



ABN 53 075 582 740

**ASX ANNOUNCEMENT**  
**27 July 2018**

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**Bionomics Presents at the 14<sup>th</sup> Annual Bioshares Biotech Summit**

Bionomics Limited (ASX:BNO, OTCQX:BNOEF), a global, clinical stage biopharmaceutical company leveraging proprietary platform technologies to discover and develop drug candidates targeting ion channels in CNS disorders, is presenting on BNC210, a novel small molecule therapeutic candidate in development for anxiety, panic, post-traumatic stress disorder (PTSD) and agitation at the 14<sup>th</sup> Annual Bioshares Biotech Summit in Queenstown, New Zealand.

The presentation is being given on Saturday July 28<sup>th</sup> at 11.00am by the Vice President of Strategic Initiatives and Innovation, Dr Sue O'Connor, in the session *CNS Drug Development and Mental Health*.

A copy of the presentation is attached to this announcement.

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**About Bionomics Limited**

Bionomics (ASX: BNO) 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 Phase 2 for the treatment of agitation and for post-traumatic stress disorder, is a novel, proprietary negative allosteric modulator of the alpha-7 ( $\alpha$ 7) nicotinic acetylcholine receptor. Beyond BNC210, Bionomics has a strategic partnership with Merck & Co., Inc (known as MSD outside the United States and Canada).

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

**About BNC210**

BNC210 is a novel small molecule, orally-administered therapeutic candidate being developed for anxiety, panic, trauma- and stressor-related disorders and agitation, that we believe has similar efficacy but improved tolerability compared to currently available drugs such as benzodiazepines, selective serotonin reuptake inhibitors, or SSRIs, and serotonin-norepinephrine reuptake inhibitors, or SNRIs. BNC210 is a first-in-class highly-selective negative allosteric modulator of the alpha-7 nicotinic acetylcholine ( $\alpha$ -7) receptor. The alpha-7 nicotinic receptor is highly expressed in the amygdala, which forms part of the emotional centre of the brain and recent data increasingly implicate acetylcholine and the alpha-7 receptor in the symptoms of anxiety and depression. To date, BNC210 has been evaluated in seven completed clinical trials in over 200 subjects.

Additionally, 193 patients have been enrolled in a Phase 2 PTSD trial, and a Phase 2 trial for hospitalised elderly patients with agitation is open to recruitment.

### **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, BNC101 and BNC105), 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.

# Bionomics



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**BNC210: in Development  
For Anxiety, Panic, PTSD  
And Agitation**

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**CREATING INNOVATIVE THERAPIES  
FOR SERIOUS HUMAN DISEASES.**

**Sue O'Connor PhD**  
**VP Strategic Initiatives and Innovation**  
14<sup>th</sup> Bioshares Biotech Summit  
27-28 July 2018

# Safe Harbor Statement

## Factors Affecting Future Performance

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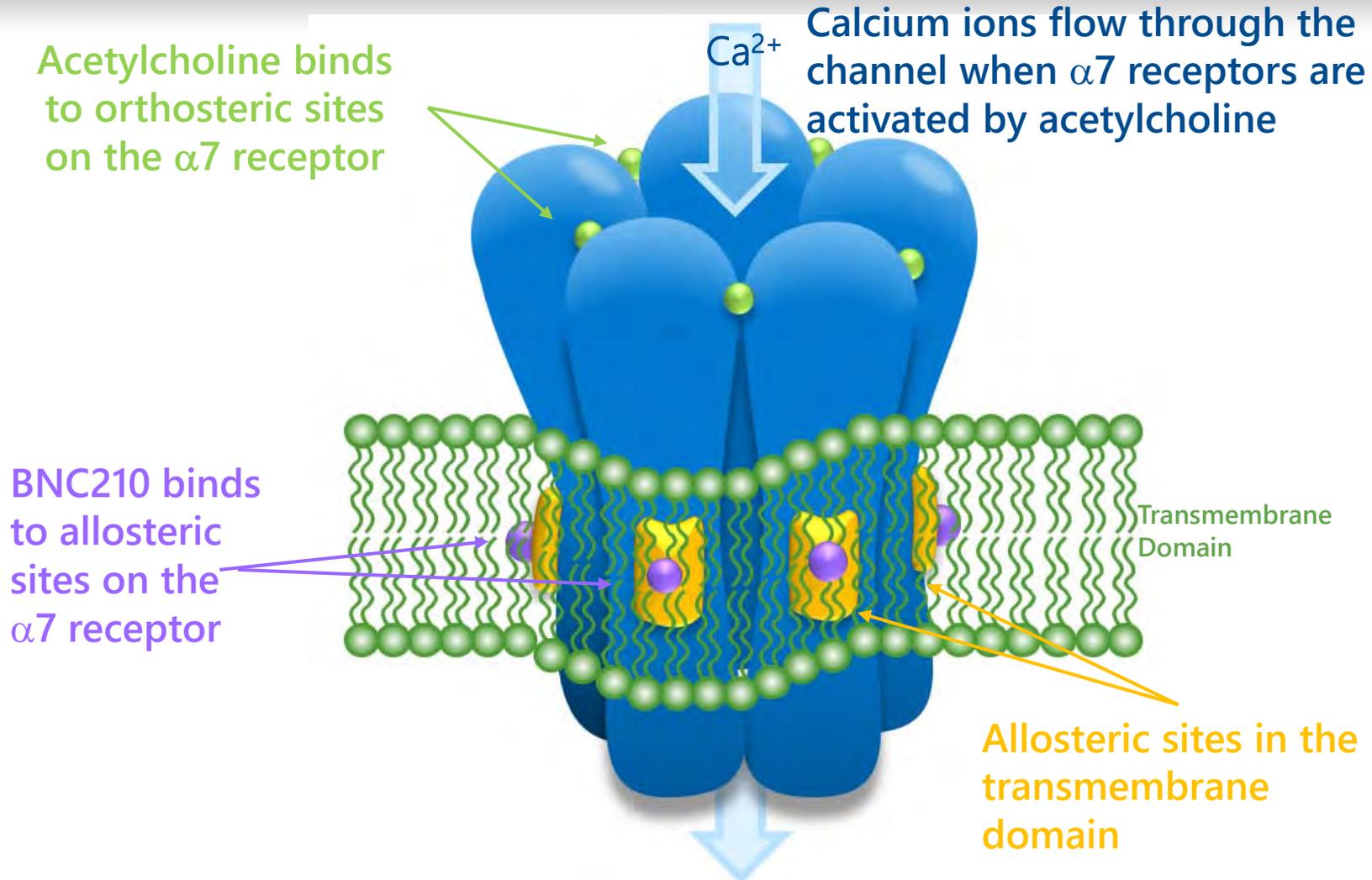
Subject to the requirements of any applicable legislation or the listing rules of any stock exchange on which our securities are quoted, we disclaim any intention or obligation to update any forward-looking statements as a result of developments occurring after the date of this presentation.

## Bionomics 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 Generalized 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\$189.5M as at 11 July 2018; Cash at 30 June 2018 US\$18.4M

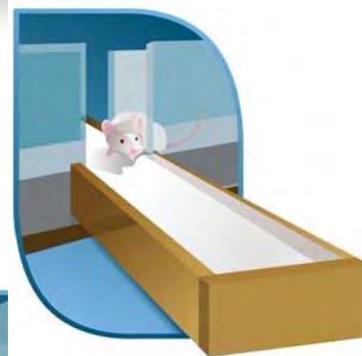
# BNC210 is a novel, negative allosteric modulator of the $\alpha 7$ nicotinic acetylcholine receptor with anxiolytic and antidepressant properties



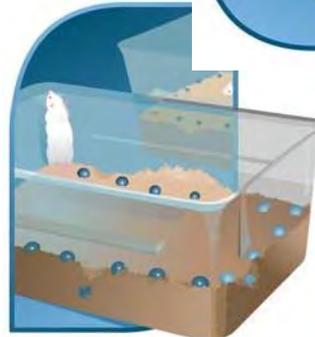
Five alpha subunits make up the  $\alpha 7$  receptor = Five potential binding sites

# Extensive pre-clinical efficacy and safety profiling demonstrated anxiolytic, antidepressant and safety properties of BNC210

- ✓ Light Dark Box
  - ✓ Marble Burying
  - ✓ Contextual Fear Conditioning
  - ✓ Elevated Plus Maze
- MICE



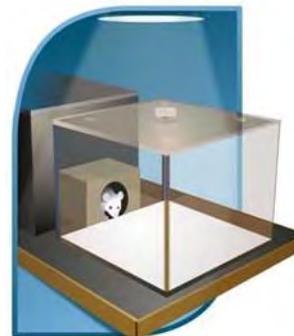
- ✓ Elevated Plus Maze
  - ✓ Pre-stress + Elevated Plus Maze
  - ✓ CCK + Elevated Plus Maze
  - ✓ Forced Swim Test
- RAT



- ✓ Isolation-induced vocalizations in guinea pig pups
- GUINEA PIG



- Open Field – dark, light
  - Rotarod
  - Modified Irwin
  - Novel Object Recognition
  - T-maze
- SAFETY



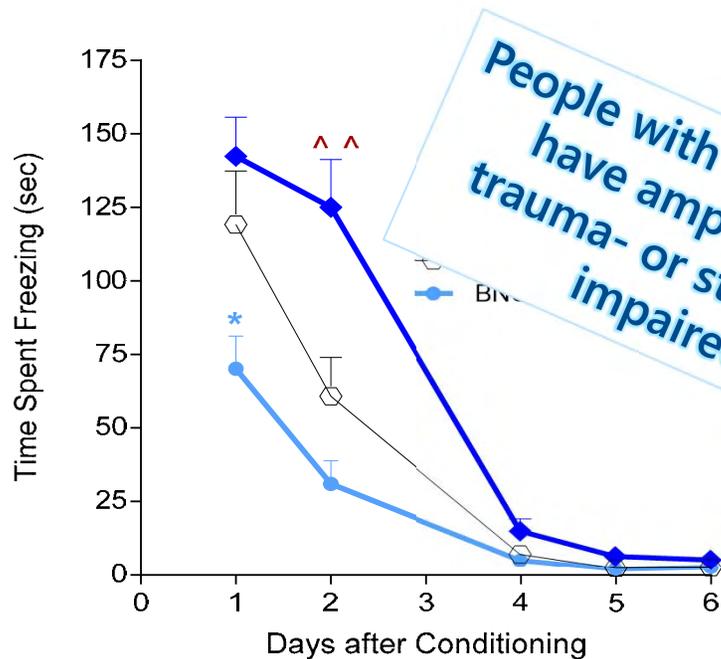
# BNC20 clinical data has demonstrated anxiolytic activity while maintaining a unique safety profile

Purpose	Description	Subjects	Location
P1 BNC210.001 & 2 SAFETY & TOLERABILITY, PK	Safety & Tolerability of Single Ascending Doses	24	Australia
P1 BNC210.003 SAFETY & TOLERABILITY & PD	Lorazepam & BNC210 Comparison plus EEG	22	France
P1 BNC210.004 EFFICACY	Panic Attack Model in Healthy Volunteers	59	France
P1 BNC210.005 SAFETY AND TOLERABILITY TARGET ENGAGEMENT	Safety & Tolerability of Multiple Ascending Doses, Target Engagement Study with Nicotine & EEG	42	France
P2a BNC210.006 EFFICACY	Imaging & Behavioural Study In Generalised Anxiety Disorder Patients		USA
P2 BNC210.007 EFFICACY	Stress Disorder		Australia
P2 BNC210.008 EFFICACY	Study in a Hospital Setting		Australia

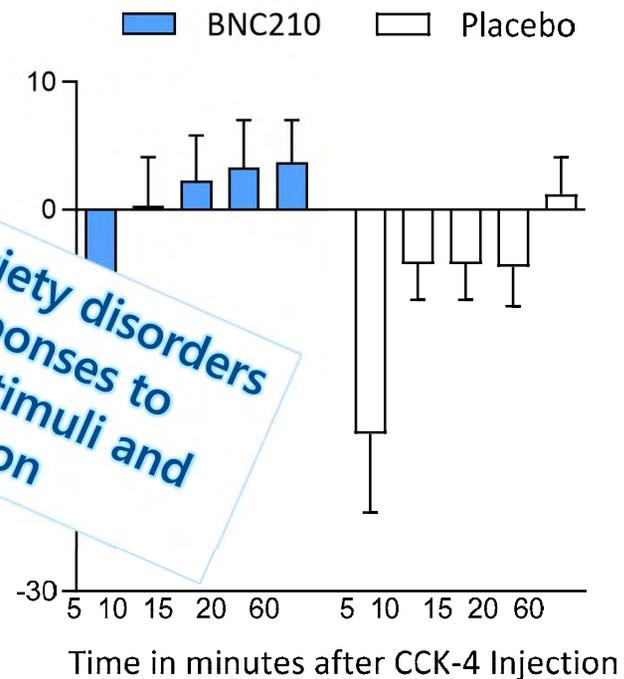
**AGITATION TRIAL:  
RECRUITING WELL  
DATA EXPECTED Q1,  
2019**

# BNC210 enhanced fear extinction in mice - this translated to rapid improvement in healthy volunteers following a CCK-4-induced panic attack

## Conditioned Fear Extinction Model



## Emotional Visual Analog Scale (eVAS)

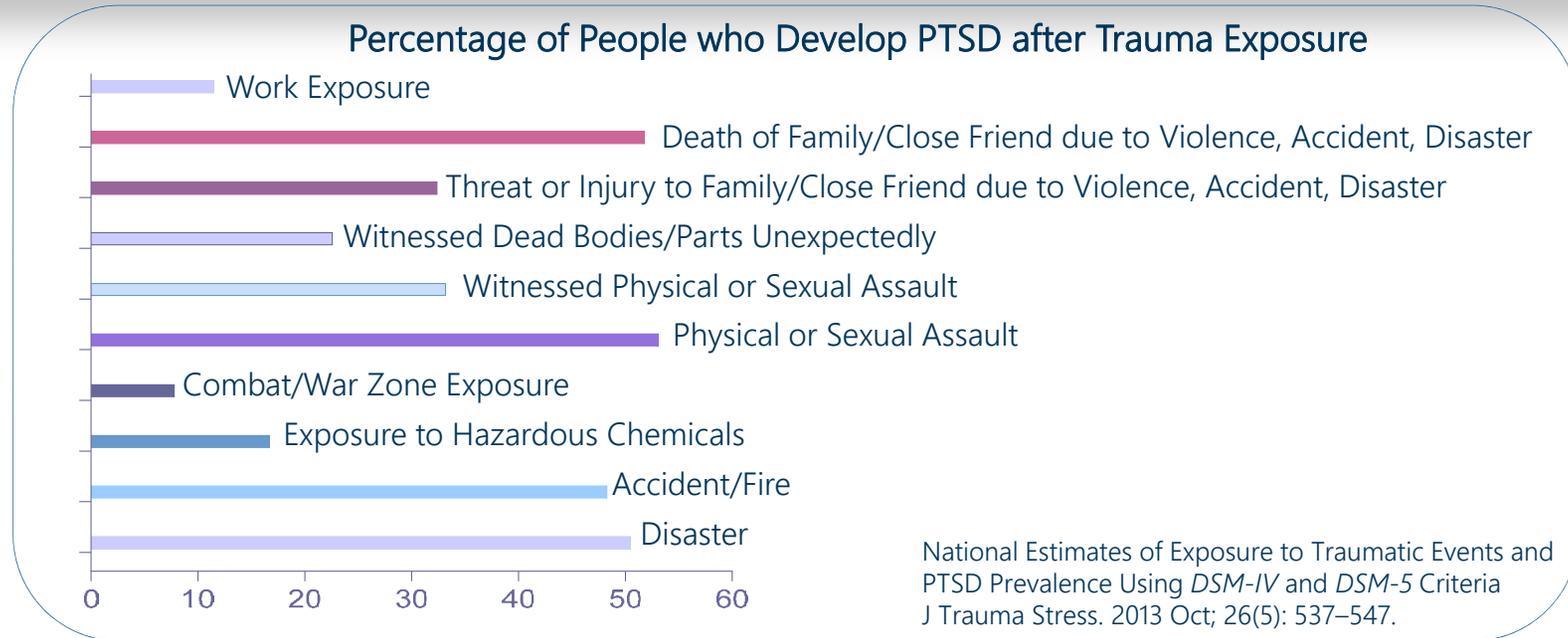


People with PTSD and anxiety disorders have amplified fear responses to trauma- or stress-related stimuli and impaired fear extinction

**MICE**  
BNC210 enhanced fear extinction following conditioned stimulus training

**HUMANS**  
BNC210 improved rate of return to emotional stability following CCK-4 challenge

# PTSD is a prevalent, world-wide disorder arising from a variety of trauma – not just combat exposure



**U.S. population Facts:** 7-8% of the population will have PTSD at some point in their lives. ♦ About 8 million adults have PTSD during a given year. ♦ About 10% of women develop PTSD sometime in their lives compared with about 4% of men.

**US Veterans with PTSD:** ♦ Operations Iraqi Freedom and Enduring Freedom: between 11-20% have PTSD in a given year ♦ Gulf War (Desert Storm): 12% have PTSD in a given year. ♦ Vietnam War: about 30% of Vietnam Veterans have had PTSD in their lifetime.

**UK Population Facts:** 10% of people develop PTSD. ♦ 20% of firefighters ♦ 30% of teenagers who have survived a horrific car crash ♦ 70% of rape victims ♦ 66% of Prisoners of War ♦ 40% of people who experienced a sudden death of a loved one ♦ An estimated 10,000 women a year following a traumatic childbirth

# Bionomics is currently recruiting for a Phase 2 Trial in Post Traumatic Stress Disorder (PTSD) in Australia and the USA



SUBJECTS	192 PTSD patients
PROTOCOL	<ul style="list-style-type: none"><li>• Double blind, placebo controlled, randomized, multi-centre</li><li>• 4 arms: 1 placebo, 3 BNC210 dose levels</li><li>• 12 weeks of dosing, twice daily oral treatment</li></ul>
PRIMARY OBJECTIVE	<ul style="list-style-type: none"><li>• To determine whether BNC210 causes a decrease in PTSD symptoms as measured by CAPS-5</li></ul>
SECONDARY OBJECTIVES	<ul style="list-style-type: none"><li>• To determine the effects of BNC210 on Anxiety (HAM-A), Depression (MADRS) and</li><li>• Functioning and Quality of Life,</li><li>• Safety and Tolerability</li></ul>
EXPLORATORY ENDPOINTS	Effects of smoking

Trial enrolled 193 PTSD patients. Data expected late Q3.

# Several rating scales included to capture efficacy of BNC210 for a range of symptoms and disorders

## PTSD Scales

CAPS-5 (Clinician-Administered PTSD Scale for DSM-5) Primary endpoint

PTSD Checklist for DSM-5 (PCL-5) Self-reporting scale

## Affective Disorders

Montgomery-Åsberg Depression Rating Scale (MADRS)

Hamilton Anxiety Rating Scale (HAM-A)

## Scales to assess symptom severity, treatment response and efficacy

Clinical Global Impressions – severity and improvement scale (CGI-S/CGI-I)

Patient Global Impression – Severity and improvement Scale (PGI-S/PGI - I)

Assessment of Quality of Life (AQoL-8D)

Social functioning: Sheehan Disability Scale (SDS)

Sleep monitoring: Pittsburgh Sleep Quality Index (PSQI)

Suicidal behavior (Columbia Suicide Severity Rating Scale, C-SSRS)



## Safety evaluations conducted throughout the study

- Adverse event reporting
- Vital signs
- Physical examinations
- Standard 12 Lead ECG
- Safety Labs: Hematology, Biochemistry, Urinalysis
- CANTAB Cognitive Assessments:
  - Paired Associates Learning (episodic memory)
  - Spatial Working Memory (working memory)
  - Rapid Visual Information Processing (sustained attention)

# 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

### Avoidance

### Negative alterations in cognition and mood.

### Arousal and reactivity

- 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 
- 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 
- 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 
- 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 

# The potential advantages of BNC210 for PTSD, Anxiety & Agitation compared to standard of care treatments, have been demonstrated in preclinical and clinical studies

## Potential Competitive Advantages of BNC210\*

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

*It Is Time to Address the Crisis in the Pharmacotherapy of Posttraumatic Stress Disorder: A Consensus Statement of the PTSD Psychopharmacology Working Group*  
*Biological Psychiatry 2017: PMID: 28454627*

### Anxiety Treatments

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

### Depression Treatments

- SSRIs and SNRIs used to treat depression and anxiety
- Modest efficacy, late onset of action, discontinuation syndrome, 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, a 70–80% increased risk of pneumonia)

- ANTI-DEPRESSANTS:
- Sertraline (Zoloft) and escitalopram (Lexapro) are only US FDA approved drugs for PTSD, vs. venlafaxine (Effexor) and Prozac
  - The 2017 VA/DoD Clinical Practice Guideline for PTSD further offers weak recommendation for other antidepressants if the four strongly recommended medications are ineffective, unavailable, or not tolerated. nefazodone (Serzone); imipramine (Tofranil); phenelzine (Nardil). Both nefazodone and phenelzine require careful management as they carry potentially serious toxicities.

- BENZODIAZEPINES:
- 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.
  - Still over-prescribed despite lack of efficacy, addictive potential and other harms associated with chronic use. An estimated 2.8M scripts are written off-label for management of PTSD symptoms.

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

## BNC210 has potential for the treatment of agitation



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



BNC210 works acutely for panic attack and in GAD patients  
Has equivalent efficacy to benzodiazepines;  
Safety profile greatly improved



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

# Agitation in the elderly: prevalence, symptoms and treatments

## Agitation in Alzheimer's Disease

- >2 million AD patients in the US.<sup>1,2</sup> Expected to nearly triple by 2050.<sup>3</sup>
- Agitation and aggression seen in approximately 45% of AD patients during 5-year period.<sup>4</sup>
- Characterized by emotional lability, restlessness, irritability, aggressive behaviors, disinhibition, and caregiver burden.<sup>5</sup>
- Agitation is associated with<sup>5,6</sup>:
  - Accelerated cognitive decline
  - Earlier nursing home placement<sup>3</sup>
  - Increased mortality
- 30% of caregivers rate stress associated with agitation / aggression as severely to extremely distressing.<sup>7</sup>
- Agitation is estimated to account for more than 12% of the healthcare and societal cost of Alzheimer's disease; currently estimated to be \$256 billion in US for 2017.<sup>3</sup>

## Agitation Treatments

- No approved medication = unmet medical need
- Current treatments include benzodiazepines and antipsychotics, buspirone,  $\beta$ -blockers, serotonergic agents, carbamazepine, lithium, and divalproex sodium.<sup>3</sup>

### Issues with Benzodiazepines:

- Sedating, cause disinhibition, cognitive and motor impairment, development of tolerance and addictive with long term use
- Decreased metabolism in the elderly leads to longer presence of drug in the body and increased risk of toxicity

### Issues with Antipsychotics:

- Adverse effects: pseudo-parkinsonism, sedation, akathisia, a form of motor restlessness.
- Lack therapeutic efficacy on wandering, apathy, withdrawal, hypersexuality, and symptoms of executive dysfunction or other cognitive aspects of dementia.
- FDA "Black Box Warning" for elderly patients- increased risk of death (pneumonia, stroke)

1. Ryu, SH, et al. Am J Geriatr Psychiatry. 2005;13:976-983.  
2. Hebert, LE, et al. Neurology. 2013;80:1778-1783.  
3. The Alzheimer's Association, <https://www.alz.org/facts/>

4. Steinberg M, et al. Int J Geriatr Psychiatry. 2008;2:170-177.

5. Antonsdottir IM, et al. Expert Opin Pharmacother. 2015;11:1649-1656

6. Rabins PV et al. Alzheimers Dement. 2013; 9:204-207.

7. Raskin, MA, Disruptive Agitation in Alzheimer's Disease: Medication Treatment

# 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

Depression, PTSD and Agitation are dominating psychiatric drug discovery and development efforts.

### 4 FDA Psychiatric Drug Approvals Since 2013

2018 -0; 2017 – 0;  
2016 – 1 (Nuplazid);  
2015 – 3 (aripiprazole, brexpiprazole, cariprazine)

### 7 Industry Run Trials in PTSD\*

P3 - 1 (Tonix),  
P2 – 3 (Bionomics, Otsuka, Azevan, + MDMA (MAPs),  
P1 – 2 (Springworks, Aptinyx,

### 9 Industry Run Trials in Agitation in the Elderly\*

5 antipsychotics, 2 anxiolytics,  
2 antidepressants  
1 Fast track  
5 Phase 2, 4 Phase 3

### 21 Trials with Ketamine\* and 5 Trials with MDMA\*

\* = Recruiting, Not yet Recruiting, Active, not Recruiting, Recruiting by Invitation

## The FDA has initiated five approaches to make potentially important new drugs available as rapidly as possible

**PRIORITY REVIEW 1992:** A *Priority Review* designation will direct overall attention and resources to the evaluation of applications for drugs that, if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications.

**FAST TRACK DESIGNATION 1997:** The purpose is to get important new drugs to the patient earlier. Fast Track addresses a broad range of serious conditions.

**ACCELERATED APPROVAL: In 2012,** Allows the FDA to base accelerated approval on whether the drug has an effect on a surrogate or an intermediate clinical endpoint for drugs for serious conditions that fill an unmet medical need)

**BREAKTHROUGH THERAPY DESIGNATION: July 9, 2012** a new designation - Breakthrough Therapy Designation -If a drug is designated as breakthrough therapy, it will demonstrate substantial treatment effects early in clinical development (P2). FDA will expedite the development and review of such a drug.

**REGENERATIVE MEDICINE ADVANCED THERAPY 2016:** Preliminary clinical evidence indicates that the regenerative medicine therapy has the potential to address unmet medical needs for such condition.

## Drugs in development for Depression and PTSD are leading the indications receiving Breakthrough Therapy Designation

2018		
Sage217	Sage Therapeutics	MDD
Balovaptan	Roche	Autism Spectrum Disorder
2017		
Valbenazine	Neurocrine Biosciences	Tardive Dyskinesia
Midomafetamine	Multidisciplinary Association for Psychedelic Studies	Posttraumatic Stress Disorder
2016		
Pimavanserin	Acadia Pharmaceuticals	Parkinson's Disease-related Psychosis
Oliceridine	Trevena	Analgesia And Pain Management
Sage 547	Sage Therapeutics	Post Partum Depression (IV)
Esketamine	Janssen	MDD With Imminent Suicide Risk
Rapastinel(Glyx-13)	Allergan	MDD Rapid Onset
Tonmya	Tonix Pharmaceuticals	Posttraumatic Stress Disorder
2014 & 2015		
-	-	-
2013		
Esketamine	Janssen	Treatment Resistant Depression

# Drugs with dissociative properties are being investigated for therapeutic benefit in many difficult-to-treat disorders.



## Ketamine\*

- Suicide Prevention (5),
- Autism Spectrum Disorder (2)
- Agitation Control in Emergency Depts (2),
- Treatment Resistant Depression (5),
- Major Depression (3),
- Bipolar Depression (1),
- PTSD (1),
- Major Depression in Veterans
- Pediatric OCD (1)



## MDMA\*

- PTSD (1)
- Startle Response (1)
- Fear Extinction (1)
- Psychotherapy –assisted treatment for PTSD (2)

**DISADVANTAGES!**

\* =Clinical Trials.gov: Recruiting, Not Yet Recruiting, Active, Not Recruiting, Recruiting by Invitation

## Clinical studies with BNC210 indicate efficacy in anxious humans and potential therapeutic benefit for other disorders

- Significantly changed anxiety-induced brain activity
- Significantly changed anxiety-induced behavior
- Acute efficacy, equivalent to Lorazepam
- Reduced Panic Symptoms

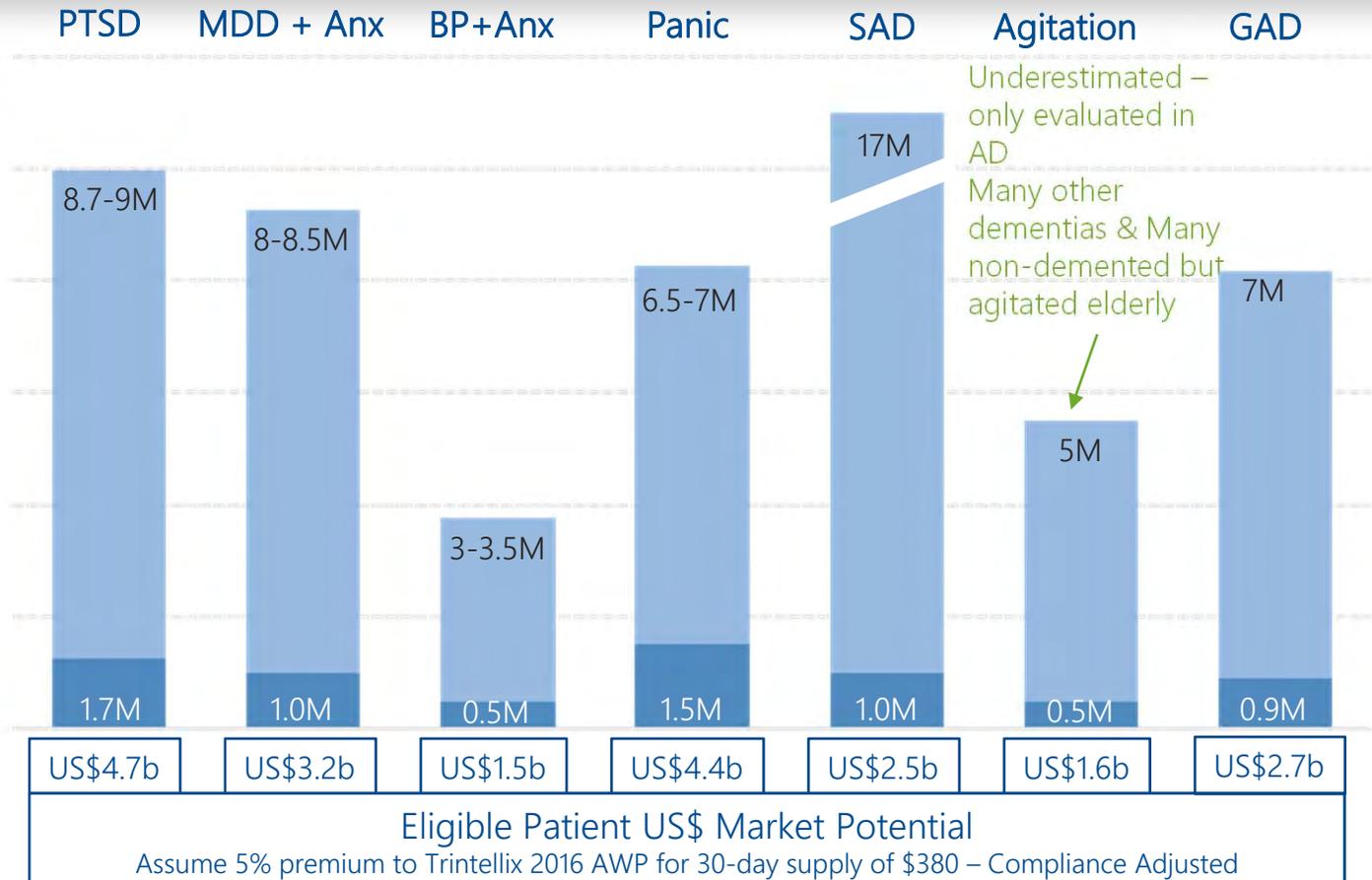
BNC210 also reduced connectivity between the ACC\* and the amygdala which, combined with dampening down of amygdala activation, indicates potential for therapeutic intervention in other disorders e.g. PTSD and Agitated Elderly which also feature hyperactive amygdala



\*ACC=Anterior Cingulate Cortex (involved in decision making and emotional regulation)

# 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



Underestimated – only evaluated in AD  
Many other dementias & Many non-demented but agitated elderly

**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

**Bionomics**



Appendices

# Competitive Landscape for Industry Trials in PTSD

Stage of Development	PI	PI	PII	PII	PII	PIII	PIV	PIV
Company / Sponsor	SpringWorks	Aptinyx	Bionomics	Azevan	Otsuka	Tonix	MSD Howard University	Takeda University of Miami
MOA	FAAH inhibitor	N-methyl-D-aspartate (NMDA)	a7 nAChR NAM	Vasopressin V1a antagonist	Dopamine	Multiple mono-amines	Orexin antagonist	Serotonin modulator and stimulator
Drug	PF-04457845	NYX-783	BNC210	SRX246	Rexulti/ Brexpiprazole	Tonmya TNX102	Suvorexant	Brintellix
Other Indications	Anxiolytic	Anti-depressant	Anxiolytic, Antidepressant, Enhances fear extinction	Anti-fear, Aggression, Depression, and Anxiety Positive results in P2 trial in intermittent explosive disorder	Atypical Antipsychotic, Antidepressant Hyperarousal	Sleep, Nightmares	Insomnia	Depression
Trial Overview	No Information other than in PI	No information <b>Fast Track</b>	192 pts, 2H, 2018	52 pts, June 2018	332 pts, Placebo, Sertraline, Sertraline+ Rexulti, Rexulti December 2018	550 pts, Oct. 2018 <b>Fast Track</b>	105 pts, March 2019 145 pts, March 2021	80 pts, July 2019

*Compounds address different specific symptoms to achieve overall benefit*

# Current Industry Sponsored Trials for Agitation and Aggression in Dementia July 2018

Stage of Development	P2	P2	P2	P2	P2	P3	P3	P3	P3
Company / Sponsor	Bionomics	Acadia	Acadia	Axovant	Mediti Pharma	Otsuka	Axsome	Avanir	Intra-Cellular Therapies
MOA	α7 nAChR NAM	5HT2a inverse agonist	5HT2a inverse agonist	5HT2a inverse agonist	mGluR2 agonist	Dopamine	Dextro-methorphan and Bupropion	Deuterated dextromethorphan and quinidine	5-HT <sub>2A</sub> receptor antagonist
Drug	BNC210	Pimavanserin	Pimavanserin	Nelotanserin	MP-101 (LY2979165)	Rexulti/ Brexpiprazole	AXS-05	AVP-786	ITI-007 Luma-teperone
Indication	Agitation in the Elderly	Treatment of Agitation and Aggression in AD	Treatment of Agitation and Aggression in Subjects With AD	REM sleep behavior in Lewy Body Dementia	Dementia-Related Psychosis and/or Agitation and Aggression	Symptoms of agitation in AD dementia - Completed Positive data on 2 scales	Agitation in Patients With Dementia of the Alzheimer's Type	Agitation in AD	Treatment of agitation in patients with Dementia including AD
Pharmacology	Anxiolytic Anti-depressant, Enhances fear extinction	Anti-psychotic	Anti-psychotic	Atypical Anti-psychotic Positive results in P2 -intermittent explosive disorder	Anxiolytic	Novel Atypical Antipsychotic, Anti-depressant	Treatment Resistant Depression	Anti-depressant Anti-psychotic Antitussive	Atypical Anti-psychotic
Trial Overview	40 pts, End 2018	432 pts, June 2019	111 pts, August 2019	60 pts, June 2017	100 pts; January 2021	Third Phase 3 trial commencing 1H, 2018	435 pts, Sept 2019 Fast Track Designation	380 pts, June 2018; 470 pts, Dec 2019; Ext study 700 pts, March	80 pts, July 2019