Athira Pharma Virtual KOL Webinar – The Predictive Nature of P300 to Determine Clinical Benefit of Alzheimer's Disease Treatments

October 28, 2020 – 4pm ET

Presenters

- Leen Kawas, PhD – President and CEO, Athira Pharma
- Larry Ereshefsky, PharmD, BCPP, FCCP – Leader in the application of translational drug development tools for neurodegenerative and psychiatric disorders. Dr. Ereshefsky is Chief Scientific Officer at Apex Innovative Sciences and a member of Athira's Scientific Advisory Board

Participating Analysts

- Paul Matteis – Managing Director, Biotechnology Equity Research at **Stifel**
- Jason Butler, PhD – Managing Director, Biotechnology Equity Research at **JMP**
- Andrew Tsai – Vice President at **Jefferies**
- Graig Suvannavejh, PhD – Vice President at **Goldman Sachs**

Video Directory (Start – 2:09; End – 65:45)

Leen Kawas

1. Presentation start – 2:09
2. Dr. Ereshefsky intro – 2:53
3. Agenda – 4:30
4. Athira overview and differentiated approach – 5:25
5. Athira platform and pipeline – 7:16
6. Mechanism of action intro – 9:43

Larry Ereshefsky

7. Intro to electrophysiology, Evoked Response Potential (ERP) P300 and quantitative electroencephalogram (qEEG) – 12:42
8. Electrode placement on scalp – 14:50
9. Intro to auditory oddball ERP paradigm – 15:58
10. Video demo of ERP acquisition – 18:14
11. ERP data processing intro – 20:04
12. ERP P300 data relationship to memory function. Standard v Deviant tone – 21:26
13. ERP P300 data is highly reliable and robust: test and re-test variability is small – 24:22
14. ERP waveform comparisons: P300 (immediate cognitive processing of an event) waveform compared to N100 (pre-attentive perception) and P200 (modulated by attention) – 25:49
15. ERP offers a reliable and robust synaptic measure for a synaptic disease such as Alzheimer's disease – 29:11
16. ERP P300 latency in Alzheimer's patients is consistently reported in published literature – 30:35

17. ERP P300 latency is more sensitive, reliable and robust compared to P300 amplitude as measured by responses to different marketed drugs – 32:46
18. ERP P300 latency data in marketed drugs, donepezil and rivastigmine, suggests a high correlation to cognitive changes as measured by ADAS-Cog– 34:11
19. Electrophysiology can be used reliably as a measure of brain function in Alzheimer's disease – 35:47

Leen Kawas

20. Presentation of Athira Phase 1b ERP P300 latency data in Alzheimer's patients. Significant and directional improvement of ERP P300 latency in every Alzheimer's patient treated with ATH-1017 compared with placebo controls – 37:26
21. Introduction to Athira clinical trials, a potentially pivotal Phase 2/3 LIFT-AD trial and ACT-AD trial. Both are for mild-moderate Alzheimer's patients with same study design and clinical endpoints, but ACT-AD is smaller and includes an ERP P300 measurement – 40:21

Analysts Q&A session – 41:50

- Paul Matteis, Stifel – 42:10
    - Have you ever seen promising P300 data for a drug in Alzheimer's that later didn't have a benefit on cognition? **Answer begins at 42:51**
    - You talked about how objective this measure is and variability is tight, and when you look at Athira's Phase 1b data and the observed effect size, is there any alternative explanation other than the drug is working? Are there any artifacts that could drive the observed difference? **Answer begins at 44:38**
- Jason Butler, JMP – 47:20
    - You showed data for healthy elderly and CIAD (schizophrenia), has anyone done any longitudinal studies looking at how P300 latency changes as disease progresses? **Answer begins at 48:43**
    - Leen mentioned the baseline data for the Phase 1 population, how representative is the baseline data for the Alzheimer's population, and any expectations for the baseline P300 latency in the ACT-AD trial? **Answer begins at 50:02**
- Andrew Tsai, Jefferies – 52:47
    - As we think about ACT-AD trial, how easy or how hard is it for a technician to pick up P300 and perform it in an accurate and consistent way? What's the learning curve like? How long does it take to fully train? How do you minimize intra-site variability? **Answer begins at 53:20**
- Graig Suvannavejh, Goldman Sachs – 56:42
    - Could you remind us for P300, outside of Alzheimer's, what's the use of P300 in other neurological conditions and what's been seen there? Has it been used to support the approval of any other products? How's it been used in the past? **Answer begins at 58:10**
    - The uniqueness of the Athira story is the novelty of the approach. What's FDA's receptivity of this approach? Give a sense of where the agency's head is in terms

of how they're really embracing the approach you're taking. **Answer begins at 60:01**

- Paul Matteis, Stifel – 61:25
    - Speed of onset question. How do you think about P300 and the kinetics of change on it vs the kinetics of change of cognitive capacity? Would you expect this drug to show a benefit that quickly? **Answer begins at 61:53**
- Leen Kawas – 63:49
    - How do you see the future for P300 and EEG? **Answer begins at 64:12**