ATTUNE Phase 2b Study Full Dataset Results

March 2024

Developing treatments for patients with underserved CNS disorders

Safe Harbor Statement

Factors Affecting Future Performance

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Bionomics is an Advanced Clinical Stage CNS-focused Biotech Company with Multiple Value-Creating Milestones

Leading expertise in ion channel targeting, advancing a pipeline of best-in class allosteric modulators

BNC210	**Ph3-ready α7 nicotinic receptor negative allosteric modulator with unique non-sedating, non-habit-forming psychoactive profile suitable for acute and chronic dosing in multiple CNS indications**
PTSD and Social Anxiety Disorder	• No new treatment for decades • Significant socioeconomic impact • Blockbuster potential
Alzheimer's Disease and Schizophrenia	Clinical Stage partnership with Merck on α7 PAM valued ~500M in regulatory and clinical milestones

2024-2026
Milestone Rich Development Plan

Q1-Q2 2024

Initiation of SAD Ph3

Q2-Q3 2024

FDA PTSD breakthrough designation decision

FDA PTSD Meeting

Q4 2024

Initiation of late-stage PTSD study

2025-2026

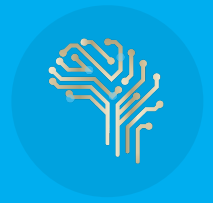
SAD Ph3 readout

Potential Merck Ph2 milestone

PTSD late-stage trial readout

EoP2 = end of Phase 2; FDA = U.S. Food and Drug Administration; NAM = Negative Allosteric Modulator; PAM = Positive Allosteric Modulator, PTSD = post-traumatic stress disorder; SAD = social anxiety disorder.

BNC210: Best- and First-in-Class α7 Nicotinic Receptor Small Molecule Negative Allosteric Modulator in Development for the Treatment of Neuropsychiatric Disorders



Unique and differentiated MoA with high confidence in rationale and probabilities of success

Rapid and durable anxiety relief with acute administration
(~60 min onset, half-life 4-5 hrs)
Chronic administration for PTSD and other indications

Non-sedating, non-habit forming, not cognition impairing*

Clinically Meaningful Effects

Reduction of PTSD symptom severity - treatment effects higher than SSRIs

Reduction of anxiety in Panic Attacks, GAD & SAD - benzodiazepine-like without the side effects

*Profile based on a safety database of ~600 subjects.
GAD = General Anxiety Disorder; MOA = Mechanism of Action; NAM = Negative Allosteric Modulator; SAD: Social Anxiety Disorder; PTSD = Post-Traumatic Stress Disorder; SSRIs = Serotonin Selective Reuptake Inhibitors.

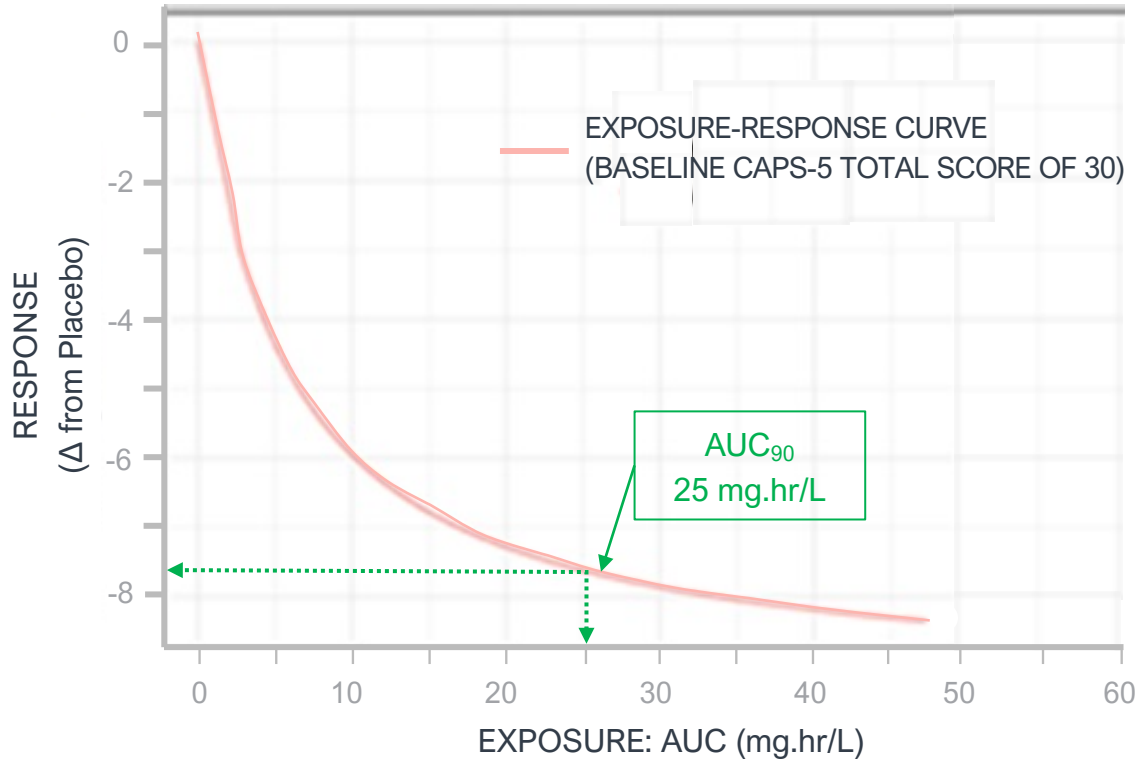
Target Exposure and Dose for ATTUNE was Determined by Model-Based Analysis of Previous Datasets

Pharmacometric (PMX) Analysis Target Exposure

PMX modelling on prior Phase 2 PTSD trial identified 25 mg.hr/L blood exposure target

Pharmacometric analysis identified a statistically significant exposure-response relationship for the CAPS-5 Total score (p value <0.01)

AUC Values (plasma exposure) = **CAPS-5 Score** (PTSD symptoms)

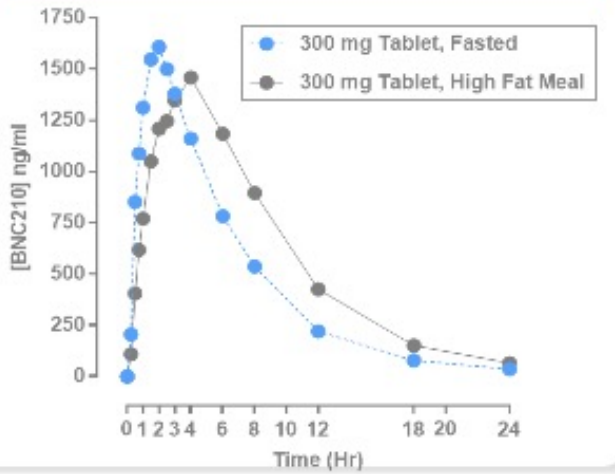


7-Day Pharmacokinetic study of BNC210 tablet formulation mean AUC (mg.hr/L) ± standard deviation

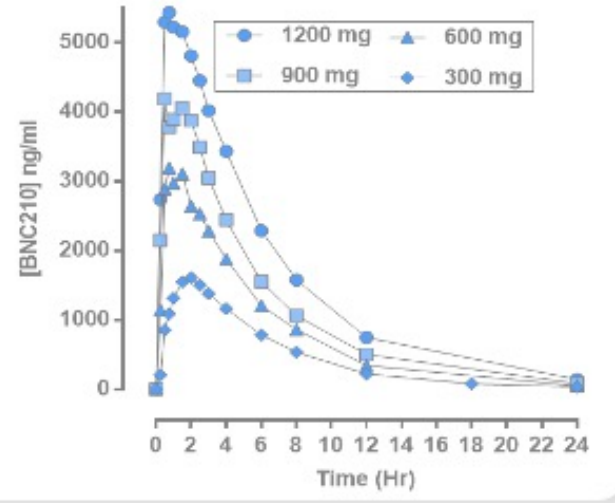
AUC = Area under the curve
PMX = Pharmacometric modelling
CAPS-5 = Clinician-Administered PTSD Scale for DSM-5

The BNC210 Proprietary Solid Tablet Formulation Used in ATTUNE was Developed with PK properties to Deliver Optimal Exposures for Out-Patient Studies

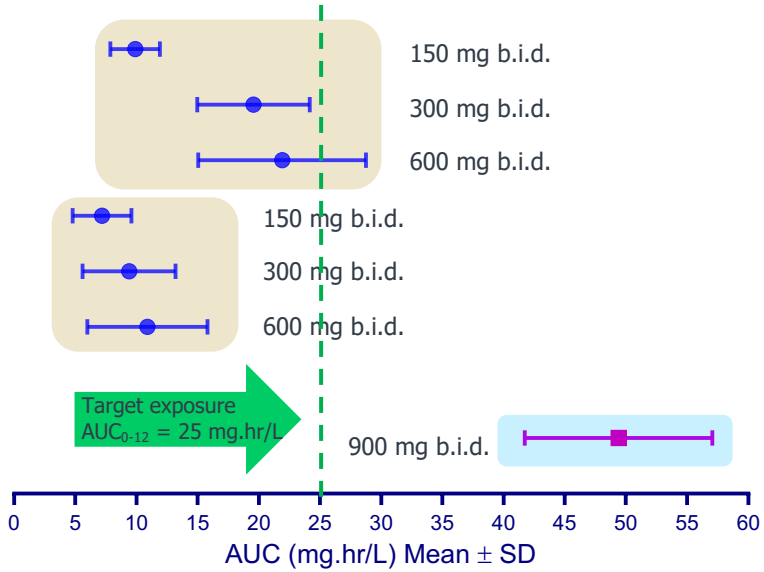
1 Tablet ***alleviates food effect***



2 Tablet has ***dose linear exposure***



3 ***Tablet exceeds target plasma exposure for future PTSD study***



A. Phase 1 8-day multiple ascending dose study **(in-clinic)**

B. Phase 2 12-week PTSD study RESTORE **(out-patient)**

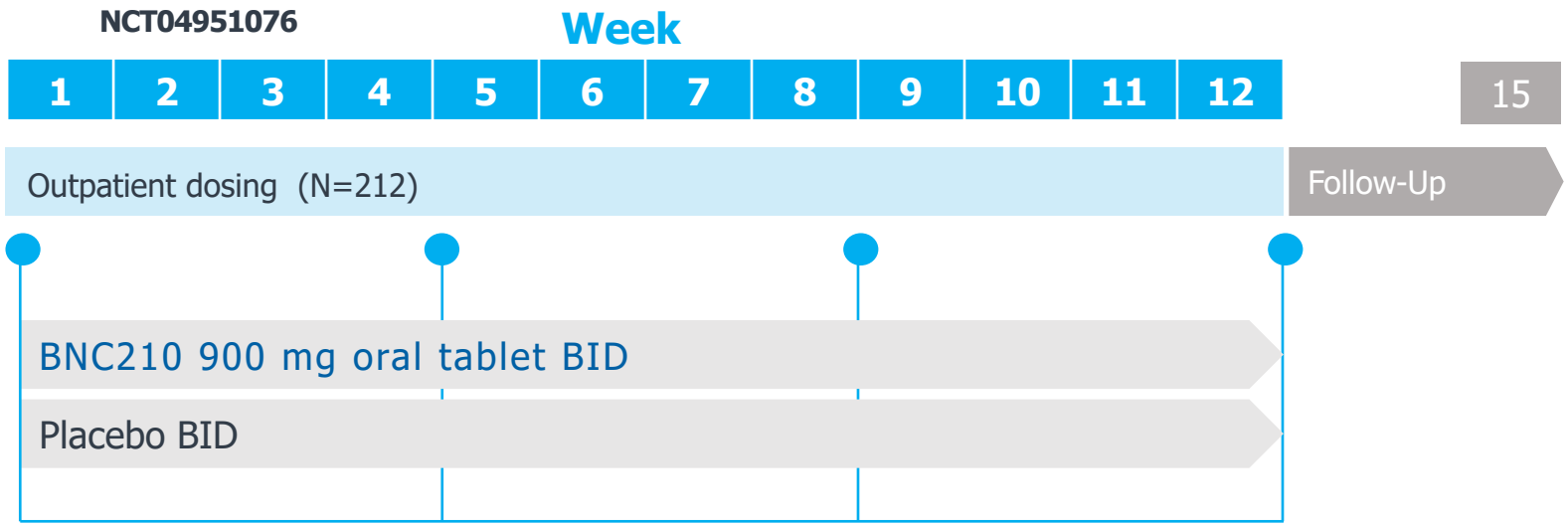
C. Phase 1 7-day multiple dosing study **(in-clinic)**

BNC210 plasma exposures: (A) and (B) **liquid suspension** formulation; (C) **tablet** formulation

- ✓ **Overcomes food effect** of the prior liquid suspension formulation
- ✓ **900 mg BID delivered ~x2 of the target exposure** and was selected as a ”no-regrets” high dose for ATTUNE Ph2b study
- ✓ **Dose linear PK parameters**
- ✓ **IP coverage** extends to ~2040’s with novel formulation

ATTUNE was Robustly Designed as Monotherapy Phase 2b Study of BNC210 in PTSD Patients

Robustly designed study based on FDA feedback, completed on-time and on-budget



Primary Endpoint

CAPS-5 Total Symptom Severity Scores in change from Baseline to Week 12 compared to placebo

Secondary Endpoints

Change from Baseline to Week 12 compared to placebo in:

- Depression (MADRS)
- Sleep (ISI)
- CAPS-5 symptom clusters
- Anxiety (HAM-A), CGI/PGI, Disability (SDS)
- Safety & tolerability endpoints

ATTUNE Study
NCT04951076

Phase 2b Study

Key Inclusion Criteria

Females and males (18 – 75 years)

Current PTSD diagnosis

CAPS-5 ≥ 30 (Screening & Baseline) & ≤ 25% decrease Screening to Baseline

Index trauma event must have occurred in adulthood

Key Exclusion Criteria

Complex PTSD

MADRS score ≥35

No antidepressants, benzodiazepines, other psychotropics

No prior history of significant psychiatric or neurological condition

Moderate or severe substance use disorder in the last 12 months

34 Sites across the US and UK

CGI-S/I = Clinical Global Impression – Severity/Improvement Scales; CAPS-5 = Clinician Administered PTSD Scale for DSM-5; HAM-A = Hamilton Anxiety rating Scale; ISI = Insomnia Severity Index; MADRS = Montgomery-Asberg Depression Rating Scale; PCL-5 = PTSD Checklist for DSM-5; PGI-S/I = Patient Global Impression – Severity/Improvement Scales; SDS = Sheehan Disability Scale

Subject Disposition and Well-Balanced Demographics

Dataset enabled robust data analysis and interpretation

Disposition	BNC210 900 mg	Placebo	Overall
Randomized Population	106	106	212
Safety Population*	105	104	209
Efficacy Population**	89	93	182
Completed Through to End of Treatment	57	66	123
Discontinued Study Early	48	38	86

Demographics - Randomized	BNC210 900 mg	Placebo	Overall
Age (years) - Mean (min, max)	42.3 (19, 67)	42.4 (21, 68)	42.3 (19, 68)
Male / Female	41 / 65	35 / 71	76 / 136
CAPS-5 Total Severity Score at Baseline – Mean (min, max)	41.9 (30, 57)	41.2 (30, 59)	41.5 (30, 59)

* Safety population includes all participants who receive any amount of the study intervention.
** Includes all randomized participants who receive any amount of study drug and have at least one post-baseline primary efficacy assessment (CAPS-5).

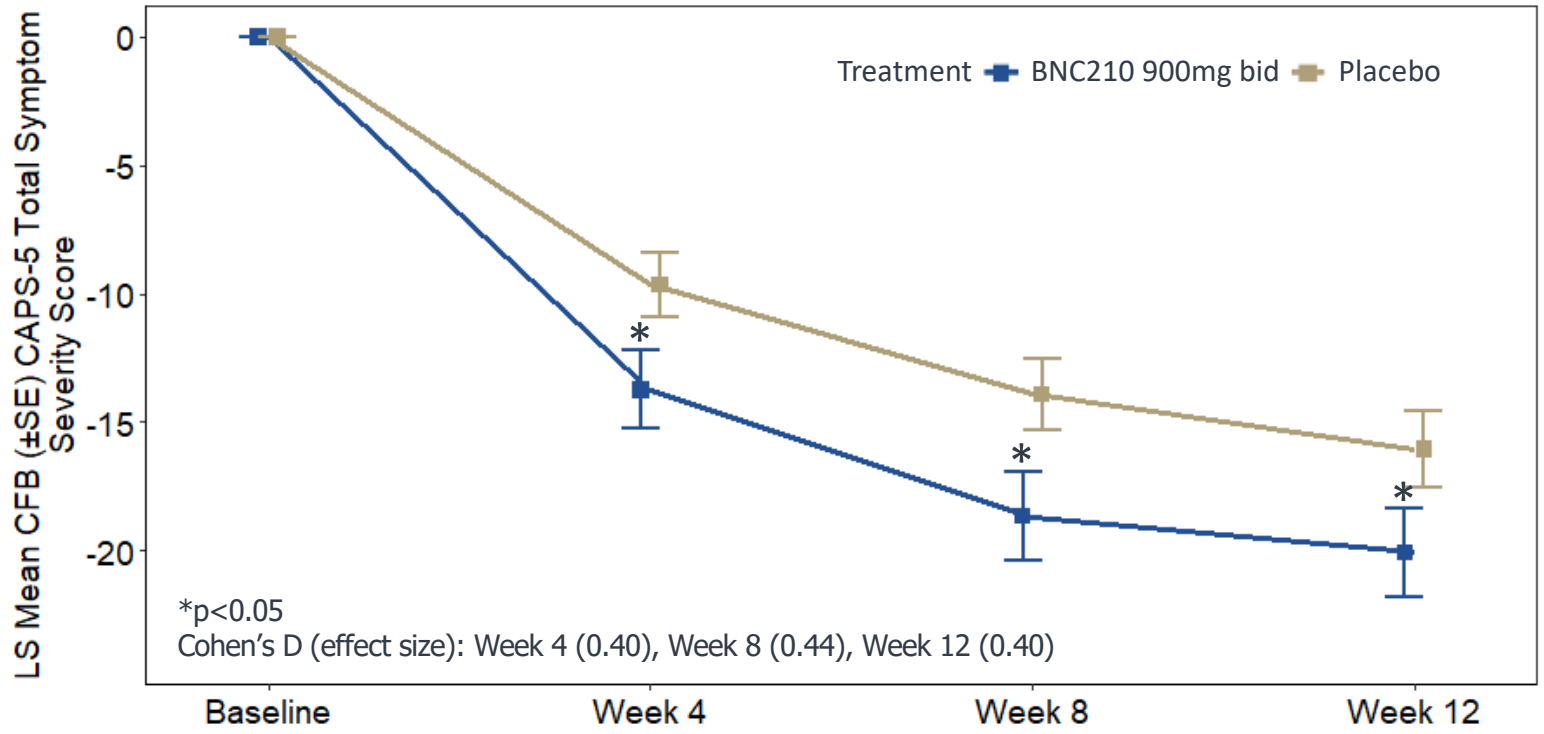
ATTUNE Enrolled Patients with a Wide Range of Index Trauma Type

Index Trauma Event	BNC210 900 mg	Placebo	Overall
Physical assault	23	19	42
Sexual assault	17	21	38
Sudden violent death	9	13	22
Assault with a weapon	10	10	20
Combat or exposure to a war zone	10	6	16
Transportation accident	10	6	16
Life-threatening illness or injury	7	5	12
Sudden accidental death	7	4	11
Captivity	3	3	6
Fire or explosion	1	4	5
Serious injury, harm, or death you caused to someone else	0	4	4
Serious accident at work, home, or during recreational activity	0	3	3
Severe human suffering	0	2	2
Other unwanted or uncomfortable sexual experience	1	1	2
Any other very stressful event or experience	8	5	13

BNC210 Significantly Reduced PTSD Symptoms During 12 Weeks of Treatment

Clinically meaningful treatment effects/effect sizes, higher than approved treatments

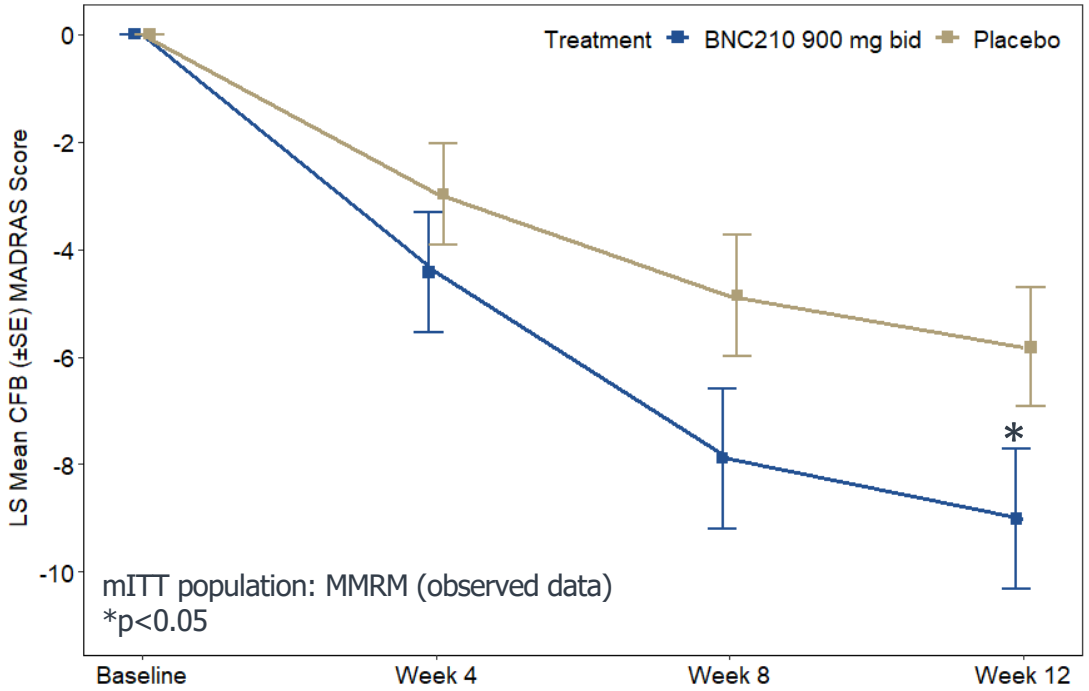
Change from Baseline in CAPS-5 Total Symptom Severity Scores



CAPS-5	Baseline	Week 4	Week 8	Week 12
n (BNC210/Placebo)	89/93	83/90	69/77	58/68
LS Mean difference from placebo		-4.11	-4.74	-4.03

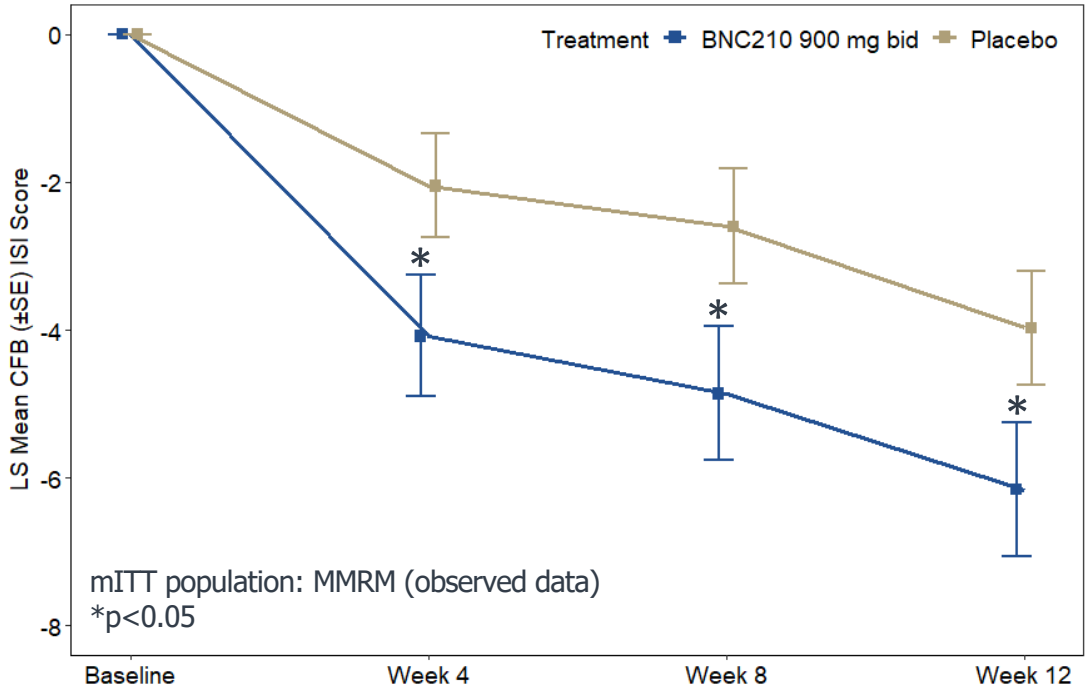
BNC210 Treatment Resulted in Improvements in Both Depression and Sleep in patients with PTSD

Montgomery-Asberg Depression Rating Scale



MADRS	Baseline	Week 4	Week 8	Week 12
n (BNC210/Placebo)	89/93	83/90	69/77	58/68
LS Mean difference from placebo		-1.46	-3.03	-3.19

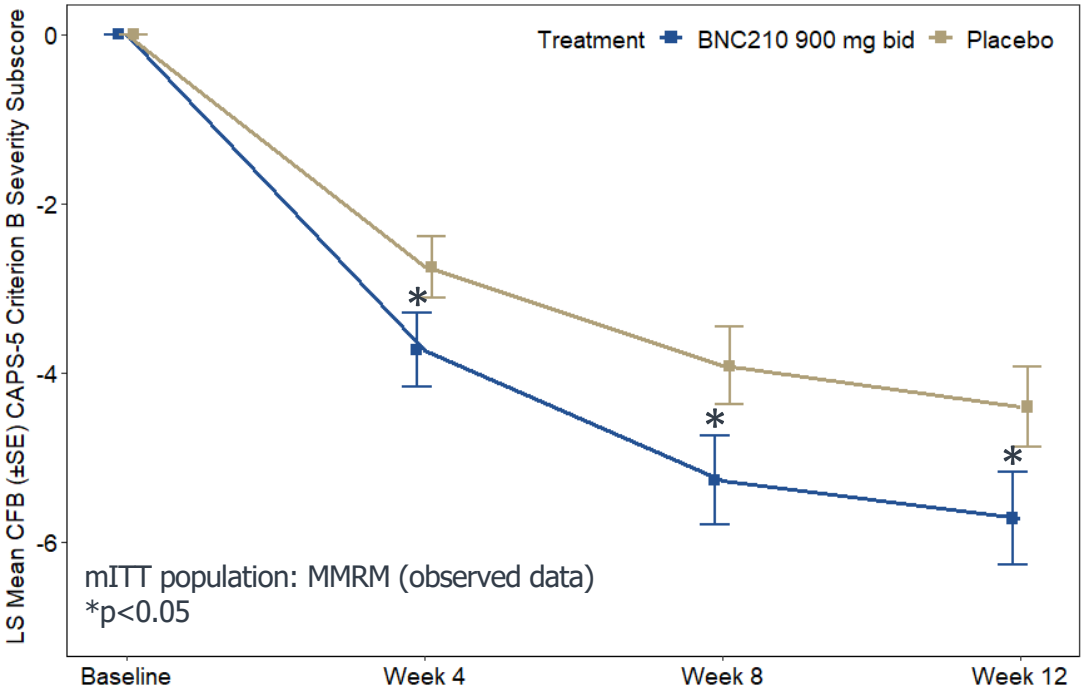
Insomnia Severity Scale



ISI	Baseline	Week 4	Week 8	Week 12
n (BNC210/Placebo)	89/93	83/90	69/77	58/68
LS Mean difference from placebo		-2.03	-2.27	-2.19

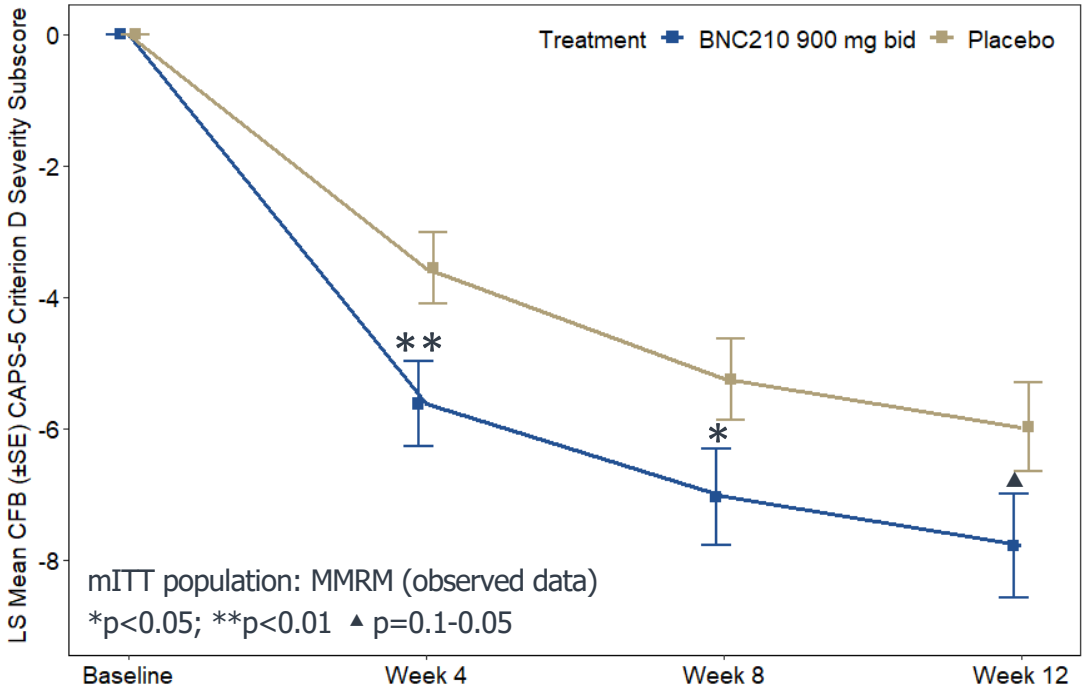
BNC210 Resulted in Improvements to Intrusive Thoughts, Mood and Cognition:
These symptoms are considered the most difficult to treat in PTSD

Criterion B: Intrusion



CAPS-5 Criterion B	Baseline	Week 4	Week 8	Week 12
N (BNC210/Placebo)	89/93	83/90	69/77	58/68
LS Mean difference from placebo		-0.98	-1.35	-1.33

Criterion D: Negative Alterations in Cognitions and Mood



CAPS-5 Criterion D	Baseline	Week 4	Week 8	Week 12
N (BNC210/Placebo)	89/93	83/90	69/77	58/68
LS Mean difference from placebo		-2.05	-1.79	-1.79

Efficacy of BNC210 in the ATTUNE Phase 2b Study: Primary and several secondary endpoints met

		No. subjects (BNC210/Placebo); LS Mean difference from placebo			
		Week 4	Week 8	Week 12	Endpoint
CAPS-5	Total score at each timepoint	83/90; -4.11* 83/90; -4.37 **	69/77; -4.74 * 69/77; -4.92 *	58/68; -4.03 * 58/68; -4.19 *	Primary (mITT) Primary (ITT) – Post-hoc
	Total score over 12 weeks			83/90; -4.35 *	Post-hoc
	Intrusion subscore	83/90; -0.98 *	69/77; -1.35 *	58/68; -1.33 *	Secondary
	Negative cognitions & mood subscore	83/90; -2.05 **	69/77; -1.79 *	58/68; -1.79 ^	Secondary
CGI-S		83/90; -0.14	69/77; -0.39 *	57/68; -0.23	Secondary
SDS		81/87; -2.15 ^	69/77; -2.00 ^	58/68; -1.38	Secondary
MADRS		83/90; -1.46	69/77; -3.03 ^	58/68; -3.19 *	Secondary
ISI		83/90; -2.03 *	69/77; -2.27 *	58/68; -2.19 *	Secondary
PGI-S		82/90; -0.23	69/77; -0.33 ^	57/67; -0.37 ^	Secondary

**p<0.01; *p<0.05; ^p=0.05-0.10

BNC210 Showed a Favorable Safety Profile for Chronic Dosing

Number of Subjects	BNC210 900 mg	Placebo	Overall
With at Least 1 TEAE	70 (66.7%)	56 (53.8%)	126 (60.3%)
Related/Not Related	55 (52.4%)/15 (14.3%)	34 (32.7%)/22 (21.1%)	89 (42.6%)/37 (17.7%)
Mild/Moderate/Severe	24.8%/37.1%/4.8%	21.2%/26.9%/5.8%	23.0%/32.1%/5.3%
SAEs Related/Not Related	0/0	0/2 (1.9%)	0/2 (1.0%)
Leading to Discontinuation	21 (20.0%)	10 (9.6%)	31 (14.8%)

Frequently reported adverse events (reported by ≥5% of subjects in either group):

Number of Subjects	BNC210 900 mg	Placebo	Overall
Nervous System Disorders: Headache	18 (17.1%)	13 (12.5%)	31 (14.8%)
Gastrointestinal Disorders: Nausea	13 (12.4%)	8 (7.7%)	21 (10.0%)
General Disorder: Fatigue	6 (5.7%)	8 (7.7%)	14 (6.7%)
Investigations: Elevated liver enzyme(s)*	14 (13.3%)	2 (1.9%)	16 (7.7%)
Subjects completed study treatment	9 (8.5%)	0	9 (4.3%)
Subjects discontinued due to liver enzyme elevation	5 (4.8%)	2 (1.9%) Both >4x ALT and >10x AST elevations	7 (3.3%)

Vital signs, physical examinations and ECG – no clinically significant results.
Clinical chemistry, hematology, urinalysis - no clinically significant results deemed related to study drug, apart from the elevated liver enzyme(s)
* No liver findings in the preclinical program or in 13 other clinical trials during administration with BNC210.

Reasons for Treatment Discontinuation: Leading Causes were Treatment Emergent Adverse Events, Subject Withdrawals and Lost to Follow-Up

Variable Category	BNC210 900 mg (N=106)	Placebo (N=106)	Overall (N=212)
Reason for Early Termination			
Subject withdrawal of consent	8 (7.5%)	13 (12.3%)	21 (9.9%)
Sponsor requests participant to be withdrawn	1 (0.9%)	1 (0.9%)	2 (0.9%)
Request of primary care physician or investigator	1 (0.9%)	0	1 (0.5%)
Non-compliance	3 (2.8%)	4 (3.8%)	7 (3.3%)
Protocol violation	1 (0.9%)	1 (0.9%)	2 (0.9%)
Lost to follow-up	13 (12.3%)	9 (8.5%)	22 (10.4%)
Adverse event	21 (19.8%)	10 (9.4%)	31 (14.6%)
Death	0	0	0
Pregnancy	0	0	0
Other	0	0	0

Adverse Events Leading to Discontinuations

Other than LFTs no other system organ category (SOC) AE clusters of note were identified

BNC210 900 BID

Adverse Event	Dosing Duration (Days)	Study Duration (Days) - Randomization to EOS
Dry Mouth	41	71
Discomfort	2	28
Paraesthesia	1	11
Tachycardia and paraesthesia	4	16
Headache	1	5
Diplopia	16	28
Swelling face and Dysguesia	8	10
Headache	8	20
Suicidal Ideation	46	46
Suicidal Ideation	19	23
Hepatic Enzyme Increased	59	59
Nausea	6	36
Chromaturia	8	62
AST and ALT Increased	45	76
Nausea and Vomiting	5	9
Hepatic Enzyme Increased	44	46
Rash, Abdominal Discomfort, and Headache	28	50
Diarrhoea	4	13
Hypersensitivity	12	30
Abdominal Pain and Liver Function Test	23	42
Lethargy and Pollakiuria	49	57

Placebo

Adverse Event	Dosing Duration (Days)	Study Duration (Days) - Randomization to EOS
Constipation	3	29
Dizziness and Fatigue	32	65
Fatigue and Anxiety	16	30
Cholelithiasis	55	70
Nausea and Derealisation	8	29
Liver Function Test Increased	58	64
Hepatic Enzyme Increased	59	63
Nausea	21	44
Blood Urine Present	11	41
Libido Decreased and Depression	57	58

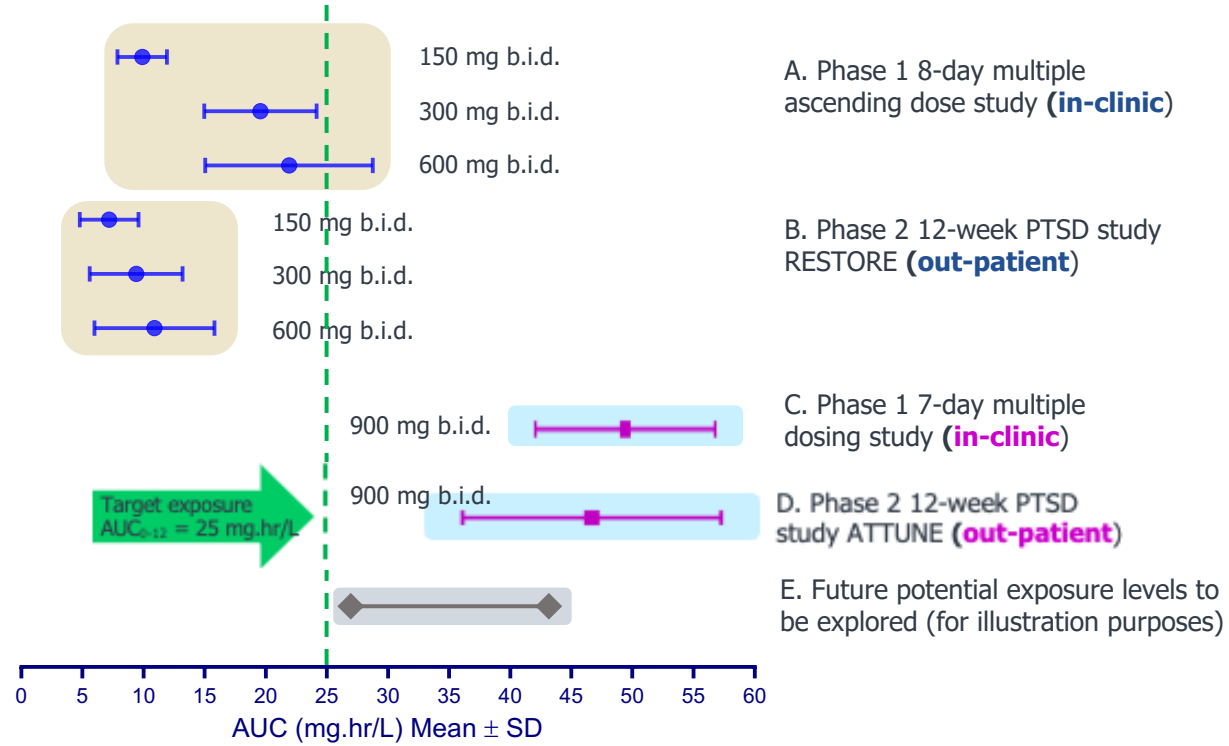
Overall Safety Summary: In ATTUNE BNC210 Continues to Demonstrate a Favorable Safety Profile for a Psychoactive Experimental Therapeutic

- No SAEs on BNC210
- Most AEs mild to moderate
- No excess of psychiatric adverse event reporting compared to placebo, differentiating BNC210 from most other psychotherapeutics used in treatment of PTSD
- Abnormal liver enzyme test results were reported leading to 5 discontinuations with BNC210 and 2 on placebo:
  - Findings were not associated with hepatic functional impairment (i.e., no liver injury, decompensation, no Hy's Law, no bilirubin level elevations)
  - No LFT elevations during dosing administration in previous studies and no liver signals in preclinical program
- There were no other system organ category (SOC) AE clusters or laboratory findings of note

BNC210 solid tablet formulation used in ATTUNE Ph2b Study Achieved ~2x the Predicted/Modeled Exposures for Efficacy Response.

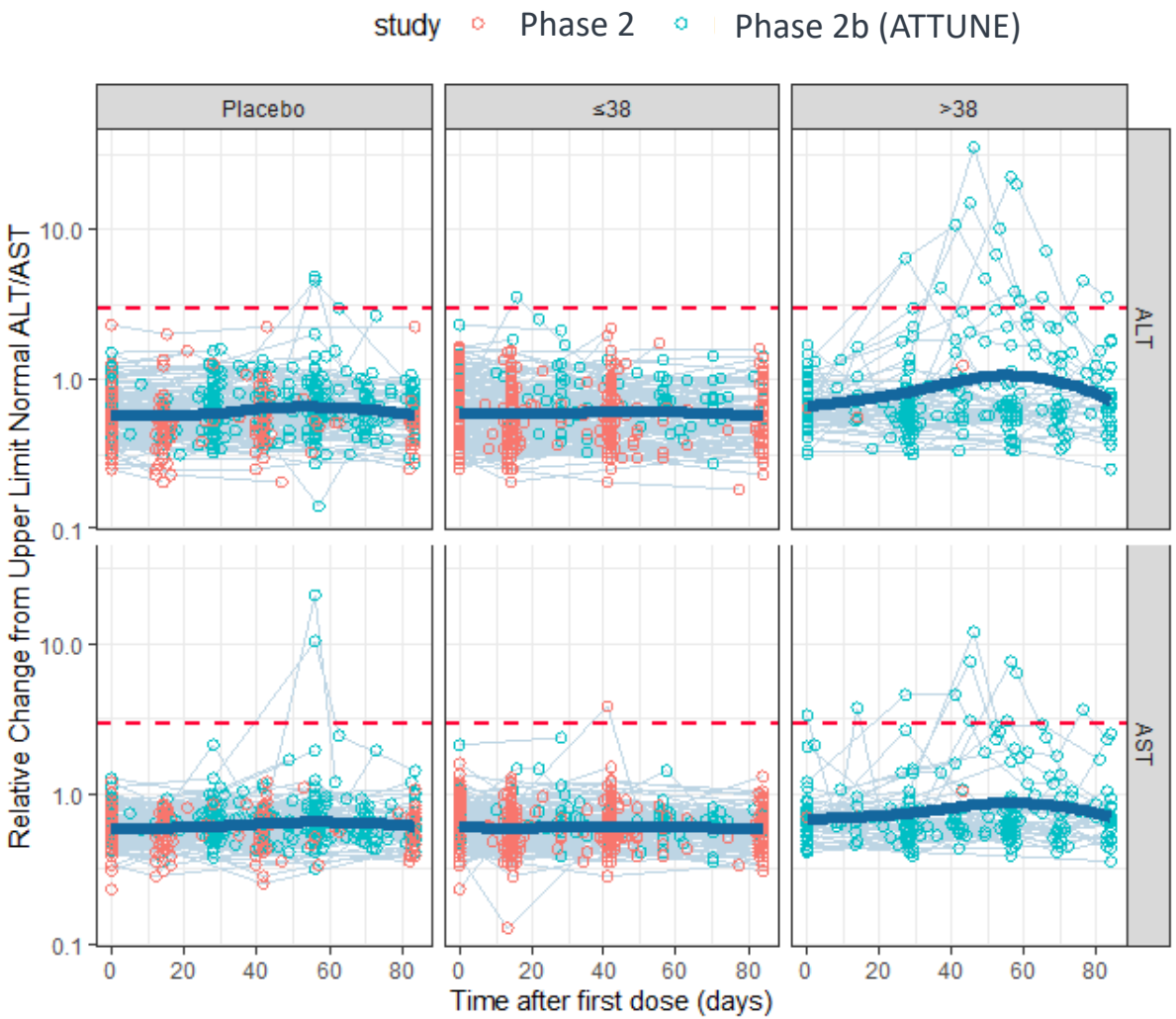
in addition to the current 900 mg BID, opportunity to test a lower dosage in upcoming trials

- BNC210 tablet formulation performed as expected in the second 12-week PTSD study in an out-patient setting (ATTUNE)
- Mean plasma exposure was 47 mg.hr/L
- 900mg BID achieved ~x2 the predicted therapeutic exposures highlighting the potential for future testing of a lower potentially efficacious dose in late-stage registrational trials



BNC210 plasma exposures: (A) and (B) **liquid suspension** formulation; (C), (D), (E) **tablet** formulation

Pharmacokinetic/Liver Enzyme Levels Analysis for BNC210 reveals an association of elevations with high drug exposures – A lower dose is predicted to alleviate elevations



Fold change from upper limit of normal (ULN) divided into AUC bins (mg.hr/L)

- No on-study elevations in LFTs were observed in previous studies and lower exposures (mean plasma exposures <~11 mg.hr/L)
- A placebo-like pattern of elevated LFTs was seen in the plasma exposure range ≤38 mg.hr/L in the combined Ph2 (RESTORE) and Ph2b (ATTUNE) datasets
- An intermediate exposure range may reduce the occurrence of elevated LFTs and still demonstrate efficacy considering the past pharmacometrics analysis that identified an exposure target of 25 mg.hr/L

ATTUNE is Expected to Enable Late-Stage Development of BNC210 in PTSD

Clear evidence of efficacy demonstrated with path forward to registrational trials

BNC210 Efficacy & Safety

- Clear evidence of **clinically meaningful efficacy** across primary and several secondary endpoint
- Positive secondary endpoints confirm overall profile of BNC210
- **Only positive dataset in PTSD** with a novel MoA small molecule and a favorable safety and tolerability profile
- **Opportunity for Breakthrough Designation** based of early onset of treatment effect, effect size and AE profile
- **Opportunity for a single additional late-stage trial** to enable an NDA submission

Study Design & Dose Identification

- CAPS-5, the gold standard endpoint for PTSD **performed robustly** for primary efficacy measure
- **Key secondary endpoints identified** for registrational trials
- Opportunity to test 900 mg BID as well as a lower dose in a registrational trial

Next Steps

- Meet with FDA to determine path forward in PTSD: **Q2/Q3 2024**
- **Engaged in strategic partnering** to co-develop BNC210 in PTSD: significant interest from multiple parties