



Update on ANAVEX[®]2-73 Program in Rett Syndrome

Adult Trial ANAVEX[®]2-73-RS-001
Preliminary Results

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SAFE HARBOR

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Adult RTT ANAVEX[®]2-73-RS-001 U.S. Trial (NCT03758924)

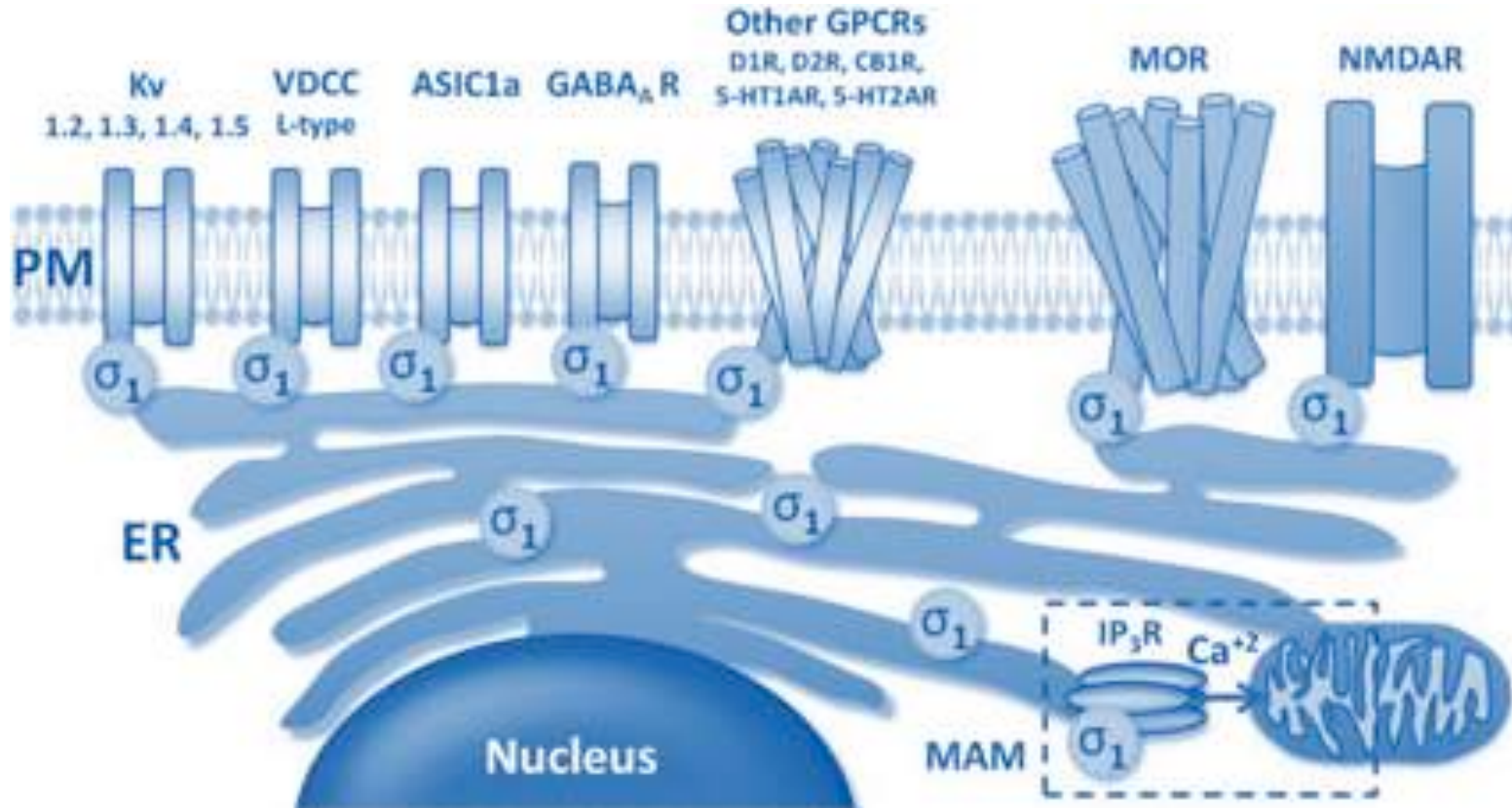
- Phase 2, safety, tolerability, efficacy
- Females > 18 years, classic RTT w/*MECP2* mutation
- Efficacy:
 - **Primary*: Global severity (RSBQ, CGI-I)**
 - Secondary: Behavior (ADAMS), Sleep (CSHQ), VAS (top caregiver concerns), Seizure diary
 - **Response Biomarker*: Glutamate, GABA**; Genetic biomarker: DNA & RNA profiles
- Part A: Intensive PK, n=6, **Completed**
- Duration: 7 weeks
- Oral, liquid formulation, 5 mg daily (relatively low dose)
- Part B: Randomized, double-blind, placebo-controlled, n=15, Ongoing

REPORT on INTENSIVE PK SUBCOHORT

- n=6, 18-36 years
- 5 mg daily for 7 weeks
- Intensive PK: Days 0 & 6
- Evaluations at baseline (Week 0), Week 4 & Week 7 (End of Treatment)
- Good safety and tolerability: No serious adverse events, only three grade 1-2 adverse events
- ***Preliminary evaluation of efficacy:** two-tailed, nonparametric tests (conservative)
- All endpoints to be analyzed at the end of the completed study (n=21)

Mechanism of Action: ANAVEX[®]2-73 Activates SIGMAR1(σ_1)

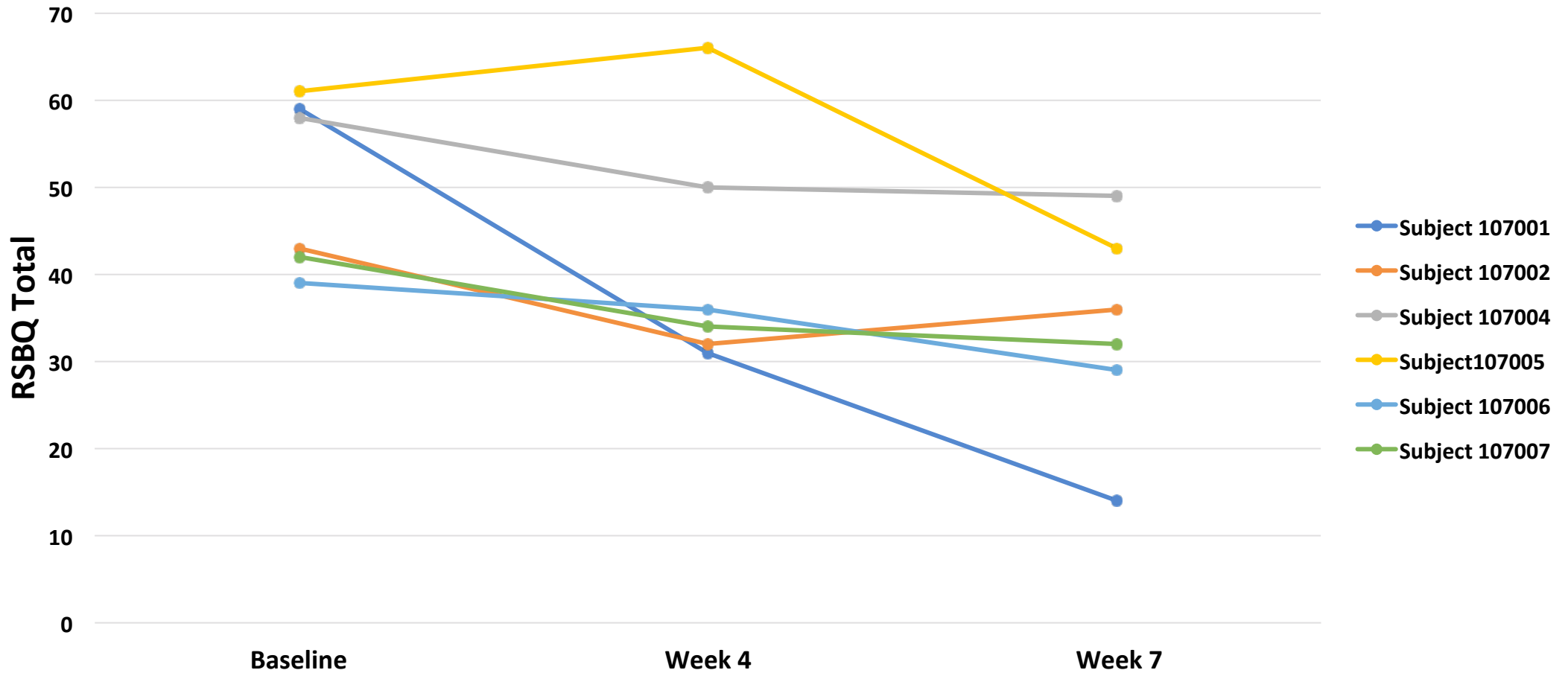
SIGMAR1 Activation has been Shown to Modulate Multiple Aspects of Neurodevelopmental and Neurodegenerative Processes



The SIGMAR1 receptor is an integral membrane protein involved in cellular homeostasis which targets restoration of neuroplasticity, response to inflammation and response to cellular stress

Efficacy: RSBQ & CGI-I Improved During Trial

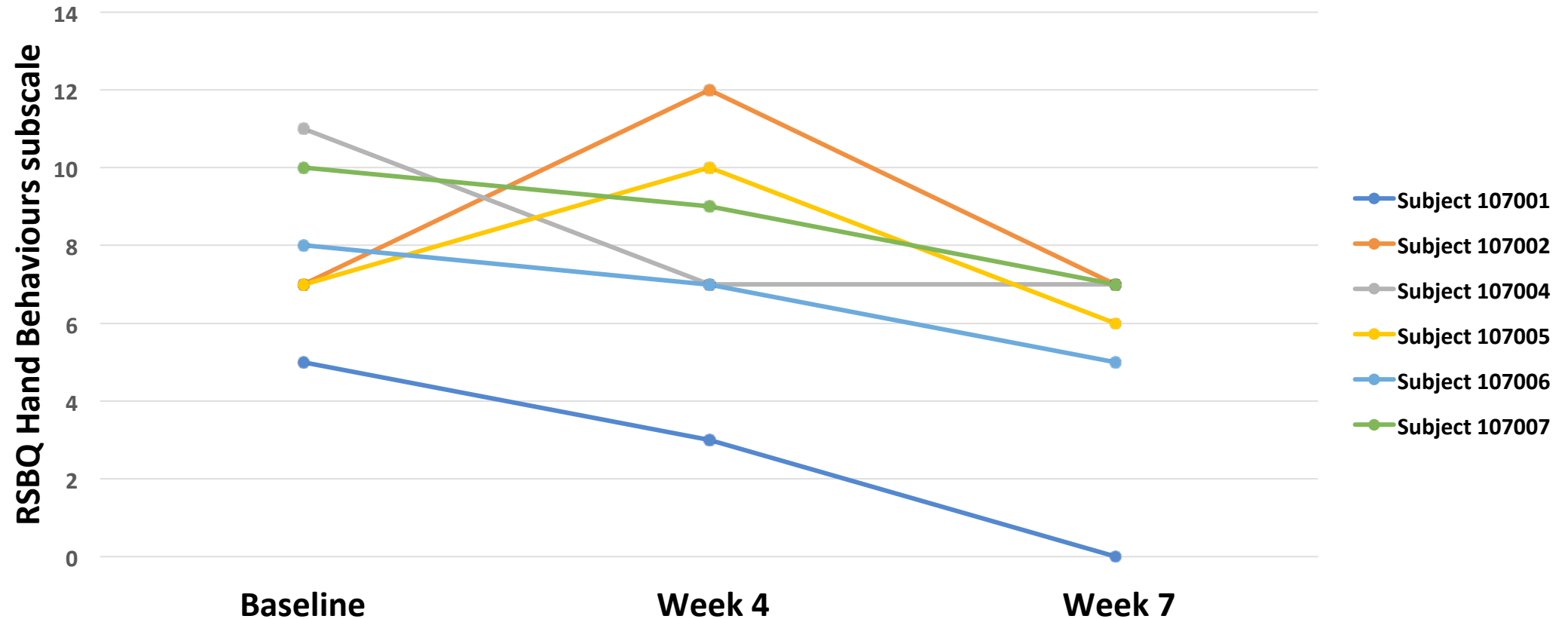
RSBQ Total Trajectory



Wilcoxon Signed Rank Test Week 0 vs. Week 7: $Z = -2.207, p = 0.027$

Efficacy: RSBQ Hand Behaviours Improved During Trial

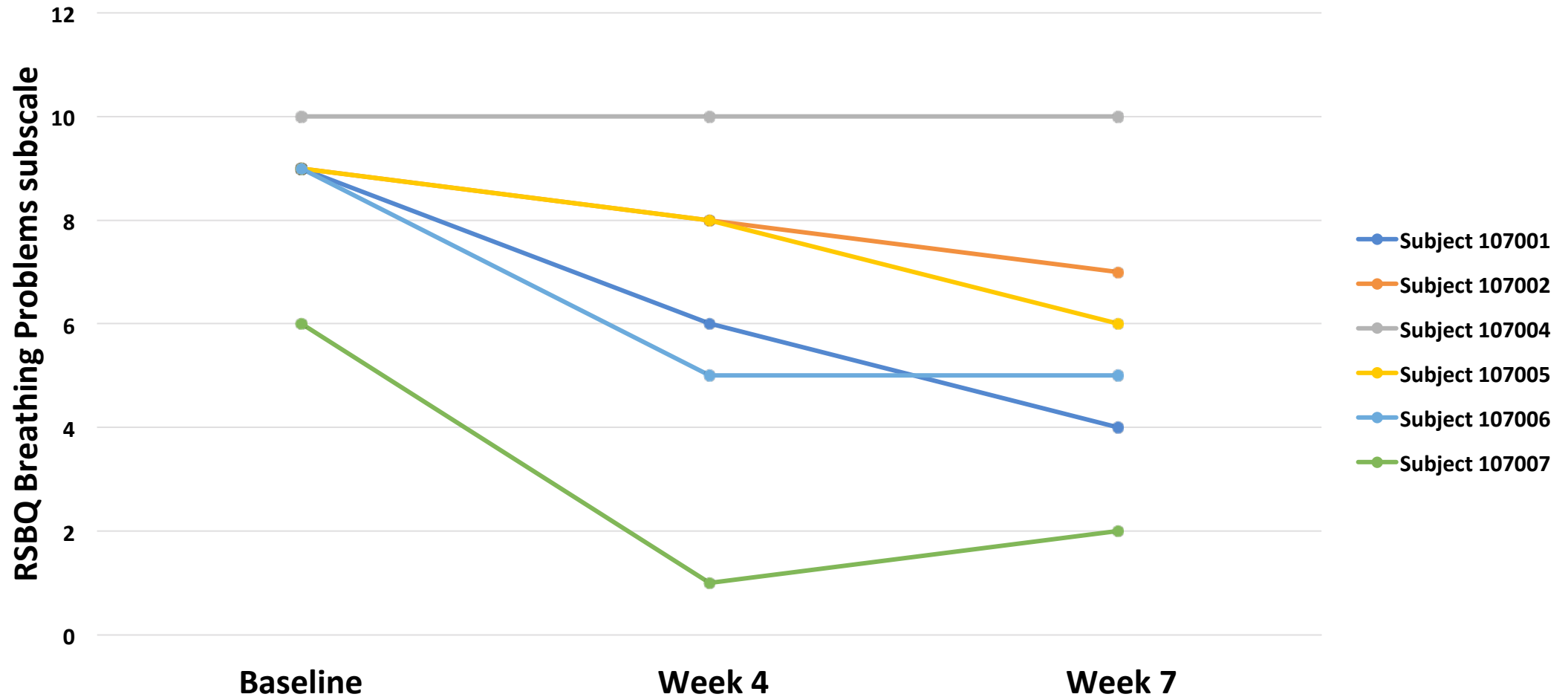
RSBQ Hand Behaviours Trajectory



Wilcoxon Signed Rank Test Week 0 vs. Week 7: $Z = -2.032$, $p = 0.042$

Efficacy: RSBQ Breathing Abnormalities Improved During Trial

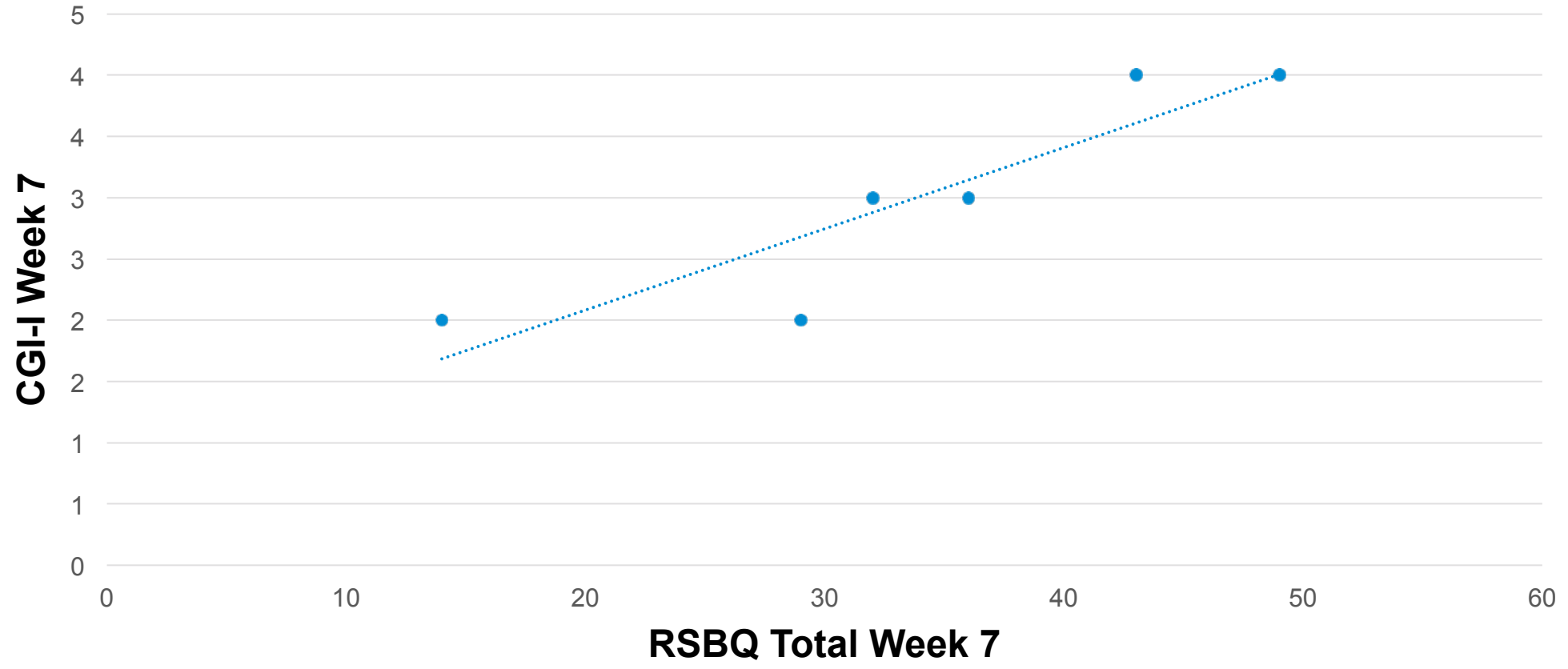
RSBQ Breathing Problems Trajectory



Wilcoxon Signed Rank Test Week 0 vs. Week 7: $Z = -2.032$, $p = 0.042$

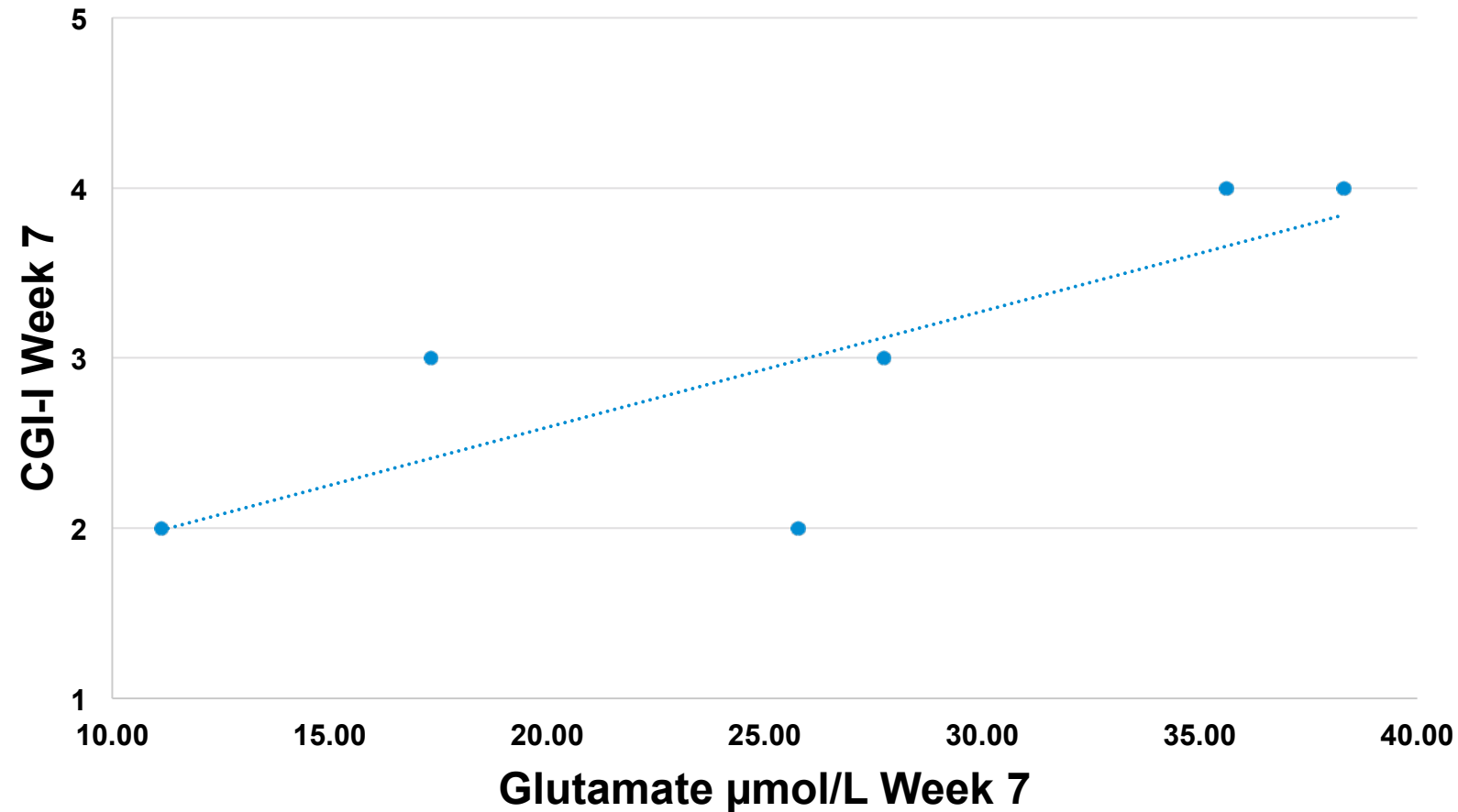
Efficacy: RSBQ & CGI-I Improved During Trial

RSBQ Total & CGI-I Correlated at Week 7



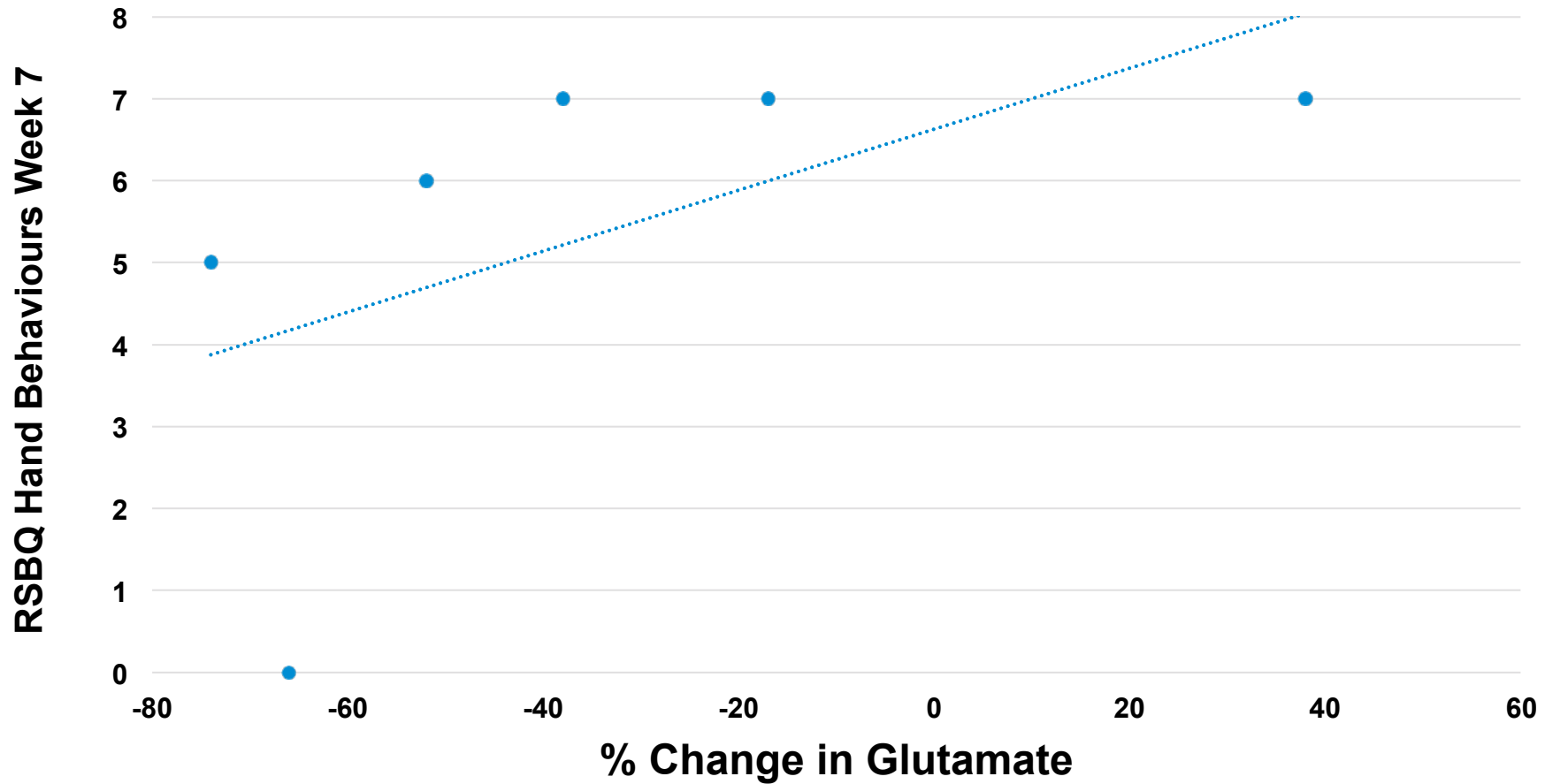
Spearman's rho = 0.956, p = 0.003

Biomarkers: Plasma Glutamate and CGI-I Correlated at Week 7



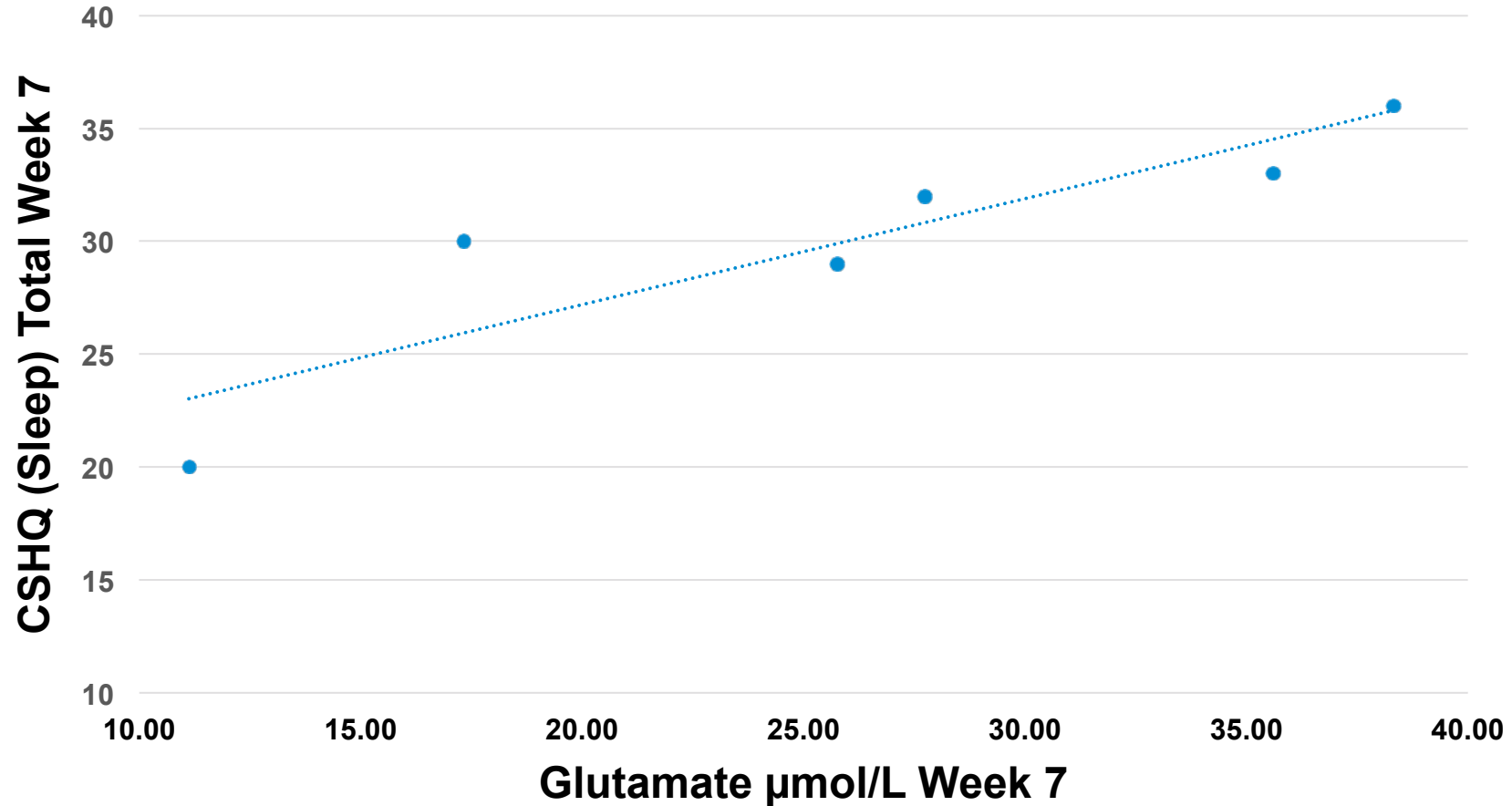
Spearman's rho = 0.837, p = 0.038

Biomarkers: Glutamate Change & RSBQ Hand Behaviours Correlated at Week 7



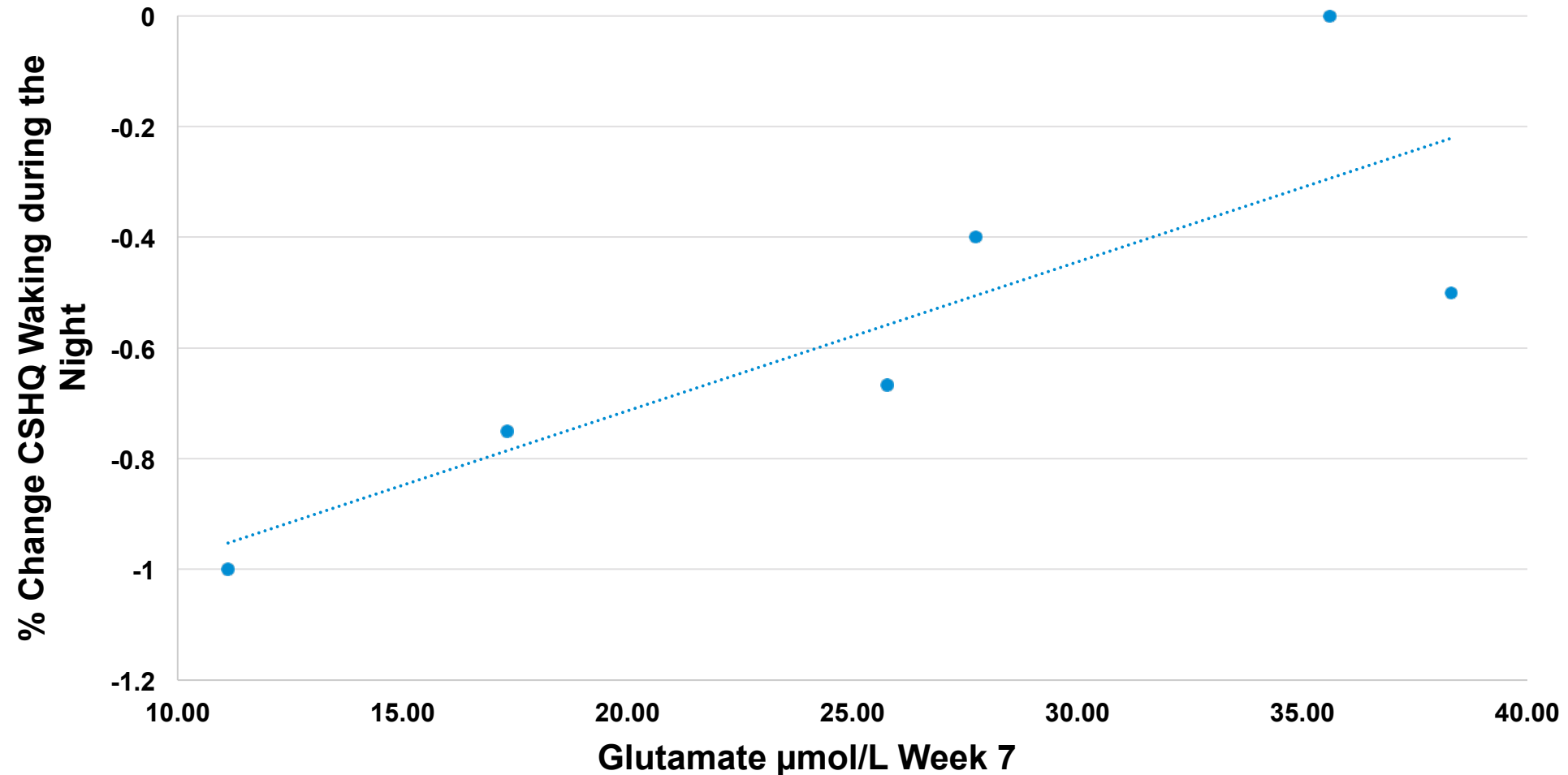
Spearman's rho = 0.880, p = 0.021

Biomarkers: Plasma Glutamate & CSHQ (Sleep) Total Correlated at Week 7



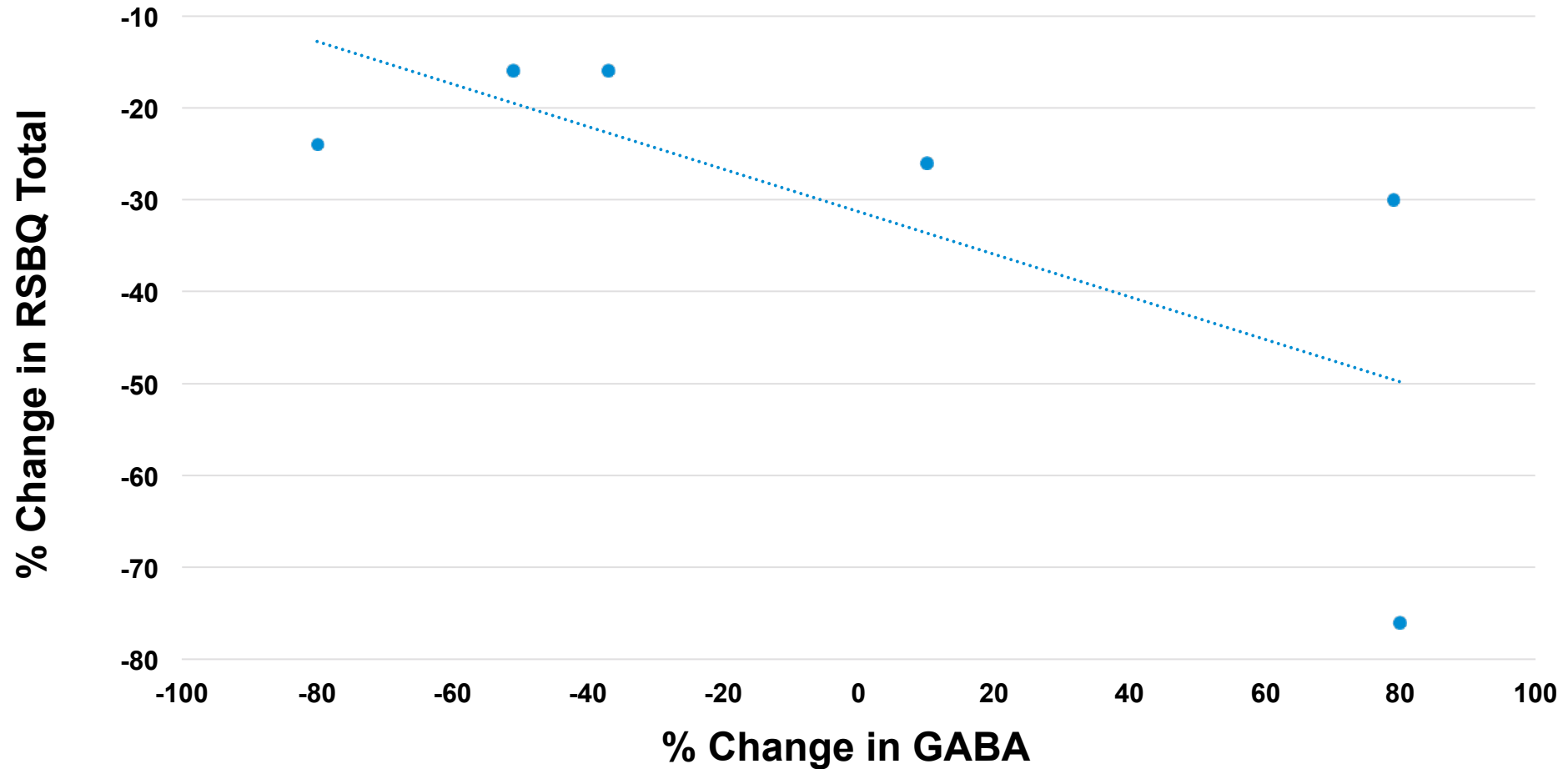
Spearman's rho = 0.943, p = 0.005

Biomarkers: Glutamate & CSHQ Waking during the Night Correlated at Week 7



Spearman's rho = 0.829, p = 0.042

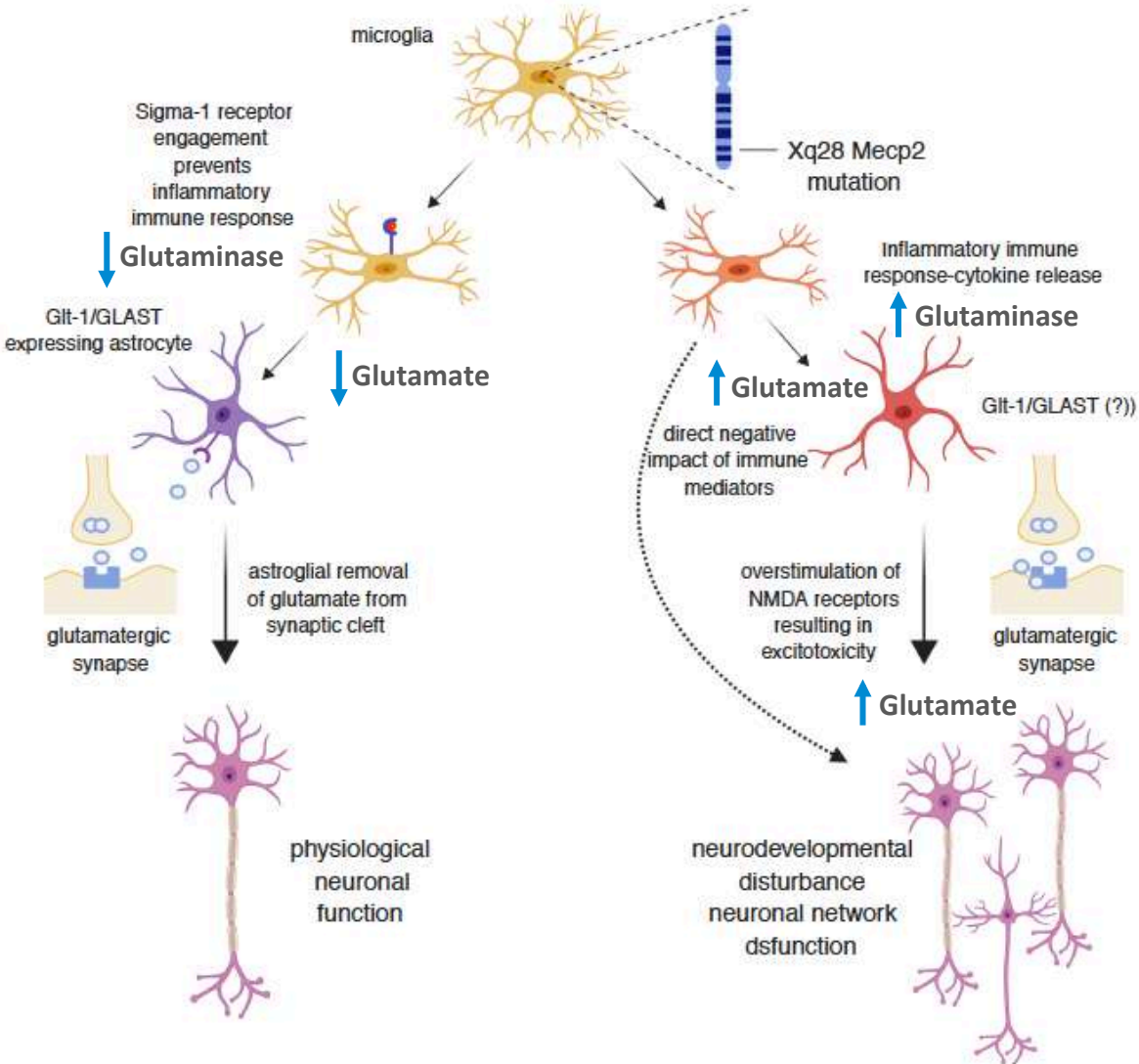
Biomarkers: GABA Change Correlated with RSBQ Total Change



Spearman's rho = -0.812, p = 0.050

Mechanism of Action

ANAVEX[®]2-73 Activation of Sigma-1 Receptor Effects on Neurons & Microglia: Glutamate as Efficacy Biomarker



Conclusions on ANAVEX[®]2-73 in Rett Syndrome

- Despite the small sample size, Preliminary data demonstrates Encouraging Safety and Efficacy Signal on *both* Caregiver- & Clinician-based measures of Severity
- Correlations with Key Biomarker related to disease Pathogenesis
- High Level of Significance: Magnitude of change (**Cohen's d: RSBQ Total 1.47; Cohen's d: Glutamate 1.11**, Large-Very Large Effect Sizes), Short duration of treatment, Older age of participants, and Clinical significance (RSBQ-CGI-I correlations)
- Anavex Rett Syndrome Program consisting of 3 clinical RTT studies including pediatric ongoing (U.S. RTT, AVATAR and EXCELLENCE)

Contact Us

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