18706 NORTH CREEK PARKWAY
SUITE 104
BOTHELL, WA 98011

Athira Pharma Virtual KOL Webinar – Educational Webinar on the Clinical Applications of ERP P300 with Drs. John Olichney, Hans Moebius and Kevin Church

November 5, 2021 – 9am PT / 12pm ET

Speakers (in order)

- Mark Litton, PhD, MBA – President and Chief Executive Officer, Athira Pharma
- Kevin Church, PhD – Executive Vice President, Research
- John M. Olichney, MD – Leader in EEG and ERP research and their applications in Alzheimer's and other neurological diseases. Dr. Olichney is Professor of Neurology at UC Davis School of Medicine
- Hans J. Moebius, MD, PhD – Chief Medical Officer, Athira Pharma

Participating Analysts (in order during Q&A)

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

Video Directory (Start – 0:40; End – 1:10:00)

Mark Litton

1. Welcome and opening – 0:40
2. Presenter intros – 1:20
3. Agenda – 1:40
4. Athira overview – 2:13

Kevin Church – *ATH-1017 mechanism of action and rationale for translational measures, qEEG and ERP P300*

5. HGF/MET neurotrophic system in normal brain function – 3:55
6. ATH-1017 intro and HGF/MET mechanism of action – 4:52
7. Promotion of HGF/MET and rationale for EEG – 6:20
8. ATH-1017 in AD mouse model demonstrating acute and sustained EEG effects – 7:30
9. ATH-1017 therapeutic rational and key points – 9:06

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John Olichney – *Introduction to Event-Related Potentials (ERPs) and Quantitative EEG (qEEG) in Alzheimer's Disease (AD)*

10. Intro slide to ERPs and qEEG and applications to AD – 10:30
11. AD is a synaptic failure (paradigm shift) – 10:41
12. Clifford Jack clinical disease progression model of AD – 12:17
13. Synapse loss is a hallmark in AD – 13:50
14. EEG measures neural synchronization and connectivity in AD – 14:49
15. Intro to EEG and ERP P300 latency measurements – 15:38
16. ERPs and relation to cognition – 16:07
17. Utility of electrophysiology in the brain – 18:12
18. Applications of ERPs in AD trials – 19:20
19. Applications of ERP/EEG for AD trials – 20:56
20. Review summarizing applications of ERP/EEG for AD trials – 22:42
21. Introduction to ERP components – 23:17
22. Introduction to auditory oddball ERP P300 paradigm – 25:37
23. Explanation of P300 amplitude – 26:53
24. ERP P300 latency is a better candidate for a consistent biomarker – 27:40
25. Diagram of cap and electrode placement – 28:50
26. ERP P300 latency and amplitude data in AD patients – 29:28
27. Summary of P300 ERP in AD studies – 30:42
28. Summary of ERP studies of treatment in AD studies – 32:25
29. ERP P300 data correlation with cognitive changes – 33:40
30. Auditory ERP components in clinical trial design – 34:36
31. Introduction to resting state EEG in AD – 35:25
32. Longitudinal studies of resting state EEG in AD – 36:10
33. Response of frequency bands to environment (stimuli/task) – 37:20
34. Electrophysiology use in measuring brain function – 39:28
35. Summary of EEG/ERP P300 in AD – 40:59

Hans Moebius – *Athira's strategy and rationale for clinical trial design and summary of ERP P300 latency data in Alzheimer's subjects*

36. Introduction to Athira's strategy and rationale with ATH-1017 in the clinic – 42:28
37. Introduction to independent partners in Athira's Phase 1a/b trial – 42:50
38. Phase 1b trial design – 44:02
39. ATH-1017 improved ERP P300 latency in AD subjects – 44:48
40. ATH-1017 improved ERP P300 latency in AD subjects – 46:29
41. LIFT-AD phase 2/3 trial design – 47:29
42. ACT-AD phase 2 trial design – 49:15

Analysts Q&A session – 51:25

- Paul Matteis, Stifel – 51:35
    - How do you think about given that ACT-AD is not powered for statistical significance, what magnitude of difference on ADAS-Cog or ADL would, in the absence of p-value, give you confidence in a real cognitive effect? **Answer begins at 52:40**
    - Athira's Phase 1b study is pretty small, based on your understanding of electrophysiology and EEG, are there any exogenous factors or intrinsic variability in the measurement that could have driven the effect like what they saw or are you confident that it was a real drug effect? **Answer begins at 53:56**
    - How well do we understand the kinetics of the effect of P300 vs cognition, does it make sense to you that we saw this so rapidly? **Answer begins at 56:49**
- Andrew Tsai, Jefferies – 58:19
    - For ACT-AD, how are you addressing potential for site-to-site variability? **Answer begins at 59:04**
    - In the Phase 1 P300 portion, it was on a 40mg dose, and on both ACT-AD and LIFT-AD, are you expecting some form of dose-response on the P300 in ACT-AD? **Answer begins at 1:01:07**
    - In ACT-AD, GST is one of the endpoints. Does this also integrate ADAS-Cog11 and ADCS-CGIC? **Answer begins at 1:02:37**
    - Is there a high correlation between P300 and cognitive improvement in other neuropsych indications? **Answer begins at 1:04:26**
- Jason Butler, JMP – 1:06:04
    - You spoke about longitudinal studies…has anyone looked to see whether in the same patient you see an improvement in P300 latency as the drug is working but as the symptomatic efficacy wanes overtime, you see a re-worsening of P300 latency? **Answer begins at 1:06:43**
    - When you think about the conduct of EEG going from Phase 1 to ACT, what do you think generally about the conduct of the EEG in ACT that are similar or different. For example, is the stimulus the same? **Answer begins at 1:08:28**

Mark Litton

43. Closing remarks – 1:09:11