



CREATING INNOVATIVE THERAPIES  
**FOR CNS DISORDERS.**

## Corporate Presentation

BNO (Australia: ASX)  
BNOEF (USA: OTCQX)

18 September 2018

Central Nervous System (CNS)

# Safe Harbor 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.

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# Bionomics Overview

- Global, clinical stage biopharmaceutical company leveraging proprietary platform technologies, ionX and MultiCore, to discover and develop a deep pipeline of novel drug candidates targeting ion channels in CNS disorders
- Lead candidate, BNC210, is a novel, orally-administered, first-in-class, negative allosteric modulator of the  $\alpha 7$  nicotinic acetylcholine receptor, in development for anxiety, panic, agitation, and PTSD:
  - Positive data from Phase 2 trial in Generalised Anxiety Disorder (GAD) patients reported in September 2016
  - Phase 2 trial in Post Traumatic Stress Disorder (PTSD) treatment completed in Australia and US with data anticipated late 3Q, 2018
  - Phase 2 trial in Agitation ongoing in Australia with data anticipated in 1Q, CY2019
- Strategic partnership with Merck & Co., (MSD):
  - Cognition therapeutic candidate entered clinical development and triggered US\$10M milestone payment in deal valued up to US\$506M in upfront, research and milestone payments plus additional royalties on net sales of licensed drugs
  - Merck & Co equity investment in October 2015, 4.5% ownership
- Robust pipeline of first-in-class ion channel programs
- Financials: Market Cap ~US\$178.9M (BNOEF) as at 5 August 2018; Cash at 30 June 2018 US\$18.4M

# Our Proprietary Platform Technologies and CNS Therapeutic Focus

## ionX

Identifies drug candidates targeting both ligand gated and voltage gated ion channels

Proprietary cell lines and screening approaches

Comprehensive *in vivo* models validate target biology

## MultiCore

A diversity orientated chemistry platform for the discovery of small molecule drug candidates

Computer aided pharmacophore modelling

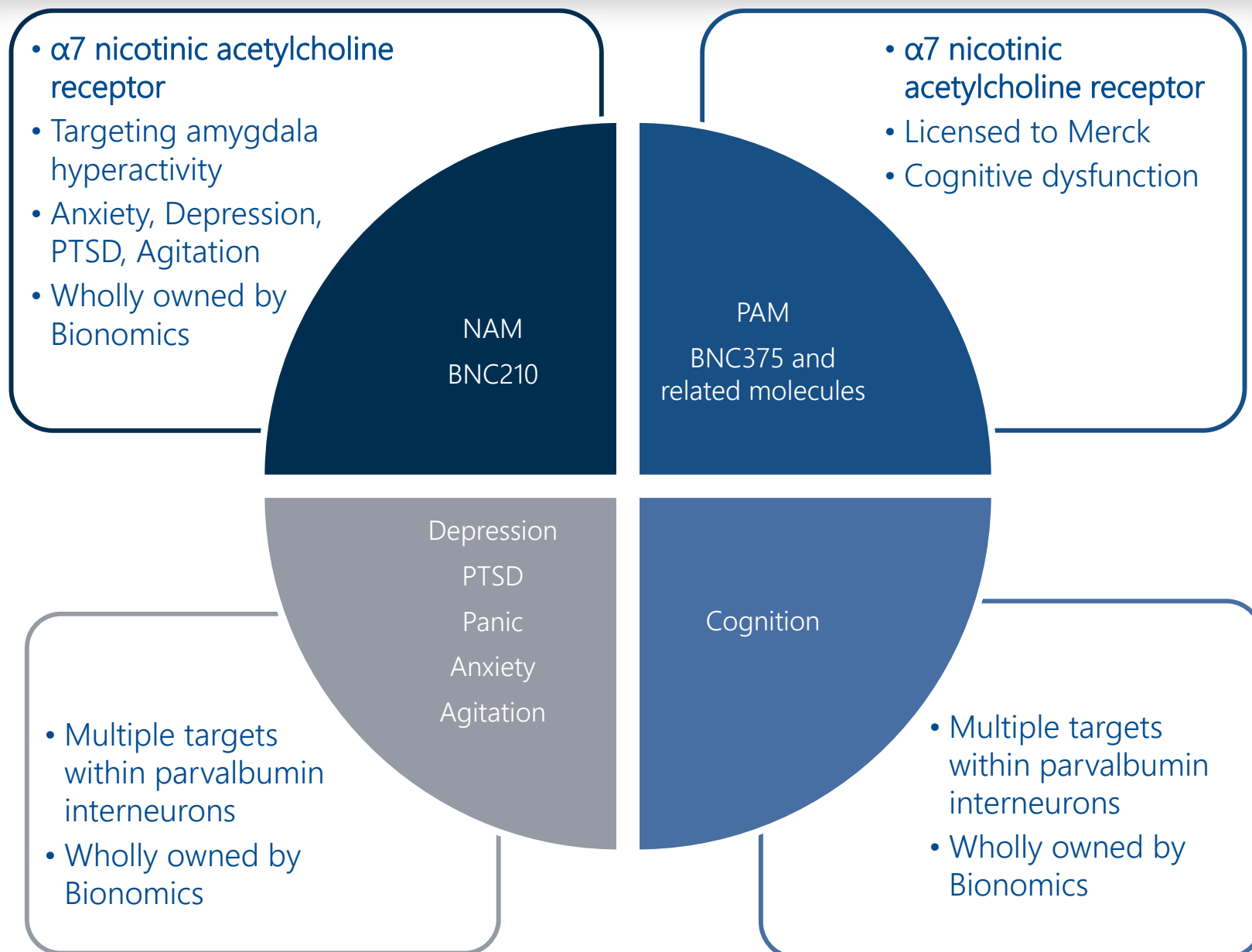
Scaffold hopping synthetic approaches rapidly create diversity in small, focused libraries

Parallel, differentiated chemical series of potential drug candidates

## Therapeutic Areas

- PTSD
- Anxiety
- Agitation
- Depression
- Cognitive/Memory Deficits
- Pain

# Bionomics' CNS Discovery Engine



# Bionomics' CNS Focused Pipeline

Program	Mechanism of Action	Indication	Pre-IND	Phase 1 / 2a	Phase 2b	Bionomics' Commercial Rights	Market Opportunity
<b>BNC210</b>	$\alpha 7$ nicotinic acetylcholine receptor NAM	PTSD	Fully recruited; results expected 2H 2018			WW	<ul style="list-style-type: none"> <li>US\$4.7B</li> <li>3.4-4% prevalence &gt;18 yrs</li> <li>~25% of patients diagnosed and treated</li> </ul>
		Agitation	Phase 2 initiated Q2 2018; results expected Q1 2019			WW	<ul style="list-style-type: none"> <li>US\$1.6B</li> <li>~3.1% dementia prevalence &gt;40yrs</li> <li>~9% agitation patients diagnosed and treated</li> </ul>
		GAD	Positive Phase 2a data			WW	<ul style="list-style-type: none"> <li>US\$2.7B</li> <li>3.1% GAD prevalence</li> <li>~25% diagnosed and treated</li> <li>~50% of SSRI patients treated are partial responders or have relapsed</li> </ul>
		Panic	Positive CCK-4 induced panic data			WW	<ul style="list-style-type: none"> <li>US\$4.4B</li> <li>2.7% prevalence</li> <li>~50% diagnosed and treated</li> <li>Assumes 5% premium to Trintellix 2016 AWP for 30-day supply of \$380 – compliance adjusted</li> </ul>
<b>MK#</b>	$\alpha 7$ nicotinic acetylcholine receptor PAM	Alzheimer's, Parkinson's	Phase 1 ongoing			WW Merck Partnership	<ul style="list-style-type: none"> <li>US\$506M total deal value including upfront and milestones payments</li> <li>Tiered royalties</li> </ul>
<b>Pain, Depression, Memory Enhancement</b>	Undisclosed					WW	



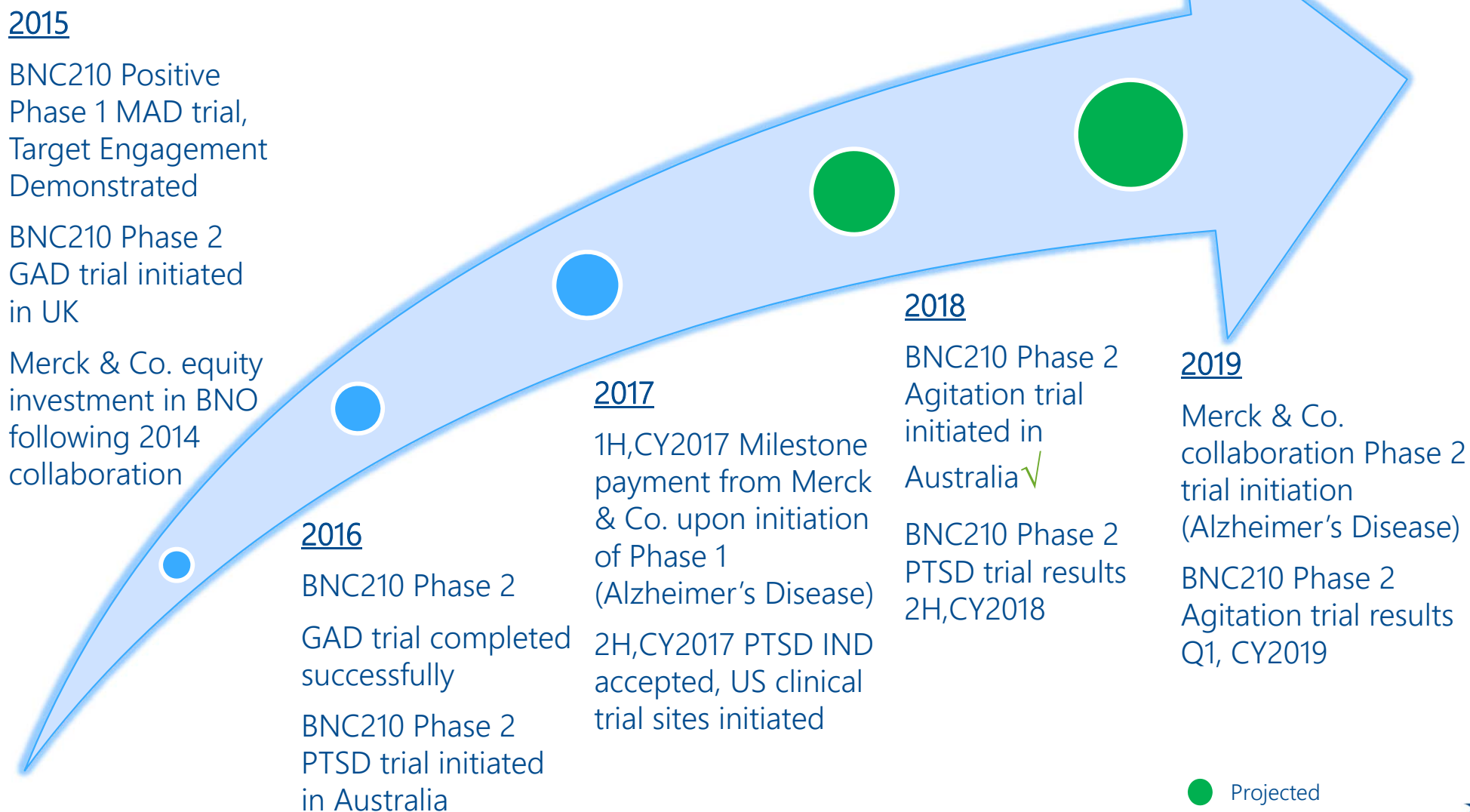
# Global License and Collaboration Agreement with Merck & Co in Cognition Provides Validation

- Validates ionX and MultiCore drug discovery platforms
- Partnership with Merck & Co in cognition generated US\$20M in upfront payment in 2014, research funding 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



- 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 and Parkinson's and other conditions

# Milestones in Value Creation





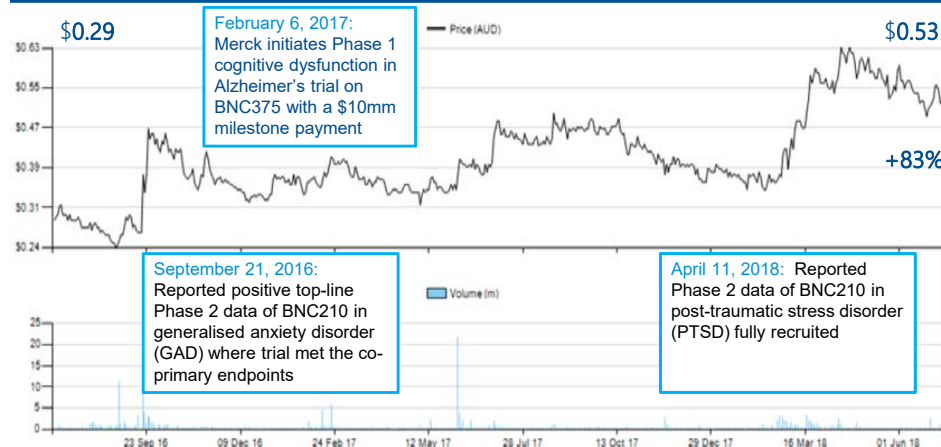
# Financial and Capital Structure Overview

Bionomics is a clinical stage biopharmaceutical company focused on the discovery and development of innovative small molecule therapeutics for conditions of the central nervous system.

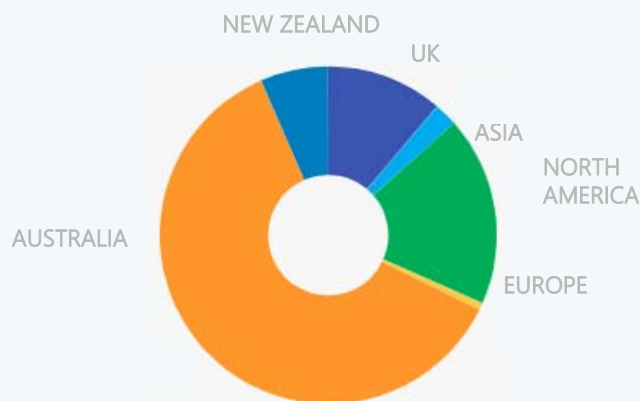
## KEY STATISTICS

<b>ASX Code/OTCQX</b>	<b>BNO/BNOEF</b>
<b>Current Share Price</b>	<b>A\$0.53</b>
<b>52 Week High</b>	<b>A\$0.64</b>
<b>52 Week Low</b>	<b>A\$0.345</b>
<b>Shares on Issue</b>	<b>482.79M</b>
<b>Market Capitalisation</b>	<b>US\$189.5M</b>
<b>Cash (6.30.18)</b>	<b>US\$18.4M</b>

## 2 YEAR SHARE PRICE PERFORMANCE (\$)



## SHAREHOLDING STRUCTURE (5.9.18)



## TOP SHAREHOLDERS

<b>BVF</b>	<b>10.2%</b>
<b>Ausbil Investment Management</b>	<b>8.1%</b>
<b>Private Portfolio Managers</b>	<b>4.9%</b>
<b>Merck, Sharp &amp; Dohme</b>	<b>4.5%</b>

# Financial Results FY18

A\$'000	30-Jun-18	30-Jun-17	
Cash & Cash Equivalents	\$ 24,930	\$ 42,874	-42%
Revenue from Continuing Operations	\$ 3,954	\$ 18,606	-79%
Other Income	\$ 8,502	\$ 9,646	-12%
Research & Development Expenses	\$(25,247)	\$(24,223)	4%
Admin	\$ (5,345)	\$ (5,726)	-7%
Occupancy	\$ (1,417)	\$ (2,595)	-45%
Compliance	\$ (713)	\$ (839)	-15%
	\$ (7,475)	\$ (9,160)	-18%
Unrealised exchange differences	\$ (3,904)	\$ 874	-547%
Gain/(Loss) on disposal of assets	\$ (20)	\$ -	
Finance expenses	\$ (2,058)	\$ (1,970)	4%
	\$ (5,982)	\$ (1,096)	446%
(Loss) before tax	\$(26,248)	\$ (6,227)	322%

Borrowings			
Current	\$ 5,696	\$ 8,496	-33%
Non-Current	\$ 15,736	\$ 10,014	57%
	\$ 21,432	\$ 18,510	16%

- Revenue consists of payments under Bionomics' agreement with MSD, contract service revenue of Bionomics' wholly-owned subsidiaries Neurofit and Prestwick and rental income.
- Other income consists of interest income received as a result of ordinary activities and the government's R&D Tax Incentive in Australia and similar incentives for the subsidiaries.
- The increased current year loss reflects the Company's investment in research and development activities and no licensing income in 2018 compared with licensing income of \$13,073,615 in 2017.
- Bionomics continues to focus on cost efficiency in supporting activities, conserving cash for research and development. Administration, occupancy and compliance expenses decreased by 9% last financial year with an additional reduction of 18% in the current financial year.

# Financial Overview

- \$24.93m Cash and cash equivalents as at 30 June 2018
- 17 months cash runway not considering income from monetisation or licensing
- Historical financial details:

(\$ in Millions)	Fiscal Year End Jun. 30,					
	2013	2014	2015	2016	2017	2018
Revenue	\$3.7	\$19.9	\$6.8	\$8.1	\$18.6	\$4.0
Other Income	\$8.1	\$7.6	\$9.8	\$13.6	\$9.6	\$8.5
R&D Expense	\$16.2	\$17.8	\$23.2	\$24.8	\$24.2	\$25.2
Total Operating Expenses	\$21.8	\$23.6	\$33.9	\$39.1	\$34.5	\$38.7
Cash & cash equivalents	\$22.5	\$10.5	\$26.6	\$45.5	\$42.9	\$24.9

# Near Term Catalysts

*Anticipated significant R&D inflection points for Bionomics in 2018 - 2019*

BNC210 PTSD	<ul style="list-style-type: none"><li>Phase 2 results anticipated in late 3Q, CY2018</li></ul>
BNC210 Agitation	<ul style="list-style-type: none"><li>Phase 2 results anticipated in 1Q, CY2019</li></ul>
Merck collaboration	<ul style="list-style-type: none"><li>Phase 2 Alzheimer's disease clinical trial initiation 1Q, CY2019 presenting the opportunity for the next milestone payment to Bionomics</li></ul>

*In addition, Bionomics' anticipates 2 new clinical candidates will enter the pipeline*

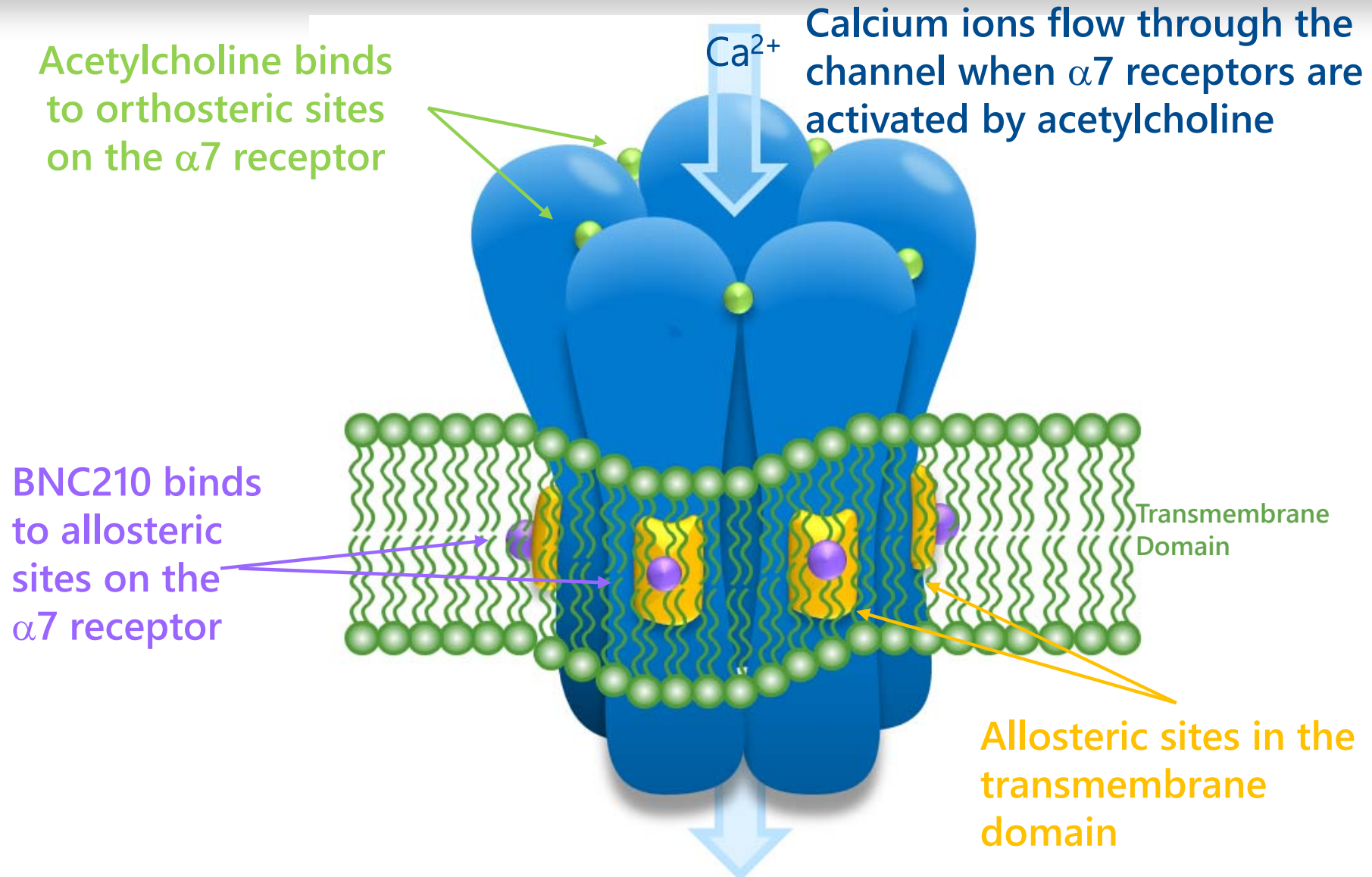


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BNC210



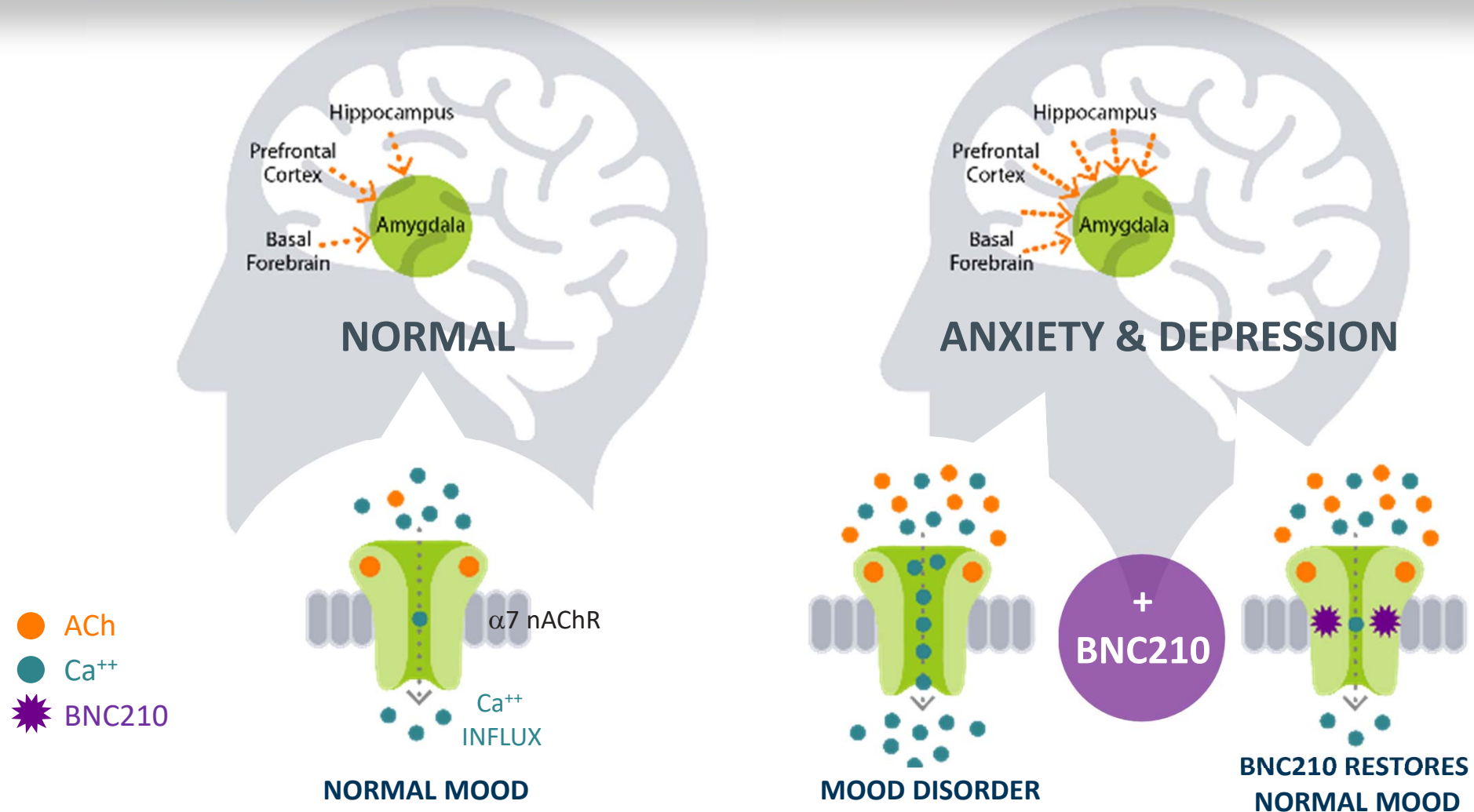
# BNC210 is a Novel, Negative Allosteric Modulator of the $\alpha 7$ Nicotinic Acetylcholine Receptor with Anxiolytic and Antidepressant Properties



Five alpha subunits make up the  $\alpha 7$  receptor=Five potential binding sites



# 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

# BNC210 Overview: Novel, Best-in-Class Modulator of $\alpha 7$ Nicotinic Acetylcholine Receptor

Mechanism of Action	Negative allosteric modulator of $\alpha 7$ nicotinic acetylcholine receptor, a ligand gated ion channel
Target Indications	<ul style="list-style-type: none"><li>• Anxiety (Generalised Anxiety Disorder &amp; Post Traumatic Stress Disorder and Agitation)</li><li>• Potential for other CNS indications, including Depression</li></ul>
Ongoing Clinical Trials	<ul style="list-style-type: none"><li>• Phase 2b multi-center trial (Australia, USA) in PTSD fully recruited and dosing completed, topline data late 3Q, CY2018</li><li>• Phase 2 multi-center trial (Australia) in Agitation, topline data 1Q, CY2019</li></ul>
Completed Clinical Trials	<ul style="list-style-type: none"><li>• 6 completed Phase 1 trials in &gt; 200 healthy subjects</li><li>• Demonstrated safety and tolerability; no sedation, cognitive impairment or impaired motor co-ordination; suppressed symptoms of CCK4-induced panic; target engagement in human brain demonstrated</li><li>• Phase 2 in GAD patients met co- primary endpoints; low dose BNC210 outperformed Lorazepam, measured by cerebral perfusion and degree of amygdala activation</li><li>• Secondary endpoint met; high and low dose BNC210 outperformed Lorazepam in an anxiety provoked behavioral task</li></ul>

# BNC210: Next Generation Drug Candidate with Potential to Treat Anxiety, Depression, Agitation, PTSD

## Potential Competitive Advantages of BNC210\*

Drug	No sedation	No withdrawal syndrome	No memory impairment	Fast acting	No drug/drug interactions	Once-a-day dosing
BNC210	✓	✓	✓	✓	✓	✓
Valium and other BZD	X	X	X	✓	✓	X
Prozac and certain other SSRI/SNRI	✓	X	✓	X	X	✓
Atypical Antipsychotics	X	X	X	✓	X	✓

### Anxiety Treatments

- Dominated by benzodiazepines (BZDs)
- Associated with sedation, abuse liability, tolerance and cognitive disturbances
- Not recommended for long-term treatment

### Depression Treatments

- SSRIs and SNRIs used to treat depression and anxiety
- Modest efficacy, late onset of action, discontinuation, weight gain, sexual dysfunction and increased thoughts of suicide in adolescents
- Many have black box warnings

### Agitation Treatments

- In addition to BZD, anti-psychotics are used to treat agitation and anxiety. They cause dizziness, sedation, weight gain, constipation, movement disorders and have black box warnings for use in elderly (stroke)

### Post Traumatic Stress Disorder (PTSD) Treatments

- Sertraline (Zoloft) and paroxetine (Paxil) are only US FDA approved drugs for PTSD.
- Despite lack of efficacy, addictive potential and other harms associated with chronic use, BZDs are still over-prescribed.
- An estimated 2.8M scripts are written off-label for management of PTSD symptoms.
- VA/DoD 'Practice Guideline for PTSD' recommends against the use of BZDs such as Valium for PTSD.
- 50% increase in overall mortality rates associated with long-term benzodiazepine use in PTSD patients – overdosing, sudden unexplained deaths, car crashes, falls.

Selective Serotonin Reuptake Inhibitors (SSRIs).  
Serotonin-Norepinephrine Reuptake Inhibitor (SNRI).  
Veteran's Affairs (VA). Department of Defense (DoD)

# BNC210 Targets Multi-Billion Dollar Markets with Unmet Need: US Market Potential

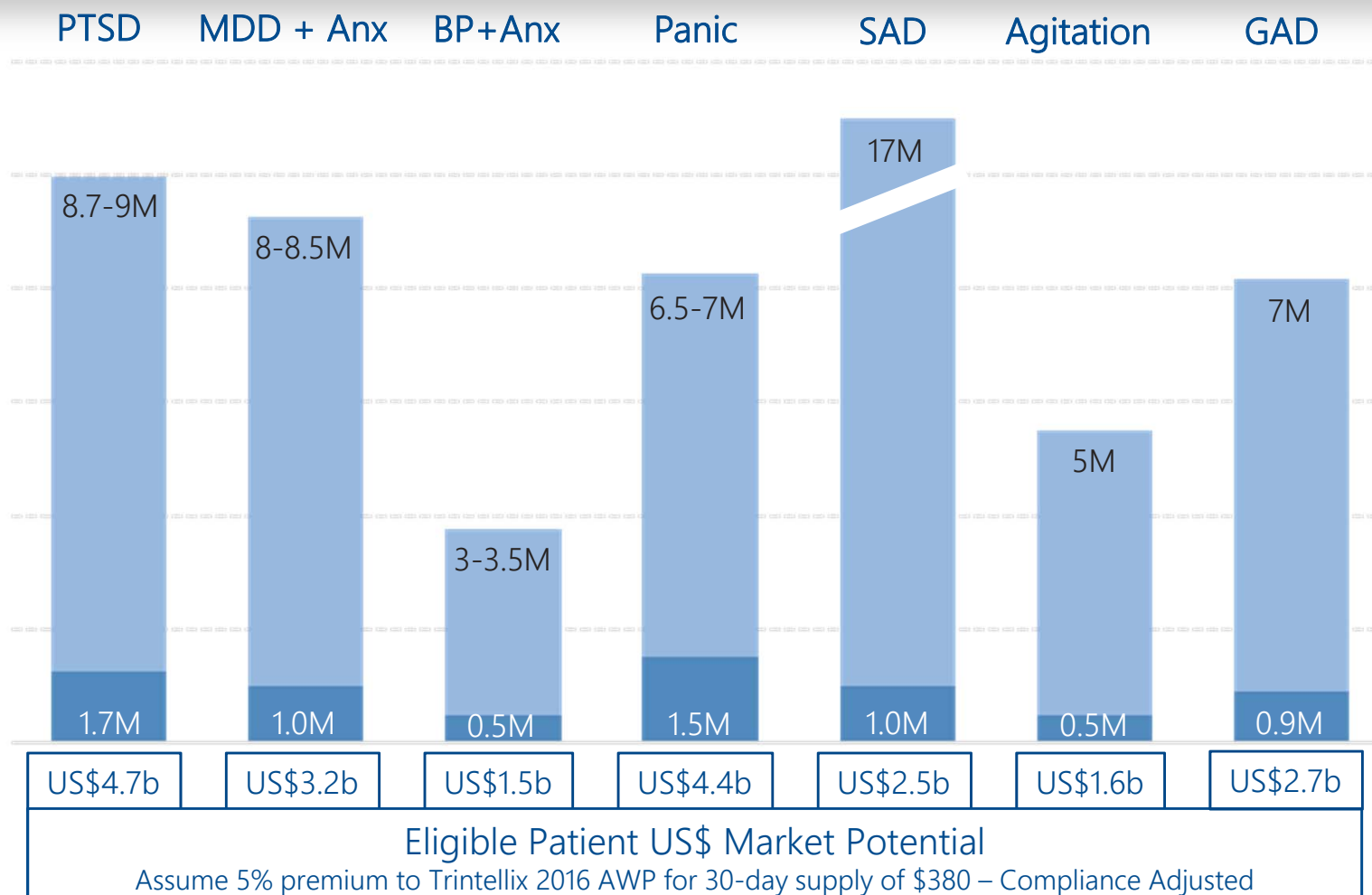
✓ Innovative, first-in-class

✓ Unmet need in large patient population

✓ Advancement in care

✓ Limited branded competition

✓ Ability to achieve large market share



US Prevalence

Eligible Patient Population

<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



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BNC210 for PTSD



# Phase 2 Trial in Post Traumatic Stress Disorder (PTSD) – Ongoing in Australia and US, Data Anticipated Late 3Q, CY18



## Subjects

- 193 PTSD Patients

## Protocol

- Double-blind, placebo controlled, randomized, multi-center
- 4 arms, 1 placebo, 3 BNC210 dose level treatment arms
- 12 weeks, twice daily oral treatment

## Primary Objective

- To determine whether BNC210 causes a decrease in symptoms of PTSD as measured by CAPS-5

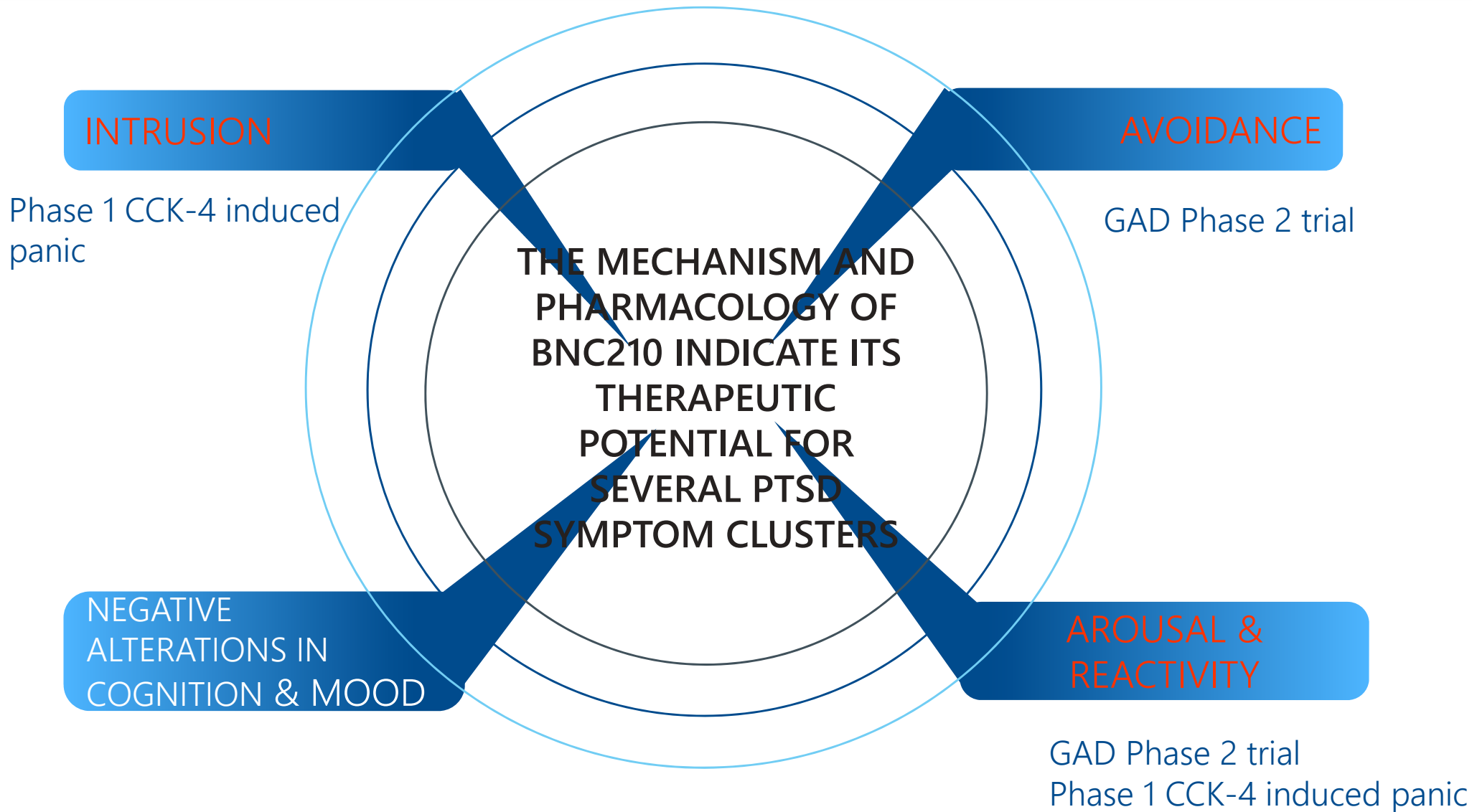
## Secondary & Exploratory Endpoints

- To determine the effects of BNC210 on anxiety (HAM-A), depression (MADRS) and cognitive functions

Clinician-Administered PTSD Scale for DSM-5 (CAPS-5)  
Diagnostic and Statistical Manual of Mental Disorders (DSM-5)  
Hamilton Anxiety Rating Scale (HAM-A)  
Montgomery-Åsberg Depression Rating Scale (MADRS)










# Human Clinical Data Indicates BNC210 May Impact Multiple PTSD Symptom Clusters Measured by CAPS-5








# The Mechanism and Pharmacology of BNC210 Indicate Therapeutic Potential for Several PTSD Symptom Clusters

## Four main PTSD symptom clusters (DSM-5 criteria)







### Intrusive thoughts Nightmares

- Anxiolytic in rodents and man   
- Acute effects on neural circuitry associated with anxiety and PTSD in man  
- Enhances fear extinction in mice and emotional recovery in man following panic attack   








### Avoidance

- Acute doses reduce defensive behavior in man   
- Antidepressant effects in rats, acute efficacy which is enhanced with repeat dosing 
- Promotes neurite outgrowth in primary neurons 

### Negative alterations in cognition and mood.

- Reduces amygdala hyperactivity – a feature shared by anxious patients and PTSD patients   
- Inhibition of  $\alpha 7$  nAChR inhibits release of excitatory neurotransmitters associated with hypercholinergic state; including NA, DA, GLUT, ACh – potential to reduce NA induced hyperarousal   

### Arousal and reactivity

- Clinical efficacy in model of panic in HVs, elevated levels of ACh stimulate the HPA axis, BNC210 treatment significantly reduced levels of ACTH in CCK study   
- $\alpha 7$  nAChRs modulate GABA and glutamate signaling in the amygdala and hippocampus    

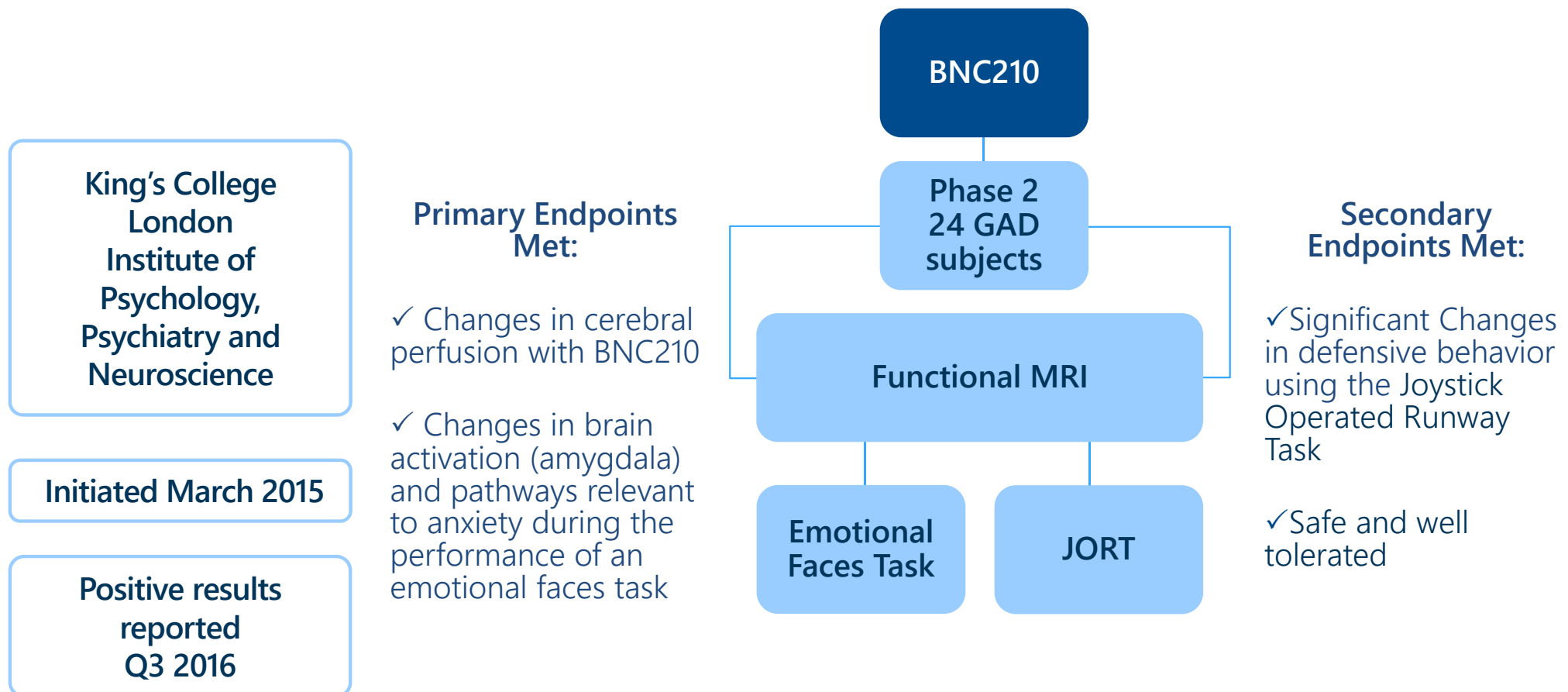


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BNC210 for GAD

# BNC210 Phase 2 Trial in Generalised Anxiety Disorder (GAD) Demonstrated Acute Anxiolytic Activity

Randomized, double-blind, placebo and Lorazepam-controlled, 4-way crossover design



*BNC210 is not sedating or addictive and does not impair memory or motor co-ordination*

# Primary Endpoints Achieved: BNC210 Outperformed Lorazepam in Anxiety Provoked Task

We believe GAD patients treated with BNC210 will have reduced activity in the amygdala during performance of an anxiety provoking task

## Emotional Faces Task

- Primary Endpoint
- Evaluate activity in the amygdala via Functional MRI
- Several FDA-approved anxiety drugs reduce amygdala activation evoked by performance of the Emotional Faces Task

### Emotional Faces Task (Hariri Faces)



*300 mg BNC210 significantly reduced bilateral amygdala reactivity to fearful faces  
 $p < 0.05$*

*Clear reduction in amygdala activity produced by lorazepam; approaching significance in the right amygdala at  $p = 0.069$*

# Clinical Data Demonstrates the Safety of BNC210 Compared to Lorazepam

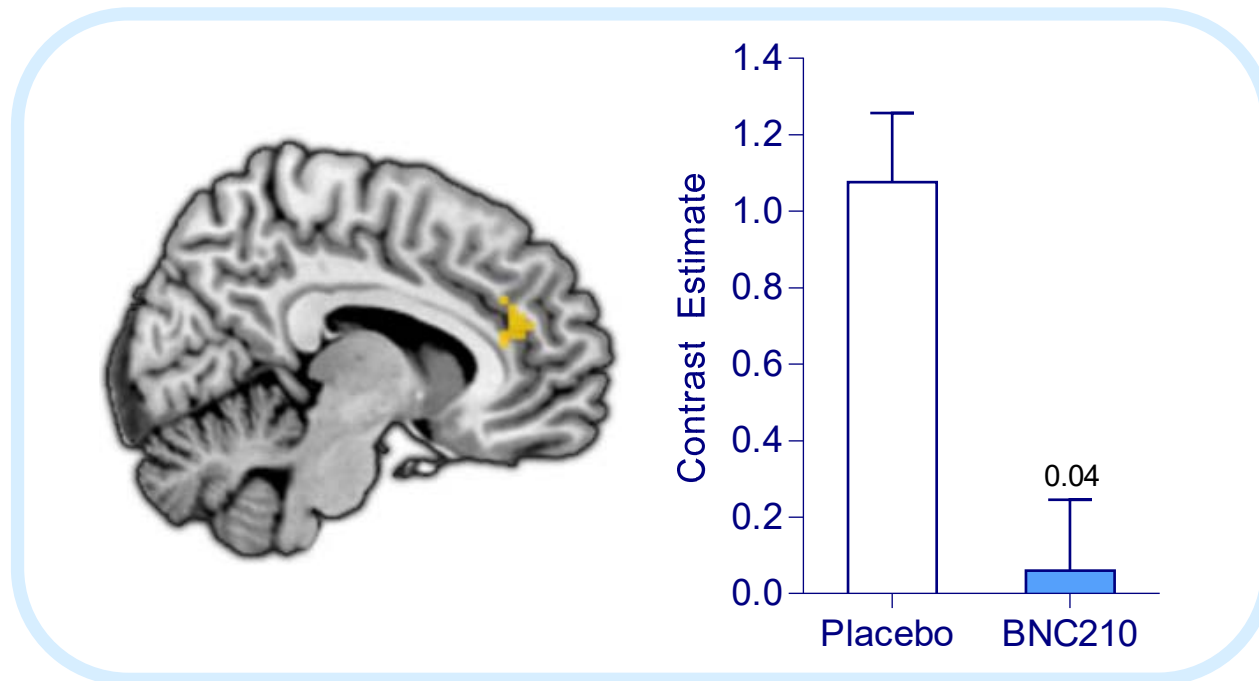
Assessments	BNC210:300 and 2000 mg	Lorazepam: 2 mg
<b>Primary Objective: Measure of Attention</b>	No Effect	Increased MCRT at 6, 9 and 12 hours
<b>Psychomotor Speed</b> Digital Substitution Test	Reduced at T+6h (300 mg only)	Reduced at T+6h and 9h
<b>Visuo-motor Co-ordination</b> Saccades	No Effect	Reduced at T+6h, 9h and 12h
<b>Emotion</b> eVAS	No Effect	Ratings Lower at T+6h and 9h
<b>Sleepiness</b> Karolinska Sleepiness Scale	No Sedation	Sedation at T+6h and 9h
<b>Memory</b> Perceptual Priming Test	No Effect on Memory	Slight Memory Impairment
<b>ACTH and Cortisol</b>	No Drug Induced Changes	Elevated ACTH and Cortisol at T+6h
<b>ARCI 49</b>	No Association with Drug Groups	Association with LSD and Phenobarbital/Alcohol Group



# BNC210 Treatment Reduced Connectivity Between the Left Amygdala and the Anterior Cingulate Cortex in GAD Patients

## FEATURE OF ANXIETY and PTSD NEUROCIRCUITRY

- BNC210 (300 mg) reduced connectivity between the left amygdala and anterior cingulate cortex while viewing fearful faces ( $p = 0.04$ )
- ✓ This finding is highly supportive for the anxiolytic activity of BNC210:
  - Interactions between the dmPFC/ACC and amygdala constitute an 'aversive-amplification' circuit - increased positive coupling between these regions is associated with elevated threat processing under stress.
  - In pathological anxiety this circuit becomes permanently 'switched-on' (Robinson et al. 2011).





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BNC210 for Panic

# BNC210 May Also Inhibit PTSD Associated Panic Attacks

Increasing evidence that panic attacks are common in people with PTSD

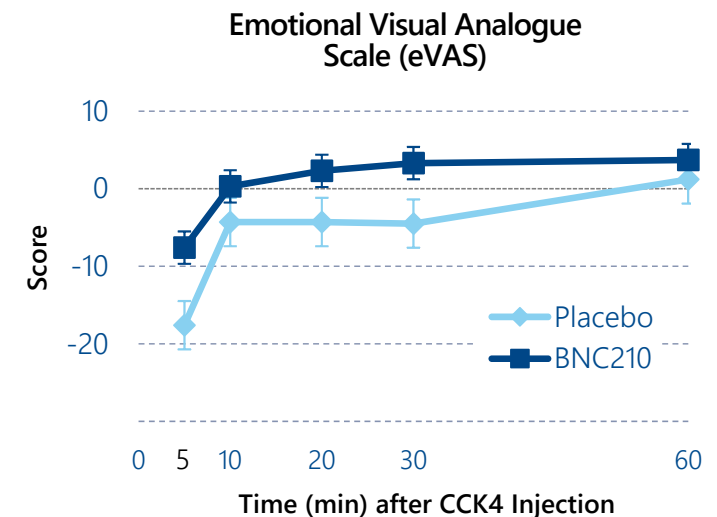
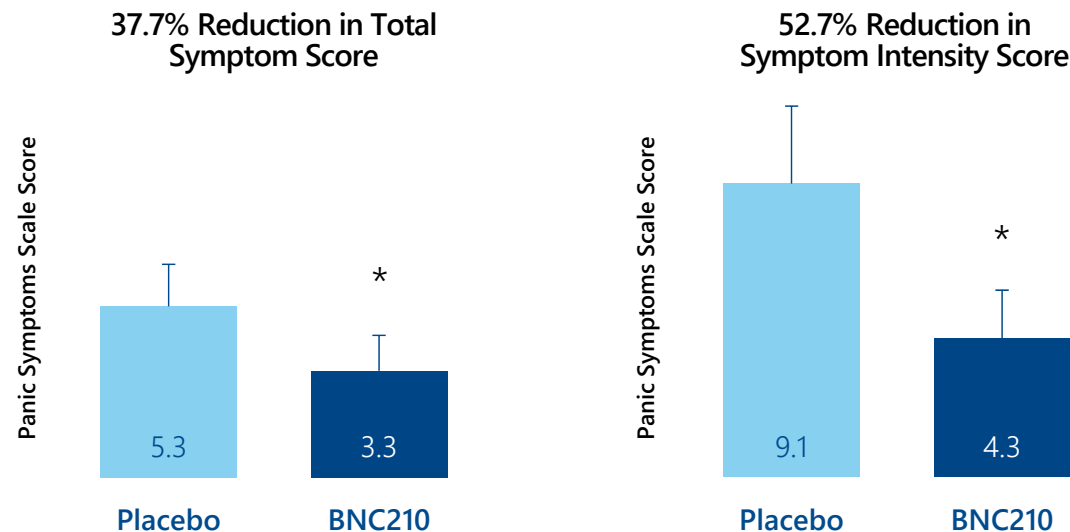
US National Comorbidity Survey found that 35% of people with PTSD had panic attacks

Evidence that panic attacks in the context of PTSD are associated with fear of trauma memories

# BNC210 Significantly Reduced CCK4-Induced Panic Symptoms in Humans

## % Reduction in Total Number of Symptoms & Symptom Intensity

## Emotional Visual Analogue Scale (eVAS)



## In a Double-blinded, Placebo Controlled Trial Subjects Experiencing Panic Symptoms When Treated with BNC210 (2000mg) Showed:

- Reduction in the number and intensity of panic symptoms compared to placebo as measured by the Panic Symptom Scale (PSS)
- More rapid return to baseline emotional stability compared to placebo reducing opportunity for embedding fear memories



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BNC210 for Agitation



# Aggression, Agitation and Dementia in the Elderly

Agitation from sundown syndrome is a common cause of institutionalization of older patients suffering from dementia  
Prevalence = 2.4% to 66%.

30% of caregivers rate stress associated with agitation / aggression as severely to extremely distressing

*Disruptive Agitation in Alzheimer's Disease:  
Medication Treatment Murray A. Raskind, MD*

- #1 Anxiety, Agitation, Aggression
- #2 Pacing, wandering
- Resistance to redirection
- Confusion, Disorientation
- Mood swings
- Abnormally demanding, Suspicious
- Visual and auditory hallucinations
- Screaming, yelling

Current treatments such as risperidone, olanzapine, aripiprazole, environmental interventions and behavioral modifications have had limited success

## ISSUES WITH BZDs

- Most commonly prescribes meds for anxiety and insomnia in elderly, not good for chronic conditions with associated psychiatric comorbidity
- PK and PD for BZDs changes in elderly, therapeutic window reduced

## ISSUES WITH ANTIPSYCHOTICS

- Frequent non-responders
- Adverse effects: pseudoparkinsonism, sedation
- Increased risk of stroke and death - FDA have issued "Black Box Warning."



# BNC210 has Potential for the Treatment of Agitation



BNC210 rapidly inhibits Amygdala activation in GAD patients during the performance of anxiety provoking tasks



BNC210 rapidly restores emotional stability after a Panic Attack



Higher prevalence of GAD in the elderly  
Amygdala activation associated with Agitation



# Phase 2 Clinical Trial to Assess the Efficacy and Safety of BNC210 in Hospitalised Elderly Patients with Agitation

## Key Selection Criteria

- Hospitalised elderly patients under the care of a specialist Geriatrician
- Presenting with agitation requiring intervention in addition to standard-of-care behavioural management

## Design

- Randomized, double-blind, placebo controlled parallel dosing, 1:1 ratio
- BNC210 300 mg and placebo (twice daily)
- 5 days treatment; 2 days follow up
- Approximately 40 participants

## Objectives

- Primary: to compare the effects of BNC210 and placebo on the time to resolution of agitation as measured by the Pittsburgh Agitation Scale (PAS)
- Secondary: to compare the effects of BNC210 and placebo on the change in global function as assessed by the Clinical Global Impression Scale (CGI-S/I)
- Exploratory: to assess safety and tolerability of BNC210 in elderly patients with agitation

# Bionomics Outlook

- Anticipated multiple near-term value accretive R&D catalysts

BNC210 PTSD	<ul style="list-style-type: none"><li>▪ Phase 2 results anticipated in late 3Q, CY2018</li></ul>
BNC210 Agitation	<ul style="list-style-type: none"><li>▪ Phase 2 results anticipated in 1Q, CY2019</li></ul>
Merck collaboration	<ul style="list-style-type: none"><li>▪ Phase 2 Alzheimer's disease clinical trial initiation 1Q, CY2019 presenting the opportunity for the next milestone payment to Bionomics</li></ul>

- Validated Platform – Merck partnership and shareholding
- Robust pipeline of first in class ion channel candidates addressing significant unmet need in Bionomics areas of strength in CNS disorders
- A well funded company to deliver on milestones