
TO IMPROVE THE LIVES OF PATIENTS WITH SERIOUS **CNS DISORDERS**

Corporate Presentation

Nasdaq: BNOX
ASX: BNO

H.C. Wainwright BIOCONNECT Virtual Conference
January 10 - 13, 2022



Factors Affecting Future Performance

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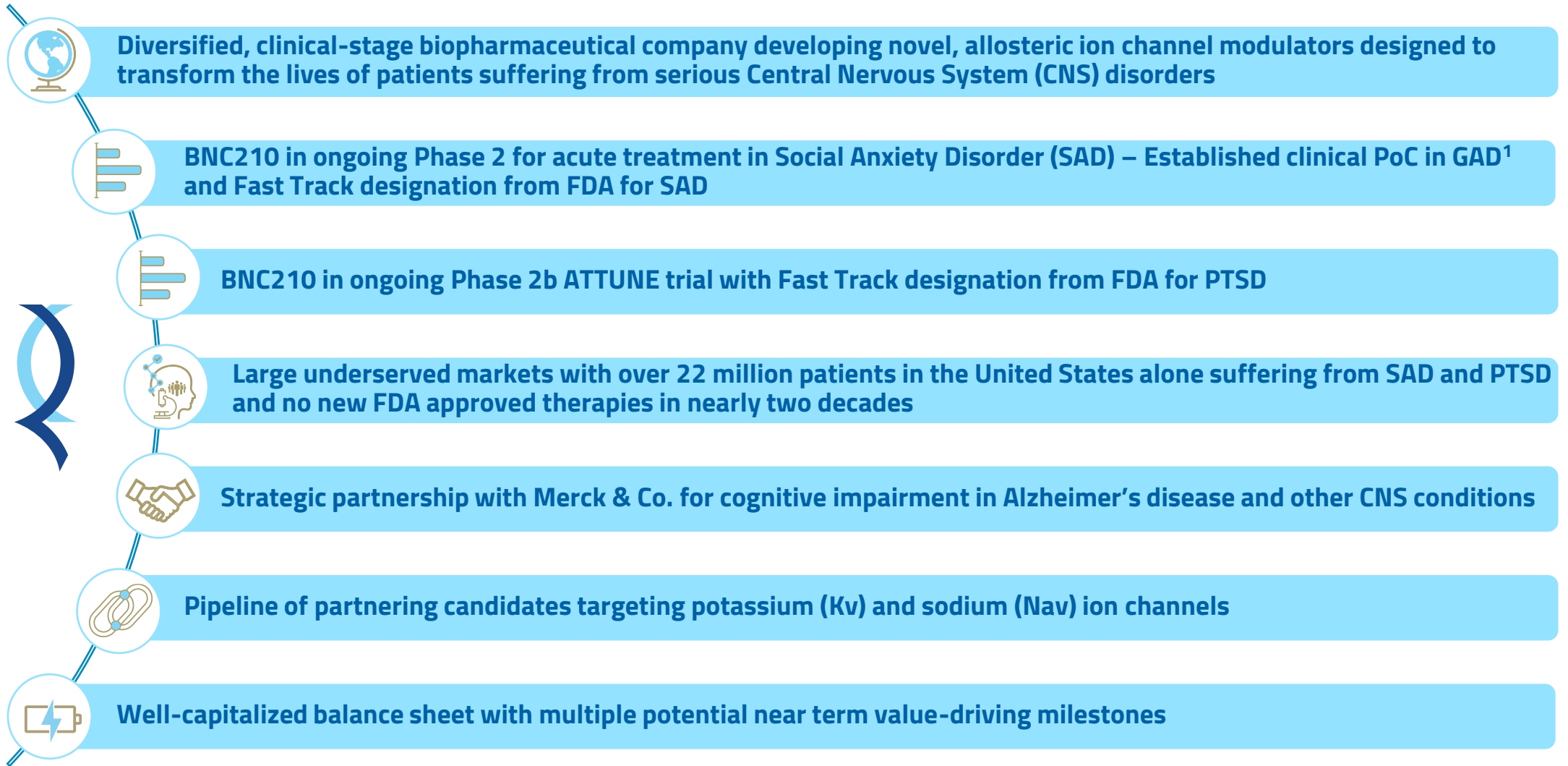
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Bionomics



Bionomics





PoC = Proof of Concept

GAD = Generalized Anxiety Disorder

PTSD = Post-Traumatic Stress Disorder

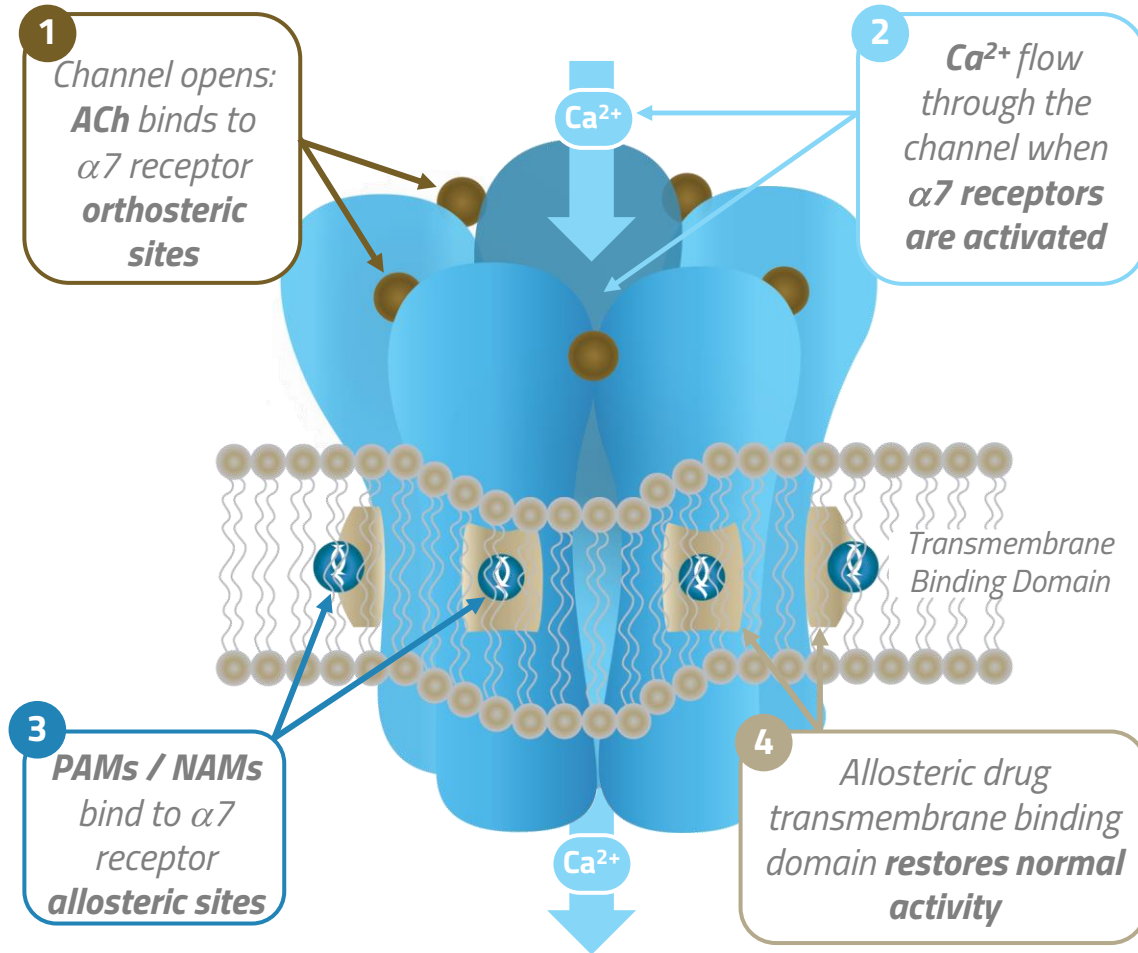
1. Wise et al 2020, Biological Psychiatry; Perkins et al 2021, Molecular Psychiatry



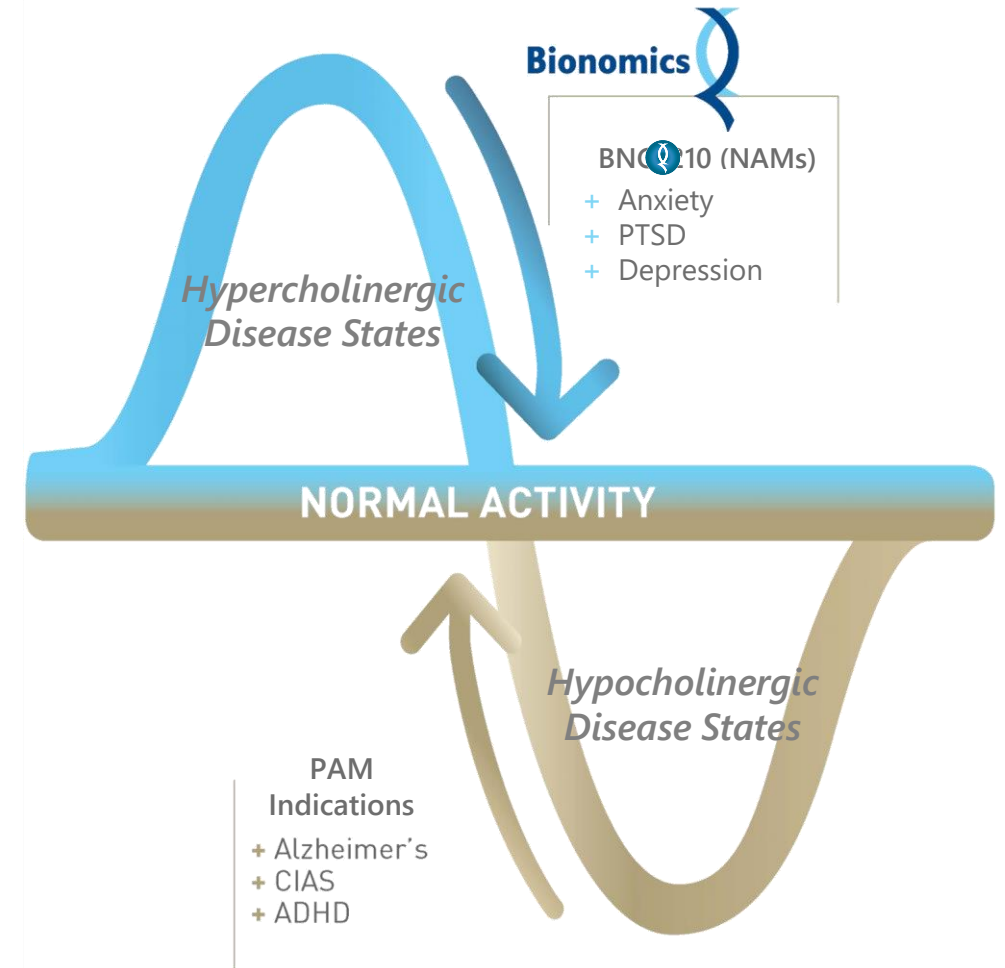
PROGRAM	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	EXPECTED TIMING
BNC210 α7 receptor NAM 	Post-Traumatic Stress Disorder (PTSD) 200 patients across ~25 centers in US 				<i>Study underway</i> <i>Topline Data: 1H'23</i>
	Social Anxiety Disorder (SAD) 150 patients across ~15 centers in US 				<i>Study underway</i> <i>Topline Data: YE'22</i>
	+MDMA derivative EMP-01 (PTSD)	<i>Memorandum of Understanding to explore combination treatment regimen for PTSD</i>			<i>Ongoing</i>
 α7 receptor PAM	2 candidates for cognitive deficits in Alzheimer's disease				<i>Phase 1 safety & biomarker studies ongoing</i>
PAIN Nav1.7/1.8 Inhibitors	Candidate				<i>Ongoing</i>
COGNITION Kv3.1/3.2 Activators	Series Lead				



Normalizing Effect Utilizing *Allosteric Modulation*

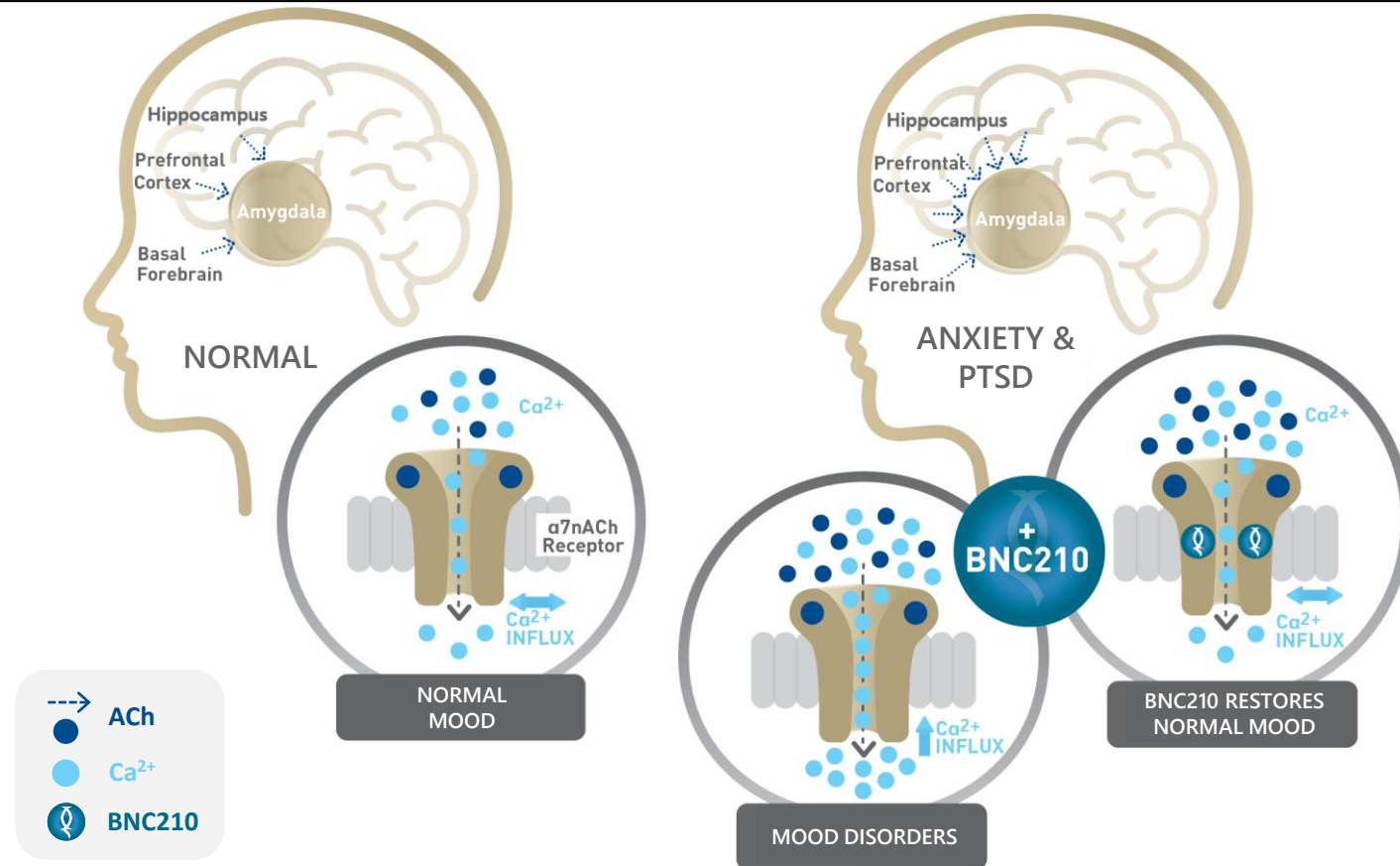


Targeting *Distinct CNS Conditions* with *Neurotransmitter Imbalance*





Action of **BNC210**
depends on
Acetylcholine
neurotransmission
and **Allosteric**
Modulation of
 $\alpha 7$ nAChR



NAMs have **self-limiting activity** determined by the **cooperative interaction** between BNC210 and Acetylcholine **binding at the allosteric and orthosteric sites, respectively**





BNC210 in Social Anxiety Disorder



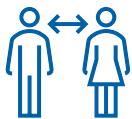
Acute Anxiety in SAD Represents a Significant Unmet Need



Social Anxiety Disorder (SAD), or Social Phobia, is a significant and persistent fear of social and performance-related situations

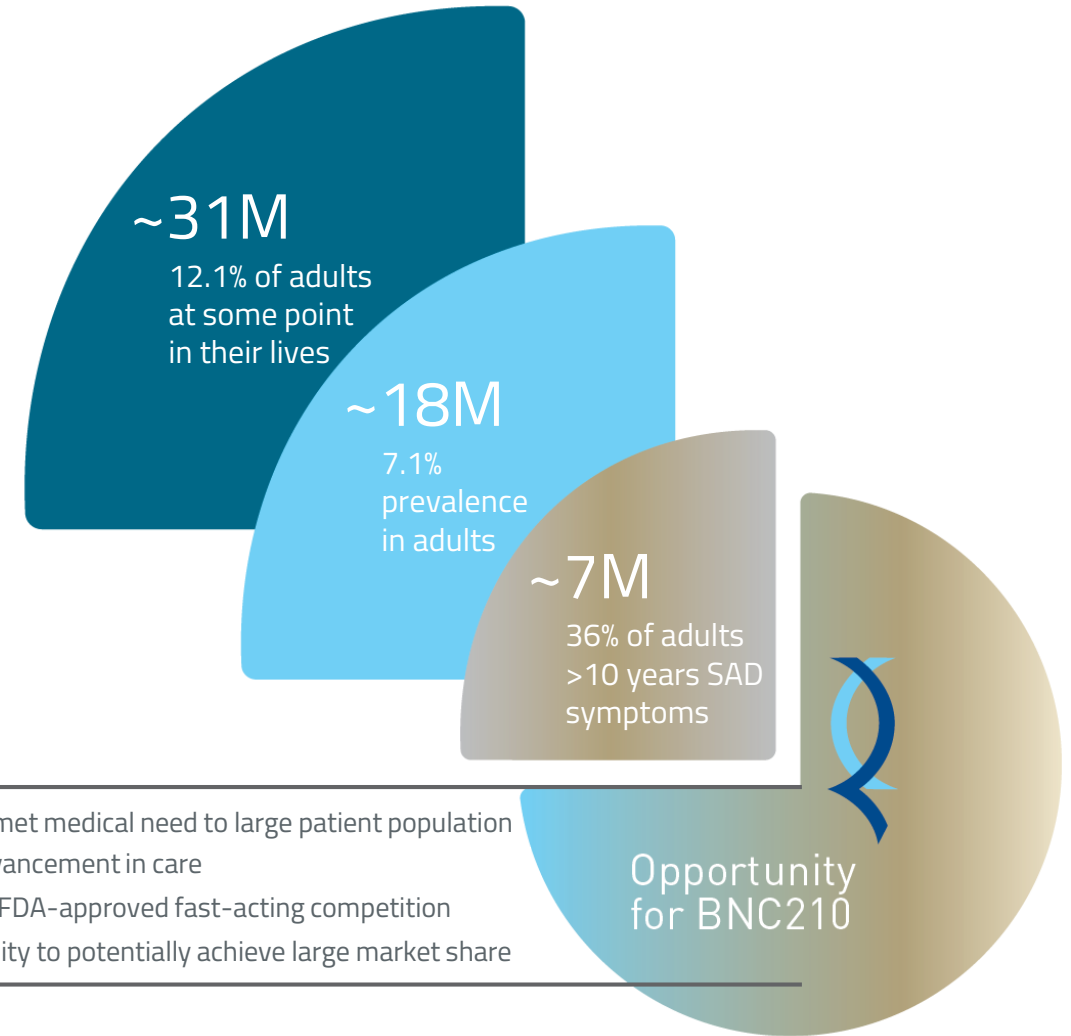


Includes anxiety from everyday social situations as well as "Fear of Public Speaking"



A disorder that substantially impacts many people's daily lives

- Amongst the largest mental health conditions with lifetime prevalence affecting >31M Americans
- No FDA-approved fast-acting medications for as-needed treatment
- Medications with the right pharmacokinetic profile and a novel mechanism are needed

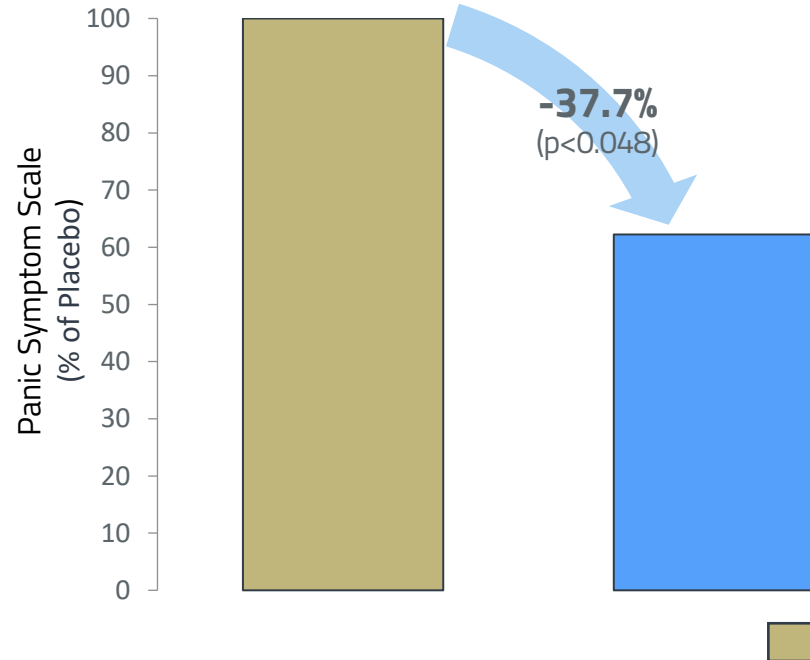




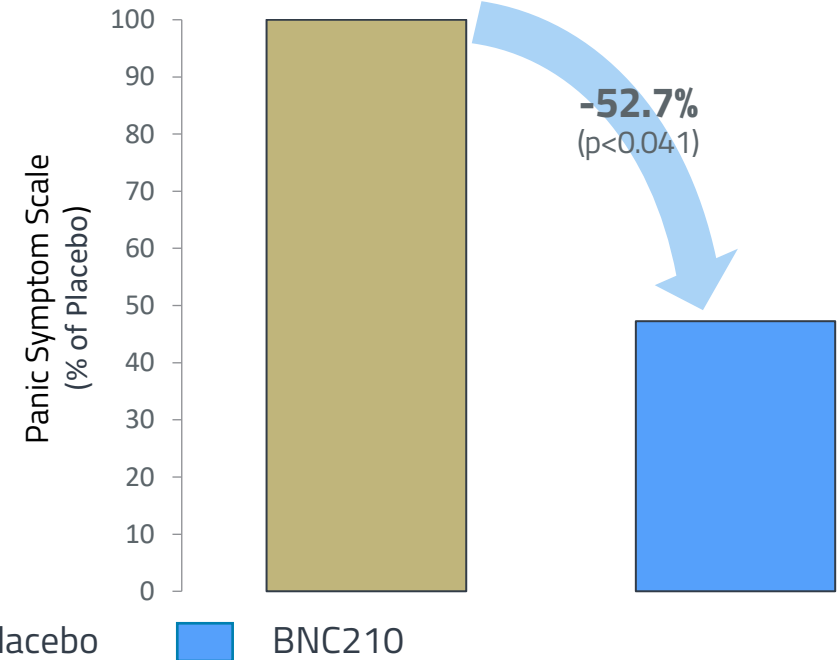
*Placebo-
controlled study
in 15 healthy
volunteers who
experienced a
CCK-4-induced
panic attack*



Total # of Panic Symptoms

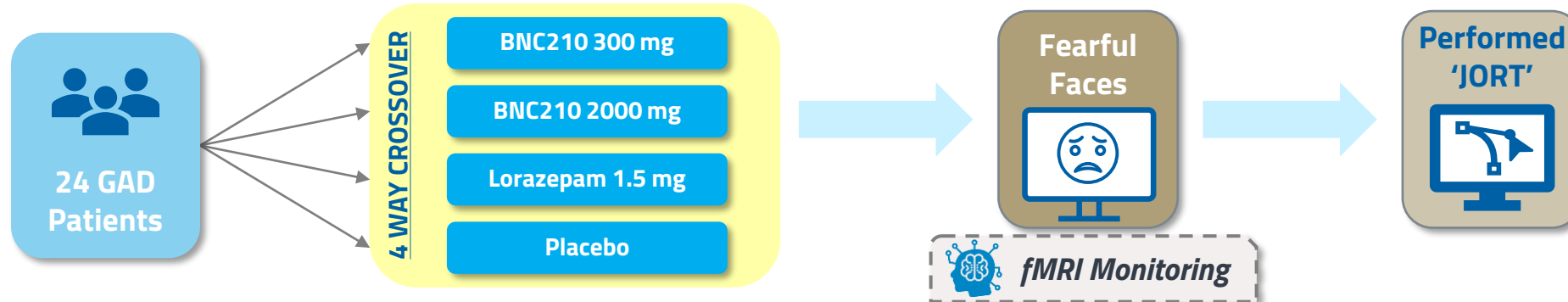


Panic Symptom Intensity



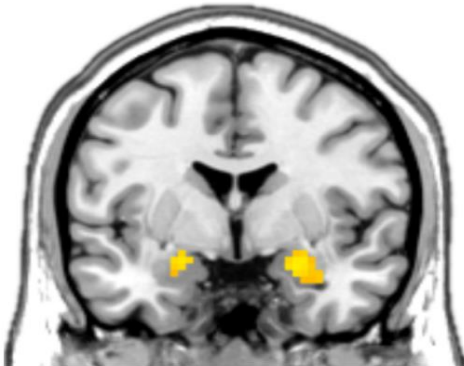
BNC210 demonstrated **statistically significant reduction in both number and intensity of panic symptoms** measured with the Panic Symptom Scale



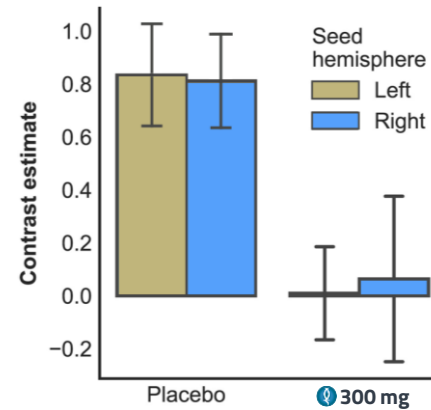


Significantly reduced activation of L & R amygdala caused by viewing fearful faces (L: $p < 0.05$; R: $p < 0.01$)

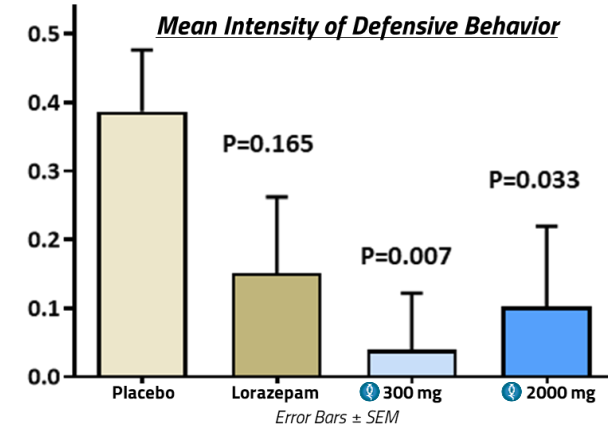
300 mg



Significantly reduced connectivity between amygdala and ACC while viewing fearful faces ($p < 0.05$)

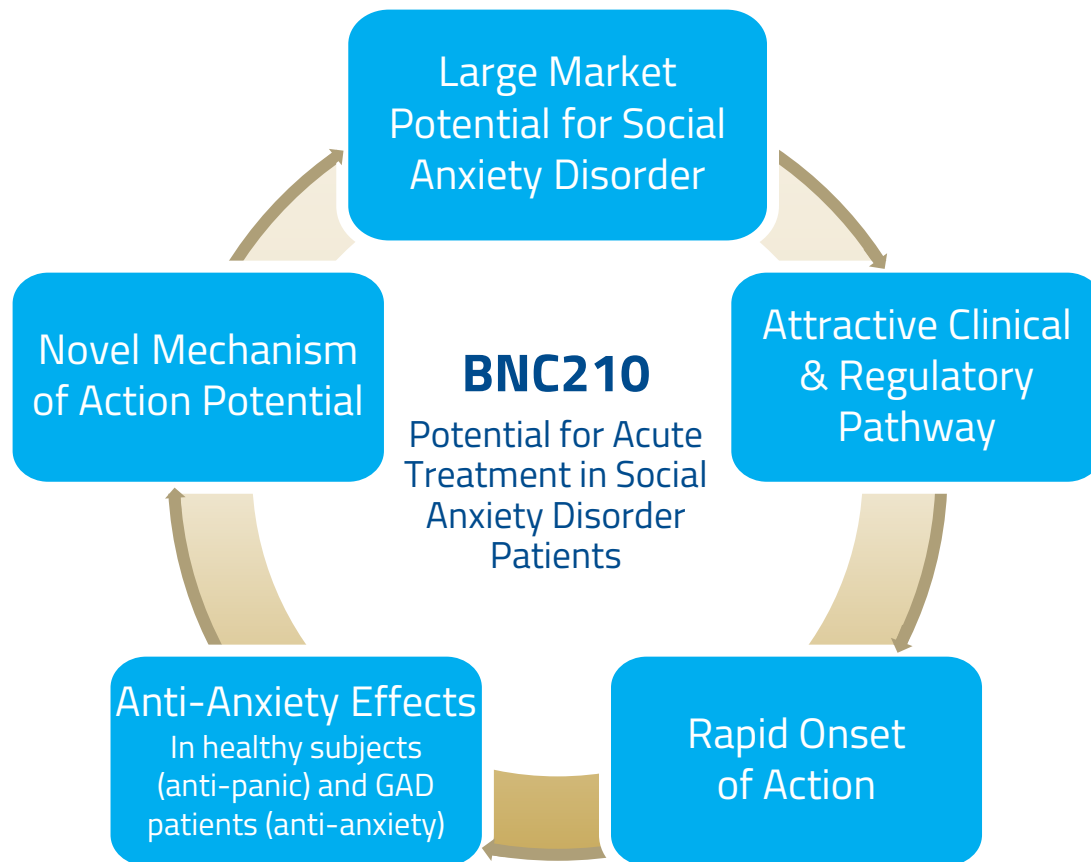


Significantly reduced threat avoidance behavior of anxious subjects in the JORT behavioral task



- **Amygdala activation** is an imaging **surrogate for anxiety**
- Connectivity between the **amygdala** and **Anterior Cingulate Cortex (ACC)** is **very strong in high anxiety**





CURRENT TREATMENTS FOR SOCIAL ANXIETY DISORDER

DRUG	FAST ACTING	NO SEDATION	NO WITHDRAWAL SYNDROME	NO MEMORY IMPAIRMENT	NO MOTOR IMPAIRMENT
Benzodiazepines ¹	✓	X	X	X	X
SSRIs / SNRIs ²	X	✓	X	✓	✓

BNC210 IS DESIGNED TO PROVIDE ADVANTAGES COMPARED TO CURRENT THERAPIES*

DRUG	FAST ACTING	NO SEDATION	NO WITHDRAWAL SYNDROME	NO MEMORY IMPAIRMENT	NO MOTOR IMPAIRMENT
BNC210	✓	✓	✓	✓	✓





✓ Emerging Regulatory Landscape & Unmet Need

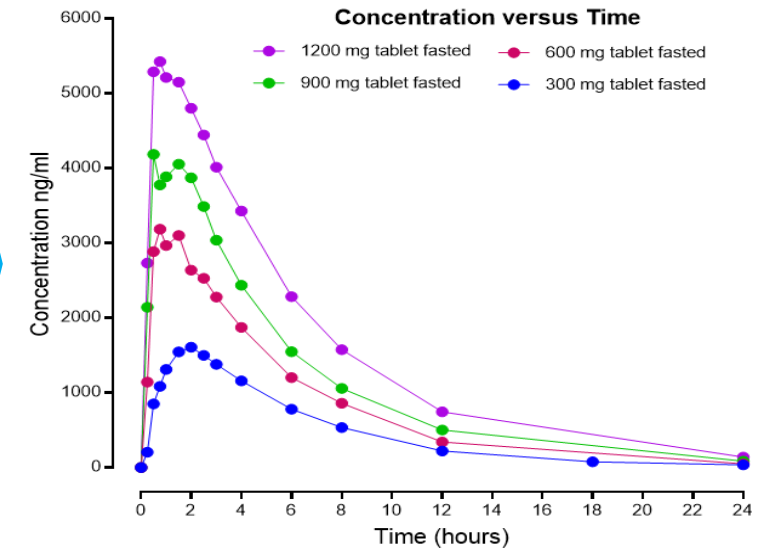
- No fast-acting FDA-approved medications for as-needed treatment of SAD
- Benzodiazepines prescribed off-label have significant side effects of sedation, cognitive impairment and potential for addiction
- Growing unmet need based on improving awareness and evolving social dynamics
- FDA precedent on simplified public speaking challenge endpoint for acute anxiety reduction vs. placebo*

✓ Rapid Onset of Action with BNC210 Formulation

- Clinically demonstrated potential for reducing anxiety in acute treatment of GAD patients and following panic induction
- Observed acute anxiolytic efficacy of BNC210 similar to lorazepam without sedative properties and addiction liability
- Formulation well-suited for acute dosing – Rapidly absorbed to high concentrations within a short period of time



**Maximum
concentrations
reached in
~45 – 105 min.
across the
dose range**

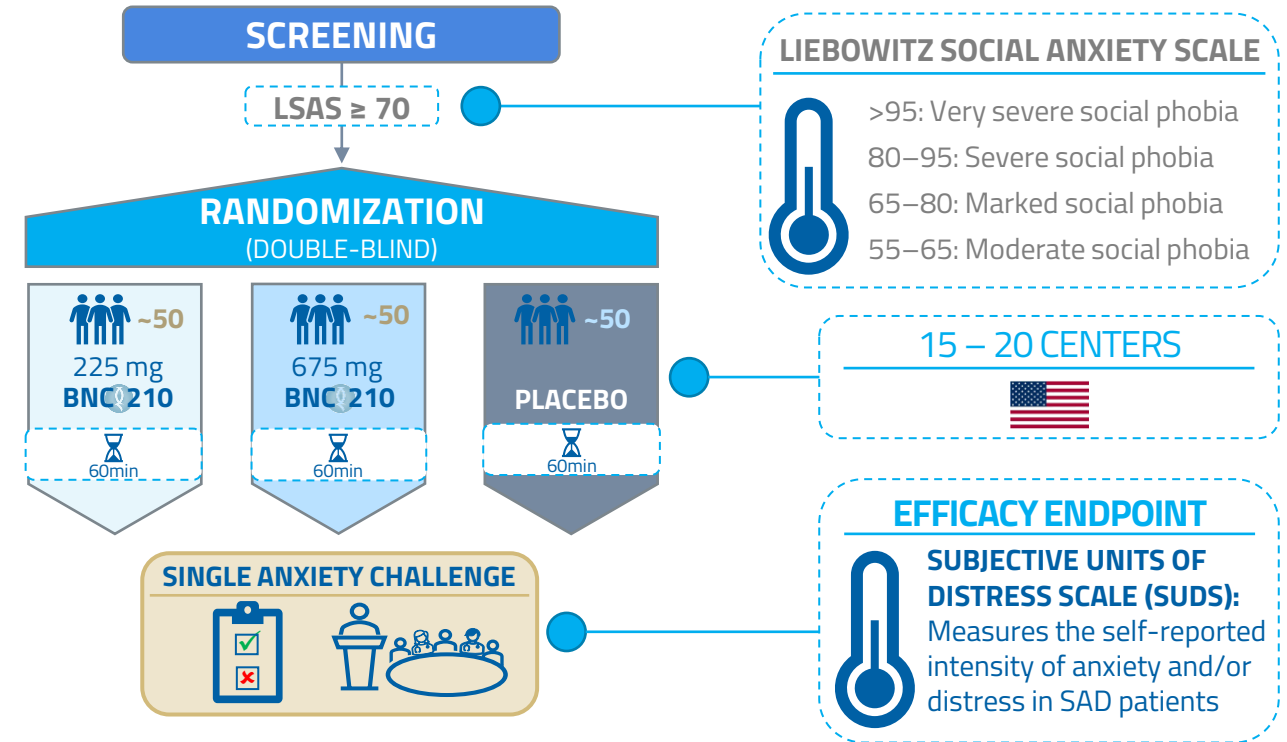




Acute Social Anxiety Disorder Study Highlights

- ✓ Potential to conduct a cost-effective trial with an efficacy endpoint conducive to rapid data generation
- ✓ Ability to leverage development strategies of other Social Anxiety Disorder public CNS trial designs
- ✓ Received FDA clearance for IND filing and **FDA Fast Track designation**
- ✓ Phase 2 trial underway and will read out topline data by end of 2022

Phase 2 PREVAIL Study Design



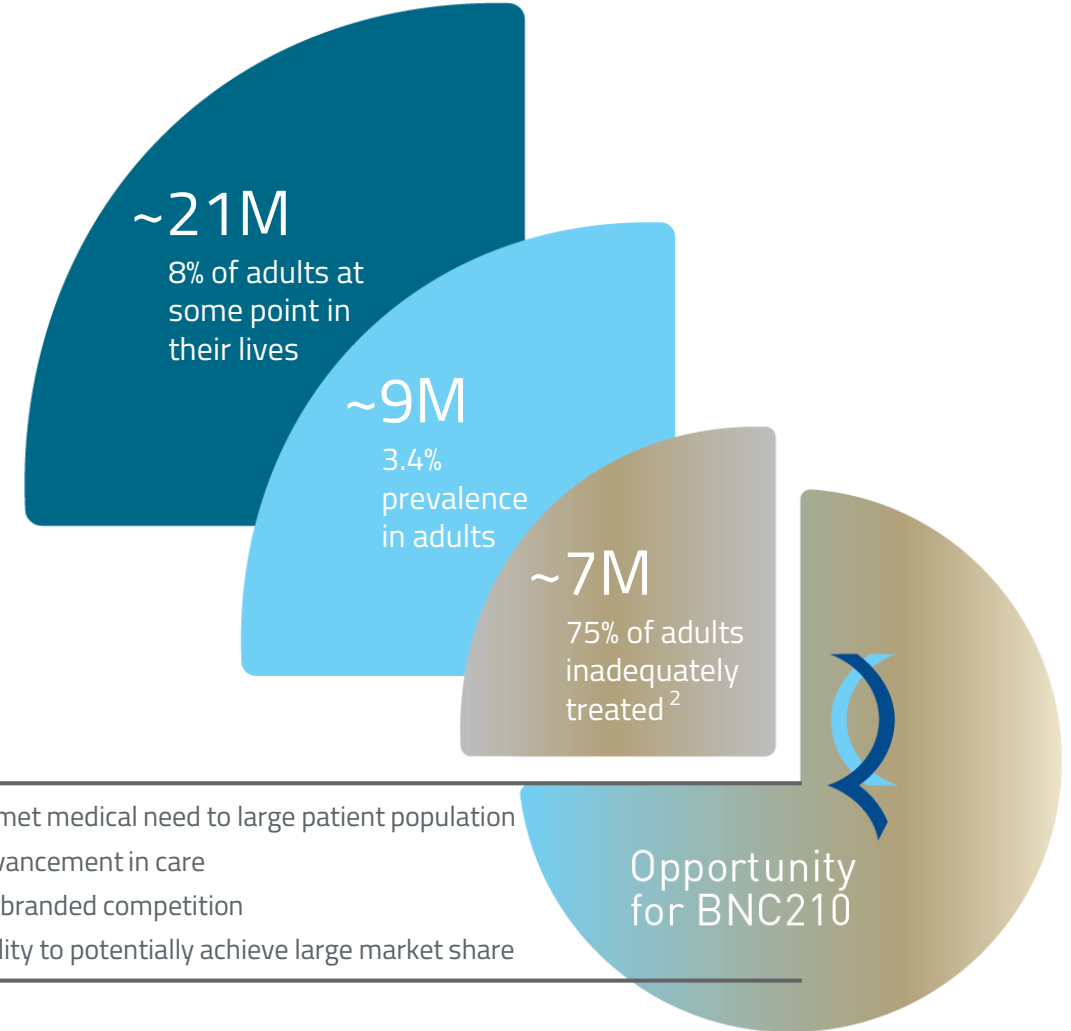


BNC210 in Post-Traumatic Stress Disorder



PTSD Represents a Significant Unmet Need

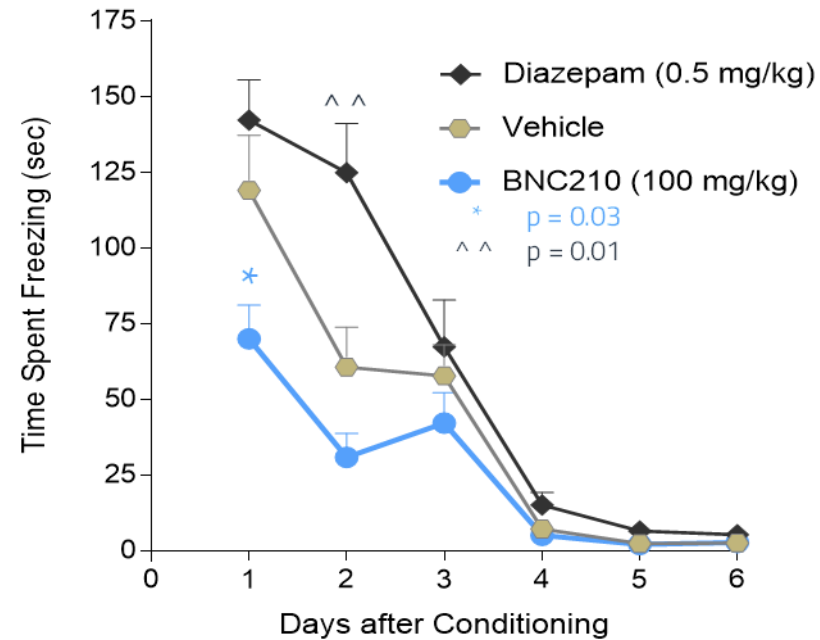
- ✓ 70% of people will experience a traumatic event in their lifetime, but most people recover normally
- ✓ PTSD results from exposure to actual or threatened death, serious injury or sexual violence
- ✓ PTSD affects up to 8% of adults during their lifetime¹
- ✓ PTSD is a global mental health problem that is associated with significant morbidity and mortality and shows up in all facets of peoples' lives
- ✓ No newly approved pharmacotherapy in almost two decades
- ✓ Medications with a novel mechanism of action that can address the pathophysiology of PTSD are needed





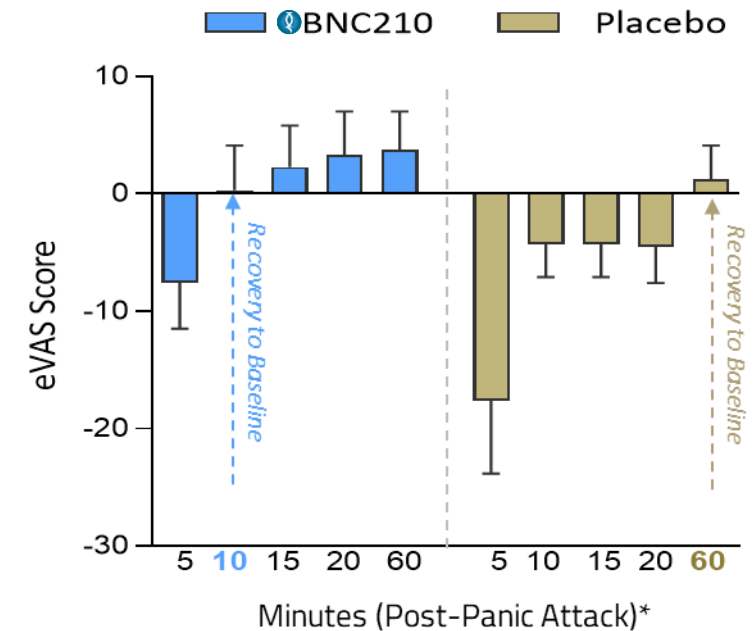
People with **anxiety disorders** and **PTSD** have **amplified fear responses** to trauma- or stress-related stimuli and **impaired fear extinction**

Conditioned Fear Extinction Model



BNC210 **enhanced fear extinction** following conditioned response training

Emotional Visual Analog Scale (eVAS)



BNC210 **enhanced emotional recovery** following a CCK-induced panic attack



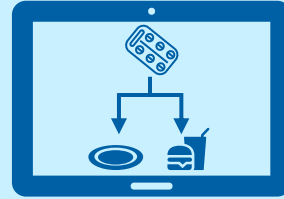


- ✓ Anti-depressant and anti-anxiety trends seen at earlier time points
- ✓ Safety profile generally well tolerated

Did not meet primary endpoint*; lower than expected exposure of liquid suspension formulation



- ✓ Pharmacometric analysis of Phase 2 PTSD data
- ✓ Predicted significant efficacy potential with adequate drug exposure achieved



- ✓ New tablet formulation overcomes food effect of suspension formulation
- ✓ Achieved exposure target predicted from pharmacometric analysis
- ✓ Extended IP coverage



- ✓ Type C meeting with FDA
- ✓ FDA granted Fast Track designation in PTSD



- ✓ Phase 2b ATTUNE trial started in July 2021
- ✓ Topline data expected 1H 2023

*Primary endpoint of CAPS-5 total symptom severity score at 12 weeks





**PMX modelling
on prior Phase 2
PTSD trial identified
liquid suspension
under-exposure**

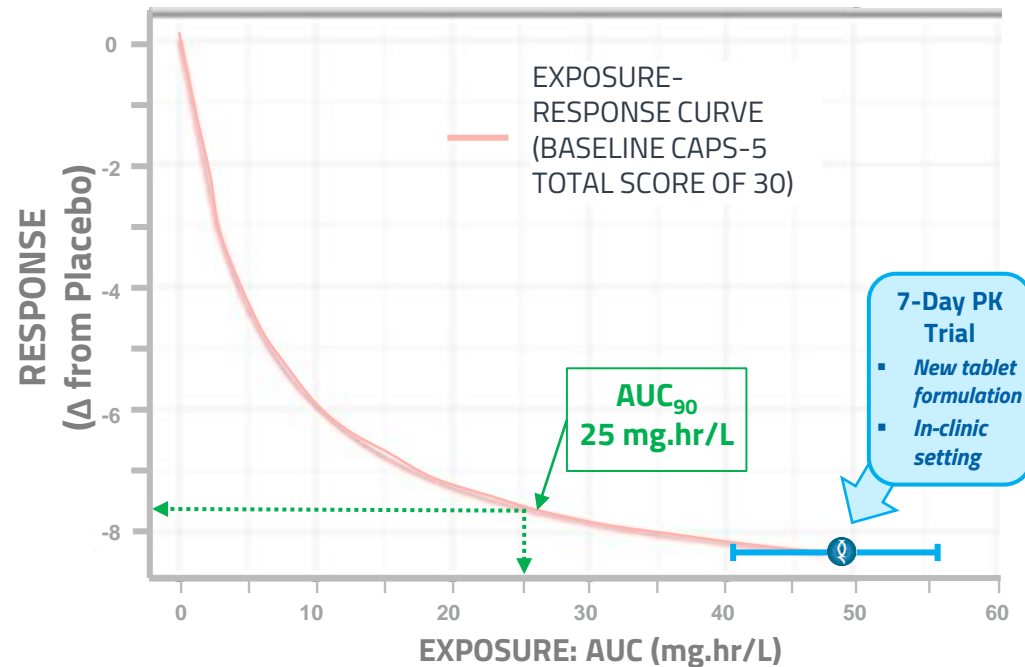


**BNC210 tablet
formulation**



**New formulation
achieves target AUC
>25 mg.hr/L
with 900 mg dose
b.i.d.**

Pharmacometric (PMX) Analysis Target Exposure



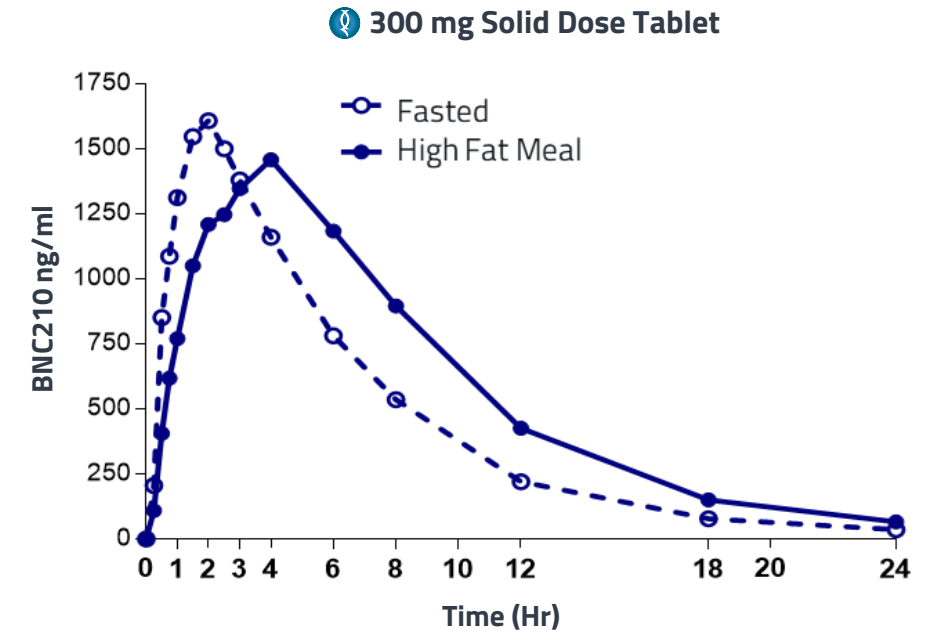
**AUC Values
(plasma exposure)**

=



**CAPS-5 Score
(PTSD symptoms)**

BNC210 Novel Spray Dry Dispersion Formulation

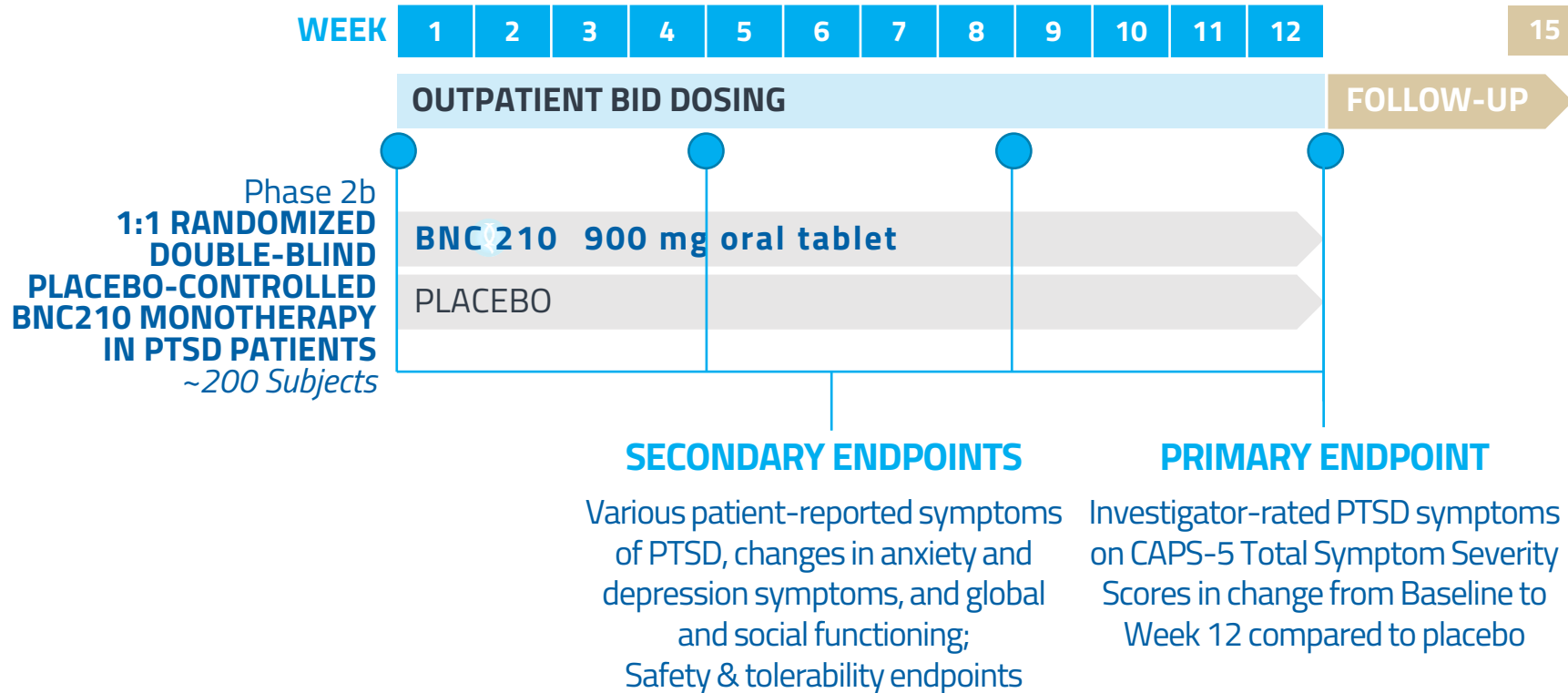


Novel tablet **overcomes food effect**
and has **dose linear exposure**

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

PMX = Population pharmacometric modelling
b.i.d = Administered twice daily





PHASE 2b

Single potential registrational-supporting trial for monotherapy treatment in PTSD

KEY INCLUSION CRITERIA

- Female and male (18 – 75 years)
- Current PTSD diagnosis
- CAPS-5 ≥ 30 (Screening & Baseline)
- (& $\leq 25\%$ decrease Screening to Baseline)

~25 Sites



Fast Track designation from FDA



Topline data expected 1H'23





CNS-focused Collaborations



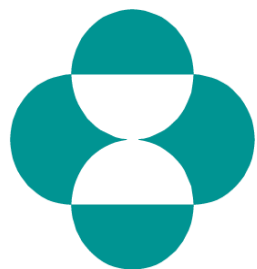
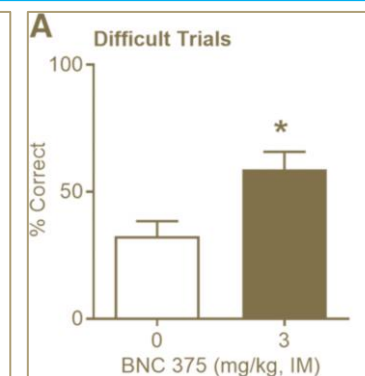
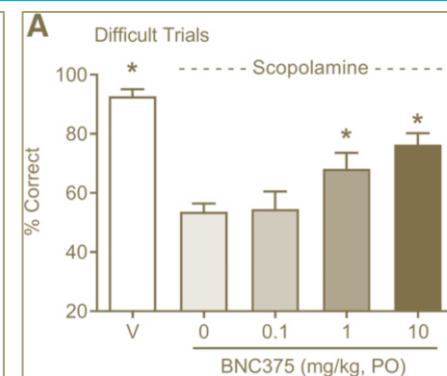
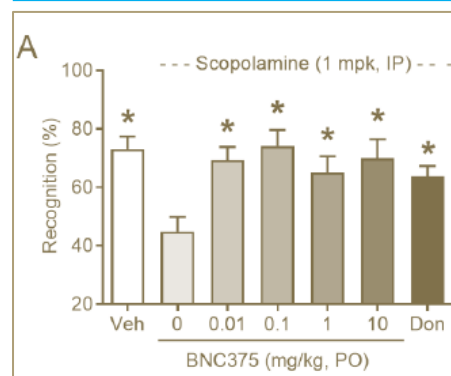
MSD Collaboration Overview

- Entered into in 2014 to develop $\alpha 7$ receptor PAMs targeting cognitive dysfunction associated with Alzheimer's disease and other central nervous system conditions
- Merck funds all R&D activities including clinical development and WW commercialization of any products from collaboration
- Milestone payments of **US\$20M upfront** and **US\$10M in 2017** when 1st compound entered Phase 1 clinical trials
- Eligible to receive **up to US\$465M in additional development and commercial milestone payments plus royalties**

Development Updates

- Includes 2 candidates which are PAMs of the $\alpha 7$ receptor in early-stage Phase 1 safety and biomarker clinical trials for treating cognitive impairment
- The 1st compound has completed Phase 1 safety clinical trials in healthy subjects and there are ongoing plans for further biomarker studies*
- In 2020, a second molecule that showed an improved potency profile in preclinical animal models was advanced by Merck into Phase 1 clinical trials*

Snapshot of Early BNC375 Studies



MERCK
PARTNERSHIP

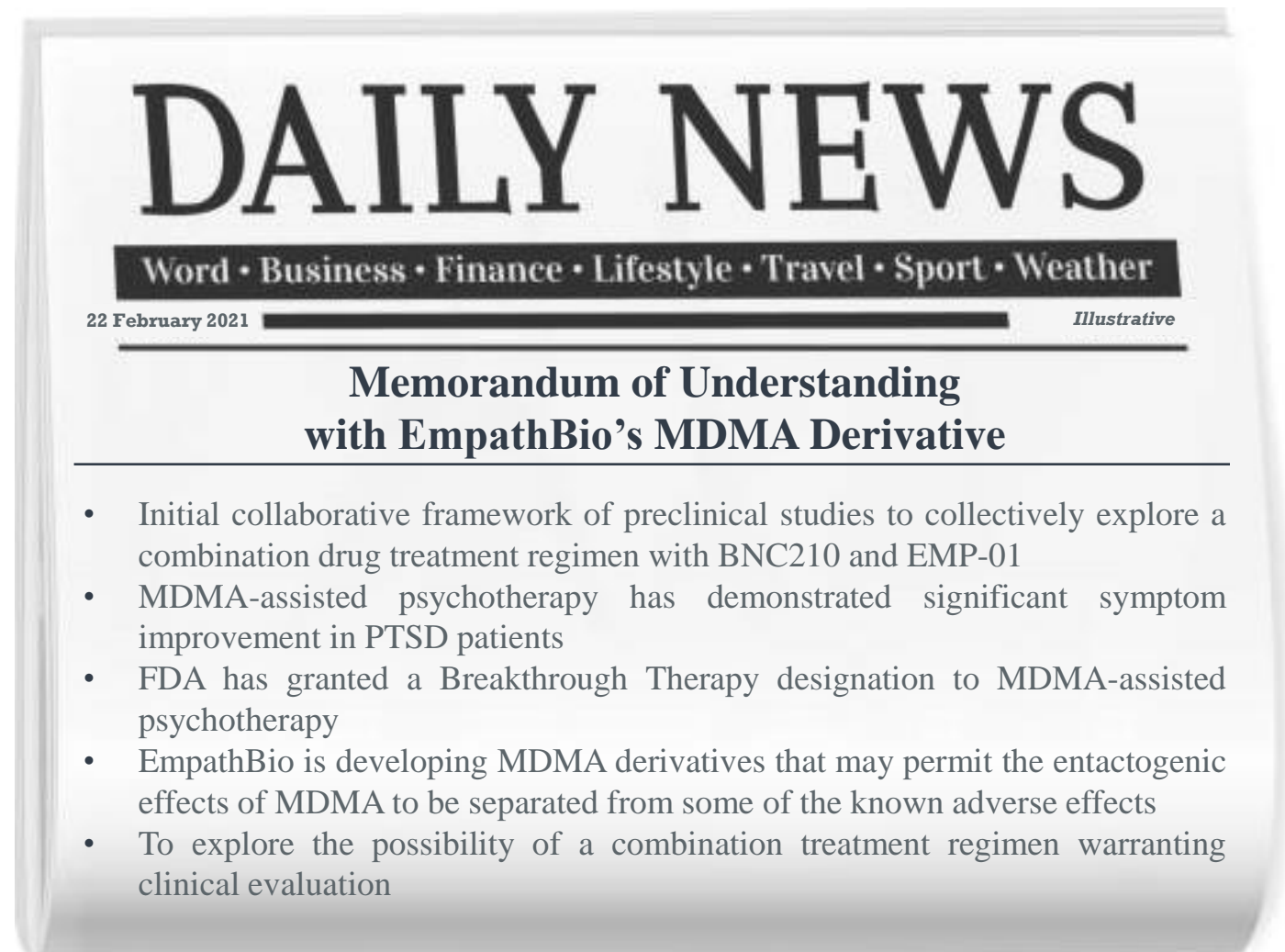


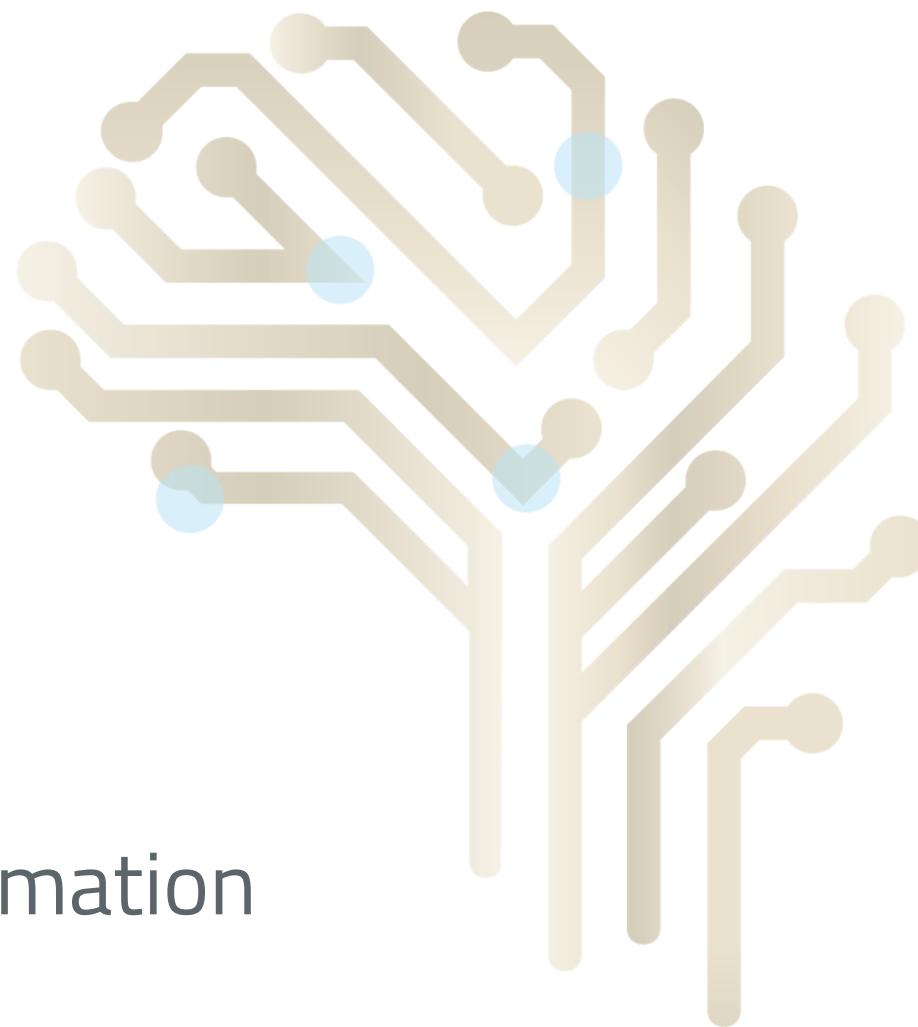


Joint Feasibility Assessment with:



EMP-01 = 3,4-Methylenedioxymethamphetamine
(MDMA) derivative





Investment Highlights & Stock and Financial Information

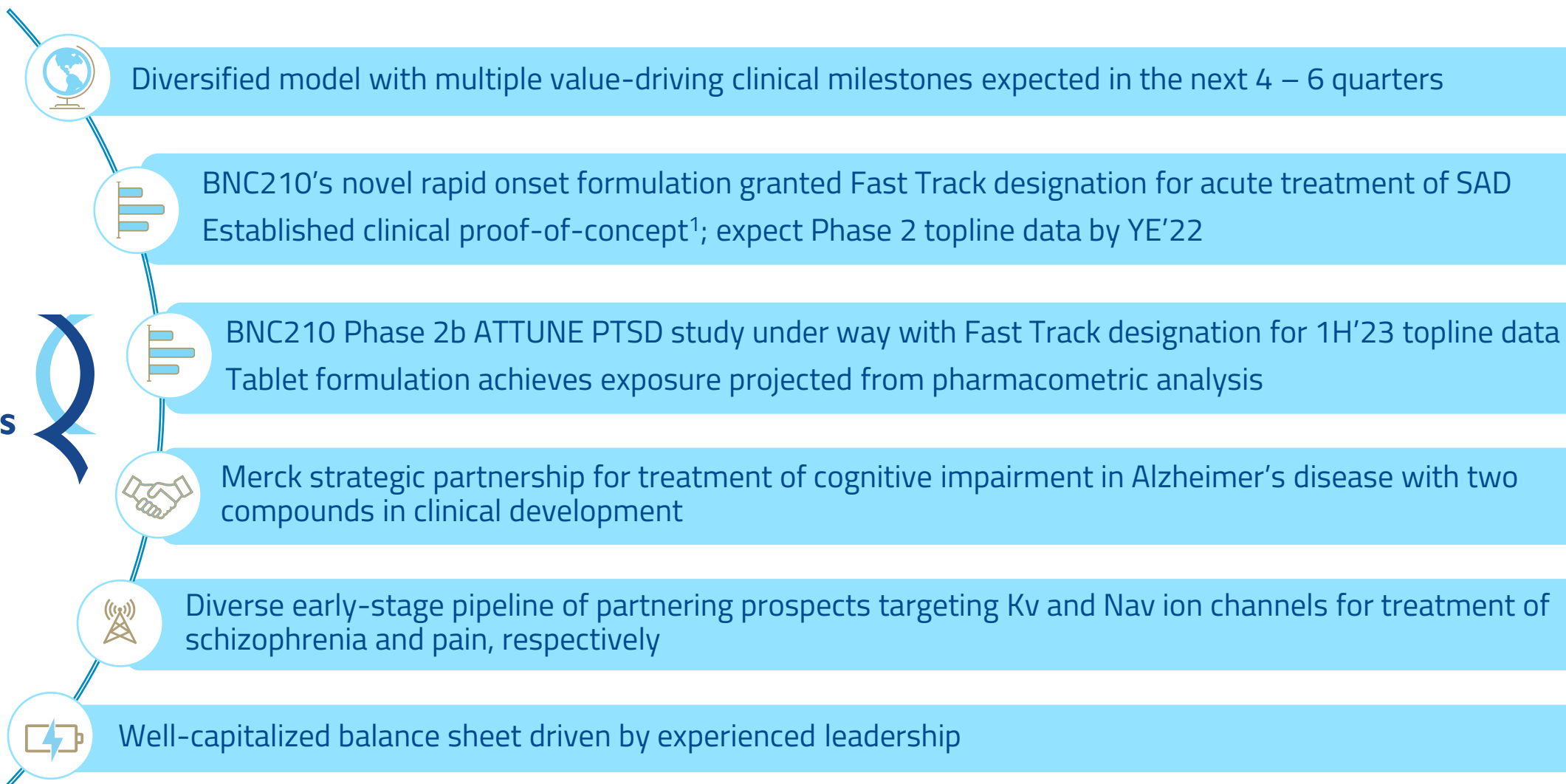


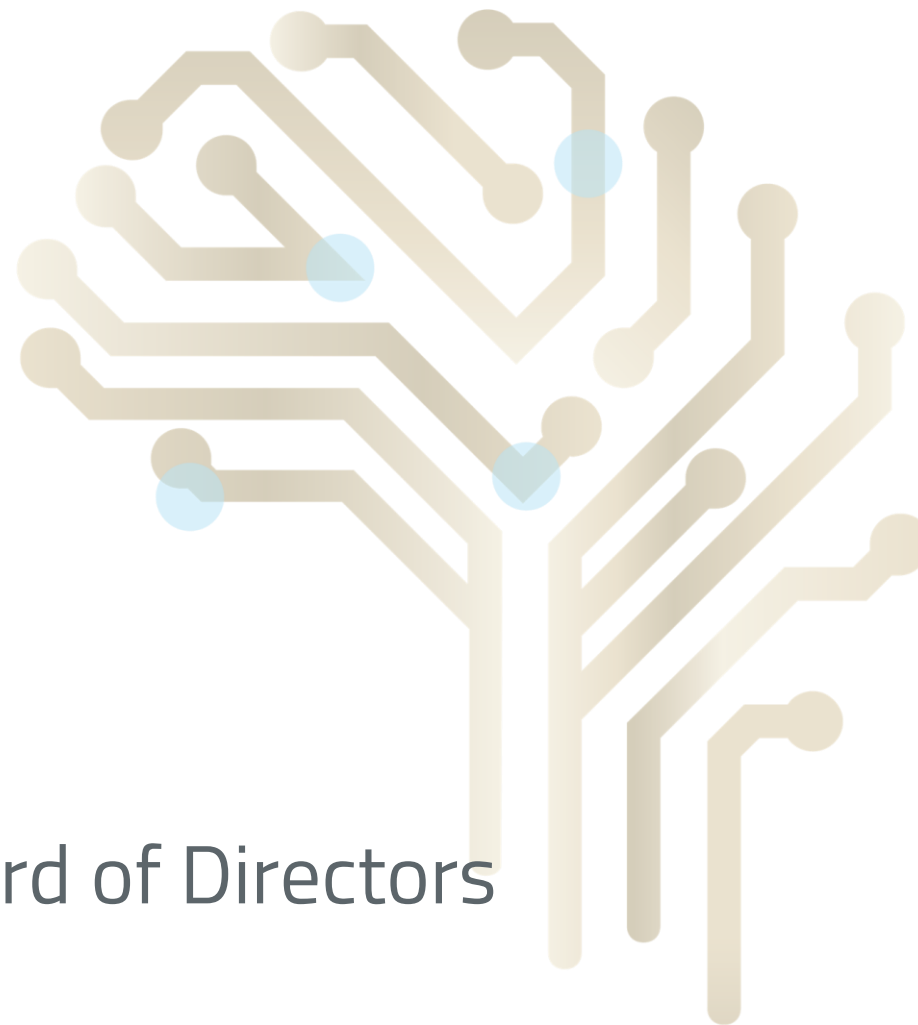
- Cash: US\$40.4M / A\$53.9M
- Debt: \$0
- Shares Outstanding: ~1,310M (NASDAQ:BNOX | ASX:BNO)
- Warrants Outstanding: 142M (WAEP = US\$0.04 / A\$0.06)
- Significant Investors:
 - Biotechnology Value Fund
 - Apeiron Investment Group Ltd.
 - Merck & Co





Bionomics





APPENDIX: Management Team & Board of Directors



Errol De Souza, PhD
Executive Chairman



Connor Bernstein
VP Strategy & Corporate Development



Liz Doolin
VP Clinical Development



Adrian Hinton
Interim Chief Financial Officer

BOARD OF DIRECTORS ¹

Errol De Souza PhD
Executive Chairman



David Wilson
Non-Executive Director



Alan Fisher
Non-Executive Director



Jane Ryan PhD
Non-Executive Director

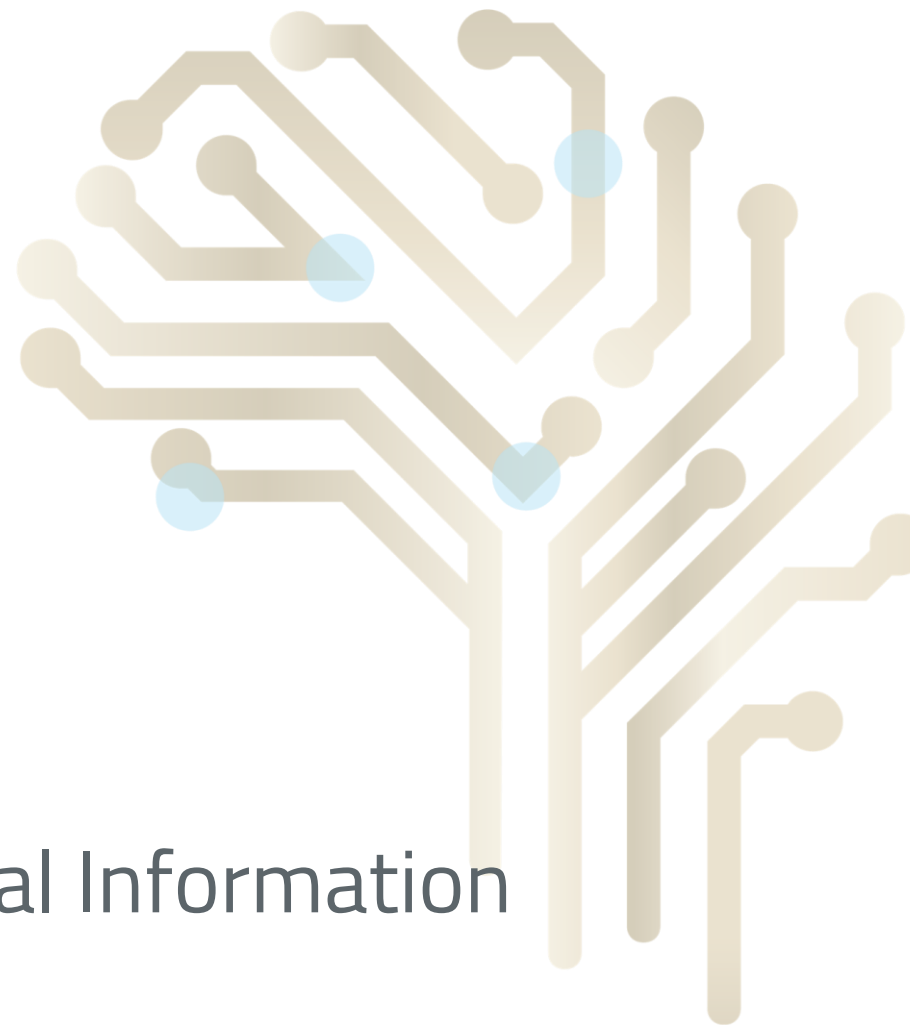


Aaron Weaver
Apeiron Nominee



Miles Davies
Apeiron Nominee





APPENDIX: BNC210 Prior Clinical Trial Information



Summary of BNC210 Clinical Trials: Excellent Safety and Tolerability Profile in Healthy Subjects and Patients

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Phase	Description	Participants / Setting	Subjects Enrolled / Administered BNC210*	BNC210 Formulation and Doses	Location
1	Single Ascending Dose Safety and PK	Healthy volunteers / In-clinic	32/24	Suspension; single doses (5 to 2000 mg)	Australia
1	Single Ascending Dose Safety and PK; Food Effect	Healthy volunteers / In-clinic	4/3	Suspension; single doses (300 to 2000 mg)	Australia
1	Single Ascending Dose Safety and PK; Food Effect	Healthy volunteers / In-clinic	47/40	Capsule; single doses (300 to 3000 mg)	US
1b	Lorazepam Comparison	Healthy volunteers / In-clinic	24/22	Suspension; single doses (300 and 2000 mg)	France
1b	CCK-4 Panic Attack Model	Healthy volunteers / In-clinic	60/59	Suspension; single doses (2000 mg)	France
1b	Multiple Ascending Dose Safety and PK; Expanded Cohort for EEG Target Engagement	Healthy volunteers / In-clinic	56/44	Suspension; multiple doses (150 to 1000 mg twice daily for 8 days)	France
1	Suspension and Tablet Formulation PK Comparison	Healthy volunteers / In-clinic	6/6	Suspension and tablet; single doses (300 mg)	Australia
1	Single Ascending Dose Safety and PK	Healthy volunteers / In-clinic	5/5	Tablet; single doses (600 to 1200 mg)	Australia
1	Multiple Dosing Safety and PK	Healthy volunteers / In-clinic	10/10	Tablet; multiple doses (900 mg twice daily for 7 days)	Australia
2a	Imaging and Behavioral Study In Generalized Anxiety Disorder	Generalized anxiety disorder patients / In-clinic	27/25	Suspension; single doses (300 and 2000 mg)	UK
2a	Agitation in the Elderly in Hospital Setting	Agitated elderly patients / Hospital	38/18	Suspension; multiple doses (300 mg twice daily for 5 days)	Australia
2	Post-Traumatic Stress Disorder	Post-traumatic stress disorder patients / Out-patient	193/143	Suspension; multiple doses (150, 300 or 600 mg twice daily for 12 weeks)	Australia US
2b	Post-Traumatic Stress Disorder	Post-traumatic stress disorder patients / Out-patient	Ongoing	Tablet; multiple doses (900 mg twice daily for 12 weeks)	US

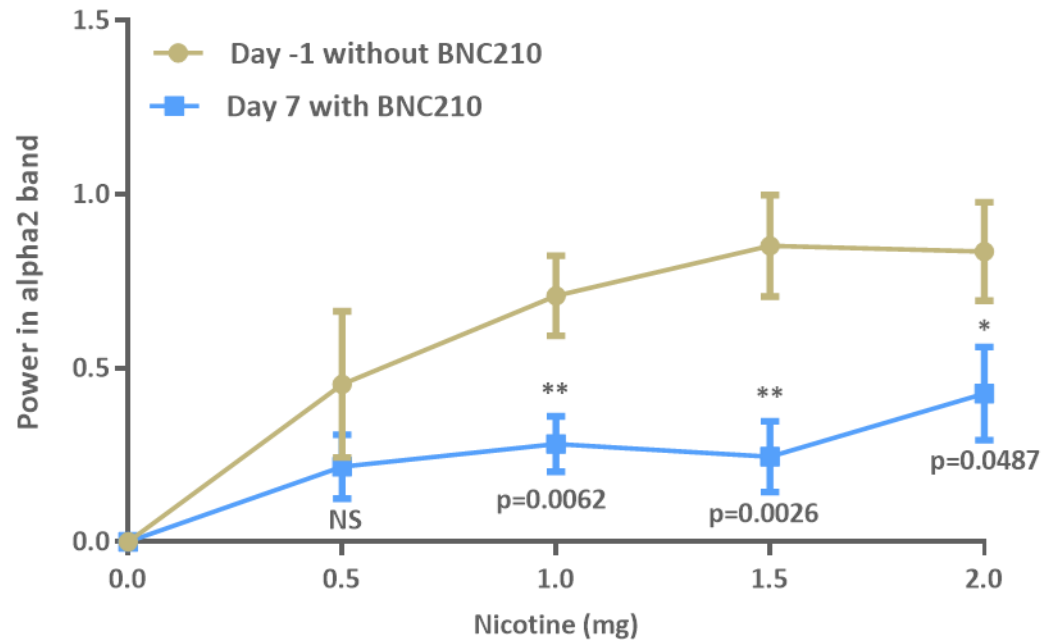
* The number of enrolled subjects who were administered BNC210; other enrolled subjects were administered placebo only
CCK-4 = Cholecystokinin Tetrapeptide
EEG = Electroencephalography
PK = Pharmacokinetic





BNC210
blood-brain
barrier
penetration and
nicotinic receptor
target
engagement in
humans

BNC210 Reduced Nicotine-induced EEG Responses



Activation of nicotinic receptors
in the brain **induces EEG response**


$\alpha 4 \beta 2$ and $\alpha 7$ receptors are the
major nAChR populations targeted

BNC210 daily oral dosing reduced
nicotine-induced EEG in the $\alpha 2$ band



Observed reduction in EEG response due to BNC210's **negative allosteric modulation** of the $\alpha 7$ receptors





Study Design	<ul style="list-style-type: none">• Multi-center, randomized, double-blind, placebo-controlled• BNC210 150 mg, 300 mg, 600 mg and placebo (1:1:1:1) (liquid suspension formulation taken twice daily, b.i.d.)• 12-week treatment period• 193 participants• 20 US sites / 6 Australian sites
Key Selection Criteria	<ul style="list-style-type: none">• Current diagnosis of PTSD as defined by CAPS-5 (Clinician-Administered PTSD Scale for DSM-5)
Key Study Objectives	<ul style="list-style-type: none">• To assess the effects of BNC210 on investigator-rated symptoms of PTSD measured by CAPS-5• To assess the safety and tolerability of BNC210 in subjects with PTSD



No overall effect on primary endpoint of CAPS-5 total severity score at 12 weeks

Australian patients had a greater improvement over placebo than US patients

- ✓ CAPS-5 statistically significant at Week 4 in Australians ($p < 0.05$)

Evidence of antidepressant effect in high dose treatment group in total population

- ✓ CAPS-5 Criterion D overall (negative alterations in cognitions and mood) statistically significant at Week 1 ($p < 0.05$)
- ✓ CAPS-5 Criterion D, Question 2 (persistent and exaggerated negative beliefs or expectations) statistically significant at Week 1 ($p = 0.001$)
- ✓ CAPS-5 Criterion D, Question 4 (persistent negative emotional state) statistically significant at Weeks 4 and 8 ($p < 0.05$)

Trend for anxiolytic effect in high dose treatment group in the total population

- ✓ Trend towards improvement on CAPS-5 Criterion E (marked alterations in arousal and reactivity), Question 3 (hypervigilance)
- ✓ Trend towards improvement on CAPS-5 Criterion E, Question 4 (exaggerated startle response)

BNC210 was well tolerated in patients with PTSD

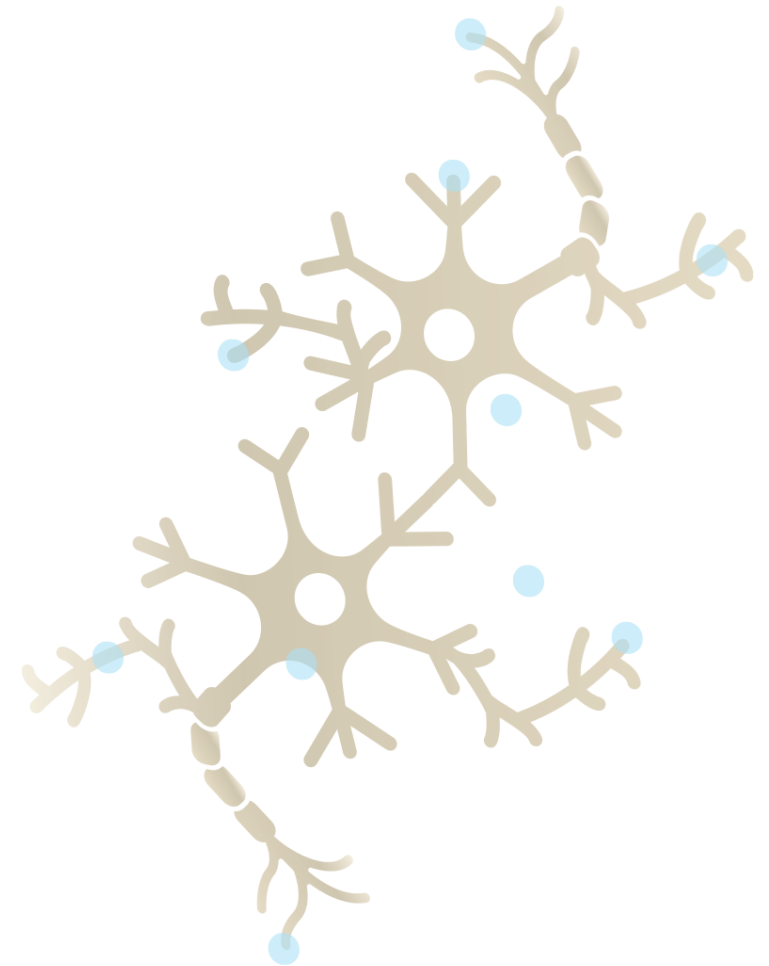
- ✓ No trend for increased adverse events with treatment
- ✓ No evidence of cognitive impairment
- ✓ No evidence of suicidal ideation or behavior worsening

Potential reasons why clinically significant effects and trends seen at early time points did not translate into significant primary endpoint on CAPS-5 at 12 Weeks

- Inadequate overall blood exposure of BNC210
- Lower compliance with liquid suspension formulation which needed to be taken with food



Emerging CNS Pipeline for Partnering





Promising therapeutic strategy for improving cognitive dysfunction and social withdrawal symptoms

Potential in *schizophrenia, Autism Spectrum disorders* and conditions with *cognitive impairments*

**~600 COMPOUNDS
SYNTHESIZED**

2 SERIES PATENTED

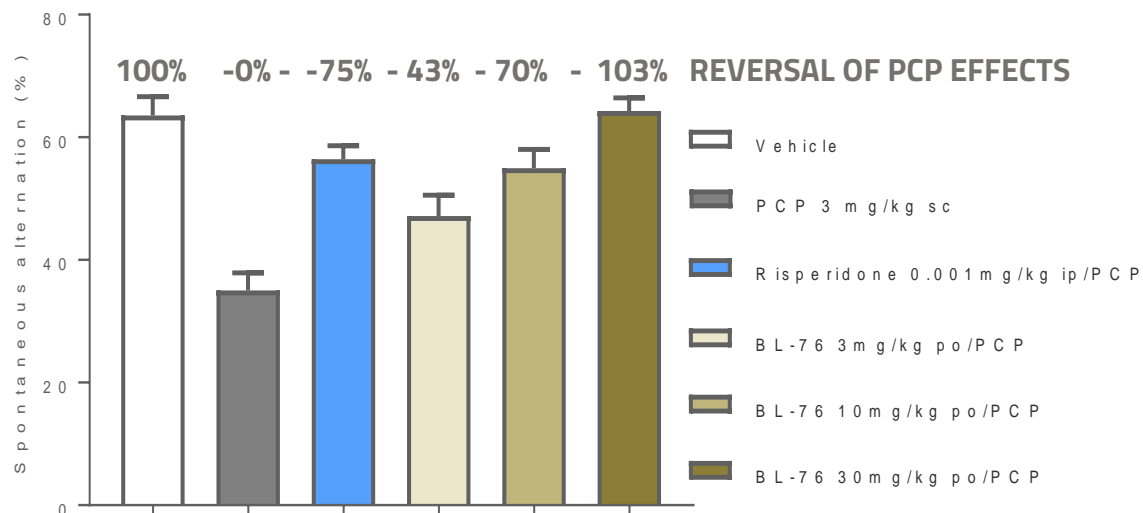
Lead
Compound
BL-76

**Back-up
Compounds**

2 Patents Published

Bionomics' molecules target Kv3.1/3.2 ion channels on parvalbumin positive, gabaergic interneurons in the pre-frontal cortex

Lead Compound BL-76 Fully Reverses PCP-induced Cognitive Deficit in Mice in the T-maze





Disease-Related Genetics

Gain & Loss-of-function mutations in Nav1.7, 1.8 and 1.9

Associated with human pain syndromes where extreme pain or no pain is experienced

BNO Pan Nav inhibitors

Small molecules with functional selectivity for voltage gated sodium channels: Nav1.7, Nav1.8 and potentially Nav1.9

1000+ COMPOUNDS SYNTHESIZED

2 SERIES PATENTED

LEAD
COMPOUND
BL-017881

BACK-UP
COMPOUNDS

3 Patents Published

Lead Candidate Identified

BL-017881

OBSERVED TO REVERSE PAIN IN THE FORMALIN PAW MODEL IN MICE



APPENDIX: Building Value Through Legacy Oncology Assets





Exclusive BNC101 Oncology License Agreement for the Development of CAR-T Therapeutics



- Exclusive Agreement to license Bionomics' BNC101 oncology drug candidate to Carina Biotech for the development of Chimeric Antigen Receptor T cell (**CAR-T**) therapy, which harnesses the body's immune system to fight cancer.
- Bionomics is eligible to receive up to A\$118 million in clinical & development milestones plus royalty payments if Carina fully develops and markets the new therapy. In the event that Carina sub-licenses the CAR-T treatment, Bionomics is eligible to share in the sub-licensing revenues in early clinical development and receive a substantial double-digit portion of the revenues in later stages of clinical development.
- ***In September 2021, Carina announced that it plans to initiate a clinical trial of BNC101 CAR-T therapy for the treatment of advanced colorectal (bowel) cancer in late 2022***
- Bionomics retains BNC101 for other types of therapies

