ASX ANNOUNCEMENT
1 June 2023

Poster Presentation at the American Society of Clinical Psychopharmacology (ASCP) Annual Meeting

Bionomics Limited (ASX: BNO, Nasdaq: BNOX), ("Bionomics" or the "Company"), a clinical-stage biopharmaceutical company developing novel, allosteric ion channel modulators designed to transform the lives of patients suffering from serious central nervous system ("CNS") disorders with high unmet medical need, presented data on BNC210 for the treatment of Social Anxiety Disorder (SAD) by way of a Poster Presentation, at the 2023 American Society of Clinical Psychopharmacology (ASCP) Annual Meeting on Wednesday, May 31, 2023, 11:15 AM(EDT), in Miami Beach, Florida.

A copy of the Poster Presentation follows and is also available at the Company's website Corporate Presentations | Bionomics Ltd.

Released on authority of the President and CEO of the Company.

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About Bionomics Limited
Bionomics (ASX:BNO, NASDAQ:BNOX) is a clinical-stage biopharmaceutical company developing novel, allosteric ion channel modulators designed to transform the lives of patients suffering from serious CNS disorders with high unmet medical need. Bionomics is advancing its lead drug candidate, BNC210, an oral, proprietary, selective negative allosteric modulator of the α7 nicotinic acetylcholine receptor, for the acute treatment of Social Anxiety Disorder (SAD) and chronic treatment of Post-Traumatic Stress Disorder (PTSD). Beyond BNC210, Bionomics has a strategic partnership with Merck & Co., Inc. (known as MSD outside the United States and Canada) with two drugs in early-stage clinical trials for the treatment of cognitive deficits in Alzheimer's disease and other central nervous system conditions.

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A Phase 2, Double-Blind, Placebo-Controlled Study for BNC210, an Alpha7 Nicotinic Receptor Negative Allosteric Modulator (NAM) for the Acute Treatment of Social Anxiety Disorder (PREVAIL): Top-Line Efficacy and Safety Results

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INTRODUCTION

- Social Anxiety Disorder (SAD) is a chronic, serious and prevalent neuropsychiatric condition characterized by feelings of intense and persistent fear and avoidance of social or performance-related situations. Functional disabilities of SAD are debilitating for patients and left untreated, can lead to worsening over time and life-altering co-morbidities such as depression, substance abuse, and suicidal ideation.
- The National Institute of Mental Health reported the 12-month prevalence of SAD in US adults to be 7.1% (~15 million), with females at 8.0% and males at 6.1% (NIMH 2023).
- Acute therapy of anxiety episodes in patients with SAD is an unmet medical need. Although there are 3 FDA-approved anti-depressants for SAD, they have delayed onset of action not suitable for acute treatment of anxiety exacerbations. Benzodiazepines are off-label, potent, fast-acting anxiolytics but have many serious side effects such as addiction, withdrawal syndrome, sedation, and memory and motor impairment. Off-label beta-blockers treat physical symptoms of SAD without alleviating anxiety.
- BNC210 is a novel, negative allosteric modulator (NAM) of the alpha7 nicotinic acetylcholine receptor (α7nAChR) that has shown anxiolytic activity comparable to benzodiazepines without severe side effects in early-stage clinical studies.
- PREVAIL study was conducted to evaluate acute anxiolytic efficacy induced by a public speaking challenge and safety of BNC210 in patients with moderate to severe SAD.

METHODS

PREVAIL was a multicenter, double-blind, placebo-controlled, single-dose, Phase 2 study.
Key Inclusion Criteria: 18-65 years of age; a current diagnosis of SAD, as defined in the DSM-5; a Liebowitz Social Anxiety Scale (LSAS) total score ≥ 70 at Screening.
Key Exclusion Criteria: history of schizophrenia, bipolar disorder, or psychotic disorders; a current clinically predominant diagnosis of any other Axis I disorder, other than SAD; HAM-D score ≥18; use of psychotropic medications within 30 days of screening.

Public Speaking Challenge: Eligible participants entered a 1-day treatment period and were randomized 1:1:1 to receive a single dose of 225 mg BNC210, 675 mg BNC210 or placebo. Approximately 60 minutes following treatment administration they took part in a public speaking challenge which involved 2-minutes for speech preparation (anticipation phase) and a 5-minute speech in front of a small audience (performance phase). The efficacy measures were the Subjective Units of Distress Scale (SUDS), the State-Trait Anxiety Inventory (STAI State subscale) and the Self-Statements During Public Speaking scale (SSPS), taken pre-dose, pre-challenge, at the anticipation and performance phases of the challenge (at 1-minute intervals for SUDS), and post-challenge, as illustrated in Figure 1.

Figure 1: Schedule of Key Efficacy Assessments

SUDS (primary and secondary measure): standard visual analog scale from 0-100 that measures self-reported intensity of anxiety and/or distress.

STAI-State (secondary measure): self-reported questionnaire with 20 anxiety-related questions marked on a 4-point scale.

SSPS-negative self-statements (secondary measure): self-reported 5-item questionnaire capturing negative cognitions during a public speaking situation. Results showed that this scale did not capture efficacy trends in this setting (no results are presented).

Statistical Methods:

SUDS data were analyzed at 3 different end points; average (primary endpoint was the average of the performance phase), peak, and area-under-the-curve (AUC), in planned and post-hoc analyses as below:

Average: Mean change in SUDS score between baseline and average of the anticipation or performance phase of the challenge separately, or the average of anticipation + performance phases together, for each dose of BNC210 compared to placebo, analysed using Mixed Model for Repeated Measures (MMRM) ± multiple-imputations (MI).

Peak: Mean change in SUDS score between baseline and the peak of the anticipation or performance phase of the challenge separately, or the peak of anticipation + performance phases together, for BNC210 compared to placebo, analysed using MMRM ± MI.

AUC: The difference in the AUC of SUDS scores between BNC210 and placebo for the performance phase using analysis of covariance (ANCOVA) model without MI.

STAI-State and SSPS data were analyzed in planned and post-hoc analyses using mean change in scores between baseline and the end of the anticipation or performance phases of the challenge using MMRM without MI.

RESULTS & DISCUSSION

Figure 2: SUDS scores were analyzed using three different endpoints across the anticipation and performance phases of the public speaking challenge


Anticipation phase is shown in yellow; Performance phase is shown in red; Avg = average; AUC = area-under-the-curve
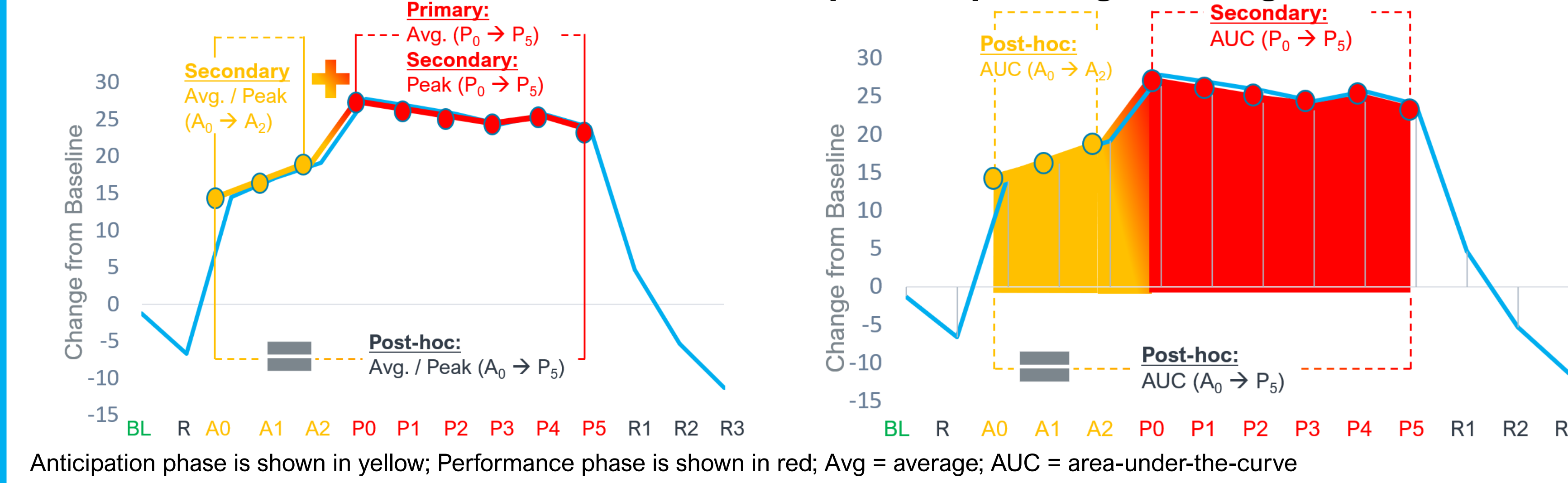
Table 1: Patient Demographics and Baseline Characteristics

	BNC210 225 mg	BNC210 675 mg	BNC210 Overall	Placebo	Overall
SAF/ FAS/Study Completer	50	51	101	50	151
Per-protocol (PP) Population	50	51	101	49	150
Mean Age in Years (Min, Max)	35.5 (18,65)	37.7 (19,65)	36.6 (18,65)	34.5 (21,58)	35.9 (18,65)
Male/Female (%Female)	17/33 (66.0)	16/35 (68.6)	33/68 (67.3)	23/27 (54.0)	56/95 (62.9)
Mean LSAS Score (SD)	98.7 (15.75)	98.3 (16.98)	98.5 (16.30)	95.3 (16.34)	97.4 (16.33)
Mean SUDS (SD)	40.3 (18.53)	37.9 (22.98)	39.1 (20.83)	32.9 (21.26)	37.0 (21.10)

SAF: Safety Population - all participants who received any amount of the study intervention
FAS: Full Analysis Set - all randomized participants who received any amount of the study intervention
PP: Per-protocol Population – participants in the FAS population who had no major protocol deviations (1 participant was removed for prior participation in a study that involved a public speaking challenge)
LSAS = Liebowitz Social Anxiety Scale at screening; SUDS = Subjective Units of Distress score at baseline (pre-dose); SD = standard deviation
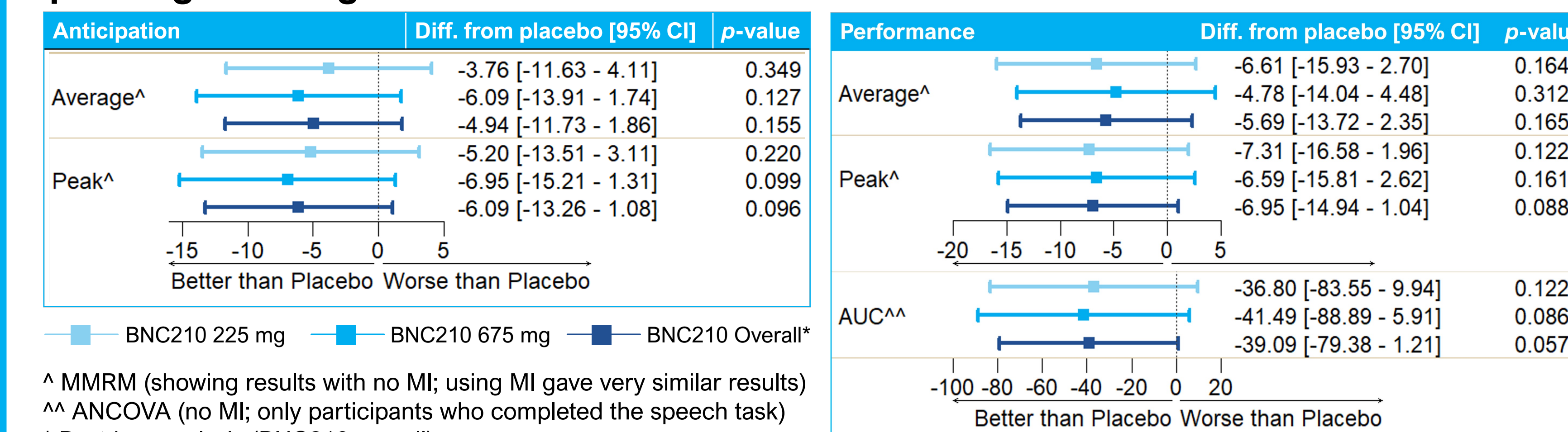
Subjective Units of Distress (SUDS)

Figure 3: Mean observed SUDS scores plotted as change from baseline demonstrating efficacy of BNC210 over the course of the public speaking challenge
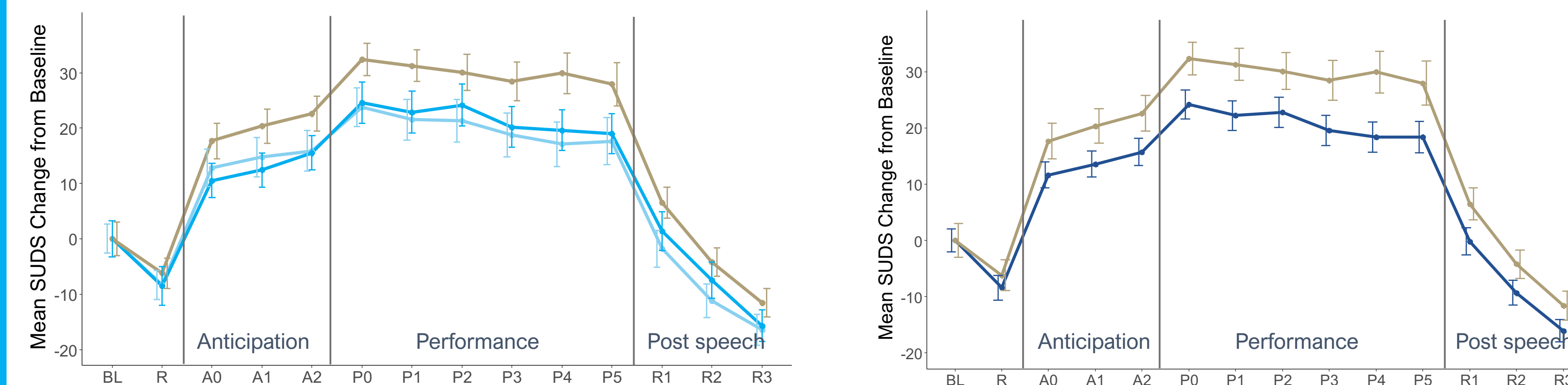

- Participants in both BNC210 groups showed reduced increases in anxiety throughout the public speaking challenge compared to participants on placebo.
- Both BNC210 groups achieved similar efficacy responses, allowing for combination of both active arms in post-hoc analyses (increasing the power of analysis).

Figure 4: SUDS Least Squares (LS) mean differences from placebo demonstrated trends for improvement during both the anticipation and performance phases of the speaking challenge

^ MMRM (showing results with no MI; using MI gave very similar results)
^^ ANCOVA (no MI; only participants who completed the speech task)
* Post-hoc analysis (BNC210 overall)

- The planned primary and secondary analyses for average, peak and AUC endpoints demonstrated consistent improvements compared to placebo for both BNC210 dose groups, although the results did not meet the pre-specified statistical threshold of p≤0.05.
- When the BNC210 dose groups were combined for increased powering in post-hoc analyses, trends for improvement (p<0.1) were observed in the peak and AUC endpoints for both phases of the challenge.
- Analysis by gender showed improvements (reduced increases in anxiety) in both female and male participants but without statistically significant differences from placebo.

Figure 5: SUDS LS Mean differences from placebo demonstrated significant improvement for BNC210 when combining the anticipation and performance phases
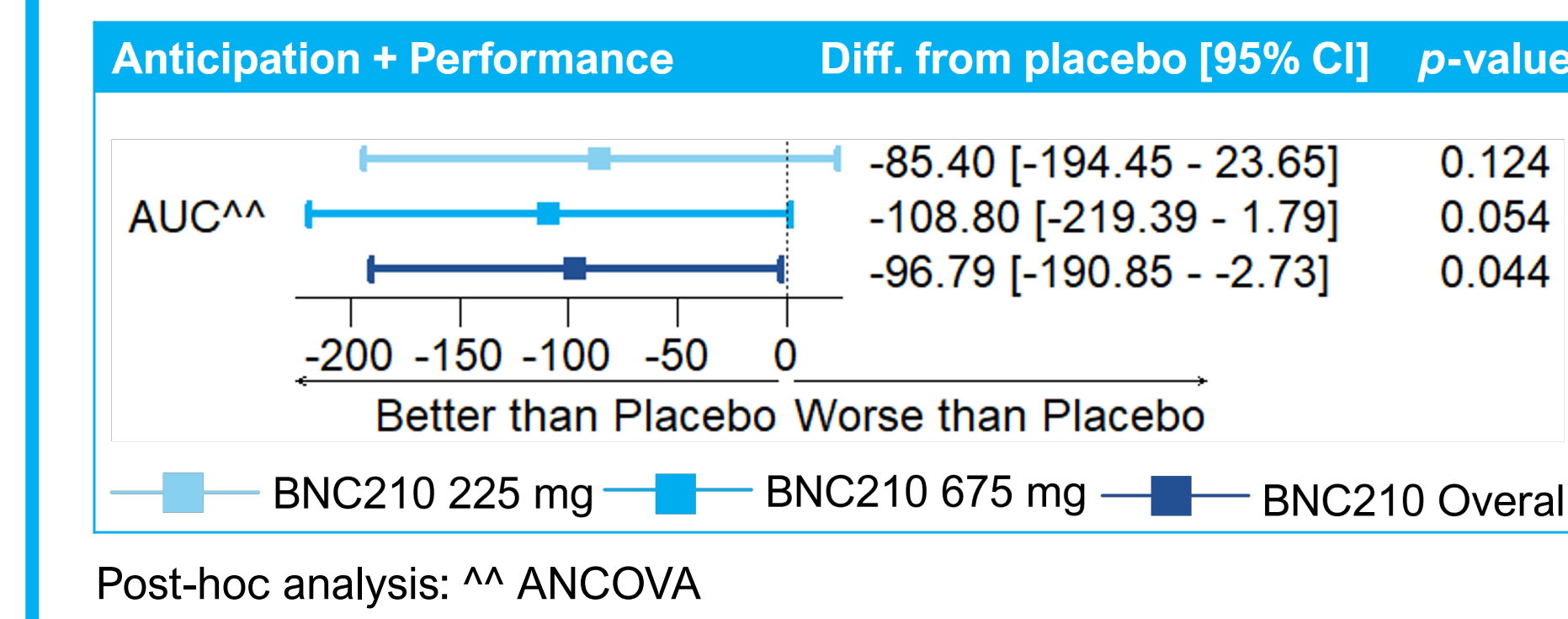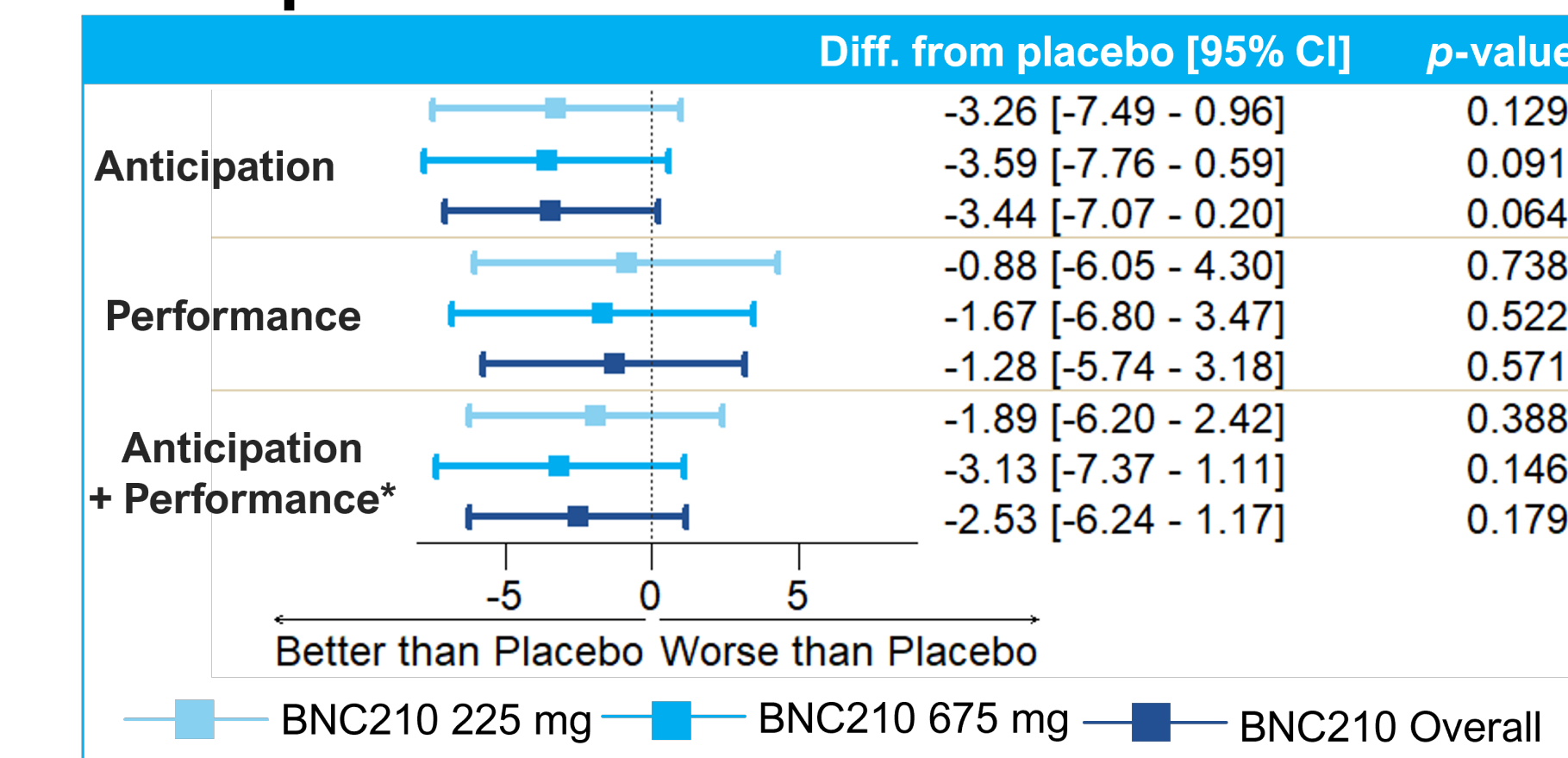

Post-hoc analysis: ^^ ANCOVA

- Anxiety is not limited to performance of a task but starts with the thought or prospect of an anxiety-inducing situation, and thus, combining the anticipation and performance phases for analysis represents a clinically-relevant outcome.

State-Trait Anxiety Inventory (STAI-State)

Figure 6: STAI-State LS mean differences from placebo demonstrated trends in favor of BNC210 during anticipation and performance phases

* Post-hoc analysis: MMRM

- STAI-State analyses showed reduced increases in anxiety, in the anticipation phase of the public speaking challenge, for both doses of BNC210 compared to placebo, consistent with the SUDS results.

Safety and Tolerability

BNC210 exhibited a highly favorable safety profile:
- 21 (out of 151) participants reported treatment-emergent adverse events (AE)
- The majority of AEs were reported as mild (for 17 out of the 21 participants)
- 4 moderate AEs 2x headache, dizziness, somnolence
- There were no severe AEs reported and no serious adverse events (SAEs)

Table 2: Treatment-Emergent Adverse Event Summary

Number of Participants	BNC210 225 mg	BNC210 675 mg	Placebo	Overall
With at Least 1 Adverse Event (%)	7 (14.0)	11 (21.6)	3 (6.0)	21 (13.9)
By Relationship to Study Drug				
Possibly/Probably/Definitely (%)	3/3/0 (6.0/6.0/0)	2/7/0 (3.9/13.7/0)	0/2/0 (0/4.9/0)	5/12/0 (3.3/7.9/0)
By Severity				
Mild/Moderate/Severe (%)	5/2/0 (10.0/4.0/0)	9/2/0 (17.6/3.9/0)	3/0/0 (6.0/0/0)	17/4/0 (11.3/2.6/0)
Serious Adverse Event	0	0	0	0
System Organ Class and Preferred Term (>1 event reported)	BNC210 225 mg	BNC210 675 mg	Placebo	Overall
Nervous System Disorders				
Somnolence (%)	2 (4.0)	6 (11.8)	2 (4.0)	10 (6.6)
Headache (%)	3 (6.0)	2 (3.9)	1 (2.0)	6 (4.0)
Dizziness (%)	1 (2.0)	3 (5.9)	0 (0)	4 (2.6)
Gastrointestinal disorders				
Abdominal pain upper (%)	0 (0)	2 (3.9)	0 (0)	2 (1.3)

CONCLUSIONS

- BNC210 225 mg and 675 mg demonstrated reduced anxiety (on SUDS and STAI-State) during the anticipation and performance phases of a public speaking challenge compared to placebo, with consistent trends for improvement in analysis of the phases separately.
- Significant effects were measured when combining the two high anxiety phases, both of which are highly relevant to the clinical experience of SAD patients.
- BNC210 was well tolerated at both doses, consistent with its overall safety profile from 13 clinical trials.
- The PREVAIL Study (NCT05193409) revealed BNC210's potential as a non-sedating anxiolytic for the acute treatment of SAD. Phase 3 trials are being planned.

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Reference: https://www.nimh.nih.gov/health/statistics/social-anxiety-disorder