Alto Neuroscience Presents New Data Leveraging EEG and Machine Learning to Predict Individual Response to Antidepressants at the 61st Annual Meeting of the American College of Neuropsychopharmacology

– Results demonstrate that individual response to antidepressants can be robustly predicted by using EEG and machine learning –

– Model presented significantly predicts observed Hamilton Depression Rating Scale score change, with successful replication on holdout dataset and generalization across studies –

– Methodology for discovery of SSRI biomarker was developed by Alto Neuroscience and is being leveraged across Alto's pipeline of first- or best-in-class clinical product candidates –

LOS ALTOS, Calif., December 8, 2022 – Alto Neuroscience today announced a presentation of new data on the discovery and validation of a machine learning model for predicting individual response to antidepressant treatment at the 61st annual meeting of the American College of Neuropsychopharmacology (ACNP) that took place in Phoenix, Arizona December 4-7, 2022.

"Although selective serotonin reuptake inhibitors (SSRIs) are the first line treatment for illnesses such as major depressive disorder (MDD), often patient response rates remain low with trial-and-error being the only option for treatment selection," said Amit Etkin, M.D., Ph.D., founder and chief executive officer of Alto Neuroscience. "The data we presented at ACNP further validate our work and exemplify the future of precision psychiatry in changing the mental health treatment landscape."

Alto developed and validated a machine learning model for predicting individual response to SSRIs using 19-channel resting-state electroencephalography (rsEEG) data from two MDD clinical trials (total N= 346). Data from 93 MDD patients in the SSRI arm of an open-label clinical trial were used for model development. A model was identified that is significantly predictive of the observed Hamilton Depression Rating Scale ($HAMD_{17}$) score change in the open label study. Prospective testing of the model on a holdout sample yielded similar results, both with a large effect size for the clinical outcome difference between those with and those without the EEG biomarker. The model also generalizes across studies, demonstrated by application of the model to the sertraline arm of a separate randomized placebo-controlled trial (RCT) in MDD patients. Importantly, the model failed to predict outcome in the placebo arm of the RCT, suggesting that the model is specific to predicting response to SSRIs. These results demonstrate that robust prediction of individual response to antidepressants can be achieved leveraging EEG and machine learning in a specific and reproducible manner developed by Alto Neuroscience.

The data were presented at ACNP in two separate formats; the details of each presentation were as follows:

Presentation Title: ACNP Meet the Expert session: Bringing Precision to Psychiatric Treatment Development: Learnings and Opportunities for Realizing Biomarker-Guided Clinical Care
Presenting Author: Amit Etkin, M.D., Ph.D., founder and chief executive officer
Presentation Date: Tuesday, December 6, 2022
Presentation Highlights:

- Historically, psychiatric drug development has failed to account for individual patient biology, leading to higher rates of failure and fewer new medications for mental health conditions
- Despite drugs demonstrating success in clinical studies and obtaining FDA approval, only a minority of patients demonstrate adequate antidepressant response
- Advancements in brain imaging techniques, including EEG, enable deeper understanding of the neurobiology of disease and effects of treatment
- Leveraging new machine learning techniques and rigorous validation, the development of treatment prediction models can be systematized to develop robust and scalable biomarkers
- Alto has discovered, developed, and validated a model for prediction of SSRI response leveraging an EEG biomarker that is dependent on core features which are stable and reliable

Presentation Title: Prediction of Antidepressant Response Using Machine Learning and Resting-State EEG
Presenting Author: Wei Wu, Ph.D., co-founder and chief data science officer
Poster Number: Poster Session III; W105
Poster Authors: Chao Wang, Ph.D., Wei Wu, Ph.D., Akshay Ravindran, Ph.D., Vinit Shah, Ph.D., Maimon Rose, Ph.D., Adam Savitz, M.D., Ph.D., Amit Etkin, M.D., Ph.D.
Presentation Highlights:

- Identified a model that is significantly predictive of the observed $HAMD_{17}$ score change in an open label study of SSRIs in patients with MDD ($r = 0.35$, $p < 0.001$)
- Applied the model to a holdout sample, resulting in prospective model validation with consistent results ($r = 0.32$, $p = 0.019$)
- The model generalized across studies, achieving prediction of the outcome in the sertraline arm of a separate RCT ($r = 0.28$, $p = 0.003$)
- The model is specific to SSRI response and was not predictive of response to placebo ($r = 0.03$, $p = 0.375$)

Leveraging the same analysis methodology and biomarker discovery approach, Alto anticipates presenting data from the Phase 2 study of ALTO-100 in January 2023, and the Phase 2 study of ALTO-300 is expected to be completed in the first half of 2023.

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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