



ABN 53 075 582 740

## ASX ANNOUNCEMENT

25 May 2021

---

### Bionomics Investor Presentation

Bionomics Limited (ASX: BNO, OTCQB: BNOEF) (**Bionomics** or **Company**), a global, clinical stage biopharmaceutical company, is pleased to provide an updated Corporate Presentation following the successful capital raisings completed during April 2021 and subsequent pipeline expansion activities.

A copy of the presentation is available on the Company's website at <https://www.bionomics.com.au>.

Released on authority of the Chairman of the Board & CEO.

#### FOR FURTHER INFORMATION PLEASE CONTACT:

Ms Suzanne Irwin  
Company Secretary  
+61 8 8354 6100  
[CoSec@bionomics.com.au](mailto:CoSec@bionomics.com.au)

#### About Bionomics Limited

Bionomics (ASX: BNO, OTCQB: BNOEF) is a global, clinical stage biopharmaceutical company leveraging its proprietary platform technologies to discover and develop a deep pipeline of best in class, novel drug candidates. Bionomics' lead drug candidate BNC210, currently in development for initiation of a second Phase 2 trial for the treatment of PTSD, is a novel, proprietary negative allosteric modulator of the alpha-7 nicotinic acetylcholine receptor. 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.

[www.bionomics.com.au](http://www.bionomics.com.au)

### **Factors Affecting Future Performance**

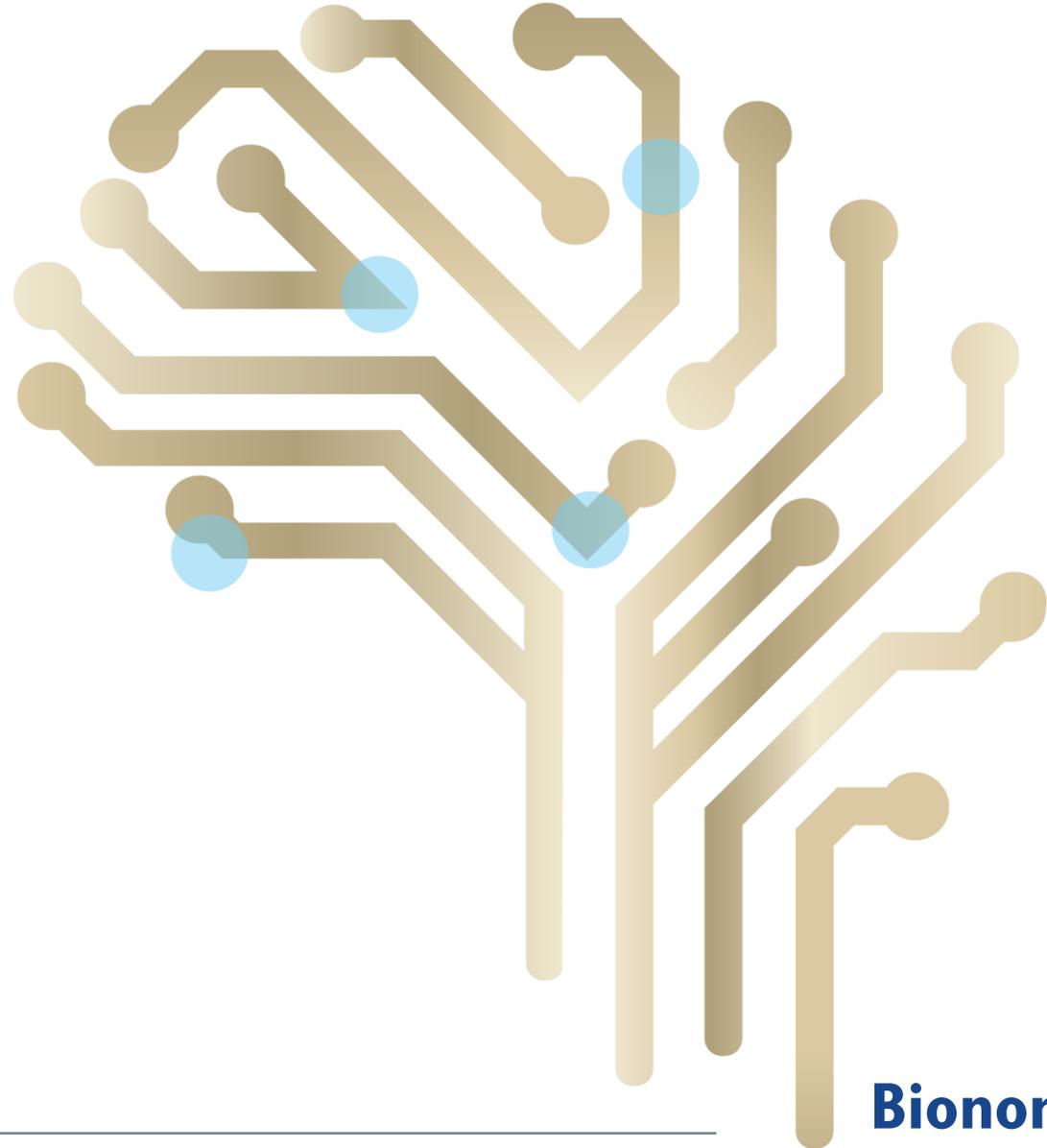
This announcement contains "forward-looking" statements within the meaning of the United States' Private Securities Litigation Reform Act of 1995. Any statements contained in this announcement that relate to prospective events or developments, including, without limitation, statements made regarding Bionomics' drug candidates (including BNC210), its licensing agreements with Merck & Co. and any milestone or royalty payments thereunder, drug discovery programs, ongoing and future clinical trials, and timing of the receipt of clinical data for our drug candidates are deemed to be forward-looking statements. Words such as "believes," "anticipates," "plans," "expects," "projects," "forecasts," "will" and similar expressions are intended to identify forward-looking statements. There are a number of important factors that could cause actual results or events to differ materially from those indicated by these forward-looking statements, including unexpected safety or efficacy data, unexpected side effects observed in clinical trials, risks related to our available funds or existing funding arrangements, our failure to introduce new drug candidates or platform technologies or obtain regulatory approvals in a timely manner or at all, regulatory changes, inability to protect our intellectual property, risks related to our international operations, our inability to integrate acquired businesses and technologies into our existing business and to our competitive advantage, as well as other factors. Results of studies performed on our drug candidates and competitors' drugs and drug candidates may vary from those reported when tested in different settings.

---

# TO IMPROVE THE LIVES OF PEOPLE LIVING WITH SERIOUS CNS DISORDERS

Corporate Presentation  
BNO (Australia: ASX)  
BNOEF (USA: OTCQB)

May 2021



## SAFE HARBOUR STATEMENT

---

### Factors Affecting Future Performance

This presentation contains "forward-looking" statements within the meaning of the United States' Private Securities Litigation Reform Act of 1995. Any statements contained in this presentation that relate to prospective events or developments, including, without limitation, statements made regarding Bionomics' drug candidates (including BNC210, BNC105 and BNC101), its licensing agreement with Merck & Co. and any milestone or royalty payments thereunder, drug discovery programs, ongoing and future clinical trials, and timing of the receipt of clinical data for our drug candidates are deemed to be forward-looking statements. Words such as "believes," "anticipates," "plans," "expects," "projects," "forecasts," "will" and similar expressions are intended to identify forward-looking statements.

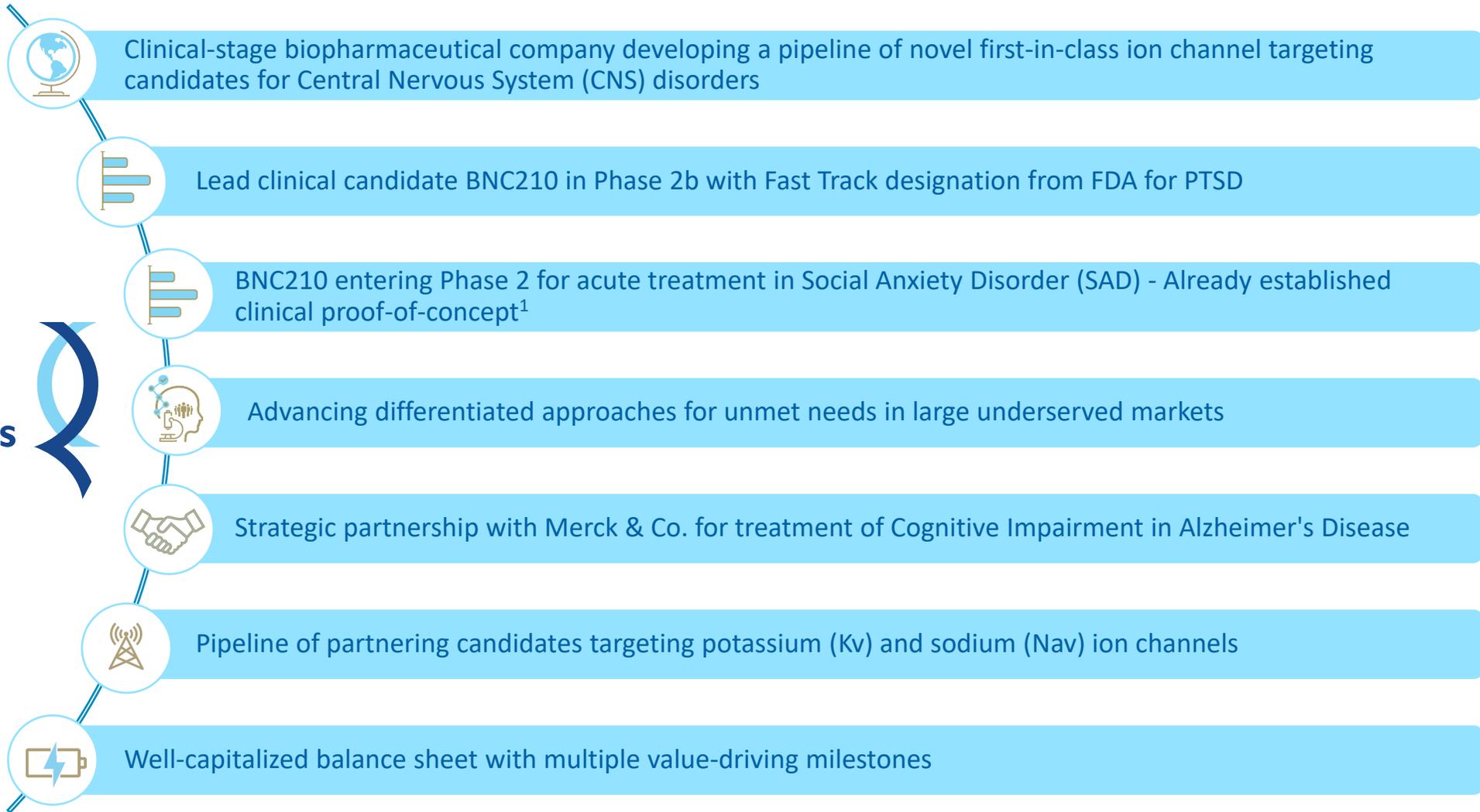
There are a number of important factors that could cause actual results or events to differ materially from those indicated by these forward-looking statements, including unexpected safety or efficacy data, unexpected side effects observed in clinical trials, risks related to our available funds or existing funding arrangements, our failure to introduce new drug candidates or platform technologies or obtain regulatory approvals in a timely manner or at all, regulatory changes, inability to protect our intellectual property, risks related to our international operations, our inability to integrate acquired businesses and technologies into our existing business and to our competitive advantage, as well as other factors. Results of studies performed on our drug candidates and competitors' drugs and drug candidates may vary from those reported when tested in different settings.

Subject to the requirements of any applicable legislation or the listing rules of any stock exchange on which our securities are quoted, we disclaim any intention or obligation to update any forward-looking statements as a result of developments occurring after the date of this presentation.





**Bionomics**



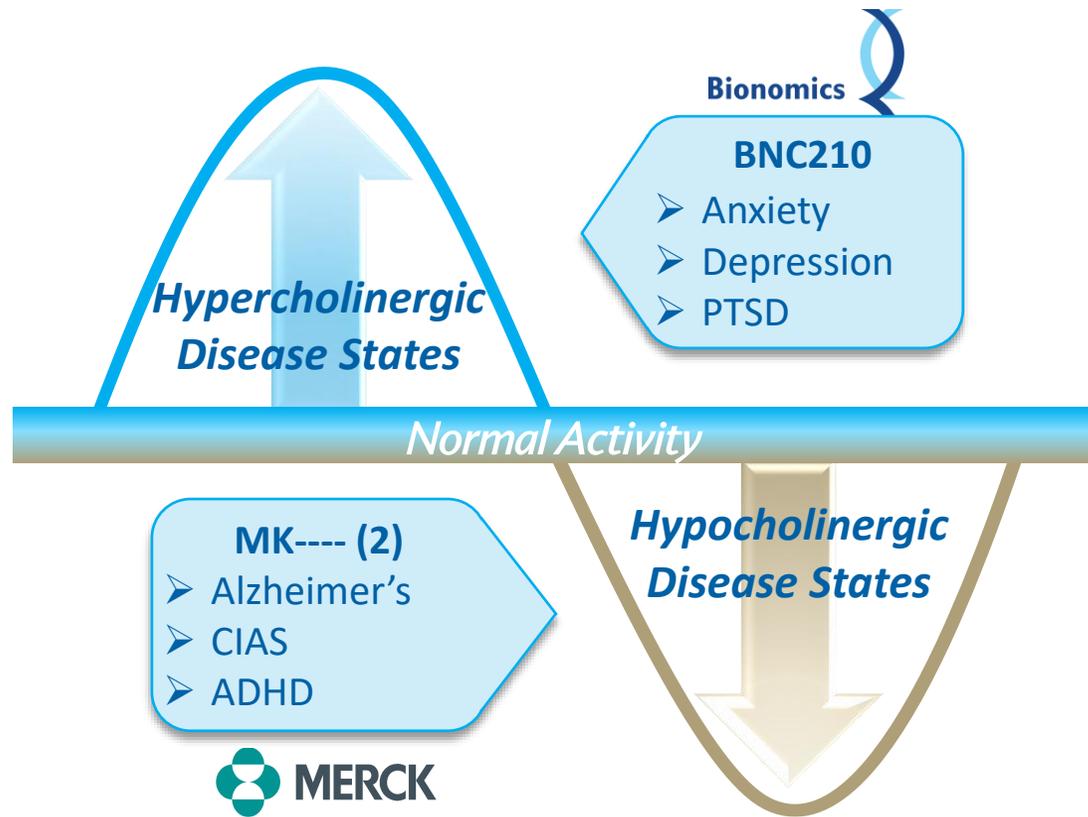
PTSD = Post-Traumatic Stress Disorder

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

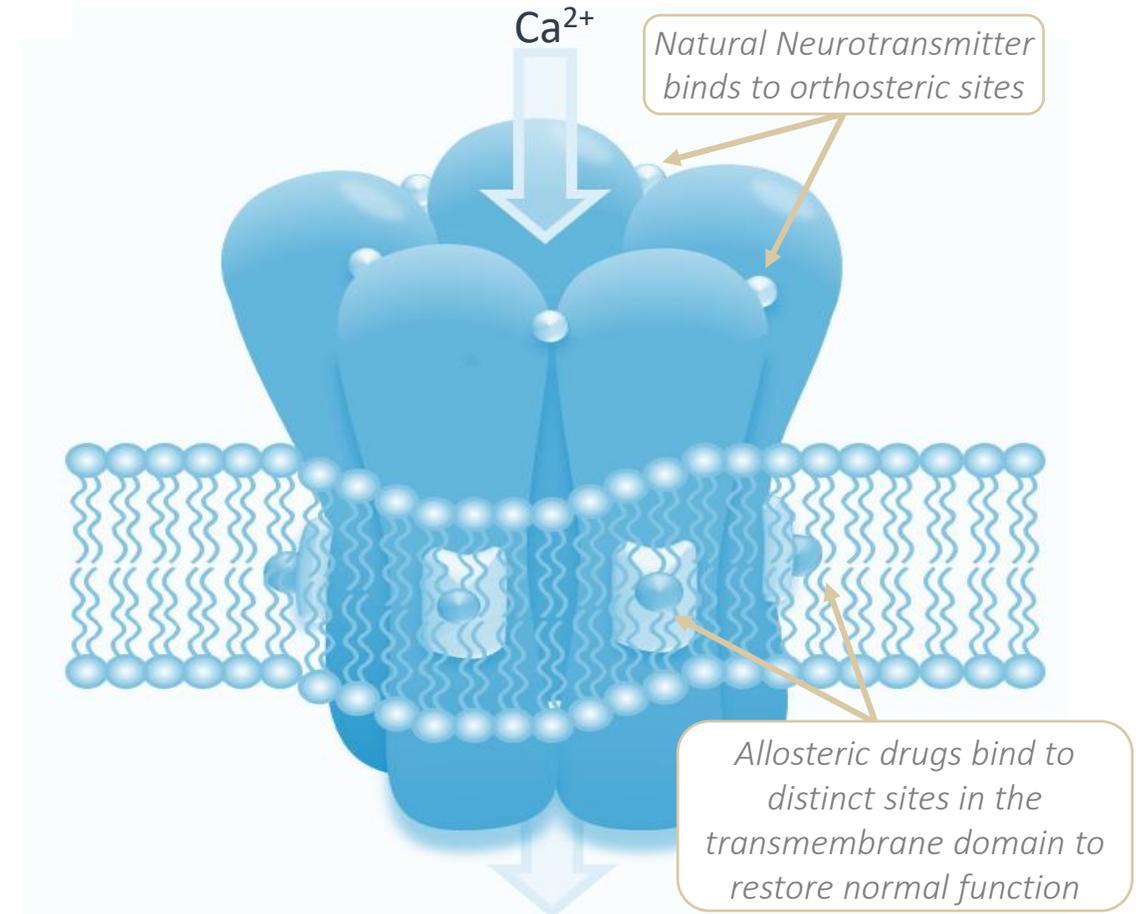




## Targeting *Distinct CNS Conditions* with *Neurotransmitter Imbalance*

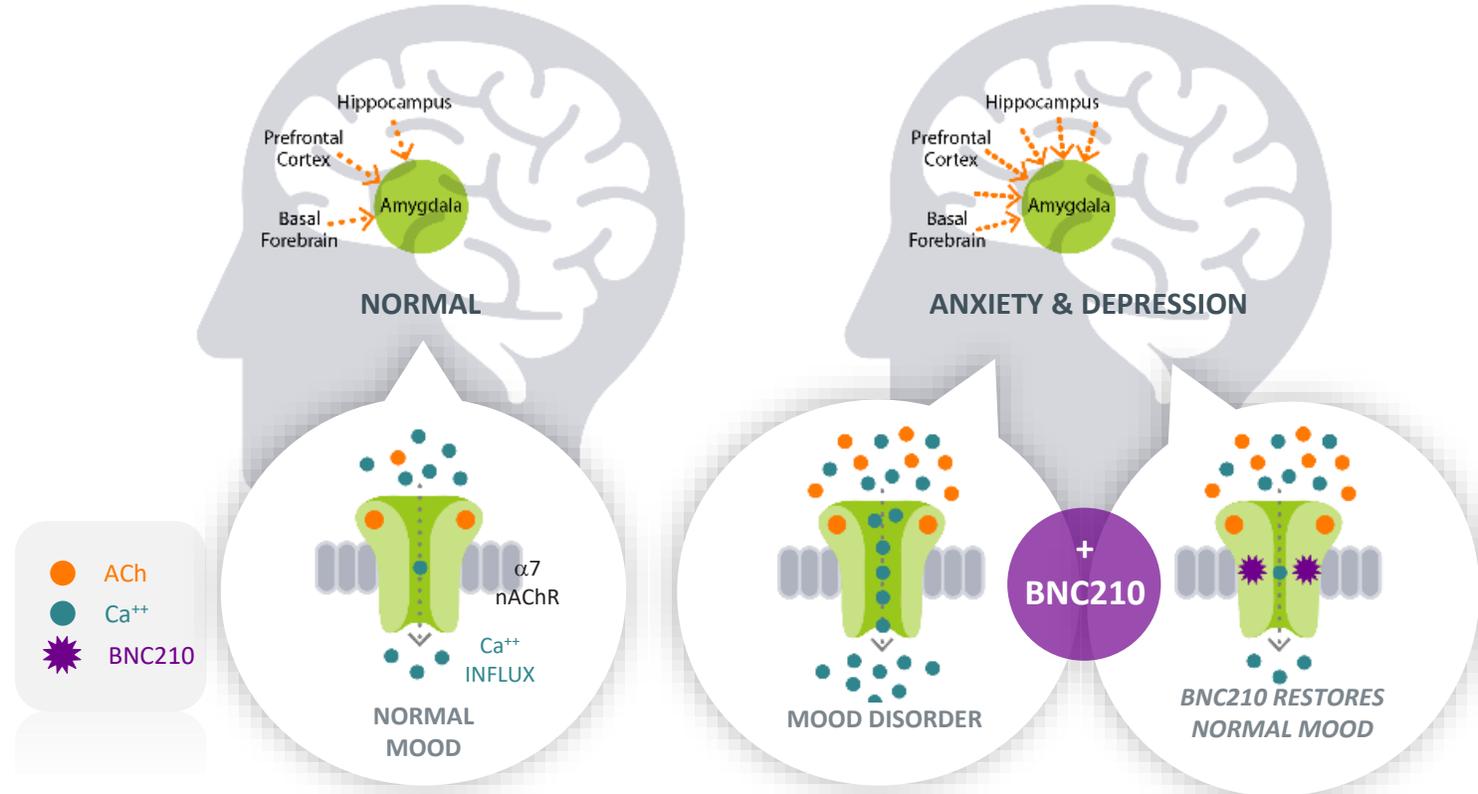


## Normalizing effect utilizing *Allosteric Modulation*





*Action of **BNC210**  
Depends on  
Acetylcholine  
Neurotransmission  
and Allosteric  
Modulation of  
 $\alpha 7$  nAChR*

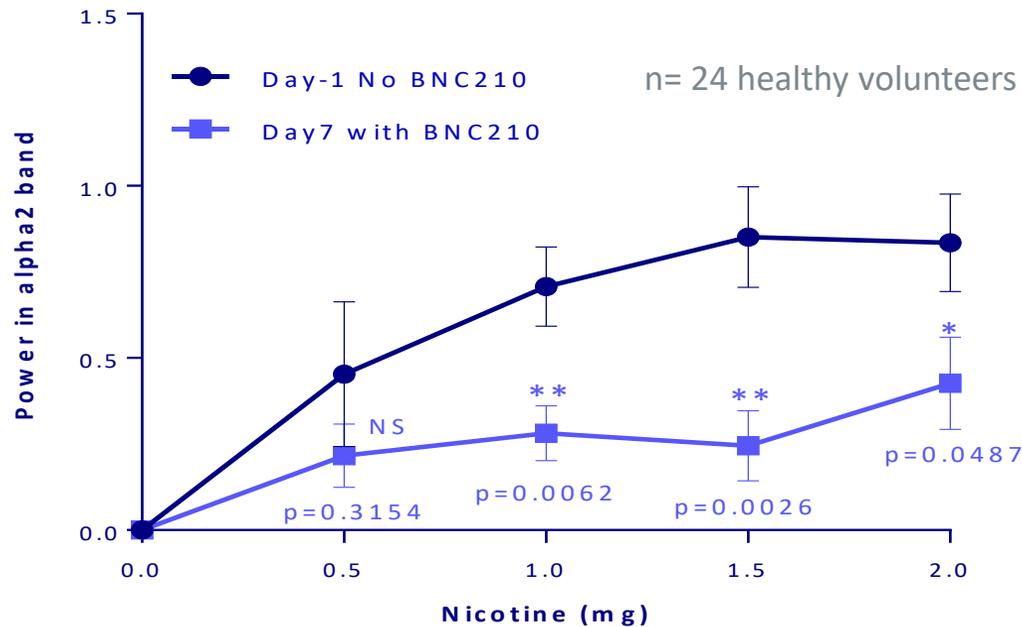


*NAMs have **self-limiting activity** determined by the **cooperative interaction** between the **compounds binding at the allosteric and orthosteric sites** e.g. BNC210 and acetylcholine*





## Demonstration of Target Engagement in Humans: *BNC210 reduced nicotine-induced EEG responses*



EEG response to nicotine is achieved through **activation of nicotinic receptors in the brain**



The major populations targeted are  $\alpha4\beta2$  and  $\alpha7$  receptors



Oral dosing with 2,000 mg BNC210 for 7 days **reduced nicotine-induced EEG power** in the  $\alpha2$  band



**Reduction in the EEG response is due to negative allosteric modulation of the  $\alpha7$  nAChR by BNC210**

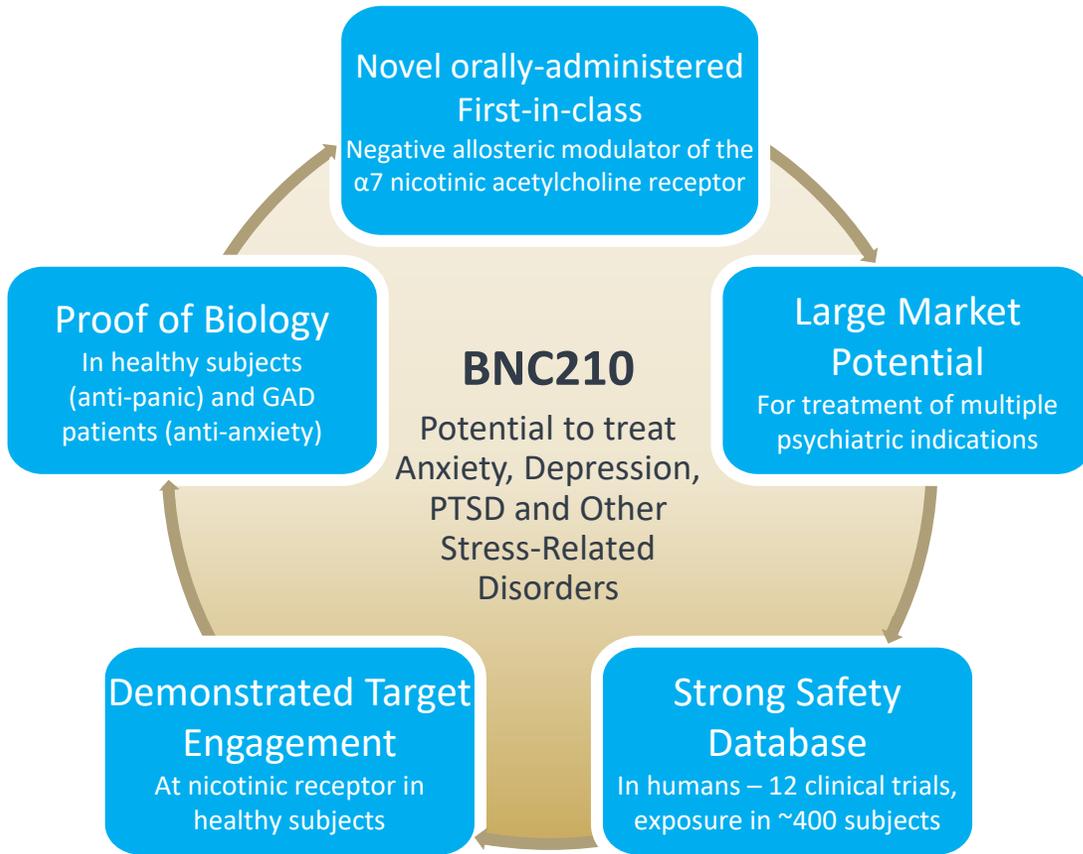




PROGRAM	PRE-IND	PHASE 1	PHASE 2A	PHASE 2B	TIMING
<b>BNC210</b> α7 nAChR* Negative Allosteric Modulator (NAM)  	<b>Post-Traumatic Stress Disorder (PTSD)</b> 200 patients across ~25 centres in US				<i>Start: Mid-2021</i> <i>Top-line data: 1H'23</i>  <i>To Be Disclosed</i>  <i>Ongoing</i>
	<b>Acute Social Anxiety Disorder (SAD)</b> Planning underway				
	<b>+MDMA derivative EMP-01 for PTSD</b> <i>Memorandum of Understanding to explore combination treatment regimen for PTSD</i>				
 <b>MERCK</b> <b>COLLABORATION</b> α7 nAChR* Positive Allosteric Modulator (PAM)	<b>2 candidates for cognitive deficits in Alzheimer's</b> Phase 1 safety & biomarker studies ongoing				<i>Undisclosed</i>
<b>PAIN</b> Nav1.7/1.8 Inhibitors	<b>Candidate</b>				<i>Ongoing</i>
<b>COGNITION</b> Kv3.1/3.2 Activators	<b>Series Lead</b>				

\* nAChR = nicotinic acetylcholine receptor





BNC210 vs. Current Therapies (Potential Advantages*)					
Drug	Fast Acting	No Sedation	No Withdrawal Syndrome	No Memory Impairment	No Drug/Drug Interactions
Benzos <sup>1</sup>	✓	✗	✗	✗	✓
SSRIs / SNRIs <sup>2</sup>	✗	✓	✗	✓	✗
<b>BNC210</b>	✓	✓	✓	✓	✓

\*Based on data from preclinical studies, Phase 1 & 2 clinical trials

1. Includes Valium and certain other benzodiazepines

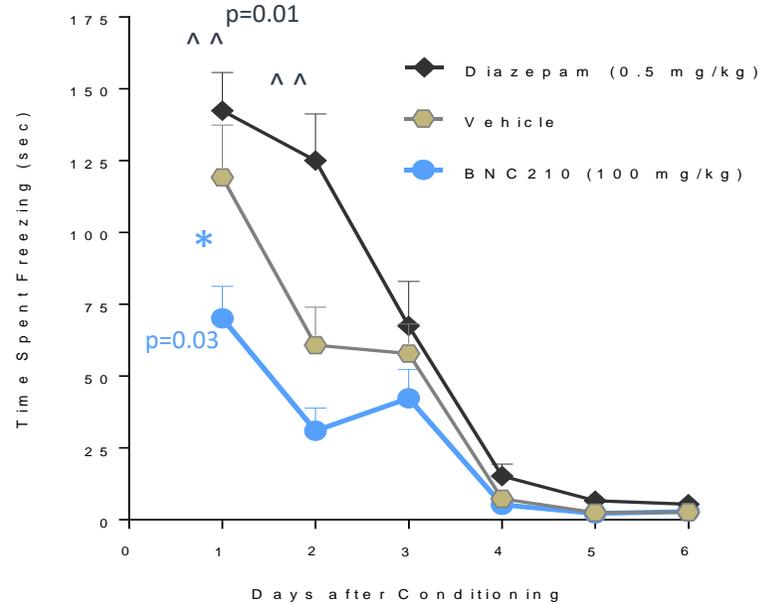
2. Includes Prozac and certain other SSRIs (Selective Serotonin Reuptake Inhibitors) / SNRIs (Serotonin-Norepinephrine Reuptake Inhibitors)





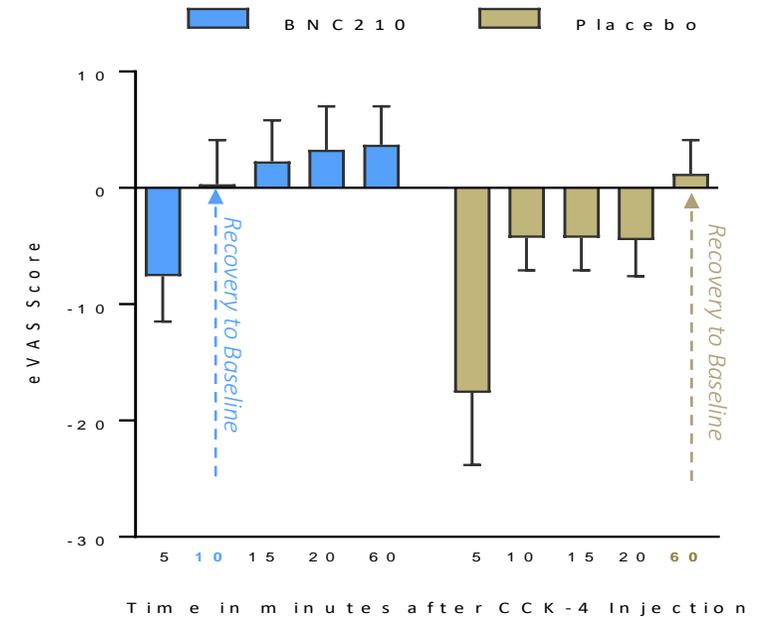
People with *PTSD* and anxiety disorders have amplified fear responses to trauma- or stress-related stimuli and *impaired* fear extinction

### 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

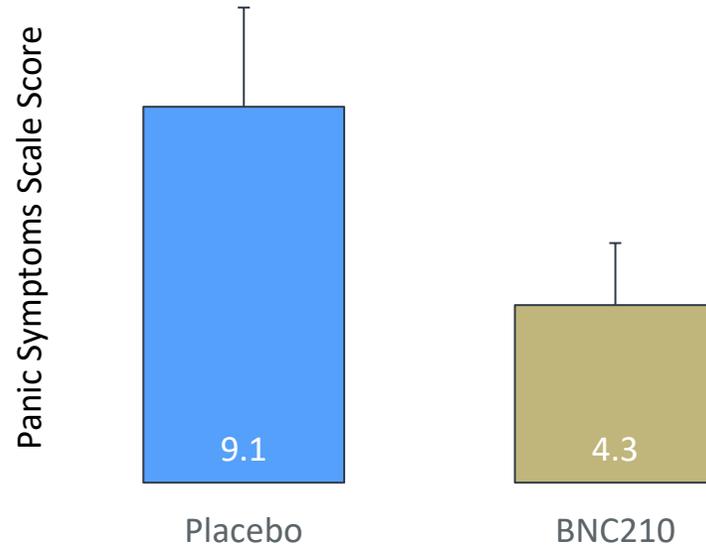
CCK4 = Cholecystokinin Tetrapeptide



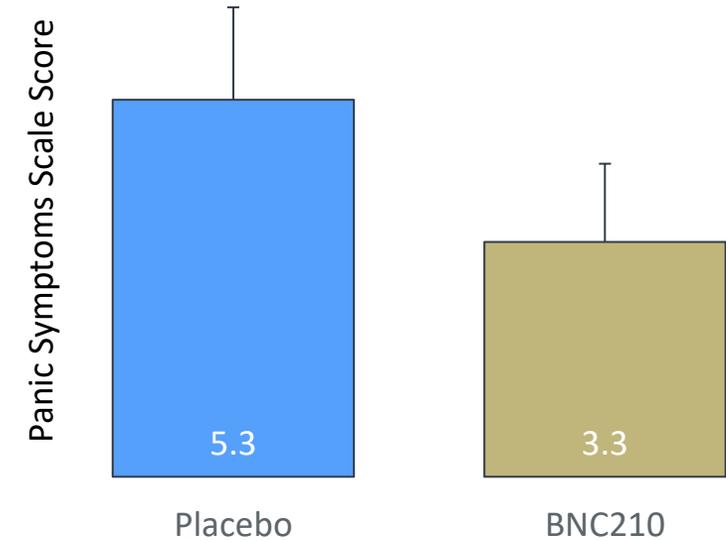


*Evaluation conducted in 15 healthy volunteers who experienced a CCK-4-induced panic attack*

↓ **Total Symptoms: 37.7% reduction (p<0.05)**



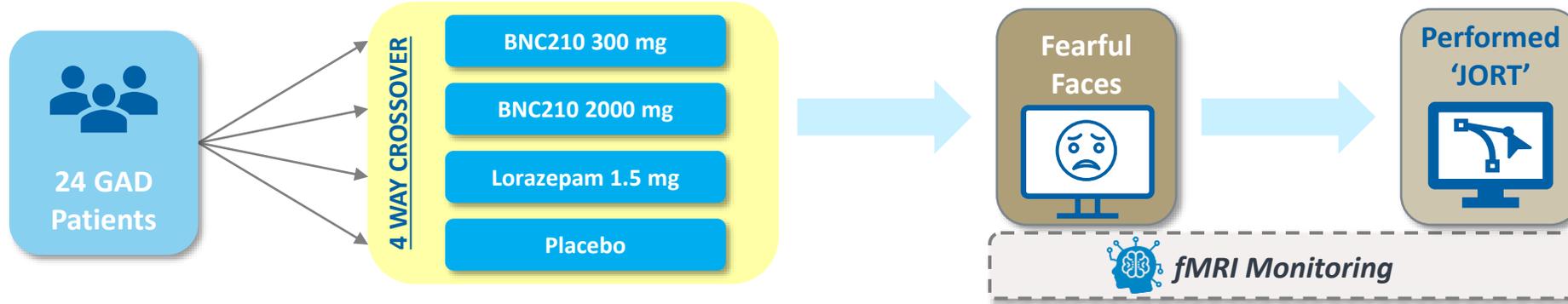
↓ **Symptom Intensity: 52.7% reduction (p<0.05)**



**Reduction in the total number of panic symptoms and panic symptom intensity - measured with the panic symptom scale**

CCK4 = Cholecystokinin Tetrapeptide





**Significantly reduced activation of L & R Amygdala** caused by viewing fearful faces ( $p < 0.001$ )

**BNC210: 300 mg**

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

**BNC210: 300 mg**

Group	Left Hemisphere	Right Hemisphere
Placebo	~0.85	~0.80
BNC210	~0.05	~0.08

**Significantly reduced threat avoidance behaviour** of anxious subjects in the JORT behavioural task

**BNC210: 300 mg 2000 mg**

Group	Mean Intensity	P-value
Placebo	~0.38	-
Lorazepam	~0.15	P=0.165
BNC210 300 mg	~0.05	P=0.007
BNC210 2000 mg	~0.10	P=0.033

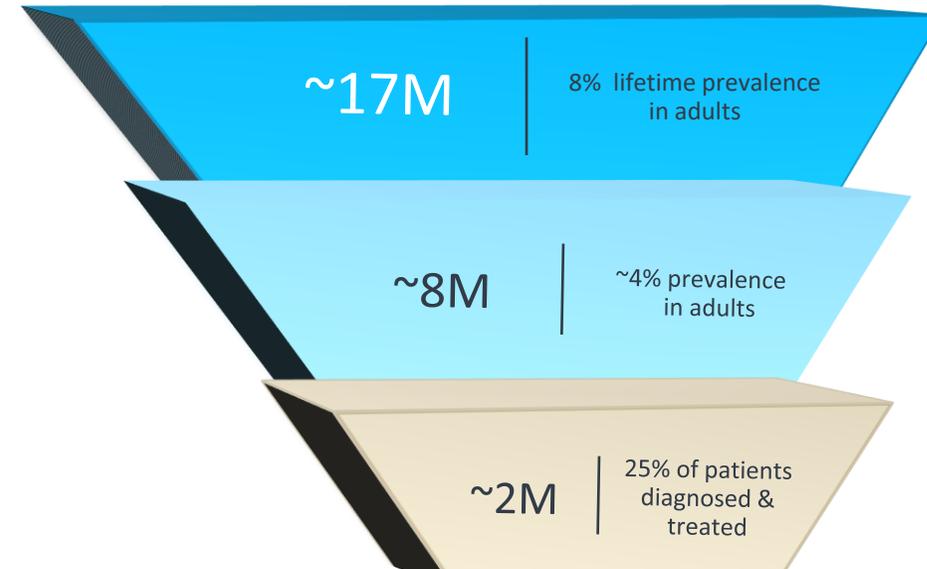
- **Amygdala activation is an imaging surrogate for anxiety**
- **Connectivity between the Amygdala and Anterior Cingulate Cortex (ACC) is very strong in high anxiety**





## . . . And 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 lifetime<sup>1</sup>
- PTSD is 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



### Opportunity for BNC210

- ✓ Unmet medical need in large patient population
- ✓ Advancement in care
- ✓ Limited branded competition
- ✓ Ability to achieve large market share





### Key Milestones Towards Continuing Development of BNC210 for the Treatment of PTSD

- ✗ Previous Phase 2 RESTORE PTSD Trial missed primary CAPS-5 endpoint at 12-weeks
- ✗ **Liquid suspension formulation with large food effect resulted in low blood exposure**, compliance and high variability

2018

- ✓ **Anti-depressant and anti-anxiety trends seen at earlier (4-week) time points**
- ✓ **Excellent safety profile**

2019  
2020

- ✓ Pharmacometric analysis of Phase 2 PTSD data showed **potential for significant patient benefit with adequate drug exposure achieved**
- ✓ Novel proprietary spray dry solid dose **formulation developed which eliminates food effect and achieves adequate exposures**
- ✓ **Positive FDA Type C Meeting** feedback on BNC210 PTSD program
- ✓ FDA granted **Fast Track designation for BNC210 in PTSD**

2021

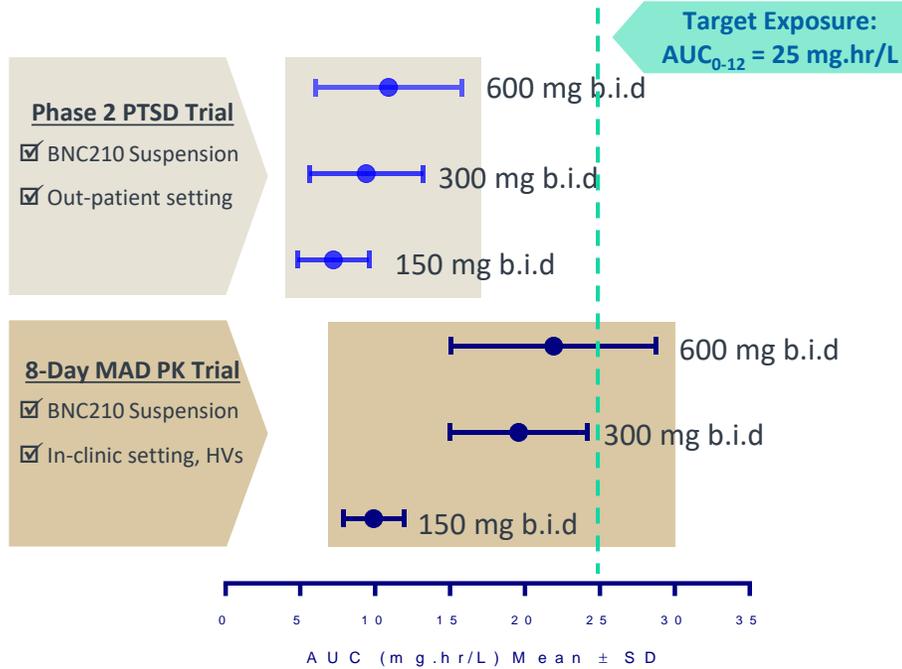
- ✓ **Determined Phase 2b PTSD trial dosing** of BNC210
- ✓ **Start of Phase 2b PTSD trial** projected for mid 2021





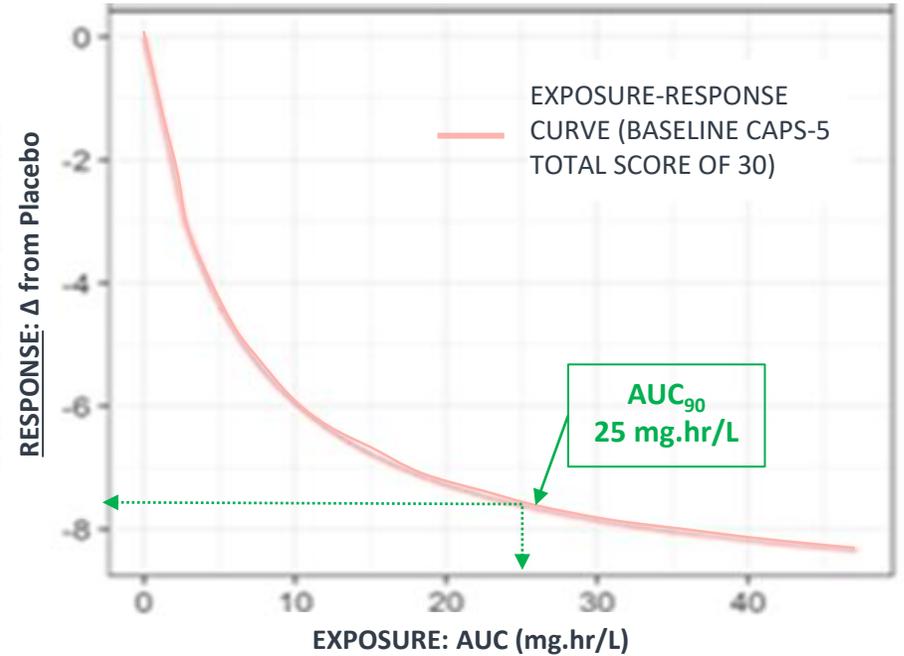
**Population pharmacokinetic modelling was done looking at the prior Phase 2 outpatient trial liquid suspension formulation**

## Pharmacokinetic Modelling:



**BNC210 plasma levels substantially lower than expected** using liquid suspension formulation

## Pharmacometric Analysis:



**↑ AUC Values (plasma exposure) = ↑ CAPS-5 Reduction (p<0.01)**





**Novel spray dry formulation overcomes food effect and has dose linear exposure**

**BNC210 Tablet formulation**

**Achieves target AUC >25 mg.hr/L with 900 mg doses b.i.d.**

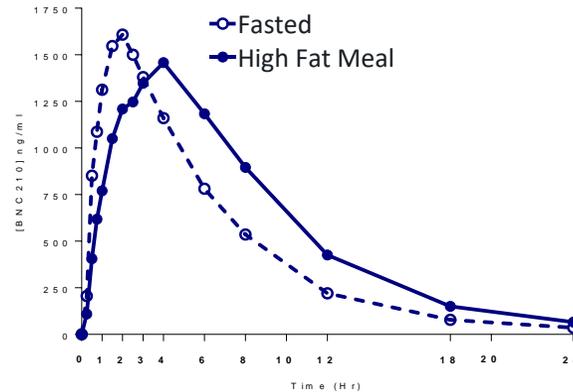
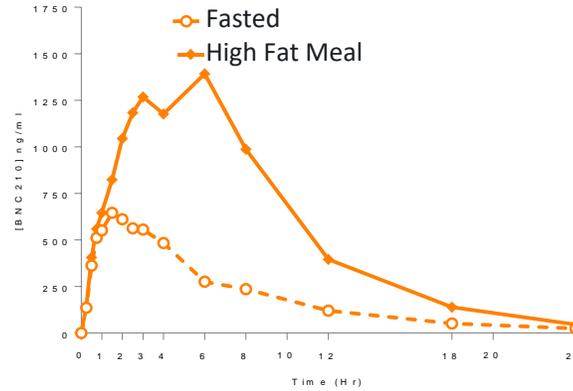
## New Tablet Formulation Eliminates Food Effect . . .

**Liquid Suspension (300 mg)**



Vs.

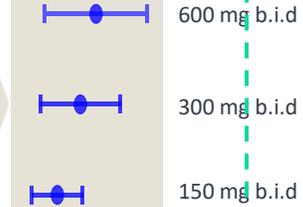
**Solid Dose Tablet (300 mg)**



## . . . And Achieves Target Exposure

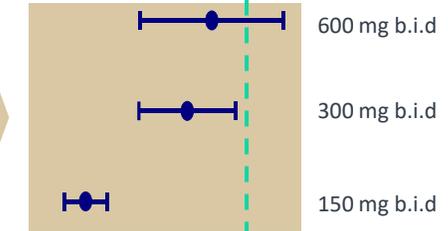
### Phase 2 PTSD Trial

- ✓ Liquid Suspension formulation
- ✓ Out-patient setting



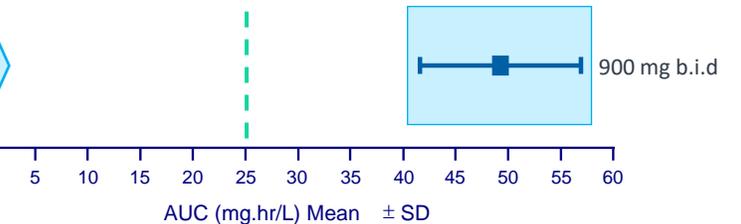
### 8-Day MAD PK Trial

- ✓ Liquid Suspension formulation
- ✓ In-clinic setting, HVs



### 7-Day PK Trial

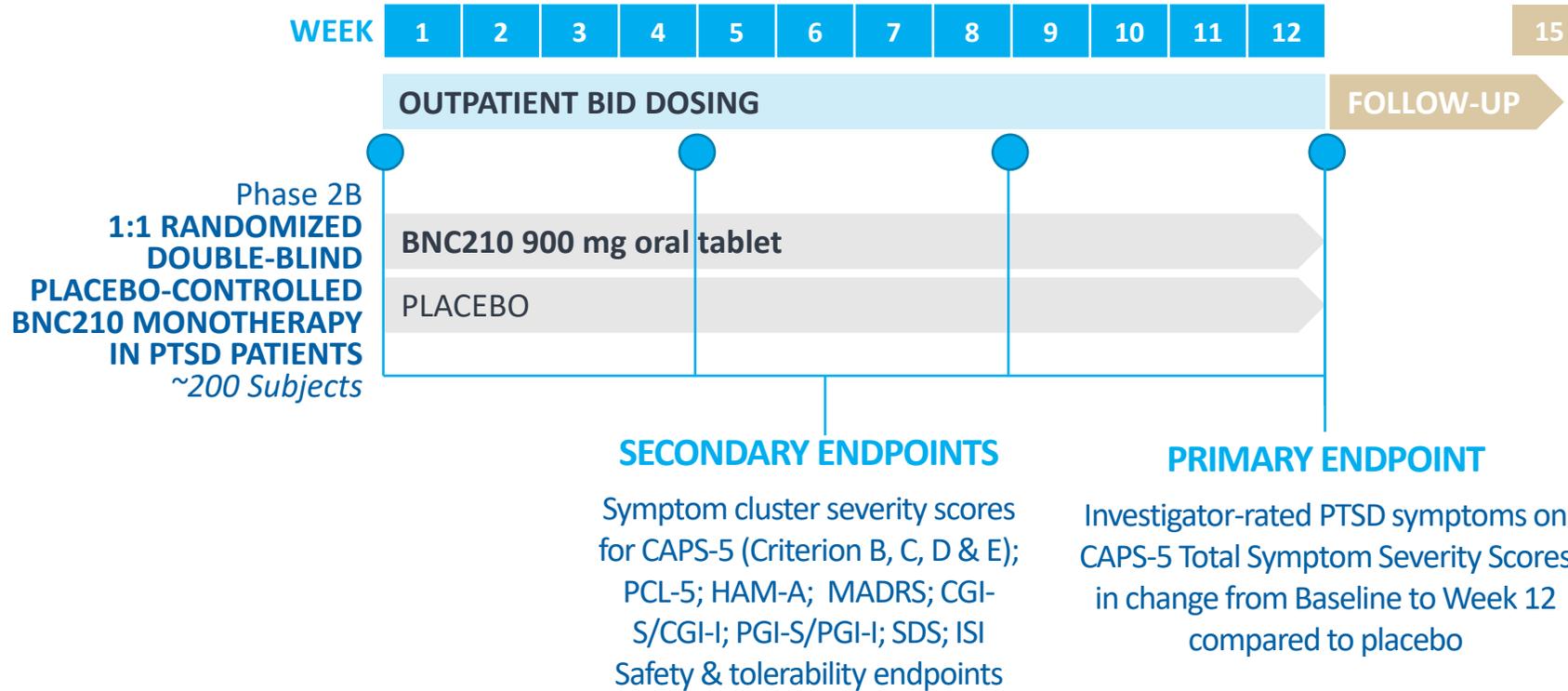
- ✓ New tablet formulation
- ✓ In-clinic setting, HVs



**Target Exposure: AUC<sub>0-12</sub> = 25 mg.hr/L**

b.i.d = Administered twice daily  
MAD = Multiple Ascending Dose





**PHASE 2B**

Single registrational-supporting trial for monotherapy treatment in PTSD

**KEY INCLUSION CRITERIA<sup>1</sup>**  
Female and male (18 – 75 years)  
Current PTSD diagnosis  
CAPS-5 ≥ 30 at Screening and Baseline (& ≤ 25% decrease Screening to Baseline)

~25 Sites  
US-based

**Top-line Data in 1H'2023**

<sup>1</sup>Full Eligibility Criteria = CAPS-5 Total Symptom Severity Score ≥ 30 at Screening and Baseline (and ≤ 25% decrease in score from Screening to Baseline)  
 CAPS-5 = Clinician-Administered PTSD Scale for the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5)  
 PCL-5 = PTSD Checklist for DSM-5  
 HAM-A = Hamilton Anxiety Rating Scale

MADRS = Montgomery-Asberg Depression Rating Scale  
 CGI = Clinical Global Impressions  
 PGI = Patient Global Impressions  
 SDS = Sheehan Disability Scale  
 ISI = Insomnia Severity Index





Joint Feasibility Assessment with:



# EmpathBio



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

# DAILY NEWS

Word • Business • Finance • Lifestyle • Travel • Sport • Weather

22 February 2021

Illustrative

## Memorandum of Understanding with EmpathBio's MDMA Derivative

- Initial collaborative framework of preclinical studies to collectively explore a combination drug treatment regimen with BNC210 and EMP-01
- MDMA-assisted psychotherapy has demonstrated significant symptom improvement in PTSD patients
- FDA has granted a Breakthrough Therapy designation to MDMA-assisted psychotherapy.
- EmpathBio is developing MDMA derivatives that may permit the entactogenic effects of MDMA to be separated from some of the known adverse effects.
- To explore the possibility of a combination treatment regimen warranting clinical evaluation





## ...And Acute Treatment of SAD Represents a Significant Unmet Need



Social Anxiety Disorder (SAD), or Social Phobia, is an acute onset of anxiety distinct from general anxiety

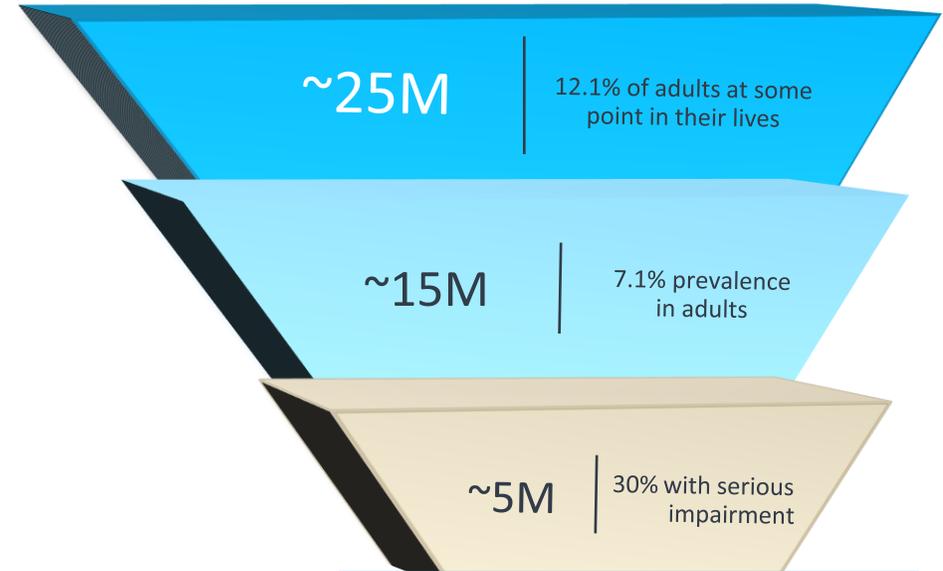


Often disguised as “Fear of Public Speaking” that includes anxiety from everyday social and performance situations



A disorder that substantially impacts people’s daily lives

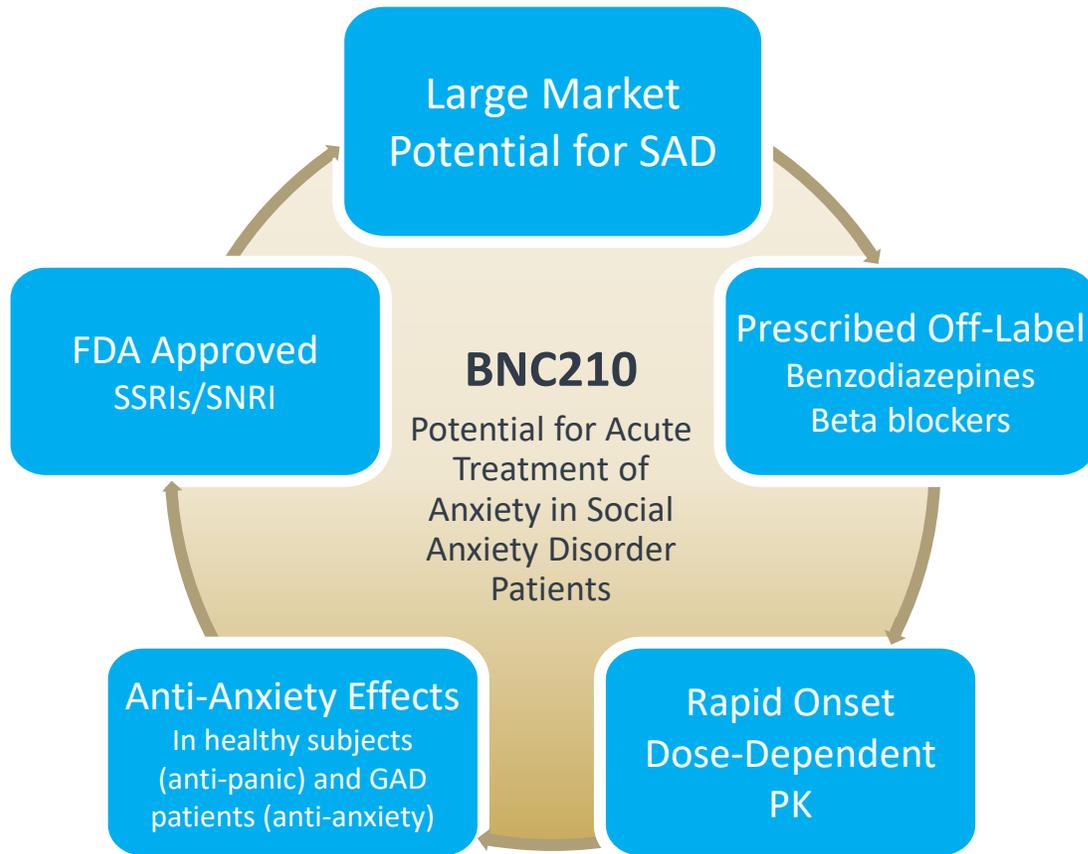
- Recognized as one of the most prevalent mental health conditions today affecting >25M Americans
- No fast-acting FDA-approved medications for, as-needed treatment of SAD
- Medications with the right pharmacokinetic profile and a novel mechanism are needed



### Opportunity for BNC210

- ✓ Unmet medical need in large patient population
- ✓ Advancement in care
- ✓ No branded competition
- ✓ Ability to achieve large market share





BNC210 vs. Current Therapies (Potential Advantages*)					
Drug	Fast Acting	No Sedation	No Withdrawal Syndrome	No Memory Impairment	No Drug/Drug Interactions
Benzos <sup>1</sup>	✓	✗	✗	✗	✓
SSRIs / SNRIs <sup>2</sup>	✗	✓	✗	✓	✗
<b>BNC210</b>	✓	✓	✓	✓	✓

\*Based on data from preclinical studies, Phase 1 & 2 clinical trials

1. Includes Valium and certain other benzodiazepines

2. Includes Prozac and certain other SSRIs (Selective Serotonin Reuptake Inhibitors) / SNRIs (Serotonin-Norepinephrine Reuptake Inhibitors)





## ✓ Emerging Regulatory Landscape and Unmet Need

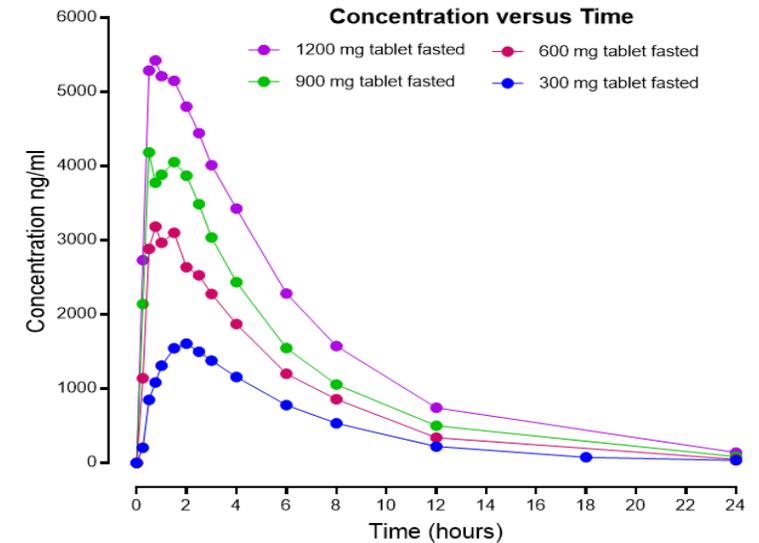
- No FDA-approved medications for fast-acting, as-needed treatment of SAD
- Benzodiazepines prescribed off-label have significant side effects of sedation, cognitive impairment and potential for addiction
- Exponentially increasing unmet need based on improving awareness and evolving social dynamics
- Buy-in from FDA on simplified public speaking challenge endpoint to evaluate the reduction in anxiety levels vs. placebo based on actions of CNS peer proceeding with registrational Phase 3 trial endpoint

## ✓ Rapid Onset of Action with BNC210 Formulation

- *Potential for reducing anxiety* following acute treatment of GAD patients and following induction of panic
- *Acute anxiolytic efficacy of BNC210 equivalent to lorazepam without sedative properties* and addiction liability
- Formulation ideal for acute dosing – *rapidly absorbed to high concentrations within a short period of time*



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

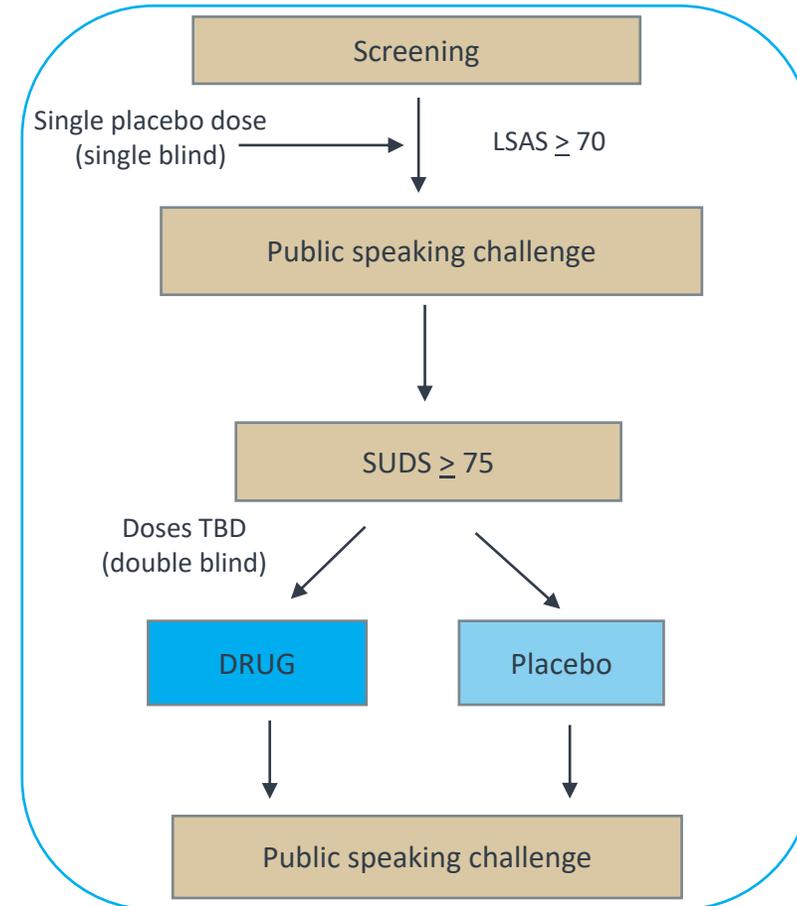




## BNC210 Phase 2 Trial Planning Underway

- ✓ Conducting preliminary background analysis around planning and study design
- ✓ Ability to significantly leverage public CNS peer's trial design for its ongoing Phase 3 in Social Anxiety Disorder
- ✓ Potential to conduct a rapid and cost-effective trial with the ability to generate compelling a data signal
- ✓ *Anticipate further clarity on advancing Phase 2 trial design in near future with potential to be underway in 2H2021*

## CNS Peer Reference Trial Design



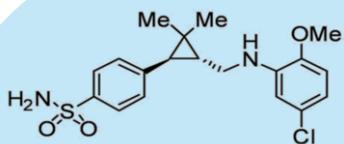


- Partnership generated US\$20M in upfront payment in 2014, research funding from 2014-2017 and US\$10M first clinical milestone in February 2017. Deal valued up to US\$506M in upfront, research and milestone payments plus additional royalties on net sales of licensed drugs
- MSD (a tradename of Merck & Co., Inc., Kenilworth NJ USA) Collaboration Update:
  - Phase 1 safety clinical trials of the lead molecule in healthy subjects have been completed and there are ongoing plans for further biomarker studies
  - A backup molecule that showed an improved potency profile in preclinical animal models versus the current lead molecule is advancing into Phase 1 clinical trials



- Agreement covers research on BNC375 and related compounds
- BNC375 demonstrated potent memory enhancing properties in animal models – both episodic and working memory improved
- Targeting cognitive impairment in Alzheimer's, Parkinson's and other conditions





BNC375 is Bionomics' Novel Partnering Candidate for Cognitive Impairment in Alzheimer's Disease and other disorders



Restores cognitive deficits in animal assays & models with Equivalent Efficacy to standard of care Aricept (Donepezil) Broad dosing range (up to 1000x)



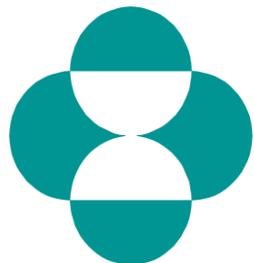
Effective in rat assays of cognition (Novel Object Recognition) Reverses scopolamine deficit



Effective in non-human primate assay of cognition (Novel Object Recognition) Reverses scopolamine deficit



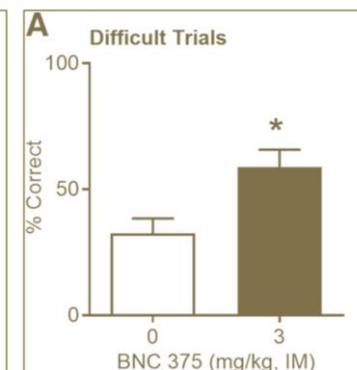
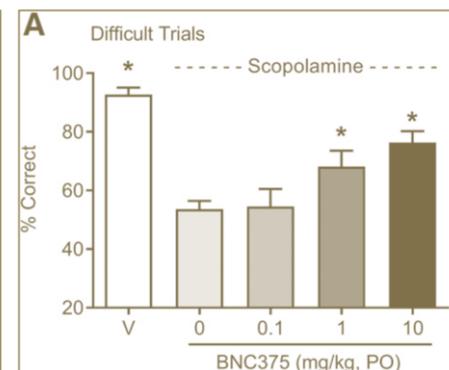
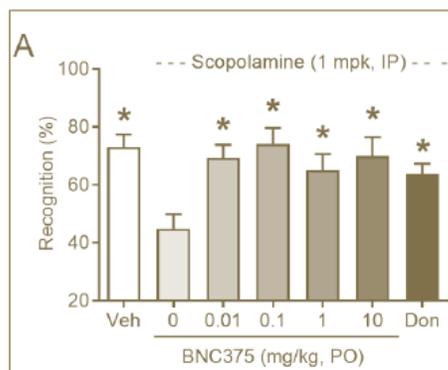
Efficacious in African Green Monkey model of Alzheimer's Disease (develop plaques with age)



# MERCK

PARTNERSHIP

## Snapshot of Early BNC375 Studies



Wang et al. J Pharmacol Exp Ther 373:311-324, May 2020 <https://pubmed.ncbi.nlm.nih.gov/32094294/>

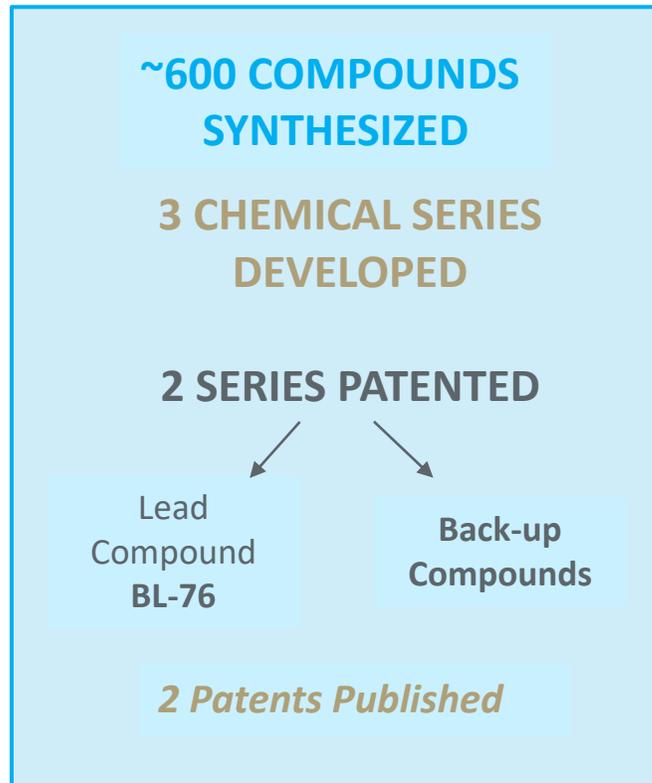


## Emerging CNS Pipeline for Partnering



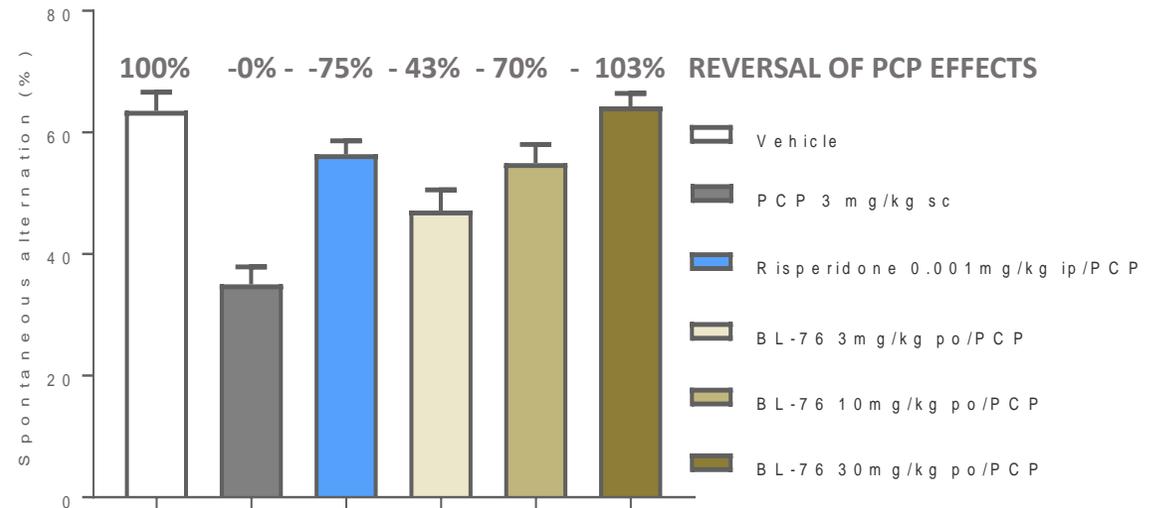
*Promising therapeutic strategy for improving cognitive dysfunction and negative symptoms*

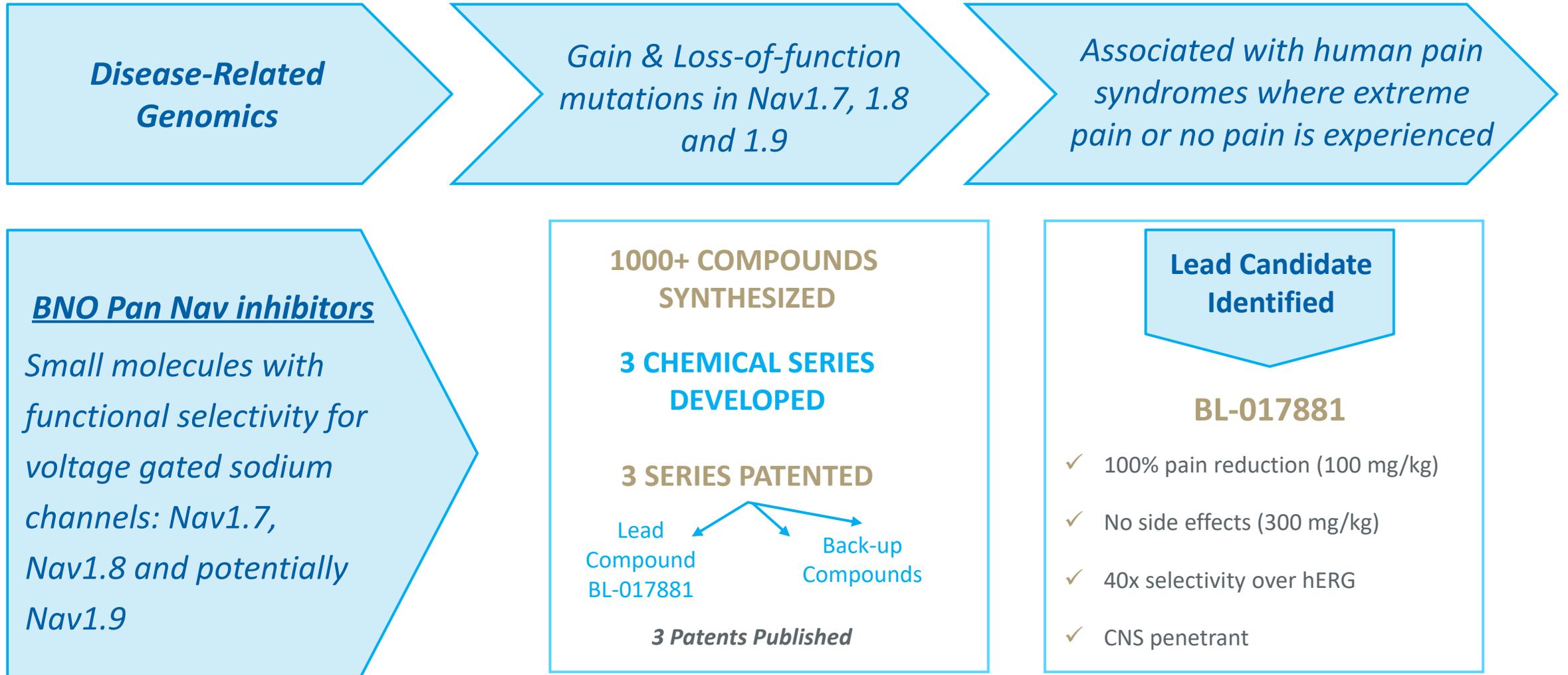
Potential in *schizophrenia* and other illnesses such as *Autism Spectrum Disorder* and *Alzheimer's Disease*



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

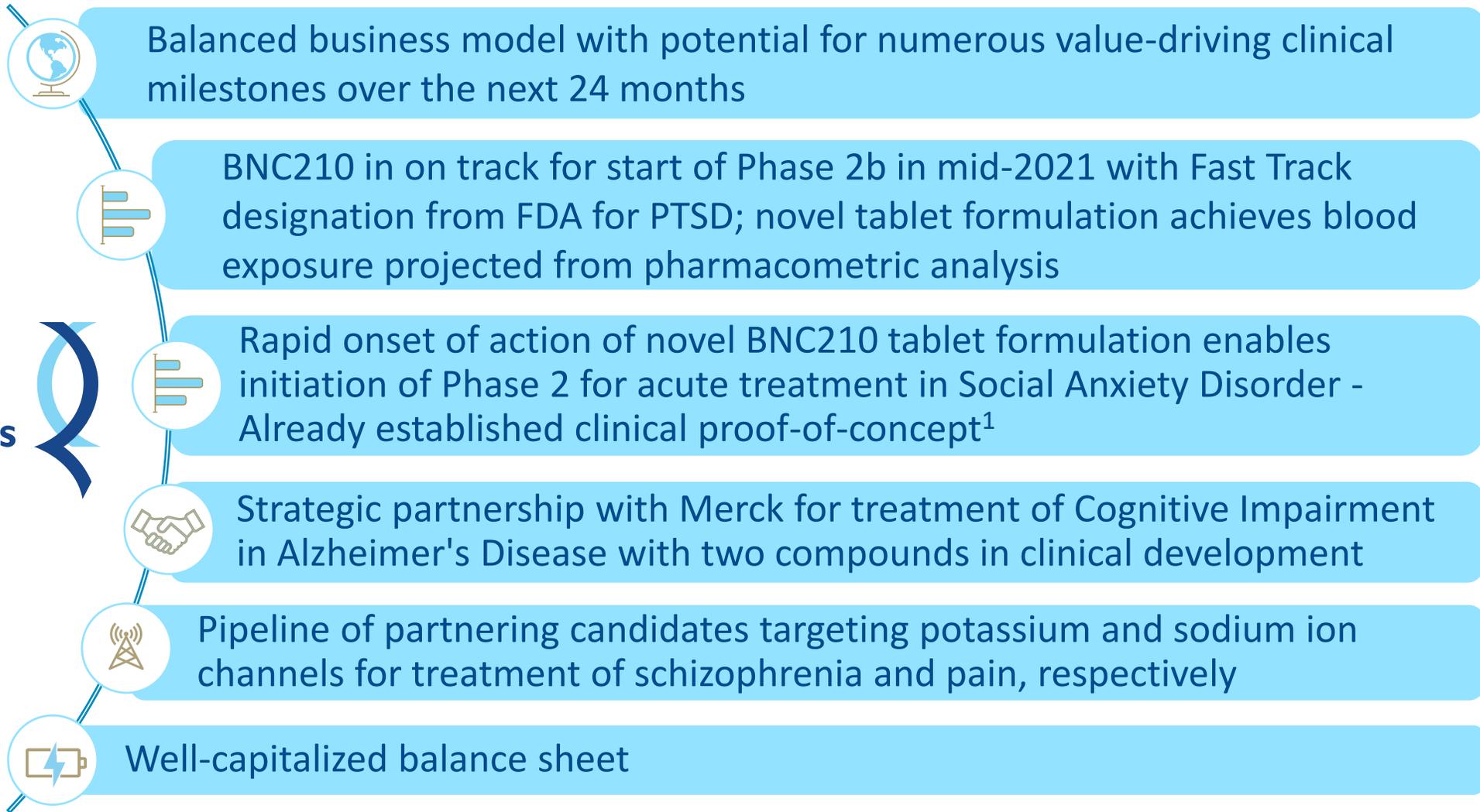
Lead Compound BL-76 Fully Reverses PCP-induced Cognitive Deficit in Mice in the T-maze







**Bionomics**





## APPENDIX





**Errol De Souza PhD**  
Executive Chairman

- More than 35 years experience in biotech, big pharma and academia
- Previous President & CEO of multiple public (Biodel, Synaptic) & private (Neuropore, Archemix) biotech companies
- Founder of Neurocrine Biosciences
- Previous SVP Aventis Pharmaceuticals
- Previous Head of CNS Diseases, DuPont Merck
- Multiple public and private boards



**Connor Bernstein**  
Vice President Strategy & Corporate Development

- 10 years experience in Life Sciences Investment Banking in strategic advisory, M&A, and equity and debt financings
- Broad execution expertise with closed deals representing >US\$38B in aggregate value
- Formerly with Apeiron Investment Group assisting various Biotech companies in finance, strategy, corporate development and investor relations
- Prior Healthcare Investment Banking roles include RBC Capital Markets, Perella Weinberg Partners, Guggenheim Securities and Piper Jaffray



**Adrian Hinton**  
Acting Chief Financial Officer

- Over a 43 year career at Deloitte (Adelaide)
- Retired in 2018 as Principal Audit and Assurance Group
- Broad-based knowledge of contemporary accounting and audit issues in a wide range of industries
- Experience in preparing Due Diligence reviews, investigative accounting reports and review of profit forecasts



**Liz Doolin**  
Vice President Clinical Development

- 25 year international career in drug discovery, clinical and life sciences research
- Joined Bionomics in 2008
- Extensive clinical operations and regulatory experience
- Oncology and CNS drug development
- Strong biotechnology research and manufacturing background





**Errol De Souza PhD**  
Executive Chairman

- More than 35 years experience in biotech, big pharma and academia
- Previous President & CEO of multiple public (Bidel, Synaptic) & private (Neuropore, Archemix) biotech companies
- Founder of Neurocrine Biosciences
- Previous SVP Aventis Pharmaceuticals
- Previous Head of CNS Diseases, DuPont Merck
- Multiple public and private boards



**Alan Fisher**  
Non-Executive Director

- 24 years at accounting firm Coopers & Lybrand as lead Advisory Partner – Melbourne Corporate Finance Division
- Last 22 years as founder of his own Corporate Advisory company specializing in M&A business restructurings, strategic advice and capital raisings for small cap companies
- Non-Executive chairman – Centrepont Alliance Ltd & IDT Aust.
- Non-Executive Director and chair of Audit and Risk committee of Thorney Technology



**David Wilson**  
Non-Executive Director

- Chairman & Founding Partner of WG Partners
- Over 30 years' experience in investment banking in City of London
- Previous CEO of Piper Jaffray Ltd
- Previous Joint Head of UK Investment Banking Group, ING Barings
- Previous head of Small Companies Corporate Finance, Deutsche Bank
- Previous Head of Small Companies Corporate Broking, UBS



**Jane Ryan PhD**  
Non-Executive Director

- Over 30 years of international experience in the pharmaceutical and biotechnology industries
- Worked in Australia, the US and the UK with companies including Peptech, Roche, Cambridge Antibody Technology and Biota Holdings
- Led many successful fundraising campaigns and Licensing initiatives inclusive of a \$230m US government contract
- Chair of the Advisory Board of the ithree Institute at the University of Technology Sydney (UTS)





**Srinivas Rao PhD**  
Non-Executive Director

- Chief Scientific Officer at ATAI Life Sciences AG
- Over 19 years of professional experience in pharmaceutical and biotechnology industries
- Has held the titles of Chief Scientific, Medical, or Executive Officer at companies ranging from Venture backed start-ups to vertically-integrated publicly traded pharmaceutical companies
- PhD in neurobiology from Yale Graduate School
- M.D. from Yale School of Medicine



**Aaron Weaver**  
Non-Executive Director

- Managing Director at Apeiron Investments focused on the life sciences sector
- Snr General Counsel supporting fundraising & IR at ATAI Life Sciences AG
- Qualified Chartered Financial Analyst (CFA) and a registered solicitor in the UK
- Previously an investor banker at Credit Suisse in London within the Capital Markets Solutions team
- Previous capital markets solicitor at Allen & Overy LLP

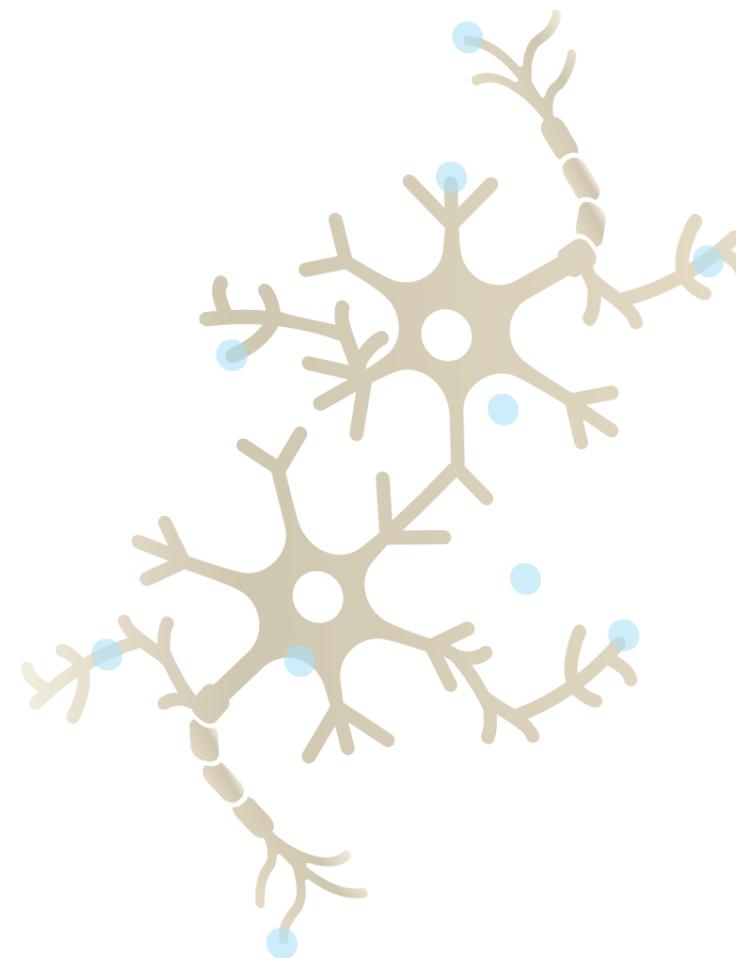


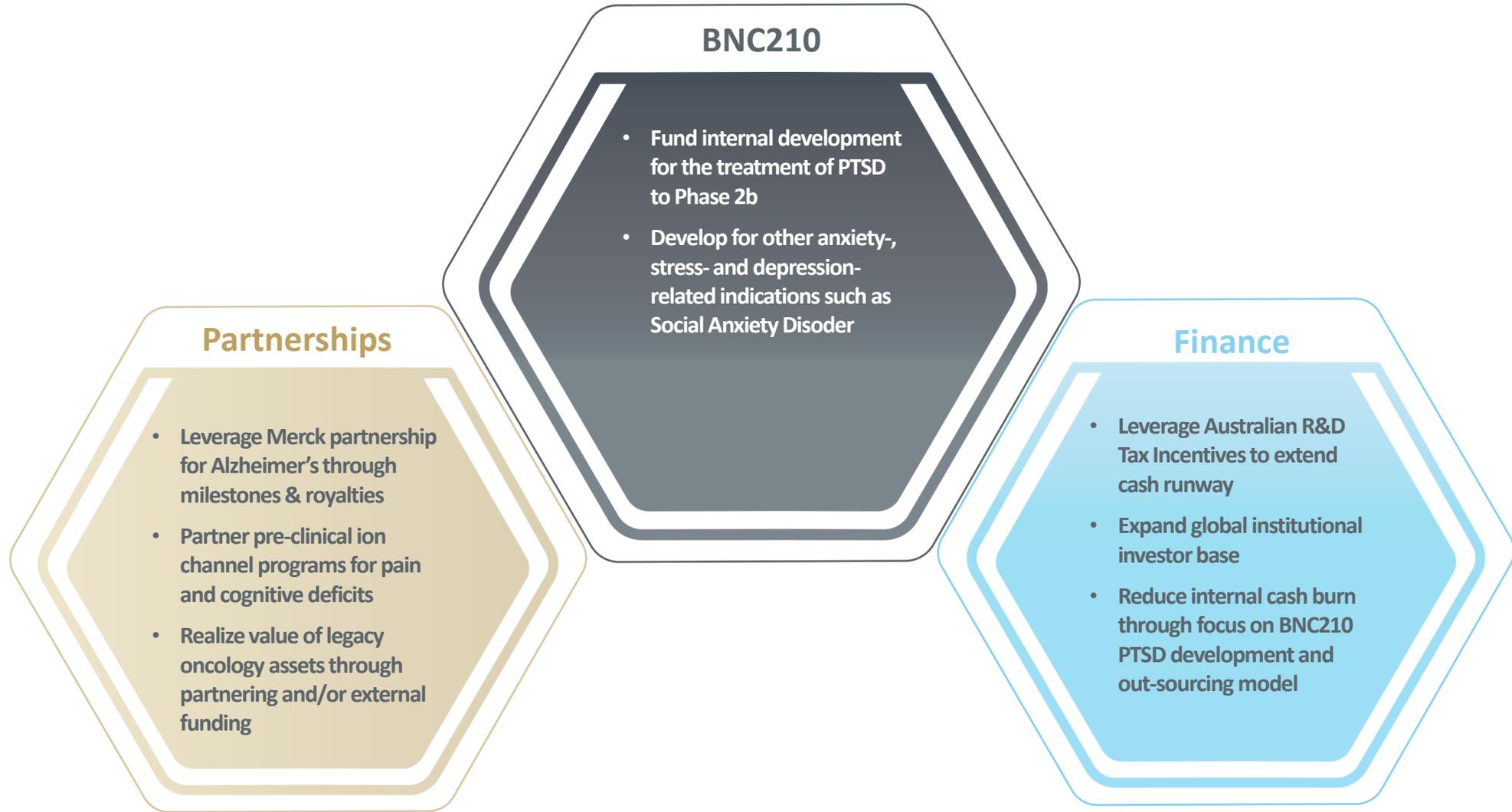
**Mitchell Kaye**  
Non-Executive Director

- COO BVF Partners
- Founding member of Xmark Opportunity Partners LLC
- Founding member of Brown Simpson Asset Management LLC
- Founder of MedClaims Liaison LLX
- Previous Managing Director Navigant Capital Advisors, Head of Navigants Financial Institutions restructuring Solutions team

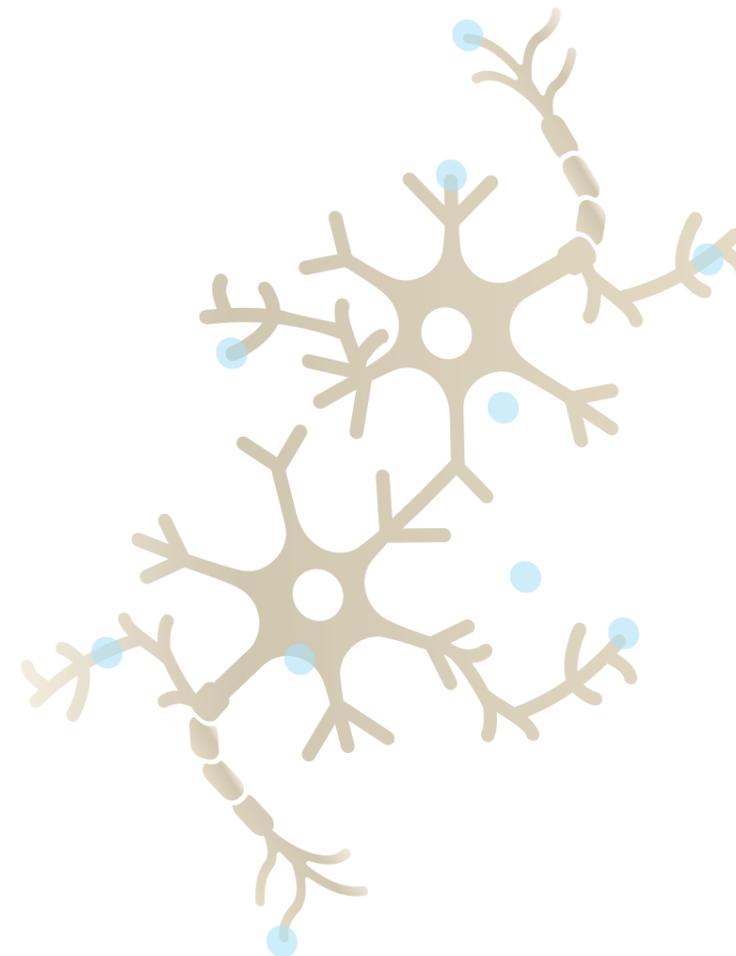


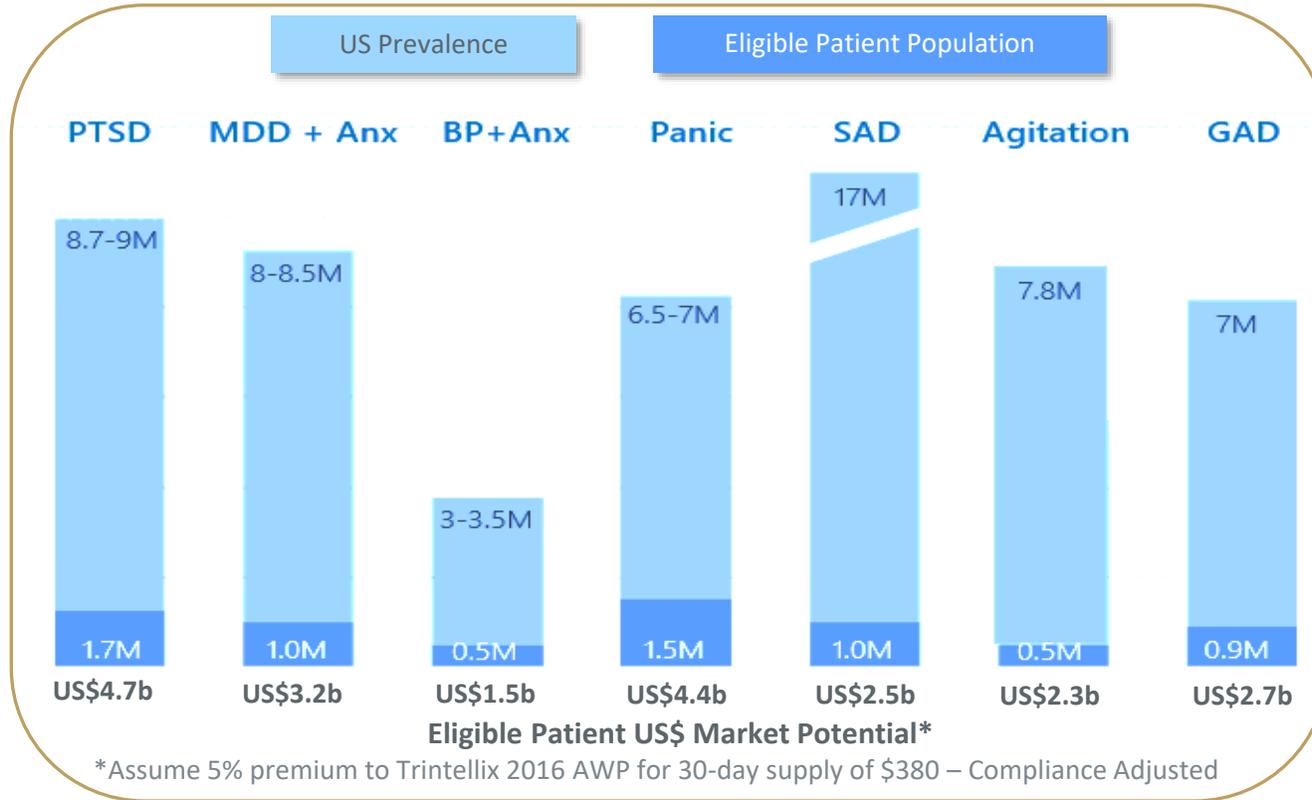
## Strategy and Value Proposition & Stock and Financial Information





## BNC210: Market Potential and Summary of Clinical Trials





- ✓ Innovative, first-in-class
- ✓ Unmet need in large patient populations
- ✓ Advancement in care
- ✓ Limited branded competition
- ✓ Ability to achieve large market share

<sup>1</sup> 3.4-4% prevalence >18yrs., ~25% of patients diagnosed and treated

<sup>2</sup> 6.7% prevalence, ~50% co-morbid anxiety, ~50% diagnosed and treated

<sup>3</sup> ~2.9% prevalence, 50% co-morbid anxiety (range in literature 25 to 75%), ~50% diagnosed and treated

<sup>4</sup> ~2.7% prevalence, ~50% diagnosed and treated

<sup>5</sup> ~6.8% prevalence, 15-20% diagnosed and treated

<sup>6</sup> ~3.1% dementia prevalence >40yrs., ~9% agitation patients diagnosed and treated

<sup>7</sup> 3.1% GAD prevalence, assumes ~25% diagnosed and treated, ~50% of SSRI patients treated are partial responders or relapsers

Post-Traumatic Stress Disorder (PTSD) Major Depressive Disorder (MDD) Bipolar Disorder (BP) Social Anxiety Disorder (SAD) Generalized Anxiety Disorder (GAD)



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

Protocol Number	Phase	Description	Subjects Enrolled / Administered BNC210	Location
BNC210.001 BNC210.002 ICP-2143-101	1	Safety and Tolerability of Single Ascending Doses in Healthy Volunteers	83/67	Australia US
BNC210.003	1b	Lorazepam & BNC210 Comparison in Healthy Volunteers	24/22	France
BNC210.004	1b	Panic Attack Model in Healthy Volunteers	60/59	France
BNC210.005	1b	Safety and Tolerability of Multiple Ascending Doses and EEG Target Engagement Study with Nicotine in Healthy Volunteers	56/44	France
BNC210.006	2a	Imaging and Behavioral Study In Generalized Anxiety Disorder Patients	27/25	UK
BNC210.007	2	Post-Traumatic Stress Disorder	193/143	Australia US
BNC210.008	2a	Agitation in the Elderly in Hospital Setting	38/18	Australia
BNC210.009 BNC210.010	1	Single Dose Pharmacokinetics of BNC210 Solid Dose Formulation in Healthy Volunteers	11/11	Australia
BNC210.011	1	7-Day Pharmacokinetics of BNC210 Solid Dose Formulation in Healthy Volunteers	10/10	Australia





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





**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 ( $p < 0.05$ )

**Evidence of 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 safe and 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

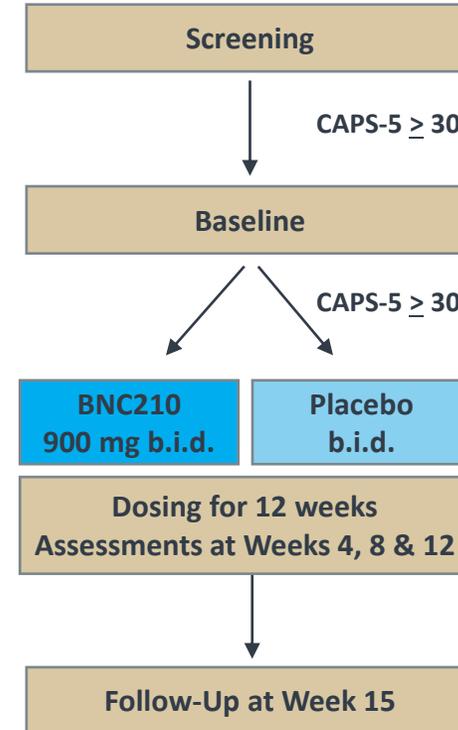
**Potential reasons why clinically significant effects and trends seen at 4 Weeks did not translate into significant primary endpoint on CAPS-5 at 12 Weeks**

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





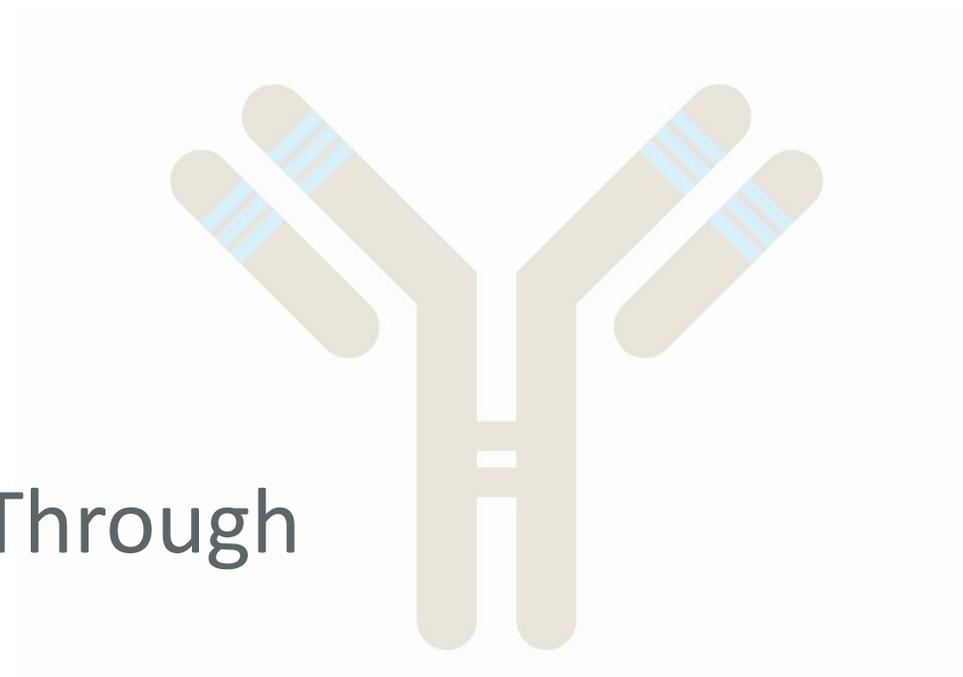
	<b>Phase 2b Post-Traumatic Stress Disorder</b>
<b>Design</b>	Randomized, double-blind, placebo-controlled, multi-center study with a 12-week, parallel 2-arm treatment period (BNC210:Placebo)
<b>Participants</b>	200 Adults 18-75 years old with PTSD randomized 1:1 (BNC210:Placebo)
<b>Eligibility</b>	CAPS-5 $\geq$ 30 at Screening and Baseline (and $\leq$ 25% decrease in score Screening to Baseline)
<b>Sites</b>	~25 sites (US)
<b>Doses</b>	BNC210 900 mg or Placebo twice daily
<b>Primary efficacy endpoint</b>	The effect of BNC210 compared to Placebo on Baseline to endpoint change in CAPS-5 Total Symptom Severity Scores after 12 weeks of treatment
<b>Secondary endpoints</b>	Efficacy: Symptom cluster severity scores for CAPS-5 (Criterion B, C, D & E); PCL-5; HAM-A; MADRS; CGI-S/CGI-I; PGI-S/PGI-I; SDS; ISI Safety & tolerability endpoints
<b>Status</b>	Commence mid-2021 in the US

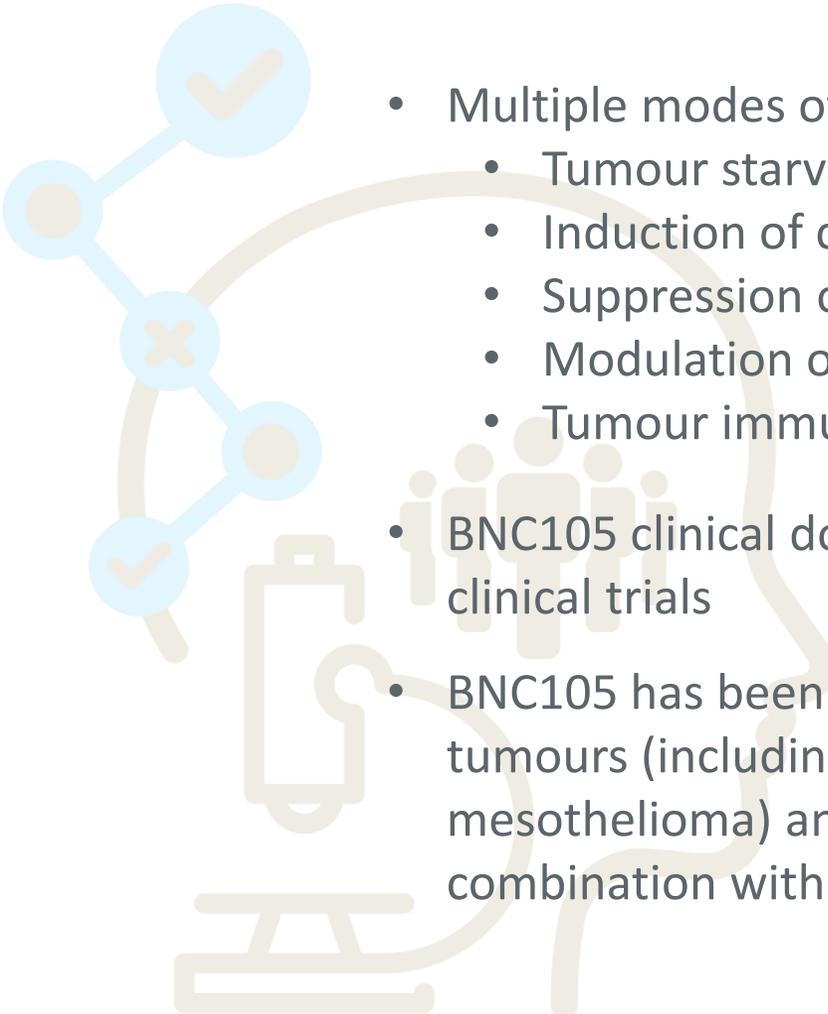


CAPS-5 = Clinician-Administered PTSD Scale for the Diagnostic and Statistical Manual of Mental Disorders, 5<sup>th</sup> Edition (DSM-5); PCL-5 = PTSD Checklist for DSM-5; HAM-A = Hamilton Anxiety Rating Scale; MADRS = Montgomery-Asberg Depression Rating Scale; CGI = Clinical Global Impressions; PGI = Patient Global Impressions; SDS = Sheehan Disability Scale; ISI = Insomnia Severity Index



## Oncology Assets: Build Value Through External Funding



- 
- Multiple modes of BNC105 anti-cancer action have been identified:
    - Tumour starvation by selective disruption of tumour vasculature
    - Induction of cancer cell death by upregulation of pro-apoptotic proteins
    - Suppression of tumour growth by inhibition of cancer cell proliferation
    - Modulation of the tumour microenvironment
    - Tumour immunomodulation with a significant reduction in PD-L1 expression
  - BNC105 clinical dose and schedule have been established in four Phase 1 and 2 clinical trials
  - BNC105 has been generally well tolerated in clinical trials in patients with solid tumours (including renal cell cancer, ovarian cancer, colorectal cancer and mesothelioma) and liquid tumours (chronic lymphocytic leukemia) (including in combination with other chemotherapeutics)

	Preclinical	Phase 1	Phase 2
<b><i>BNC105: a multi-modal, small molecule tubulin polymerization inhibitor</i></b>			
Solid Cancers	COLORECTAL: in combination with nivolumab; externally funded; Phase 2 completed		
	RENAL: in combination with everolimus; Phase 2 completed; biomarker-based Phase 2/3 ready		
	MESOTHELIOMA: monotherapy; Phase 2 completed		
	OVARIAN: in combination with gemcitabine + carboplatin; Phase 1 completed; Phase 2 ready		
	ADVANCED SOLID TUMOURS: monotherapy dose escalation; Phase 1 completed		
Blood Cancers	CHRONIC LYMPHOCYTIC LEUKEMIA: in combination with ibrutinib; externally funded; Phase 1 completed		
	ACUTE MYELOID LEUKEMIA: preclinical data available; Phase 1/2 ready		
<b><i>BNC101: a first-in-class humanized monoclonal antibody to LGR5, a cancer stem cell receptor</i></b>			
Solid Cancers	COLORECTAL: monotherapy dose escalation; Phase 1 completed; Phase 2 ready		
	PANCREATIC: in combination with SOC; preclinical data		
	COLORECTAL: in combination with anti-PD-1; preclinical data		
	ANTIBODY DRUG CONJUGATE: preclinical data		



Study ID	Indication	Design	Intervention	#Subjects Dosed with BNC105P (Doses)	Key Objectives	Location	Status
BNC105P.001	Advance Stage Solid Tumours	Ph 1; Dose escalation	BNC105P monotherapy	21 (2.1-18.9 mg/m <sup>2</sup> )	MTD; PK	Australia	Complete
B2P2M2	Advanced Malignant Pleural Mesothelioma	Ph 2; Single arm	BNC105P monotherapy	30 (16 mg/m <sup>2</sup> )	PFS; Response Rate	Australia	Complete
ANZGOG-1103	Partially Platinum Sensitive Relapsed Ovarian Cancer	Ph 1; Dose escalation	BNC105P + carboplatin/gemcitabine <i>(with sequential BNC105P monotherapy)</i>	15 (12-16 mg/m <sup>2</sup> )	RP2D; PFS; Response Rate	Australia NZ USA	Complete
GU09-145	Metastatic Clear Cell Renal Cell Cancer	Ph 1/2; Randomized two arm	BNC105P + everolimus vs everolimus monotherapy <i>(with sequential BNC105P monotherapy)</i>	113 (4.2-16 mg/m <sup>2</sup> )	MTD & RP2D; 6-month PFS; Response Rate	USA Australia Singapore	Complete
CA209-99U	Microsatellite Stable Refractory Colorectal Cancer	Ph 2	BNC105P + nivolumab	(16 mg/m <sup>2</sup> )	PFS; Response Rate	Australia	In progress
D14234	Relapsed/Refractory Chronic Lymphocytic Leukemia	Ph 1; Dose escalation + expansion	BNC105P+ ibrutinib	(8-16 mg/m <sup>2</sup> )	MTD; EFS; Response Rate	USA	In progress

EFS = event-free survival; MTD = maximum tolerated dose; PFS = progression-free survival; PK = pharmacokinetics; RP2D = recommended Phase 2 dose



- LGR5 is a cancer stem cell receptor overexpressed in a number of solid cancers such as colorectal, pancreatic, breast and lung cancers, and has a role in tumour growth and survival
- BNC101 binds to LGR5 with high affinity and selectivity and internalizes the receptor
- BNC101 clinical dose and schedule were established in a Phase 1 trial in patients with metastatic colorectal cancer (CRC) - the recommended Phase 2 dose (RP2D) was identified
  - BNC101 was safe and well tolerated with no dose-limiting toxicities (DLTs)
  - Co-localization of BNC101 and LGR5 was demonstrated in patient tumour tissue

## **Future development:**

- **Phase 2 ready: BNC101 in combination with standard of care treatment for gastro-intestinal cancers overexpressing LGR5**
- **BNC101 has the potential to be developed as an Antibody-Drug-Conjugate (ADC) therapeutic or in combination with CAR-T therapy**



- 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.
- Bionomics retains BNC101 for other types of therapies.

