New Exploratory Alzheimer’s Drug ANAVEX 2-73: Changes in Electrophysiological Markers in Alzheimer’s Disease - First Patient Data from an ongoing Phase 2a Study in mild-to-moderate Alzheimer’s Patients

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Background

ANAVEX2-73 acts by activating specific stress reducing and survival protein Sigma-1 receptor as well as muscarinic receptors that are believed to be responsible for cognitive effects and can potentially combine symptomatic with neuroprotective and disease modifying properties (Villard 2011, Lahmy 2013). The neuroprotective properties may carry the initial cognitive effect over a longer period of time than current therapies. Sigma-1 Receptor is a Multi-Targeted Key Cellular Modulator:

• Reducing protein misfolding
• Enabling neuroprotection
• Modulating Ca2+
• Reducing oxidative stress
• Reducing retrograde dysfunction
• Blocking NOS

A previously completed randomized, placebo-controlled single ascending dose Phase 1 study of ANAVEX-73 in 22 healthy volunteers reported no serious adverse events. At highest doses, observed adverse events included moderate and reversible dizziness and headache, common in drugs that target the central nervous system. Blood pressure and resting heart rate and clinical laboratory parameters, vital signs and 12-lead ECG did not show any clinical relevant or dose-dependent changes. QT interval and QTc did not reveal any clinically significant changes. PK of ANAVEX-73 was found suitable for daily oral dosing (Schindler 2014).

Phase 2a with Adaptive Trial Design

Part A is an open-label extension for an additional 26 weeks, with daily oral dosing so as to establish a longer drug effect.

Electrophysiological Markers

EEG/ERP P300 signal is a real-time physiological measure of cognitive processes with demonstrated sensitivity to Alzheimer’s disease and more proximal to disease pathology and pharmacological intervention than psychometric measures (Polich 1990, Jeong 2004).

Electrophysiological Changes

Part A

- Initial cognitive EEG/ERP P300 ANAVEX2-73 data of 12 mild-to-moderate Alzheimer’s patients (MMSE 16-28) mostly on donepezil, the current standard of care.
- ANAVEX2-73 data is from 12 patients at baseline and day 36 with on-off-on dosing regimen without dose optimization.

Part B

- ANAVEX2-73 improves P300 signal in 10 out of 12 (83%) patients. ANAVEX2-73 data is from 12 patients at baseline and day 36 with on-off-on dosing regimen without dose optimization.

CONCLUSIONS

• This poster reports positive cognitive EEG/ERP P300 data of the initial 12 out of 32 mild-to-moderate Alzheimer’s patients’ (MMSE 16-28) mono on donepezil, the current standard of care at end of Part A (day 36).
• ANAVEX2-73 data is from 12 patients at baseline and day 36 with on-off-on dosing regimen without dose optimization. Further data will show if dose optimization leads to further increased P300 signal.
• Cognitive EEG/ERP P300 amplitude increased by 38% from baseline. A published data comparison shows that this is about 4 times higher than donepezil at the same time point and already higher than what donepezil reaches after 6 months of continuous administration.
• ANAVEX2-73 improves the P300 signal in 10 out of 12 (83%) patients.
• ANAVEX2-73 appears to show early measurable strong cognitive EEG/ERP effects.
• The study is continuing on schedule with finishing Part A for the remaining patients and progressing into longitudinal Part B.

REFERENCES

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