reduction in QIDS-SR scores versus placebo for patients treated with 40 mg of NSI-189 in Stage 2 (-2.5, p=0.04), but not Stage 1. Differences for the 80 mg dose versus placebo on these three self-report measures were not statistically significant.

In addition, the 40mg dose also showed statistical advantages on objective measures of attention and memory as per the Cogscreen test, but not the Cogstate test: Simple Attention (SATADRTC, p=0.034; Complex Attention (SATACACC, p = 0.048) and Memory (SDCDRACC, p = 0.002; also seen with 80mg dose, p = 0.015).

Both doses were well-tolerated with 0, 0 and 7 subjects discontinuing treatment with 40mg, 80mg and placebo, respectively, due to intolerance in Stage 1, and 1,0 and 1 subjects discontinuing treatment with 40mg, 80mg and placebo, respectively, due to intolerance in Stage 2. Furthermore, no subjects treated with NSI-189 experienced a serious adverse event during the study.

“We are extremely pleased that the novel, neurogenic, neurotrophic mechanism of action of NSI-189 has shown both antidepressant and pro-cognitive activity in depressed patients, and which appears to result in meaningful benefit as reported both by the patients themselves and by objective computerized measurements. These results further support those from the previous Phase 1b in subjects with MDD, which demonstrated potential efficacy on both depression and cognition scales. We look forward to meeting with the Food and Drug Administration (FDA) in the first half of 2018 to further define the clinical development and regulatory paths for NSI-189, as well as to submit the results of this study to a peer reviewed publication by the end of this year,” said Rich Daly, Chairman and CEO, Neuralstem.

**Conference Call and Webcast**

In connection with this announcement, Neuralstem will host a conference call today, Tuesday, December 5, at 8:30 a.m. ET. The call can be accessed by dialing 1 (833) 584-0034 (U.S. and Canada) or 1 (409) 350-3602 (international). The conference ID number is 4382159. To access the live webcast, or the subsequent archived recording, visit the "Events" section of the Neuralstem website at www.neuralstem.com. An archived presentation will be available for 90 days.

**About NSI-189**

NSI-189, a benzylpiperazine-aminopyridine, is a small molecule in clinical development for MDD and in preclinical development for Angelman syndrome, irradiation-induced cognitive impairment, Type 1 and Type 2 diabetes, and stroke. NSI-189 is a novel compound developed for the treatment of MDD. Data suggest that NSI-189 works by promoting synaptogenesis or neurogenesis in the hippocampus; a different mechanism of action than currently marketed antidepressants. Based on preclinical studies, NSI-189 has shown to stimulate neurogenesis of human hippocampus-derived neural stem cells in vitro and stimulates neurogenesis in mouse hippocampus in vivo. These studies suggest that NSI-189 may have broad utility as a neuroregenerative drug. NSI-189 was discovered using the Company's stem cell-based screening platform. The Company's portfolio of small molecule compounds, which includes NSI-189, are covered by 10 U.S. exclusively owned issued and pending patents and over 60 exclusively owned foreign issued and pending patents.

**About Neuralstem**

Neuralstem is a clinical-stage biopharmaceutical company developing novel treatments for nervous system diseases of high unmet medical need. NSI-189 is a small molecule in clinical development for major depressive disorder (MDD) and in preclinical development for Angelman syndrome, irradiation-induced cognitive impairment, Type 1 and Type 2 diabetes, and stroke. NSI-566 is a stem cell therapy being tested for treatment of paralysis in stroke, chronic spinal cord injury (cSCI) and Amyotrophic Lateral Sclerosis (ALS). Neuralstem's diversified portfolio of product candidates is based on its proprietary neural stem cell technology.

**Cautionary Statement Regarding Forward Looking Information**

This news release contains "forward-looking statements" made pursuant to the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements relate to future, not past, events and may often be identified by words such as "expect," "anticipate," "intend," "plan," "believe," "seek" or "will." Forward-looking statements by their nature address matters that are, to different degrees, uncertain. Specific risks and uncertainties that could cause our actual results to differ materially from those expressed in our forward-looking statements include risks inherent in the development and commercialization of potential products, uncertainty of clinical trial results or regulatory approvals or clearances, need for future capital, dependence upon collaborators and maintenance of our intellectual property rights. Actual results may differ materially from the results anticipated in these forward-looking statements. Additional information on potential factors that could affect our results and other risks and uncertainties are detailed from time to time in Neuralstem's periodic reports, including the Annual Report on Form 10-K for the year ended December 31, 2016, and Form 10-Q for

the three and nine months ended September 30, 2017, filed with the Securities and Exchange Commission (SEC), and in other reports filed with the SEC. We do not assume any obligation to update any forward-looking statements.

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