

Anavex Life Sciences Announces Preliminary Clinical Efficacy Data of its U.S. Phase 2 Clinical Trial of ANAVEX®2-73 in Patients with Rett Syndrome

- ***Both global efficacy endpoints, RSBQ and CGI-I, showed significant improvement with respect to baseline after 7 weeks of treatment with ANAVEX®2-73 (blarcamesine)***
- ***ANAVEX®2-73 (blarcamesine) treatment effect was significantly correlated with changes in two different biomarkers linked to the neurobiology of Rett syndrome, Glutamate and GABA***
- ***Detailed Data to be Presented at 6th Annual European Rett Syndrome Conference in Tampere, Finland, September 27-28, 2019***

NEW YORK – September 16, 2019 – Anavex Life Sciences Corp. (“Anavex” or the “Company”) (Nasdaq: AVXL), a clinical-stage biopharmaceutical company developing differentiated therapeutics for the treatment of neurodegenerative and neurodevelopmental disorders including Alzheimer’s disease, Parkinson’s disease, Rett syndrome and other central nervous system (CNS) disorders, today announced preliminary clinical data of the U.S. Phase 2 Rett syndrome clinical trial.

Preliminary Clinical Data is derived from the ANAVEX®2-73-RS-001 study on the first 6-patient cohort ranging in age from 18 to 36 years, who completed the pharmacokinetic (PK) part of the study and who received a low dose of approx. 5 mg daily oral liquid dose of ANAVEX®2-73 (*blarcamesine*) for 7 weeks. Patients are continuing participation in the ANAVEX®2-73-RS-001 open label extension study.

Both efficacy endpoints, the Rett Syndrome Behaviour Questionnaire (RSBQ) and the Clinical Global Impression – Improvement (CGI-I) showed significant improvement with respect to baseline after 7 weeks of treatment. The RSBQ Total average scores improved from 50 to 34 points (2-tailed Wilcoxon signed rank test, $p = 0.027$) and the CGI-I scores were positively correlated with RSBQ Total scores at 7 weeks (2-tailed Spearman’s $\rho = 0.956$, $p = 0.003$).

Supporting the clinical assessments, plasma levels of the biomarker Glutamate also decreased significantly (Week 0 vs. Week 7; 2-tailed Wilcoxon signed rank test, $p = 0.046$) and levels of Glutamate at Week 7 were directly correlated with CGI-I scores at Week 7 (2-tailed Spearman’s $\rho = 0.837$, $p = 0.038$) with greater decreases in Glutamate associated with greater improvement in these efficacy scores.

Glutamate is the main excitatory neurotransmitter in the brain and is known to be higher in patients with Rett syndrome compared to healthy subjects in the brain, as measured by magnetic resonance imaging spectroscopy (MRS), as well as in cerebrospinal fluid (CSF) and blood plasma.

Additionally, the magnitude of GABA change was inversely correlated with the magnitude of decrease in RSBQ Total scores (2-tailed Spearman’s $\rho = -0.812$, $p = 0.050$) and GABA changes demonstrated an inverse correlation of the magnitude of Glutamate changes (2-tailed Spearman’s $\rho = -0.829$, $p = 0.042$). GABA is the main inhibitory neurotransmitter in the brain, known to be deficient in animal models of Rett syndrome. Excitatory-inhibitory imbalances postulated in many neurologic disorders, including Rett syndrome, have been linked to imbalances between Glutamate and GABA^{1,2}.

¹ Kaufmann et al. Expert Opin Orphan Drugs 4:1043-1055, 2016

² Banerjee et al. Brain 142:239-248, 2019

An independent DSMB review determined that ANAVEX[®]2-73 (*blarcamesine*) was well tolerated, with no SAEs reported and with all patients completing the study. Therefore, the DSMB issued a positive recommendation for the continuation of the Phase 2 Rett syndrome study without any modifications.

“This is a remarkable first strong signal for patients with Rett syndrome especially given that the strong effects were seen in adult patients, and we look forward to discussing these results with the FDA and the European regulatory agency as we continue our Rett Syndrome Program including pediatric patients,” said Walter E Kaufmann, MD, Principal Investigator of the study and Chief Medical Officer of Anavex. “Importantly, we've now observed that the ANAVEX[®]2-73 (*blarcamesine*) effect is correlated with changes of Glutamate and GABA levels, objective measures and biomarkers in several neurodevelopmental disorders.”

Detailed results will be presented at the 6th European Rett Syndrome Conference in Tampere, Finland, September 27-28, 2019 and submitted for publication in a peer-reviewed journal.

Neurobehavioral effects of ANAVEX[®]2-73 (*blarcamesine*) previously observed in preclinical studies were also detected in patients with Rett syndrome, pointing to the ability of translation of preclinical to clinical data. ANAVEX[®]2-73 (*blarcamesine*) has received orphan drug designation from the FDA and EMA for the treatment of Rett syndrome.

Christopher U Missling, PhD, President and Chief Executive Officer of Anavex stated, “We are encouraged by the insights gleaned from these first clinical data for ANAVEX[®]2-73 (*blarcamesine*) in patients with Rett syndrome and we look forward to both confirm this clinical data and continue the Rett syndrome program with determination. In addition to Rett syndrome³, Anavex has ongoing clinical development programs for ANAVEX[®]2-73 (*blarcamesine*) for the treatment of Alzheimer’s disease⁴ and Parkinson’s disease dementia⁵.”

About Rett Syndrome

Rett syndrome is a devastating, non-inherited genetic postnatal progressive neurodevelopmental disorder that occurs almost exclusively in girls and leads to severe impairments, affecting nearly every aspect of the child’s life: their ability to speak, walk, eat and even breathe easily. The hallmark of Rett syndrome is near constant repetitive hand movements while awake. It is characterized by normal early growth and development (6 to 18 months) followed by a slowing of development, loss of purposeful use of the hands, distinctive hand movements, autistic features, slowed brain and head growth, ataxia, seizures and intellectual disability. There is currently no cure for Rett syndrome. Rett syndrome is caused by mutations in the *MECP2* gene and strikes all racial and ethnic groups and occurs worldwide in approximately one in every 10,000 to 15,000 live female births.

About ANAVEX[®]2-73-RS-001 Clinical Study

The Phase 2 trial is a randomized double-blind, placebo-controlled safety, tolerability, pharmacokinetic and efficacy study of oral liquid ANAVEX[®]2-73 (*blarcamesine*) to treat Rett syndrome. Pharmacokinetic and dose-finding elements in a total of 21 patients over a 7-week treatment period will be evaluated

³ ClinicalTrials.gov Identifier: NCT03758924; NCT03941444

⁴ ClinicalTrials.gov Identifier: NCT03790709

⁵ ClinicalTrials.gov Identifier: NCT03774459

incorporating precision medicine biomarkers. Preceding the placebo-controlled randomization of 15 patients, a 6 patient cohort underwent a 7-week pharmacokinetic (PK) assessment with safety, tolerability, pharmacokinetic and efficacy evaluation of ANAVEX®2-73 (*blarcamesine*). All patients who participate in the study will be eligible to receive ANAVEX®2-73 (*blarcamesine*) under an open label extension protocol.

About ANAVEX®2-73

ANAVEX®2-73 (*blarcamesine*) activates the Sigma-1 receptor (S1R) protein, which serves as a molecular chaperone and functional modulator involved in restoring homeostasis. In a Phase 2a Alzheimer's disease (AD) study, ANAVEX®2-73 (*blarcamesine*) has shown dose dependent improvement in exploratory endpoints of cognition (MMSE) and activities of daily living (ADCS-ADL). Full genomic analysis of ANAVEX®2-73 (*blarcamesine*) Phase 2a AD patients was performed. The ANAVEX®2-73 (*blarcamesine*) Phase 2 Rett syndrome study design includes genomic biomarkers identified in the ANAVEX®2-73 (*blarcamesine*) Phase 2a AD study. Studies of ANAVEX®2-73 (*blarcamesine*) in a mouse model with a heterozygous *Mecp2*-null mutation (HET) that causes neurological symptoms that mimic Rett syndrome, ANAVEX®2-73 (*blarcamesine*) was evaluated in automatic visual responses and breathing tests in 7-month old mice, an age at which advanced pathology is evident. Vehicle-treated HET mice demonstrated fewer automatic visual responses and more frequent expiratory apneas than wild-type mice. Treatment with ANAVEX®2-73 (*blarcamesine*) for four weeks significantly increased these visual responses in the HET mice ($p < 0.05$). Additionally, chronic oral dosing daily for 3-6.5 weeks of ANAVEX®2-73 (*blarcamesine*) starting at ~5 weeks of age was also conducted in the HET mouse model of Rett syndrome, and dose-dependent improvements in a variety of sensory and motor deficits, including those involving motor coordination, balance, and learning, were also observed. Notably, one of the strongest effects was on hindlimb claspings, a postural response that resembles the characteristic hand stereotypies present in Rett syndrome. These experiments were sponsored by Rettsyndrome.org.

About Anavex Life Sciences Corp.

Anavex Life Sciences Corp. (Nasdaq: AVXL) is a publicly traded biopharmaceutical company dedicated to the development of differentiated therapeutics for the treatment of neurodegenerative and neurodevelopmental disorders including Alzheimer's disease, Parkinson's disease, Rett syndrome and other central nervous system (CNS) diseases, pain and various types of cancer. Anavex's lead drug candidate, ANAVEX®2-73 (*blarcamesine*), recently completed a successful Phase 2a clinical trial for Alzheimer's disease. ANAVEX®2-73 (*blarcamesine*) is an orally available drug candidate that restores cellular homeostasis by targeting sigma-1 and muscarinic receptors. Preclinical studies demonstrated its potential to halt and/or reverse the course of Alzheimer's disease. ANAVEX®2-73 (*blarcamesine*) also exhibited anticonvulsant, anti-amnesic, neuroprotective and anti-depressant properties in animal models, indicating its potential to treat additional CNS disorders, including epilepsy. The Michael J. Fox Foundation for Parkinson's Research previously awarded Anavex a research grant, which fully funded a preclinical study to develop ANAVEX®2-73 (*blarcamesine*) for the treatment of Parkinson's disease. ANAVEX®3-71, which targets sigma-1 and M1 muscarinic receptors, is a promising preclinical drug candidate demonstrating disease-modifying activity against the major hallmarks of Alzheimer's disease in transgenic (3xTg-AD) mice, including cognitive deficits, amyloid and tau pathologies. In preclinical trials, ANAVEX®3-71 has shown beneficial effects on neuroinflammation and mitochondrial dysfunction. Further information is available at www.anavex.com. You can also connect with the company on [Twitter](#), [Facebook](#) and [LinkedIn](#).

Forward-Looking Statements

Statements in this press release that are not strictly historical in nature are forward-looking statements. These statements are only predictions based on current information and expectations and involve a number of risks and uncertainties. Actual events or results may differ materially from those projected in any of such statements due to various factors, including the risks set forth in the Company's most recent Annual Report on Form 10-K filed with the SEC. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement and Anavex Life Sciences Corp. undertakes no obligation to revise or update this press release to reflect events or circumstances after the date hereof.

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