Background
This proof-of-concept study of 32 patients with mild-to-moderate Alzheimer’s disease (AD) demonstrated a favorable safety and tolerability/risk profile for ANAVEX 2-73, which activates the stress-reducing and survival protein, the Sigma-1 receptor. Presented here is preliminary exploratory efficacy data through 31 weeks (26-week PART B including 5-week PART A) from the randomized (into different treatment regimens) open-label study with ANAVEX 2-73 oral daily dosing ranging from 10mg to 50mg (not optimized in PART B). Further analysis will be performed. PART A: Bioavailability Adaptive Cross-Over Design and PART B: 52-Week Voluntary Extension

PART A: Efficacy Data Measurements Cognition and Function
- Cognitive measures (MMSE; Cogstate battery)
- Functional measures (ADCS-ADL)
- ERPs: fundamental measures of synaptic network performance and target engagement
- ERPs target detection task measures: direct measures of attention, speed of brain processing, and simple functional performance

PART B: Efficacy Data Measurements Cognition and Function
- Cognitive measures (MMSE; Cogstate battery)
- Functional measures (ADCS-ADL)
- ERPs: fundamental measures of synaptic network performance and target engagement
- ERPs target detection task measures: direct measures of attention, speed of brain processing, and simple functional performance

MMSE MCI and Mild-to-Moderate Patients
- Given unequal sample size, data after stratification are considered preliminary
- Similar effect on MMSE in both MCI and Mild-to-Moderate AD patients

ADCS-ADL MCI and Mild-to-Moderate Patients
- Given unequal sample size, data after stratification are considered preliminary
- Similar ADCS-ADL score effect between MCI and Mild-to-Moderate AD patients

Hamilton Depression Rating Scale (HAMD) 31 Weeks
- ANAVEX 2-73 treatment demonstrates reduction in overall HAMD score after 31 weeks

Reduction of Insomnia, Anxiety and other Symptoms
- Improved forms of HAMD: Reduced insomnia, anxiety, and agitation
- Agitation: 0 vs 2.0
- Appetite: 0 vs 2.0
- Sleep: 0 vs 2.0
- Hypersomnia: 0 vs 2.0
- Loss of interest or other general symptoms: 0 vs 2.0

ANAVEX 2-73 Improves Components of Cogstate Tasks
- Cognitive decision: ANAVEX 2-73 > Donepezil
- Cognitive improvement: ANAVEX 2-73 > Donepezil

EEG/ERP: ANAVEX 2-73 Rescues Cognitive Effects on a Cellular Level

Conclusions
Despite the relatively small sample size of this proof-of-concept, randomized, open-label study with oral daily doses (not optimized) of ANAVEX 2-73 ranging from 10mg to 50mg, data seems to indicate a converging and consistent response for all measurements (MMSE, ADCS-ADL, Cogstate, EEG/ERP) currently throughout 31 weeks (7 months) of ANAVEX 2-73 treatment. Patient retention rate at week 31 is 84%.

Data suggest that treatment of ANAVEX 2-73 demonstrates reduction in overall HAMD score after 31 weeks, notably through reductions in insomnia, anxiety and agitation.

Over 31 weeks of treatment, ANAVEX 2-73 was associated with a sustained benefit in psychomotor function, attention and working memory. The specificity and consistency of these benefits suggest that ANAVEX 2-73 can sustain activation of attentional and working memory functions with repeated dosing in Alzheimer’s disease.

When the group is tentatively stratified into mild-to-moderate and MCI (mild cognitive impaired) AD patients, no significant difference was observed within the MMSE or the ADCS-ADL (PART B) score, respectively. Given the small sample size, this trend would require confirmation in a larger study.

For cognitive assessment using the Cogstate test batteries, ANAVEX 2-73 continues to show benefits over baseline at 17 weeks and 31 weeks. ANAVEX 2-73 related improvement in psychomotor function, attention and working memory are preserved through 17 weeks and 31 weeks of treatment. Repeated-measures ANOVA reveals that Cogstate values maintained the baseline values through week 31.

Mathematical modeling of the pharmacodynamic results is in progress. ANAVEX 2-73 is well tolerated and patients have requested to continue on the study drug, hence a further study extension after PART B has been granted. This will permit continued collection of longitudinal safety data on ANAVEX 2-73 for up to 3 years. The 17-week and 31-week data supports the plan to prepare for a larger, double-blind, placebo-controlled study of ANAVEX 2-73 in Alzheimer’s disease patients.