Alto Neuroscience Announces Positive Results from Phase 2 Study of ALTO-100 in Post-Traumatic Stress Disorder

– ALTO-100 exhibited a favorable safety and tolerability profile and clear evidence of effect as measured by marked improvements in CAPS-5 total scores –

– Patients exhibiting a biomarker-defined cognitive profile demonstrated a greater improvement in CAPS-5 scores than the patient group without the biomarker profile –

– Validation of biomarker across MDD and PTSD populations support transdiagnostic approach to neuropsychiatric drug development leveraging Alto's Precision Psychiatry Platform™–

LOS ALTOS, Calif., September 26, 2023 – Alto Neuroscience Inc. today reported results from the post-traumatic stress disorder (PTSD) cohort in its Phase 2a study of ALTO-100, demonstrating clear evidence of efficacy and favorable safety in patients with PTSD. In the study, a subpopulation of patients defined by a certain cognitive profile exhibited a greater improvement in PTSD symptoms as measured by CAPS-5 scores, the clinician administered PTSD scale for DSM-5, than those not exhibiting the cognitive profile. This first-of-its-kind Phase 2 study in PTSD leveraged Alto's Precision Psychiatry Platform™ to identify likely drug responders by matching a distinct neurobiological profile with the novel mechanism of ALTO-100. The outcome from the PTSD cohort builds on the major depressive disorder (MDD) dataset reported in January 2023 and continues to support the robust therapeutic potential of ALTO-100 in patients with comorbid mood and affective disorders and plasticity deficits.

"Positive data from the PTSD cohort of our ALTO-100 study, following favorable results in MDD, represents further validation of our platform," said Amit Etkin, M.D., Ph.D., founder and chief executive officer of Alto Neuroscience. "This result in PTSD, leveraging the same biomarker as discovered in MDD, strengthens confidence in Alto's approach and the replicability of our data. PTSD is highly heterogeneous and notoriously difficult to treat, and these results suggest the potential to meaningfully de-risk future development in additional indications following the anticipated MDD readout in 2024. These data move us closer to transforming neuropsychiatric treatment through a robust understanding of biological drivers of treatment response at the level of individual patients."

Topline results from the ALTO-100 Phase 2a study in PTSD include:

- The biomarker-defined PTSD patient group (n=44) demonstrated a 17.5-point mean reduction in CAPS-5 scores compared to 12.9 points in the patient group without the biomarker profile (n=40) at week 4, the primary outcome timepoint (p=0.04, d=0.37).
- 46% of biomarker-defined patients achieved clinical response (defined as a CAPS-5 PTSD symptom reduction of 50% or more from baseline) compared to 26% of patients without the biomarker profile (p=0.065).

- ALTO-100 has been studied in 395 subjects across a therapeutic course and has displayed a favorable tolerability profile. As reported in January, no new safety signals were observed in this study.

The study was an 8-week open-label, holdout dataset-controlled study to evaluate the efficacy and safety of ALTO-100 in patients with MDD or post-traumatic stress disorder. The study included 133 patients with primary MDD (moderate to severe) and 90 patients with primary PTSD. Alto utilizes a rigorous data science approach and prospective replication to predict clinical efficacy in holdout datasets and define reliable drug predictors while avoiding false discovery. The primary endpoint was change from baseline in CAPS-5 score at week 4, with a replication threshold pre-specified as a Cohen's d effect of 0.25 or greater between those with and without the cognitive biomarker profile. The study focused on the effect size on enrichment and was not powered for statistical significance, though significance was achieved on the CAPS-5 reduction endpoint. The CAPS-5 score is the gold standard in PTSD assessment that consists of 20-item structured interview that can be used to diagnose and assess symptoms of PTSD.

About Alto Neuroscience

Alto Neuroscience is pioneering precision psychiatry by developing targeted medicines to help patients get better faster. Differences in individuals' biology impact how they respond to treatment. Alto's Precision Psychiatry Platform™ measures brain biomarkers by analyzing EEG activity, behavioral task performance, wearable data, genetics, and other factors to match each patient with the right Alto drug. The company's work in identifying and categorizing core domains of mental function (cognition, emotion, and sleep processes) has resulted in a multiple modality approach that supports robust drug-response predictions. Alto's clinical-stage pipeline includes first- or best-in-class novel drug candidates in depression, PTSD, and other mental health conditions, resulting in the broadest and most-advanced precision psychiatry effort. For more information, visit https://www.altoneuroscience.com or follow us on Twitter.

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