Deploying User-Friendly Portable EEG to Measure Response to a Novel Antidepressant with Resting and Task-Driven Neurophysiological Endpoints

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Background

- Many people with major depressive disorder (MDD) fail to respond adequately to first-line therapies
- DLX-001 is a non-hallucinogenic, non-dissociative neuroplastogen designed to promote structural and functional neuroplasticity
- In a previous first-in-human study, DLX-001 produced dose- and time-dependent changes in quantitative EEG (qEEG) consistent with plasticity-promoting mechanisms
- This Phase 1b study of DLX-001 in people with MDD evaluates pharmacodynamics, safety, and tolerability
- The Cumulus NeuLogiq® platform enabled high-frequency, repeated measurements (McWilliams et al., 2021; Barbey et al., 2022) of cognition, and of neurophysiology – both resting-state and task-driven neural markers of target engagement and neuroplasticity
- **Here, we report interim results from the first 9 participants (cohort A). Results from cohort B will be presented at a future conference**

Cumulus NeuLogiq® Platform for Use in Real-World Settings

Developed in collaboration with leading pharma companies and KOLs (below).

Cumulus provides full service:

- Protocol / study / SAP design
- On-site training, off-site support
- Data package
- Reporting and custom analytics

Audit ready including FDA 510(k), UKCA, HIPAA, GDPR, ISO13485.

Designed for and with patients and clinicians, deployed in Phase 0–1b CNS trials.

Secure automatic upload and QC.

Real-time dashboard monitoring of decentralized and home-based data collection.

Cumulus cognitive and EEG / ERP tests are designed to be highly repeatable, with large banks of non-repeating stimuli.

- Objectively administered and automatically scored
- Results (including EEG metrics) available in minutes, enabling remote monitoring and QC
- Suitable for detecting change over time

Relaxation: Resting State EEG

Symbol Swap: Digit symbol substitution/coding task

Biogen · Boehringer Ingelheim · Bristol Myers Squibb · GSK · J&J · Lilly · MSD · Pfizer · Roche · Takeda

Methods

EEG and cognitive endpoints were collected in-clinic using the NeuLogiq® platform, which integrates a 16-channel dry EEG headset with a tablet delivering gamified tasks. Assessments included:

- **Resting State EEG (*Relaxation*)** – 90 s eyes-open + 210 s eyes-closed to assess spectral power
- **40 Hz Auditory Steady-State Response Task (ASSR - *Soundbites*)** – 4-minute task presenting amplitude-modulated auditory tones to measure evoked gamma oscillations
- **Symbol Coding Task (*Symbol Swap*)** – digital adaptation of the task also known as the digit symbol substitution task (DSST), repeated up to twice daily, capturing broad executive function (processing speed, attention, memory, and visuo-motor) (Dyer et al., 2025). Outcome is number of correct responses in 90 seconds

Study Objectives:

- To obtain early evidence of target engagement and neuroplastic effects of DLX-001 in patients with MDD, using portable EEG and tablet-based cognitive tasks to capture resting-state and task-driven neural markers
- To evaluate cognitive task performance as an indicator of the safety profile of DLX-001

Study Design & Protocol:

- Phase 1b, dose-blinded, single-centre study in untreated adults with recurrent MDD
- 18 participants, stratified by CYP2D6 activity (100 / 170 / 250 mg DLX-001)
- Two regimens: Daily dosing (Days 1–7, n=9) or Intermittent dosing (Days 1 & 4 , n=9). **Data from the first 9 patients (who received DLX-001 once daily for 7 days) are included in this report**
- Baseline assessments were conducted on Days -2 and -1. Tablet-based cognitive tasks were completed on every day in the clinic. EEG and cognitive tasks were additionally performed 4 hours post-dose on Days 2, 3, 5, and 6. Data from follow-up Days 22 and 36 are not included here

Results

1. Resting state theta band trended upwards after first dose of DLX-001

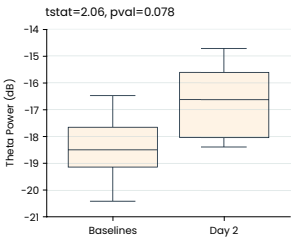

Figure 1: Boxplot of mean fronto-central theta power (6-8.5Hz). The baselines boxplot includes data averaged within participant across the two baseline timepoints. Paired t-test results including t-statistics and p-value are displayed at the top of the figures. The data presented includes 8 patients who contributed to a total of 23 sessions.

2. Spontaneous gamma band power fell after first dose of DLX-001

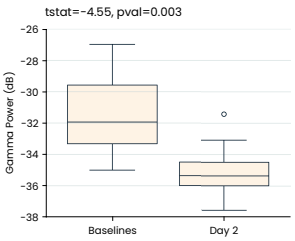

Figure 2: Boxplot of mean fronto-central gamma power (30-40Hz). The baselines boxplot includes data averaged within participant across the two baseline timepoints. Paired t-test results including t-statistics and p-value are displayed at the top of the figures. The data presented includes 8 patients who contributed to a total of 23 sessions.

3. Digital symbol swap task showed no measurable impairment of executive function following administration of DLX-001

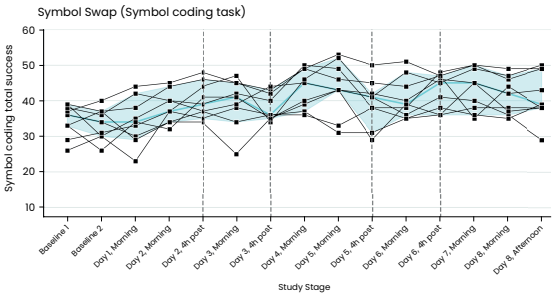

Figure 3a: Individual trajectories of the number of correct answers in the digital DSST. The vertical dotted lines indicated the acute 4hr post-dose timepoints. The blue line represents the median across all participants. The blue shaded area represents the 95% confidence interval. The data presented includes 9 patients who each contributed 15 sessions.

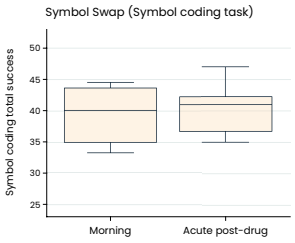

Figure 3b: Boxplot of the number of correct answers in the digital DSST collected on Day 2, Day 3, Day 5, and Day 6. The data presented includes 9 patients who each contributed 8 sessions (4 morning and 4 acute post-drug sessions).

4. Auditory steady-state response task showed inter-trial coherence (ITC) rose acutely after DLX-001 administration

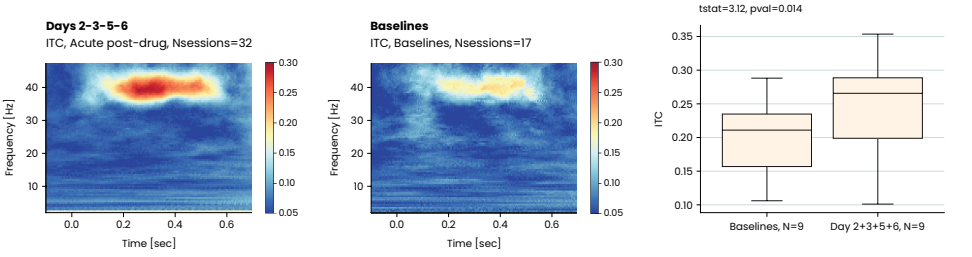

Figure 4: Left & centre: Heatmaps of the ITC averaged over Days 2, 3, 5 and 6 (left), and over the two Baselines (centre). Right: Boxplot of the mean ITC averaged over the two baseline days compared to the average of Days 2, 3, 5 and 6. Paired t-test results including t-statistics and p-value are displayed at the top of the figures.

Conclusions

- There was no evidence of acute or persistent cognitive impairment during the drug administration period, providing further evidence that DLX-001 is a safe non-hallucinogenic and non-dissociative neuroplastogen
- Slow wave brain activity has previously been described as a marker of neuroplasticity and synaptic strength (Duncan et al., 2013). Observed acute EEG effects confirm brain engagement, and are consistent with an increase in plasticity
- Increases in ITC 4h post administration compared to the baseline sessions suggest an increase in strength of the auditory entrainment and the capacity of the brain to oscillate in the gamma range
- Easy-to-use EEG hardware can be deployed to trial sites for frequent objective measurement of neurophysiological markers. Beyond translational questions, the same scalable technology could be used more broadly, on multisite phase 1 studies, or phase 2 studies, measuring mechanistic response in individuals, and to explore candidate companion diagnostics

References

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Duncan WC, Sarasso S, Ferrarelli F, et al. Concomitant BDNF and sleep slow wave changes indicate ketamine-induced plasticity in major depressive disorder. Int J Neuropsychopharmacol. 2013;16(2):301-311.
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