

Anavex Life Sciences Announces ANAVEX®2-73 (*Blarcamesine*) Meets Primary and Secondary Endpoints in Placebo-Controlled U.S. Phase 2 Clinical Trial for the Treatment of Adult Patients with Rett Syndrome

Primary safety, pharmacokinetics and secondary efficacy endpoints met, with consistent improvements in RSBQ Total scores and CGI-I

Efficacy endpoints demonstrated statistically significant and clinically meaningful reductions in Rett syndrome symptoms and correlated with changes in biomarker (glutamate) of disease pathology

Key milestone met to advance regulatory approval pathway for adult patients with Rett syndrome

NEW YORK – December 15, 2020 – 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 reported top-line results from a U.S. Phase 2 randomized, double-blind, placebo-controlled trial of ANAVEX®2-73 (*blarcamesine*) in adult female patients with Rett syndrome.

The primary endpoint of the trial was safety. The convenient oral liquid once-daily dosing of 5 mg ANAVEX®2-73 was well-tolerated and demonstrated dose-proportional PK (pharmacokinetics). Adverse events related to study drug were similar between ANAVEX®2-73 (13.3%) and placebo (10%), with no reported serious adverse events (SAEs). The safety profile of ANAVEX®2-73 in this trial is consistent with prior clinical trial data.

All secondary efficacy endpoints of the trial showed statistically significant and clinically meaningful sustained improvements for ANAVEX®2-73 compared to placebo, consisting of the Rett Syndrome Behaviour Questionnaire (RSBQ) ($p = 0.048$) and the Clinical Global Impression Improvement Scale (CGI-I) score ($p = 0.014$) in the intent-to-treat (ITT) population ($n = 25$). Statistically significant differences in patient symptoms between the active and placebo groups occurred as early as 4 weeks following the initiation of ANAVEX®2-73 administration. Improvements in RSBQ Total scores were correlated with parallel decreases (improvements) in glutamate plasma levels.

ANAVEX®2-73 activates the sigma-1 receptor (SIGMAR1). Data suggests that activation of the sigma-1 receptor (SIGMAR1) is pivotal to restoring neural cell homeostasis and promoting neuroplasticity.¹ Consistent with previous ANAVEX®2-73 clinical trials, patients carrying the common form of the SIGMAR1 gene treated with ANAVEX®2-73 experienced stronger improvements in the prespecified efficacy endpoints.

¹ Advances in Experimental Medicine and Biology Volume 964 (2017) Sigma Receptors: Their Role in Disease and as Therapeutic Targets.

All twenty-five patients in this randomized study elected to enter a 12-week ANAVEX®2-73 extension study. Anavex will be advancing its Expanded Access Policy in order to provide long-term therapy to current participants with Rett syndrome under an expanded access program for ANAVEX®2-73.

“The outcome of this trial is very promising in terms of both safety and clinical improvement. Despite the challenges of the older age of the cohort (patients were over 18 years of age) and the relatively low dose (5 mg daily), ANAVEX®2-73 demonstrated clinically meaningful improvements in outcome measures evaluating multiple impairments,” commented Walter E Kaufmann, MD, Principal Investigator. Subsequent to his appointment as Principal Investigator of this Phase 2 ANAVEX®2-73 trial in adult Rett syndrome patients, Dr. Kaufmann joined Anavex as Chief Medical Officer. He also said, “Moreover, the convergent clinical evidence was supported by parallel changes in a key biomarker of disease. This strong body of data opens the possibility of successful treatment for both adults and children with Rett syndrome and early interventions for modifying the course of the disease.”

Based on the results in this first of its kind U.S. Phase 2 (ANAVEX®2-73-RS-001)² study in adult patients with Rett syndrome, Anavex is planning to meet with FDA to discuss the approval pathway. There are no FDA-approved drugs for Rett syndrome. ANAVEX®2-73 has Fast Track designation, Rare Pediatric Disease designation and Orphan Drug designation from the FDA for the treatment of Rett syndrome and may be considered for accelerated approval.

ANAVEX®2-73 is currently being evaluated for Rett syndrome in two other ongoing placebo-controlled clinical studies: The Phase 2 AVATAR trial in adult Rett syndrome (ANAVEX®2-73-RS-002)³ and the EXCELLENCE Phase 2/3 pediatric Rett syndrome study (ANAVEX®2-73-RS-003)⁴.

“These are strong and consistent data demonstrating tolerability and rapid and clinically meaningful improvements in key measures of Rett syndrome symptoms in the ANAVEX®2-73 treatment group compared to placebo,” said Christopher U Missling, PhD, President & Chief Executive Officer of Anavex. I would like to thank the patients and caregivers who participated in this trial, the Anavex team, trial clinics, and doctors who have worked tirelessly on this program. Special thanks go to the Rett syndrome.org Foundation, which provided financial support for this trial; we look forward to continuing the journey together.”

Summary of Top-line ANAVEX®2-73 (blarcamesine) Placebo-Controlled Phase 2 U.S. Rett Syndrome Trial Results

The study evaluated the safety, pharmacokinetics and efficacy of ANAVEX®2-73 in 25 adult female patients diagnosed with Rett syndrome (positive MECP2 gene mutation).

Effect on Rett Syndrome Symptoms:

- ANAVEX®2-73 treatment yielded a statistically significant, drug exposure-dependent response in the RSBQ Total scores, when compared to placebo, in the ITT cohort (all participants, p = 0.048).

² ClinicalTrials.gov Identifier: NCT03758924

³ ClinicalTrials.gov Identifier: NCT03941444

⁴ ClinicalTrials.gov Identifier: NCT04304482

- 66.7% of ANAVEX®2-73 treated subjects showed a statistically significant improvement in drug exposure-dependent RSBQ response as compared to 10% of the subjects on placebo in the ITT cohort (all participants, p = 0.011).
- Improvements in this adult population with Rett syndrome, assessed by RSBQ Total scores, are considered clinically meaningful according to published criteria applied to neurodevelopmental disorders.⁵
- ANAVEX®2-73 treatment resulted in a sustained improvement in CGI-I scores throughout the 7-week study, when compared to placebo in the ITT cohort (all participants, p = 0.014).
- 86.7% of ANAVEX®2-73 treated subjects showed a statistically significant CGI-I response, defined as sustained improvement to treatment, as compared to 40% of the subjects on placebo in the ITT cohort (all participants, p = 0.014).

Safety and Tolerability:

- ANAVEX®2-73 was found to be well tolerated with very good medication compliance during the trial.
- All 25 subjects completed the study. The overall incidence of patients who experienced adverse events related to study drug, which were mild, or moderate was 13.3% (2) for the ANAVEX®2-73 treatment group and 10% (1) for the placebo group.
No serious treatment emergent adverse events were reported during the course of the trial.
- There were no clinically significant differences in vital signs, lab values and EKG parameters between the active drug and placebo groups.
- Collectively, the study results are consistent with the known safety profile of ANAVEX®2-73.
- There was no signal for increased risk for common disorder-related manifestations.

About Rett Syndrome

Rett syndrome is a devastating, non-inherited genetic post-natal 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 easily breathe. The hallmark of Rett syndrome is near constant repetitive hand movements while awake. The disease 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.

Rett syndrome is caused by mutations in the *MECP2* gene and strikes all racial and ethnic groups. The disease occurs worldwide in approximately one in every 10,000 to 15,000 live births. The population of patients with Rett syndrome is estimated to be between 6,000 to 9,000 patients in the U.S. There is currently no cure for Rett syndrome.

About ANAVEX®2-73-RS-001 Clinical Study (NCT03758924)

The Phase 2 trial is a randomized double-blind, placebo-controlled safety, tolerability, pharmacokinetic and efficacy study of oral liquid ANAVEX®2-73 to treat Rett syndrome in a total of 31 adult patients with Rett syndrome over a 7-weeks treatment period were evaluated incorporating precision medicine biomarkers. Preceding the placebo-controlled randomization of 25 patients (Part B), a 6-patient cohort

⁵ Chatham et al. Adaptive behavior in autism: Minimal clinically important differences on the Vineland-II. *Autism Res.* 2018;11(2):270-283. doi:10.1002/aur.1874; Luu et al. Response to Placebo in Fragile X Syndrome Clinical Trials: An Initial Analysis. *Brain Sci.* 2020 Sep 11;10(9):629. doi: 10.3390/brainsci10090629

(Part A) underwent a 7-weeks pharmacokinetic (PK) assessment with safety, tolerability, pharmacokinetic and efficacy evaluation of ANAVEX®2-73. All patients who participated in the study were eligible to receive ANAVEX®2-73 under an open label extension protocol.

About Rettsyndrome.org

Rettsyndrome.org is the most comprehensive nonprofit organization dedicated to accelerating research of treatments and a cure for Rett syndrome and related disorders while providing information and family empowerment. As the world's leading private funder of Rett syndrome research, Rettsyndrome.org has funded over \$40M in high-quality, peer-reviewed research grants and programs to date. The organization hosts the largest global gathering of Rett researchers and clinicians to establish research direction for the future. Rettsyndrome.org, a 501(c)(3) organization, has earned Charity Navigator's most prestigious 4 star rating year after year. To learn more about our work and Rett syndrome, visit www.rettysyndrome.org or call (800) 818-7388 (RETT).

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, recently completed successfully a Phase 2a clinical trials for Alzheimer's disease and a Phase 2 proof-of-concept study in Parkinson's disease dementia. ANAVEX®2-73 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 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 for the treatment of Parkinson's disease. ANAVEX®3-71, which targets sigma-1 and muscarinic receptors, is a promising clinical stage 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 mitochondrial dysfunction and neuroinflammation. 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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