ABN 53 075 582 740

ASX ANNOUNCEMENT
10 May 2017

Bionomics to Host KOL Meeting Focused on BNC210, PTSD and Anxiety on 10th May 2017 in London

Bionomics Limited (ASX:BNO, OTCQX:BNOEF), a biopharmaceutical company focused on the discovery and development of innovative therapeutics for the treatment of diseases of the central nervous system (CNS) and cancer, today announced that it will host a Key Opinion Leader (KOL) lunch focused on BNC210, including data supporting its development in generalized anxiety disorder (GAD) and post-traumatic stress disorder (PTSD), on Wednesday, May 10, 2017 in London.

The meeting will feature keynote presentations from:

- Professor Allan H Young, MB ChB, MPhil, PhD, FRCPsych, FRCPC, FRSB., Director for the Centre for Affective Disorders in the Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience at King's College London.
- Dr Adam Perkins, Ph.D., Lecturer in the Neurobiology of Personality for the Centre for Affective Disorders, in the Department of Psychological Medicine, Institute of Psychiatry, Psychology & Neuroscience at King's College London.
- Dr Sue O'Connor, Ph.D., Vice-President, Neuroscience Research, Bionomics Limited.

Additionally, Dr Deborah Rathjen, Bionomics' CEO & Managing Director, will provide an overview of Bionomics recent pipeline progress and the commercial opportunity for BNC210.

Please find attached the presentation to be given at the event.

FOR FURTHER INFORMATION PLEASE CONTACT:

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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 focused on the treatment of serious central nervous system disorders and on the treatment of cancer. Bionomics' lead drug candidate BNC210, currently in Phase 2 for the treatment of generalized anxiety disorder and for post-traumatic stress disorder, is a novel, proprietary negative allosteric modulator of the alpha-7 (α7) nicotinic acetylcholine receptor. The Company is also developing BNC101, its lead humanized monoclonal antibody targeting a key receptor on cancer stem cells that is

overexpressed in metastatic colorectal cancer, metastatic pancreatic cancer and many other solid tumours; BNC101 entered clinical trials in the first quarter of 2016. Bionomics has strategic partnerships with Merck & Co., Inc (known as MSD outside the United States and Canada) in pain and cognition.

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 and BNC101), 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.

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 announcement.

Bionomics

Creating and developing innovative therapies

Bionomics Lunch Symposium - BNC210: Next Generation Drug Candidate to Treat Anxiety & Depression.

London, UK

Wednesday May 10th, 2017

Bionomics Overview

- Leveraging proprietary platform technologies to discover and develop deep pipeline of novel drug candidates focused on treatment of serious central nervous system disorders and cancer.
- Strategic partnership with Merck & Co.:
  - Deal valued up to US$506M in upfront, research and milestone payments plus additional royalties on net sales of licensed drugs
  - Received US$10M milestone payment for initiation of Phase 1 study of cognition drug candidate
  - Merck & Co equity investment in October 2015, 4.5% ownership
- Lead drug, BNC210, is novel, orally-administered, first-in-class, modulator of α7 nicotinic acetylcholine receptor, in development for treatment of anxiety and depression
  - Positive top line data reported in September 2016 from Phase 2 clinical trial in Generalized Anxiety Disorder (GAD)
  - Phase 2 trial in Post Traumatic Stress Disorder (PTSD)
- BNC101 is first-in-class anti-LGR5 antibody targeting cancer stem cells, in development for treatment of colon cancer and other solid tumours
  - Ongoing Phase 1 trial in colon cancer patients
- BNC105 in development for treatment of both solid and blood cancers
  - Novartis funding biomarker study in renal cancer
  - US investigator initiated study in patients with Chronic Lymphocytic Leukemia to start in 2017
  - Keytruda combination trial in melanoma patients to start 1H 2017

Platform Technologies Deliver Broad Drug Pipeline

Drug Candidate	Indication(s)	Preclinical	Phase 1	Phase 2	Milestones (Calendar Year)
Central Nervous System (ionX and MultiCore)					
BNC 210	Generalized anxiety disorder				Positive P2 results Q3 2016
	Other indications including PTSD				Initiated P2 trial in PTSD H1 2016
Undisclosed	ADHD, Alzheimer's, cognition, Parkinson's, schizophrenia				
Undisclosed	Chronic and neuropathic pain				
Others	Pain, Parkinson's dyskinesia, epilepsy				
Cancer Stem Cells (CSCRx)					
BNC101	Colorectal cancer				Initiated P1 trial in Q1 2016
	Pancreatic cancer				
	Other solid tumors				
Cancer Stem Cells (CSCRx and MultiCore)					
MELK*	Solid tumors				
Others	Solid tumors				
Other Programs					
BNC105	Solid tumors, renal, ovarian, mesothelioma				
BNC420	Solid tumors, melanoma, breast				
BNC164	Psoriasis, uveitis				

Speaker Introduction

- **Dr. Deborah Rathjen**
  CEO and Managing Director, Bionomics

- **Dr. Sue O'Connor**
  VP Neuroscience Research at Bionomics

- **Professor Allan Young**
  Director, Centre for Affective Disorders, Department of Psychological Medicine
  Institute of Psychiatry, Psychology and Neuroscience
  King's College London

- **Dr. Adam Perkins**
  Lecturer in the Neurobiology of Personality
  Centre for Affective Disorders, Department of Psychological Medicine
  The Institute of Psychiatry, Psychology & Neuroscience
  King's College London

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Dr. Sue O'Connor

Overview of BNC210

BNC210: Unique Molecule in Development for Treatment of Anxiety Disorders

Novel

- Bionomics has broad IP protection and full freedom to develop compound

α7nAChR

- Unique mechanism targeting negative allosteric modulator of α7 nicotinic acetylcholine receptor, with demonstrated anxiolytic and antidepressant activity in animal models

Selective

- Selective for α7 nAChR, no activity seen at related ion channels or when evaluated for off target activity in over 700 assays

NAM

- Negative allosteric modulation (NAM) facilitates safety, selectivity and efficacy; binds to receptor at different site from agonists that activate the receptor (acetylcholine or nicotine), only active when agonists are bound

Efficacious

- Significantly reduced symptoms of anxiety in CCK-challenge model of panic; target engagement demonstrated; significantly reduces amygdala activity and avoidance behavior in GAD patients

Safe

- Safe and well tolerated in clinical studies in >200 subjects; no cognitive impairment, sedation or effects on motor coordination

Phase II Study in PTSD Expected to Complete Enrollment by End Q1 2018

Clinical studies with BNC210 have provided information about safety, efficacy formulation and dosing

Protocol Number	Phase	Description	No. Subjects	No. Received BNC210	Formulation	Doses	Location
BNC210.001	Ia	SAD – Fasted	32	24	Oral suspension	5 – 2000 mg	Australia
BNC210.002 *Food Effect*	Ia	SAD - Fed	4	3	Oral suspension	300 – 2000 mg	Australia
ICP-2143-101 *Formulation*	Ia	SAD and food effect	47	40	Oral, powder-filled capsule	300 – 3000 mg	USA
BNC210.004 *Efficacy*	Ib	CCK4 challenge	60	59	Oral suspension	2000 mg	France
BNC210.003 *Safety/Lorazepam comparison*	Ib	Single dose PD / EEG	24	22	Oral suspension	300, 2000 mg	France
BNC210.005 *Dosing and target engagement*	Ib	MAD and nicotine shift	54	42	Oral suspension	300 – 2000 mg / day (b.i.d)	France
BNC210.006 *Efficacy*	IIa	fMRI in GAD	24	24	Oral suspension	300, 2000 mg	UK
BNC210.007 Ongoing	II	PTSD	192	-	Oral suspension	300, 600, 1200 mg/day b.i.d.	Australia USA

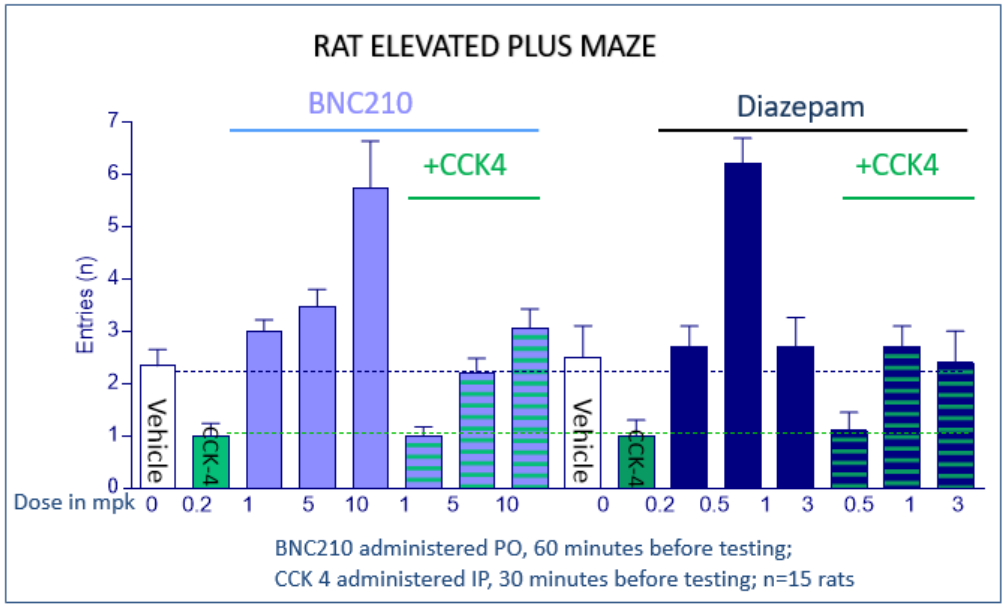
SAD = single ascending dose
MAD = multiple ascending dose
CCK = cholecystokinin tetrapeptide
b.i.d = twice daily;
fMRI = functional magnetic resonance imaging
GAD = generalised anxiety disorder
PD = pharmacodynamic

A single dose of BNC210 was evaluated in a human model of Panic Attack

Subjects	• 59 healthy subjects administered CCK4 to induce panic symptoms • 15 responders (consistent with panic attack rates in other studies)
Protocol	• Randomized double-blinded, placebo controlled • Subjects received single dose of placebo and BNC210 (2,000 mg)
Primary Endpoints	• Changes in the PSS (Panic Symptom Scale)
Secondary Endpoints	• Change in anxiety symptoms by means of the e-VAS (emotional-Visual Analog Scale) scales

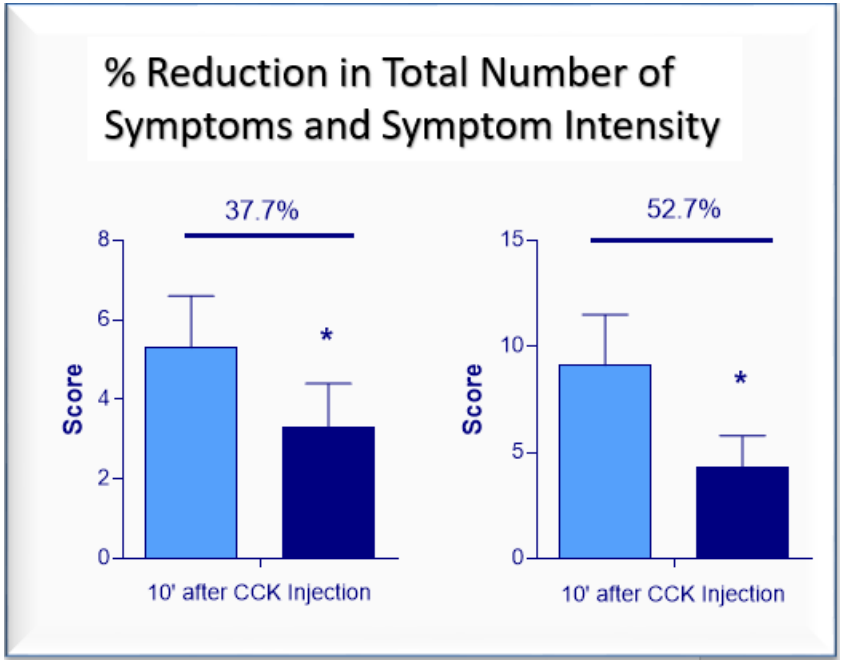
Preclinical efficacy of BNC210 translated to efficacy in human subjects

BNC210 Significantly Reduced CCK-4 Induced Anxiety in Rat Model of Panic



- ✓ Equivalent potency to Diazepam
- ✓ Broader therapeutic window
- ✓ Potential for POC in man

Following a CCK-4 Induced Panic Attack, Healthy Volunteers Treated with BNC210 Showed Significant Reduction in Number and Intensity of Panic Symptoms



Rats

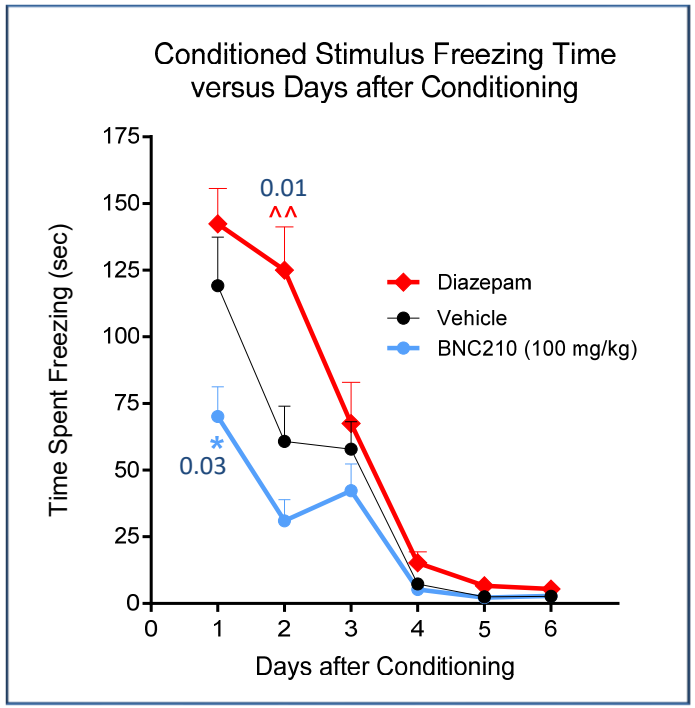
BNC210 reversed CCK-4 induced panic in a dose responsive manner

HUMANS

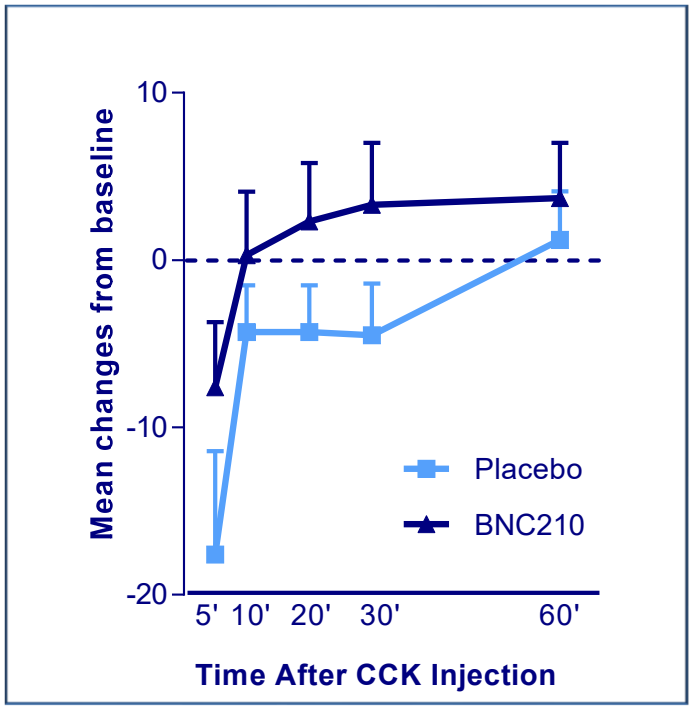
BNC210 reduced CCK-4 induced panic symptoms in healthy humans

BNC210 Enhanced Fear Extinction in a Mouse Assay: this Effect Translated to the eVAS Data Following a CCK-4 Challenge in HVs

Conditioned Fear Extinction Model



Emotional Visual Analog Scale (eVAS)



MICE

BNC210 enhanced fear extinction following conditioned stimulus training

HUMANS

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

Phase Ib Study Confirmed BNC210 -Differentiated EEG, Safety and Side-Effect Profile Compared to Lorazepam

Double-Blinded, Double-Dummy, 4-way Crossover Design; Lorazepam & Placebo Controlled

PERIOD 1	PERIOD 2	PERIOD 3	PERIOD 4
BNC210 300 mg & PLACEBO	**BNC210 2000 mg & PLACEBO**	**LORAZEPAM 2 mg & PLACEBO**	**PLACEBO & PLACEBO**

MEASUREMENTS: Attention - Reaction Time - Quantitative Wake EEG - Psychomotor Speed – Memory - ARCI49 -Visuomotor Coordination - Mood - Sedation

RESULTS: Compared to Lorazepam, 24 subjects treated with BNC210 ❶ did not experience effects on attention, memory, psychomotor speed, visual-motor coordination or ❷ eVAS; ❸ no sedation or ❹ no signs of addiction using ARCI 49 scale

Increase in δ spectral power during vigilance control session is signature of Lorazepam-induced sedation

Drug/EEG Spectrum	δ	γ	α	α1	α2	β	β1	β2	β3
BNC210			↓		↓	↑			↑
Lorazepam	↑	↓	↓	↓	↓	↑	↑	↑	↑

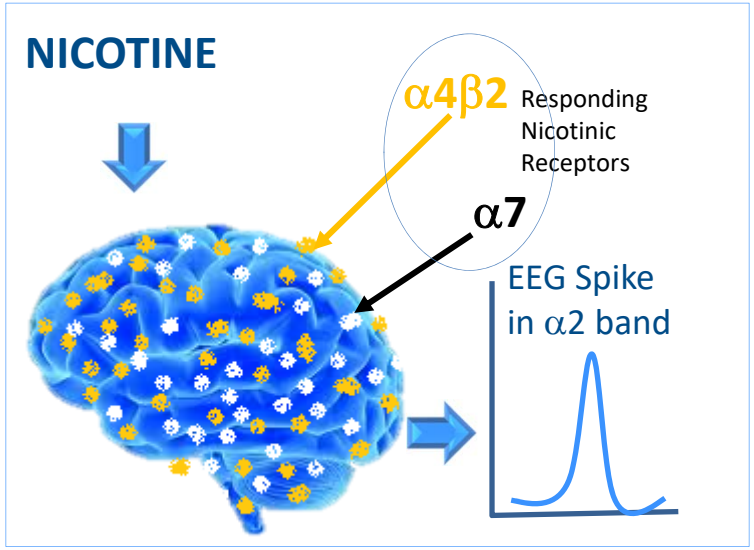
Increase in β3 spectral power is associated with the anxiolytic activity of Lorazepam

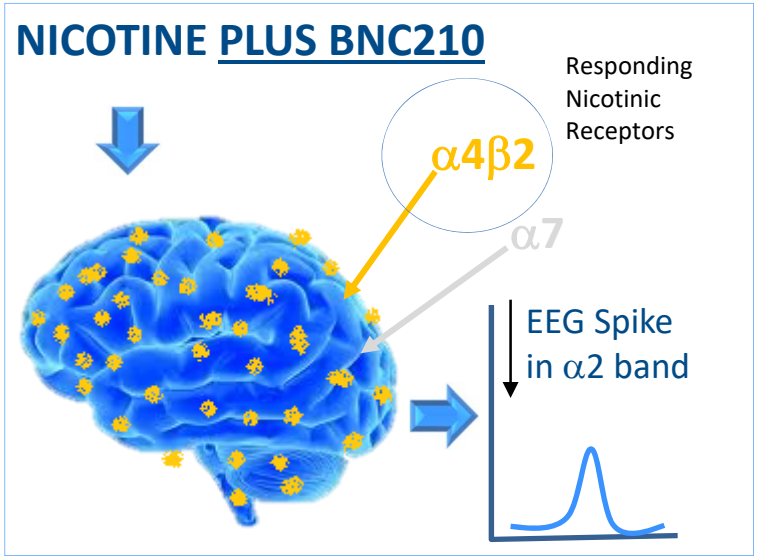
qEEG showed ❶ BNC210 effects the brain ❷ lack of sedation, and ❸ the signature associated with the anxiolytic effects of Lorazepam

BNC210 Phase 1 Multiple Ascending Dose Trial Provided Evidence of Target Engagement

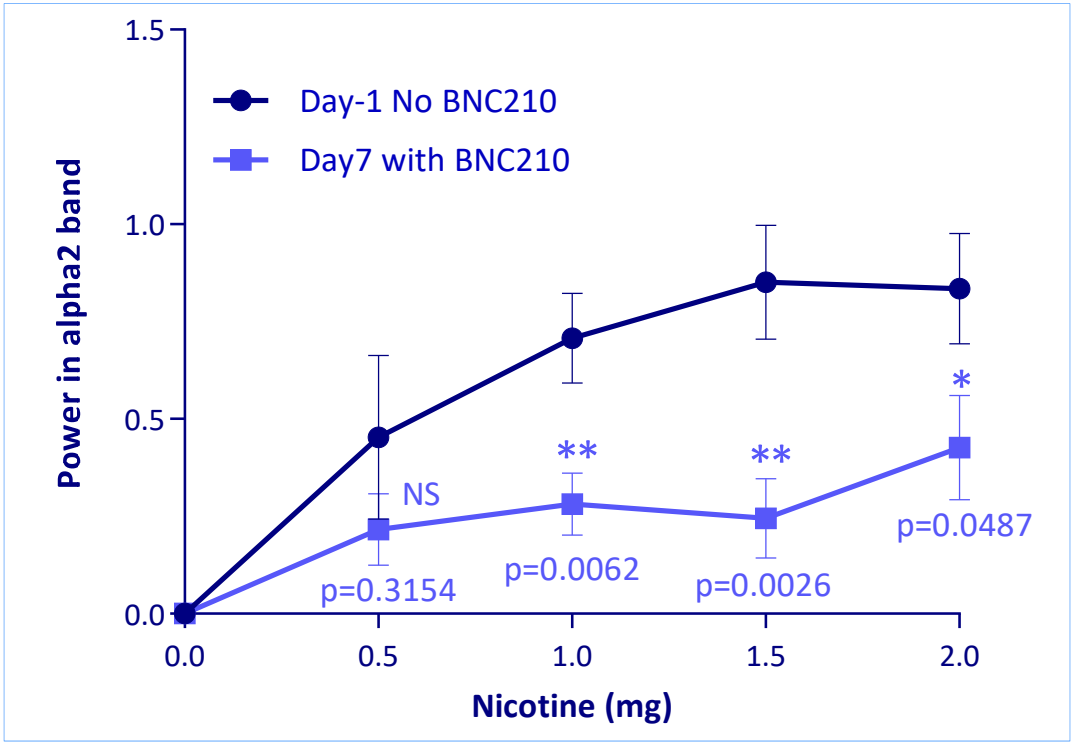
Subjects	▪ 54 healthy subjects
Protocol	▪ Double-blind, placebo controlled ▪ Subjects received multiple ascending dose ▪ Twice daily treatment for 8 days
Primary Endpoints	▪ Safety and tolerability of multiple doses
Secondary Endpoints	▪ Changes in cognitive functions ▪ Pharmacodynamic profile on nicotine shift assay (EEG) (2,000 mg dose level) ▪ Pharmacokinetics of multiple ascending doses
Results	▪ All primary and secondary endpoints met ▪ No adverse effects on cognition or emotional stability and no abuse potential indicated ▪ BNC210 reduced the effect of nicotine, as measured by EEG, consistent with its mechanism of action

Phase 1 Multiple Ascending Dose Trial: BNC210 Treatment Reduced Nicotine-Induced EEG Responses and Provided Evidence for BNC210 Target Engagement





The EEG response to nicotine is achieved through activation of nicotinic receptors in the brain. The major populations targeted are α4β2 and α7 receptors. Reduction in the response is due to negative allosteric modulation of the α7 receptors by BNC210



Oral dosing with BNC210 (2000 mg) for 7 days reduced EEG power in the α2 band

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Results from the Phase II Trial of BNC210 in Generalized Anxiety Disorder Patients

BNC210.006: Phase IIa Study in GAD patients used a creative and successful recruitment strategy

GOAL:
TO RECRUIT 24 UN-MEDICATED GAD PATIENTS

TRAIT SELF DESCRIPTION INVENTORY

4468 people completed personality test online

HIGH NEUROTICISM CORRELATES WITH HIGH ANXIETY

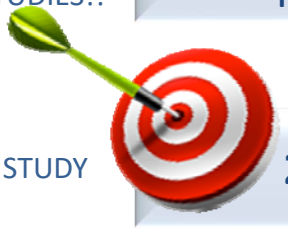
862 people scored ≥1 SD on Neuroticism

TELEPHONE SCREENING, MINI ANXIETY AND DEPRESSION SCALES, 30'

266 volunteered to be screened for the study

NO TATTOOS OR PIERCINGS ALLOWED IN IMAGING STUDIES!!

39 came in to the clinic for screening



24 COMPLETED STUDY

27 recruited

GAD Clinical Trial Objectives

Primary objectives:

(A) To determine whether BNC210 causes significant changes in cerebral blood flow using Arterial Spin Labelling in the resting state

(B) To determine whether BNC210 causes significant changes in task-related brain activity using the emotional faces task during functional magnetic resonance imaging (fMRI)

Secondary objective:

- To determine the effect of BNC210 on defensive behaviour using the Joystick Operated Runway task (JORT).

Study Design

Study Population

27 Generalised Anxiety Disorder patients enrolled:

- 4 male patients, 23 female patients
- 24 completed all four periods of the protocol (3M, 21F)
- 3 patients dropped out
  - 1 protocol violation (UDS positive for THC)
  - 1 patient request
  - 1 related to technical problems (with MRI)

Comorbidities in 2 or more patients (MINI):

Panic disorder with agoraphobia (7.4%); agoraphobia (7.4%); social phobia (7.4%); generalized social phobia (7.4%).

MRI Protocol - Procedures and Timing

3 TESLA MRI SCANNER

Primary Objectives

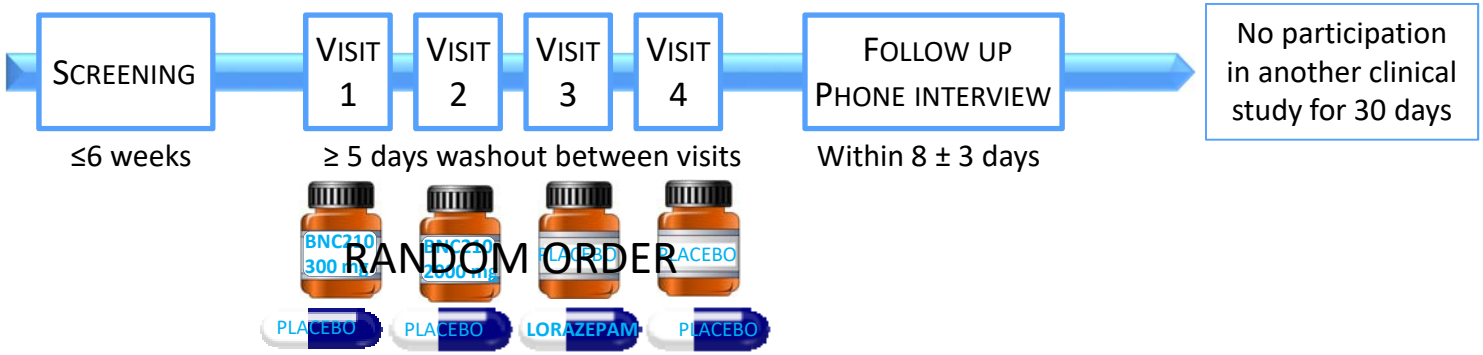
1. Set up for scanning (10')
2. Structural scans (5')
3. Resting state connectivity (8')
4. Arterial spin labelling (6')
5. Emotional faces task (fearful faces vs neutral faces) (12')

Secondary Objectives

6. Set up Joystick Operated Runway Task (JORT) (15')
7. JORT (18')

Study Methodology

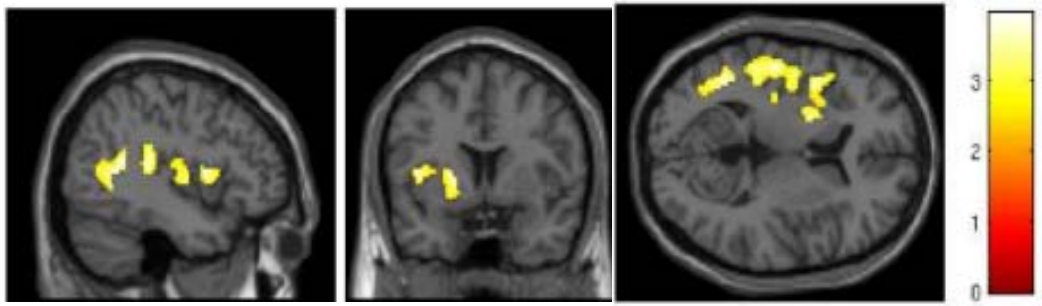
Each patient made 4 visits to the site and experienced 4 treatments in a **random order** – BNC210 300 MG, BNC210 2000 MG, LORAZEPAM 1.5 MG, PLACEBO.



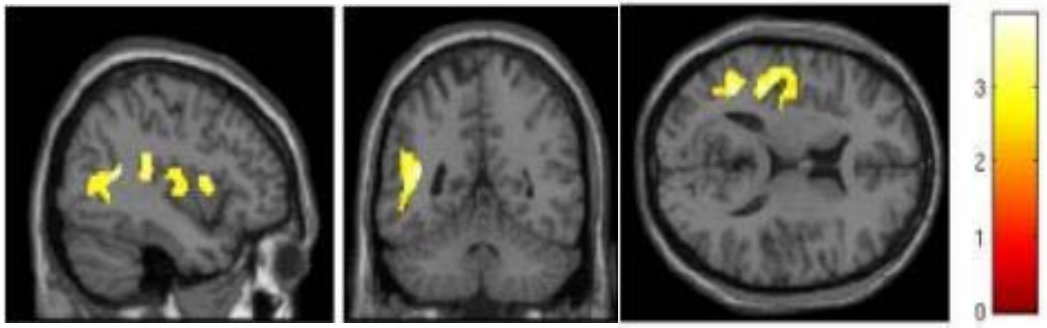
Low Dose BNC210 Caused Significant Local CBF Changes

Primary Objective met

BNC210 low dose >Placebo, all FWE corrected 0.05



P=0.047, cluster size=356, peak located at -42/6/8

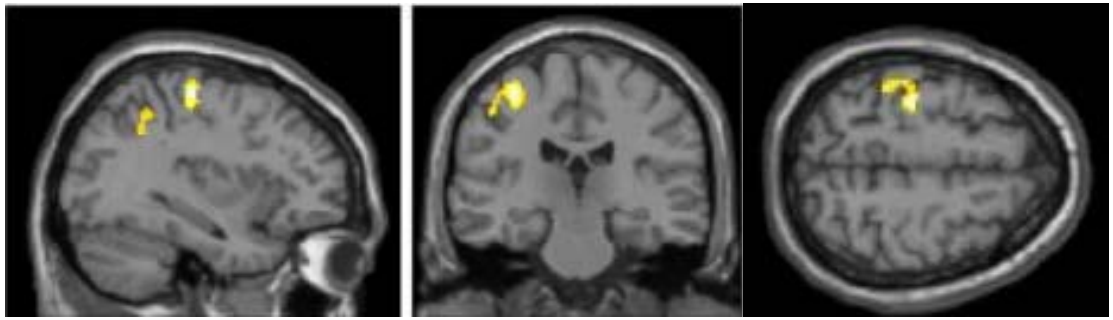


P= 1.72e-08, cluster size=1758, peak located at -40/-50/14

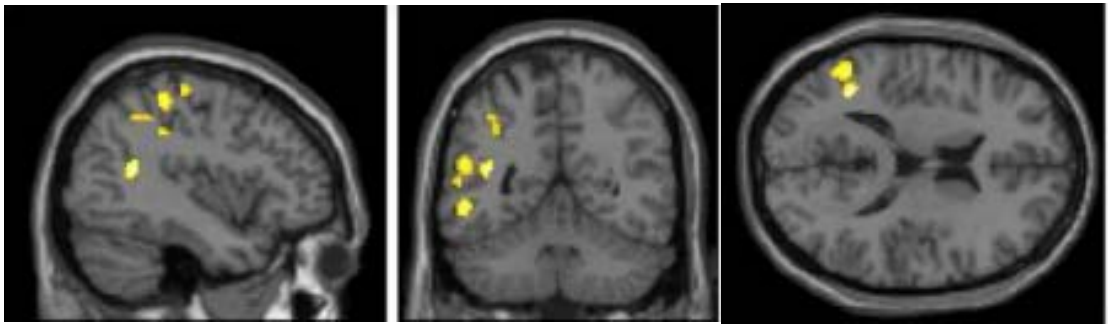
High Dose BNC210 Caused Significant Local CBF Changes

Primary Objective met

BNC210 high dose>Placebo, all FWE corrected 0.05



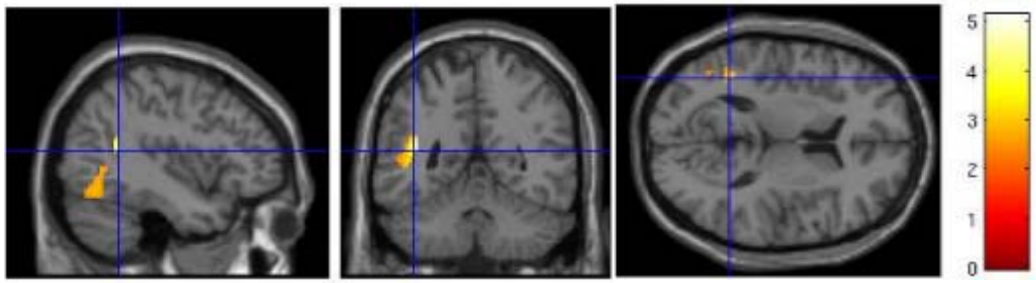
P=0.030, cluster size=387, peak located at -34/-24/58



P=0.010, cluster size=466, peak located at -40/-52/16

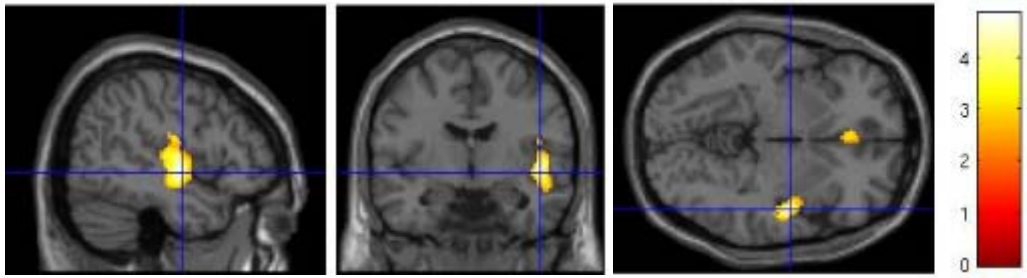
Lorazepam Produced Significant Changes in CBF

- Corrected for multiple comparisons at $p<0.05$
- Lorazepam > Placebo

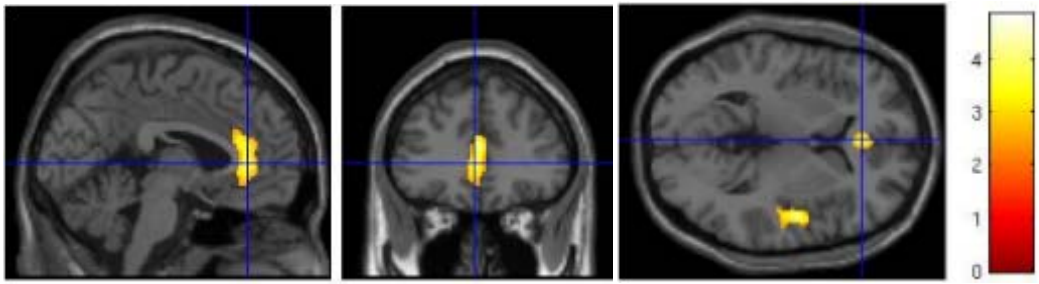


p= 3.87E-4
Cluster size 873 voxels
Peak in left superior temporal lobe

- Lorazepam < Placebo



p=0.0026
Cluster size 680 voxels
Peak in right superior temporal lobe

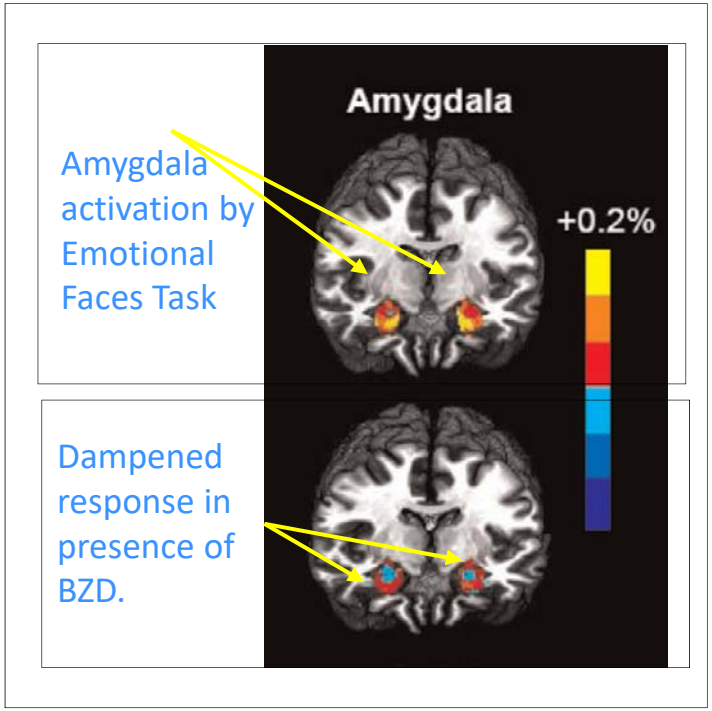


p= 0.0359
Cluster size 442 voxels
Peak in the anterior cingulate cortex

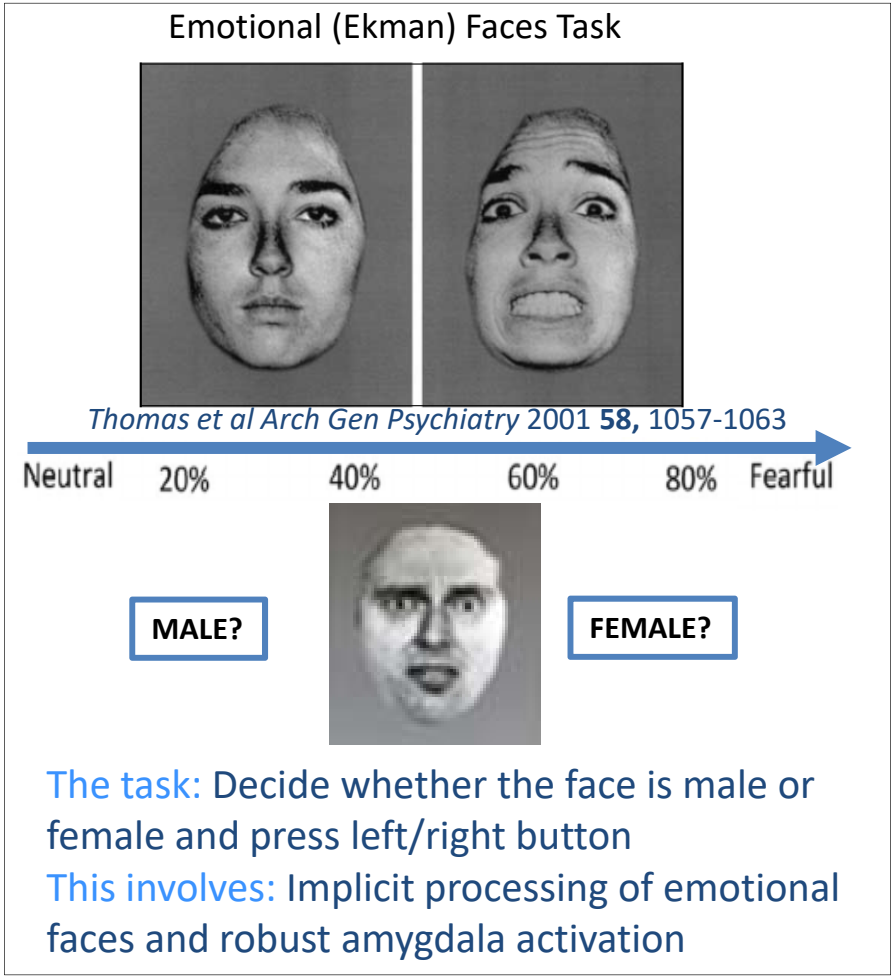
The Emotional Faces Task (fearful faces) is an Anxiety- Provoking Task Which Reproducibly Causes Amygdala Activation

GAD patients were treated with BNC210 to see if it would reduce the amygdala activity induced by the emotional faces task

- Primary Endpoint
- Activates the amygdala
- Measured using Functional MRI
- FDA-approved anxiety drugs reduce amygdala activation evoked by performance of the Emotional Faces Task



G. G. Brown et al. *Psychiatry Res.* 2015 Sep 30;233(3):394-401

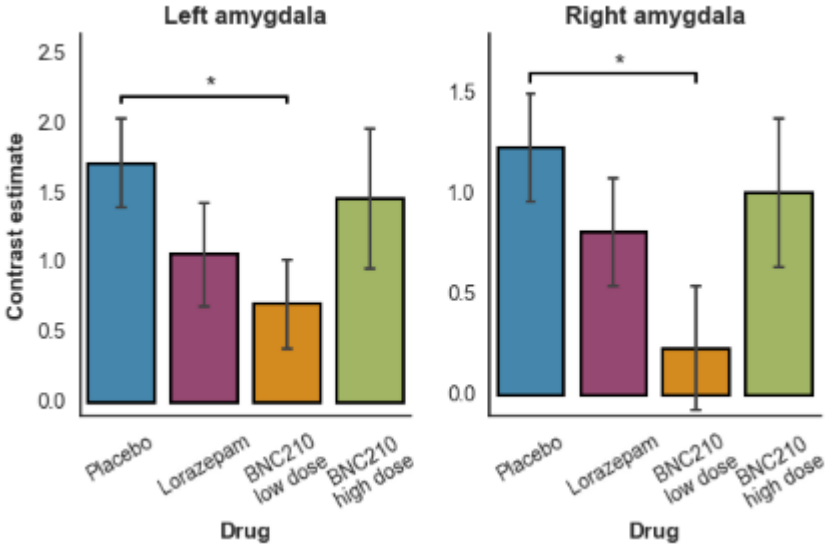


Fu et al Am. J. Psychiatry **164,** 599–607 (2007)

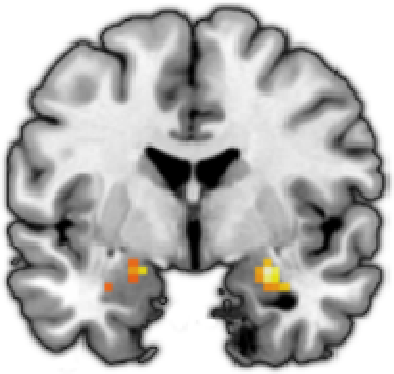
BNC210 Causes Significant Changes in Anxiety-Related Brain Activity Using Emotional Faces Task During fMRI

Statistically significant response to fearful faces in both left ($t(20) = 5.32$ $p < .001$) and right ($t(20) = 4.51$, $p < .001$) amygdala.

- 300 mg of BNC210 significantly reduced bilateral amygdala reactivity to fearful faces (p=0.027 for L and R)
- No significant effect with the 2000 mg dose of BNC210
- Lorazepam reduced left (t(20) = 2.16, p = 0.086, d = 0.5) and right (t(20) = 1.32, p = 0.19, d = 0.4) amygdala reactivity but this did not reach significance after multiple comparison correction.



Note: N = 21 (19 Female, 2 Male). Three subjects were excluded for excessive head movement.* Significant difference between placebo and BNC210 (300 mg), p < .05. Error bars: +/- SEM



Effect of BNC210 low dose on amygdala activity, thresholded at p < .05 uncorrected for illustration (Figure B).
Yellow areas indicate reduced amygdala reactivity to fearful faces. The size of the yellow area indicates scale of reduction)

Usual Adult Dose of Lorazepam for Anxiety
Initial dose: 2 to 3 mg orally per day administered 2 to 3 times per day
Maintenance dose: 1 to 2 mg orally 2 to 3 times a day

Key Takeaways from the GAD Study

This study provides strong evidence for the acute anxiolytic effects of BNC210 in anxious patients in **3 ways**:

- ✓ BNC210 significantly reduced **anxiety-induced brain activity**
- ✓ BNC210 significantly reduced **anxiety-induced behaviour**
- ✓ **Outperformed acute Standard of Care drug, Lorazepam**

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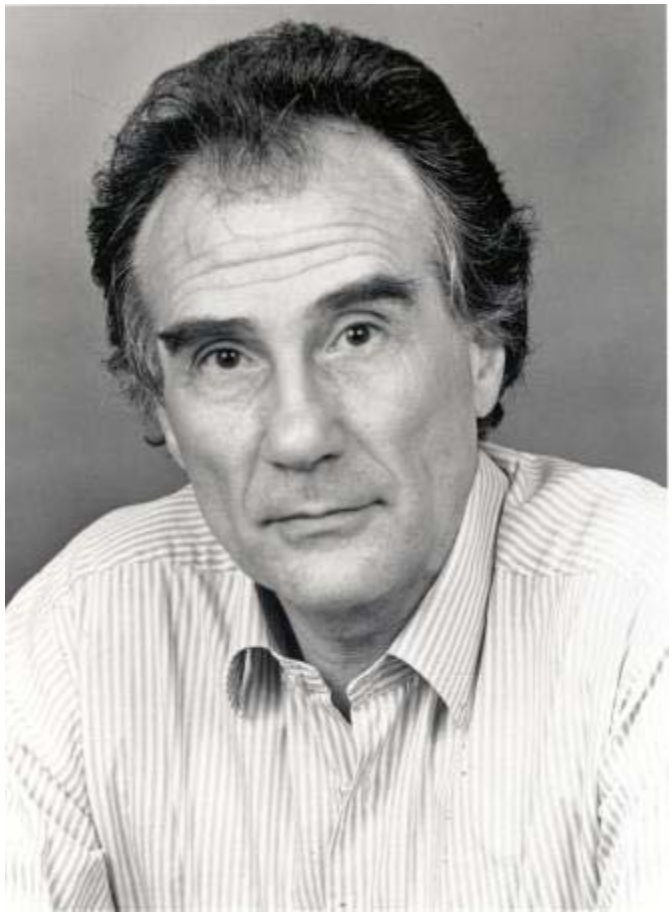
Dr. Adam Perkins

Overview of the Joystick Operated Runway Task and Results from Phase II Study of BNC210 in GAD

What is anxiety?

Jeffrey Gray's definition of anxiety is whatever is affected by anti-anxiety drugs. This is not a circular argument because he found these drugs also affect punishment-related behaviour in rodents, increasing approach to locations or stimuli that have been associated with painful electric shock.



Jeffrey Gray 1934-2004

Etho-experimental research

Drugs with clinical effectiveness against anxiety disorders systematically affect the innate defensive behaviour of rodents.

Caroline and Robert Blanchard

Etho-experimental research

Drugs with clinical effectiveness against anxiety disorders systematically affect the

innate defensive behaviour of rodents.

Caroline and Robert Blanchard

In rodents, therefore, threat → anxiety

The Janus face of anxiety: Gray's theory explaining why some people more prone to anxiety than others

State anxiety is produced by activity in brain systems that control responses to threat BUT:

Above average reactivity in threat systems = high levels of trait anxiety

Average reactivity in threat systems = medium levels of trait anxiety

Below average reactivity in threat systems = low levels of trait anxiety

The Janus face of anxiety: Gray's theory explaining why some people more prone to anxiety than others

State anxiety is produced by activity in brain systems that control responses to threat BUT:

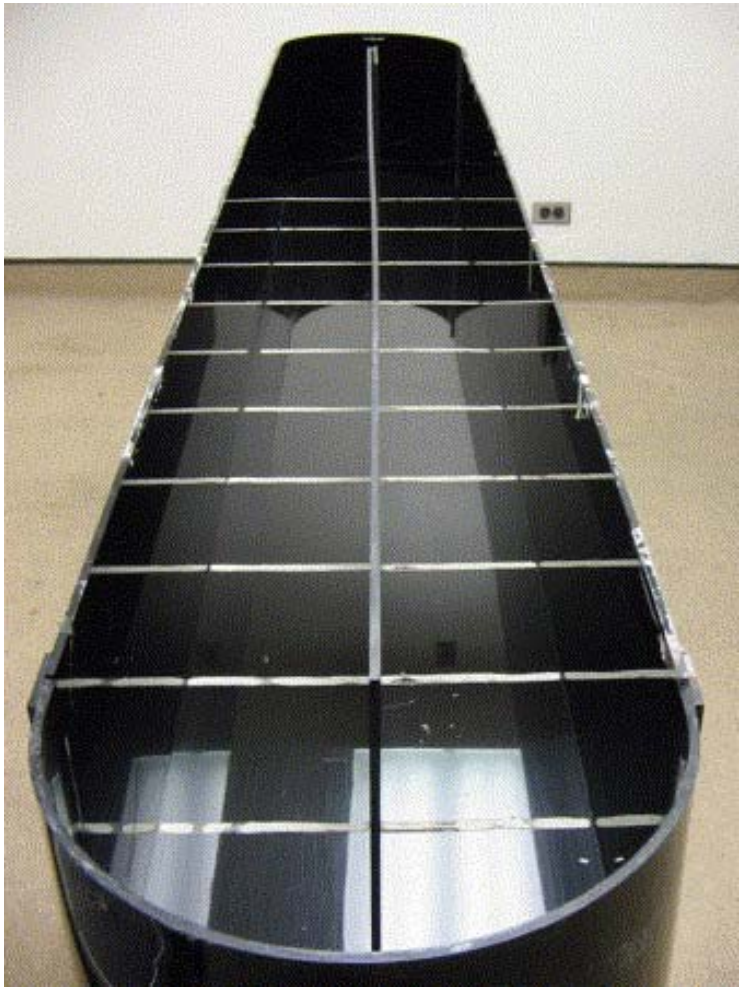
Above average reactivity in threat systems = high levels of trait anxiety

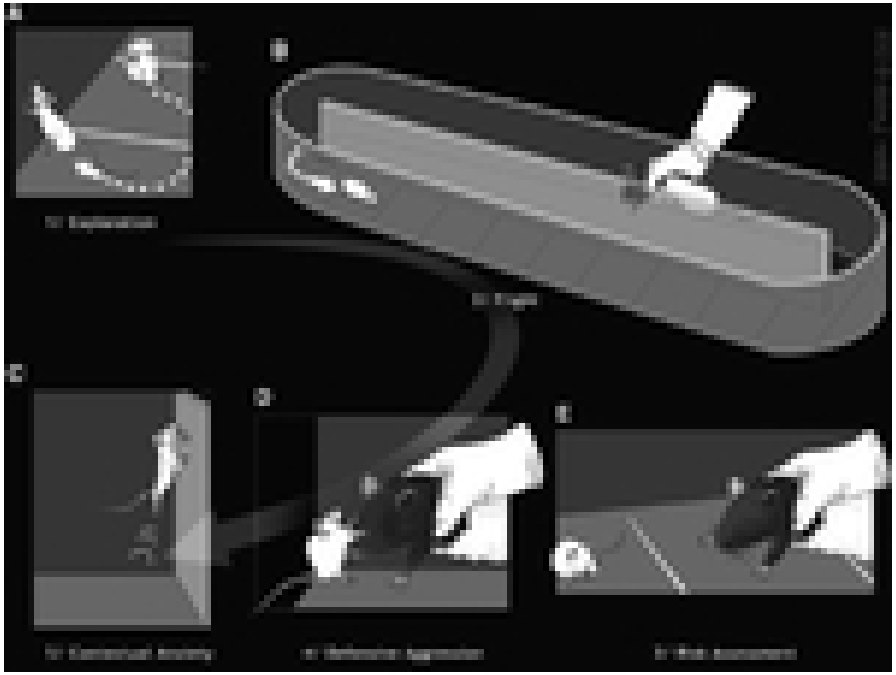
Average reactivity in threat systems = medium levels of trait anxiety

Below average reactivity in threat systems = low levels of trait anxiety

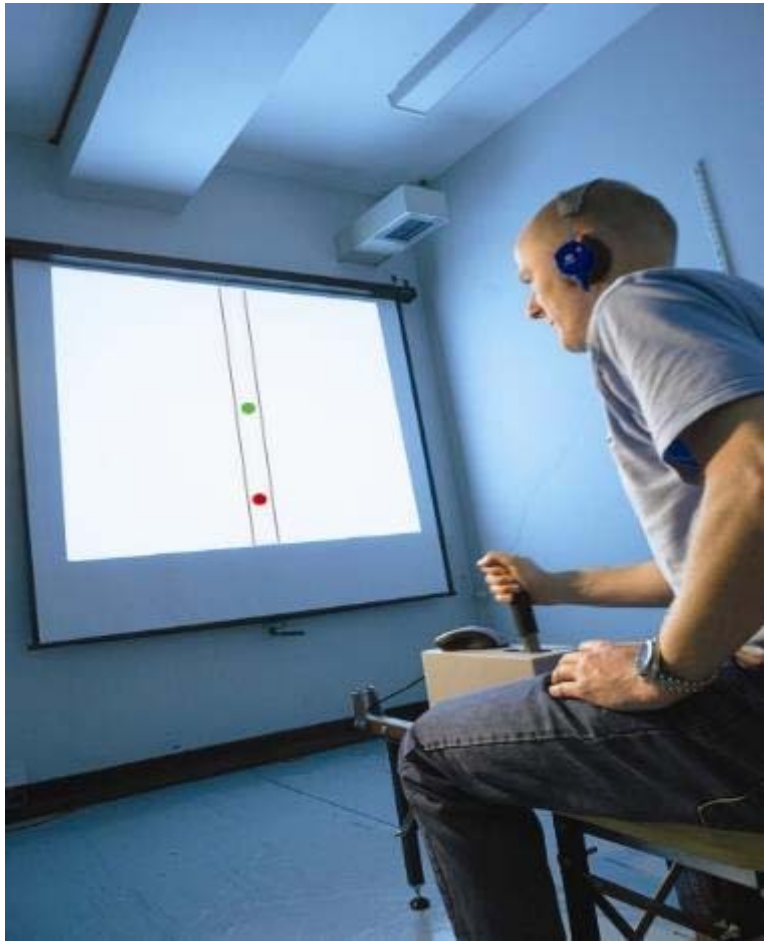
Effect of anti-anxiety drugs

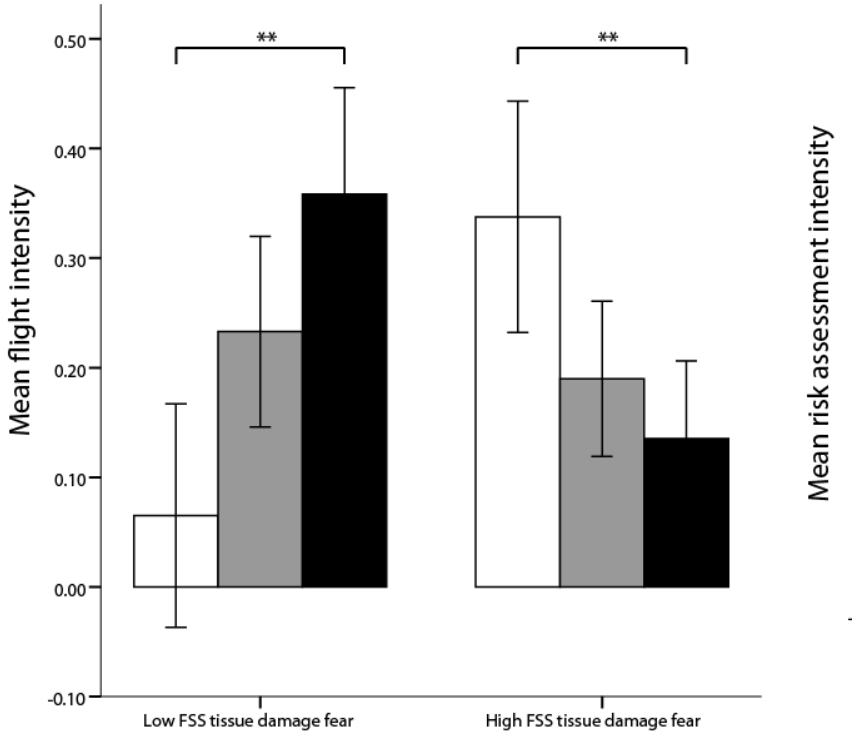
The Mouse Defense Test Battery (MDTB)





The Joystick Operated Runway Task (JORT)

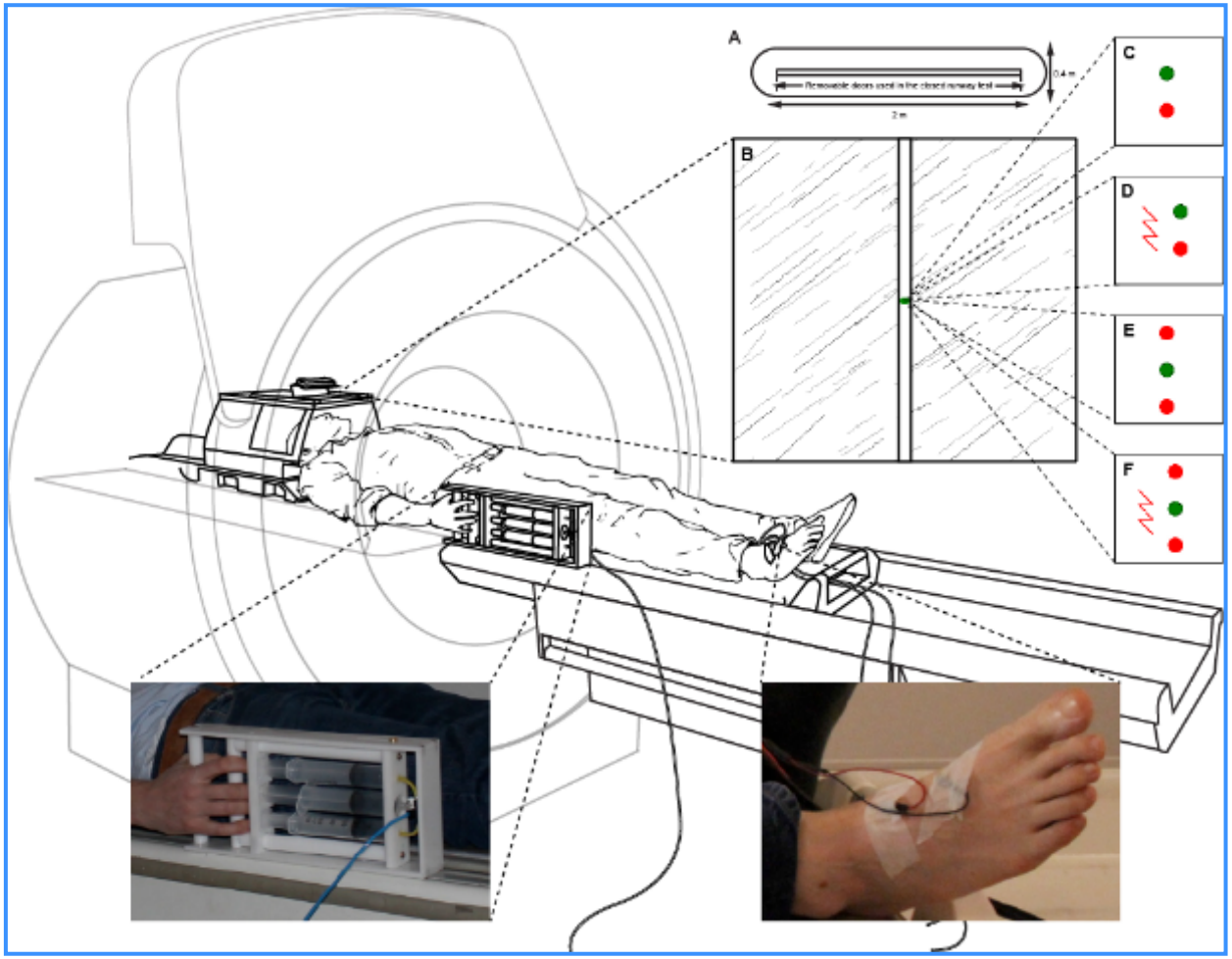




Perkins, A. M., Ettinger, U., Weaver, K., Schmechtig, A., Schrantee, A., Morrison, P. D., Sapara, A., Kumari, V., Williams, S. C. R., & Corr, P. J. (2013). Advancing the defensive explanation for anxiety disorders: lorazepam effects on human defense are systematically modulated by personality and threat-type. **Translational Psychiatry**, 3, doi:10.1038/tp.2013.20

Secondary Objective in GAD Study

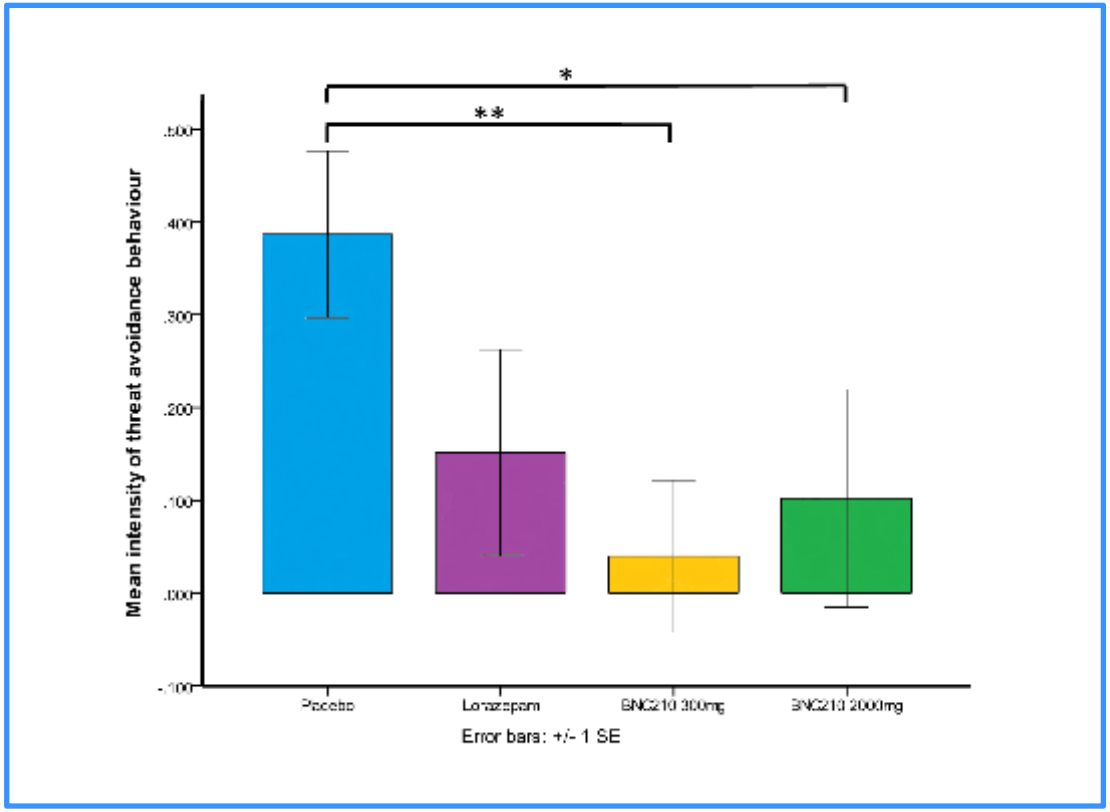
To determine the effect of BNC210 on defensive behaviour. In this study defensive behaviour was indexed using the Joystick Operated Runway Task.



Results - Secondary Objective Met

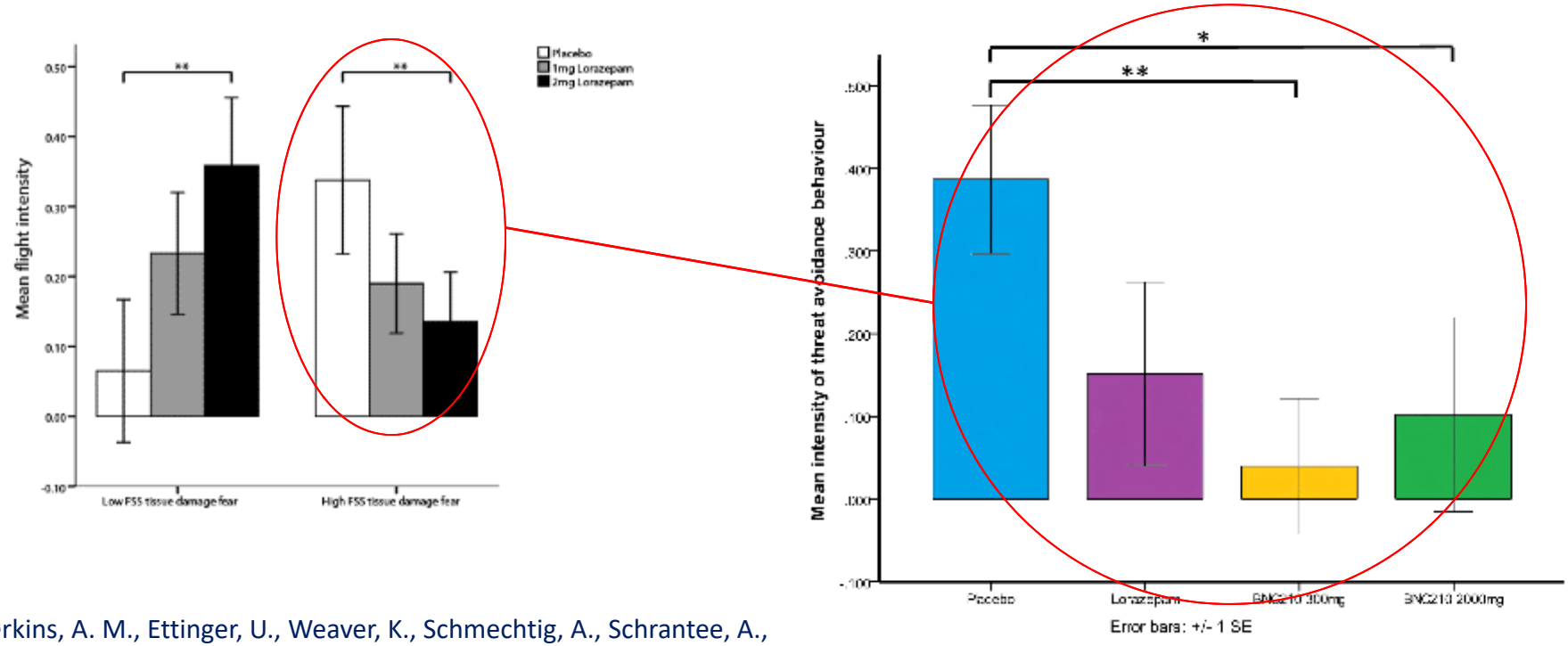
Significant separation from placebo occurred in the case of both the low and high dose of BNC210 (simple contrasts showed F values = 8.897, p = .007 and 5.217, p = .033 respectively).

Lorazepam showed a similar direction of effect but it failed to separate significantly from placebo (F = 2.072, p = .165). Note: n = 21 (females only).



Discussion - Secondary Objective

These new data in our GAD sample recapitulate the results published in 2013 which showed that for highly fearful individuals lorazepam reduced the intensity of simple avoidance behaviour.



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Key Takeaways from the GAD Study

This study provides strong evidence for the acute anxiolytic effects of BNC210 in anxious patients in **3 ways**:

- ✓ BNC210 significantly reduced **anxiety-induced brain activity**
- ✓ BNC210 significantly reduced **anxiety-induced behaviour**
- ✓ **Outperformed acute Standard of Care drug, Lorazepam**

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Creating and developing innovative therapies

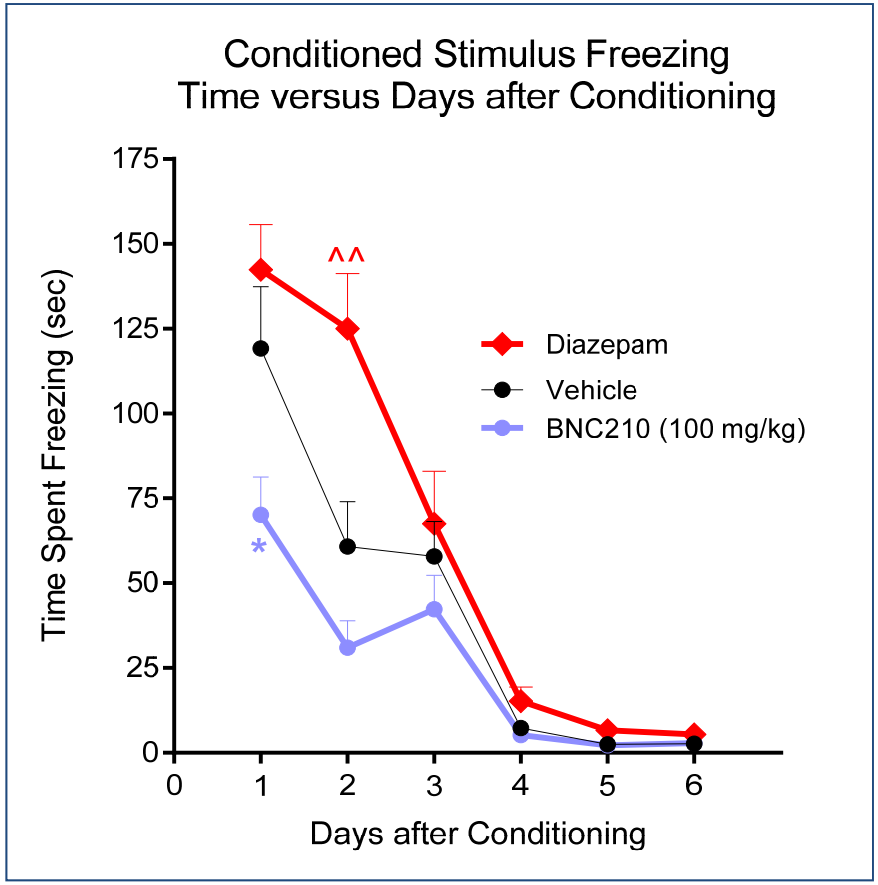
Professor Allan Young

PTSD Treatment Landscape and Overview of Phase II Study of BNC210 in PTSD

The mechanism and pharmacology of BNC210 indicate therapeutic potential for several PTSD symptom clusters

The four main PTSD symptom clusters of the DSM-5 criteria	
Intrusion. nightmares, unwanted thoughts of the traumatic events, flashbacks, and reacting to traumatic reminders with emotional distress or physiological reactivity.	BNC210 enhances fear extinction and is anxiolytic – may result in improved sleep
Avoidance. avoiding triggers for traumatic memories including places, conversations, or other reminders.	BNC210 reduces anxiety and may help to overcome avoidance BNC210 enhances fear extinction
Negative alterations in cognitions and mood. distorted blame of self or others for the traumatic event, negative beliefs about oneself or the world, persistent negative emotions (e.g., fear, guilt, shame), feeling alienated, and constricted affect (e.g., inability to experience positive emotions).	BNC210 has antidepressant effect which is more pronounced over time – potential to overcome negative mood
Arousal and reactivity. angry, reckless, or self-destructive behaviour, sleep problems, concentration problems, increased startle response, and hypervigilance.	BNC210 reduces amygdala hyperactivity – a feature shared by anxious patients and PTSD patients Inhibition of a7 nAChR inhibits release of excitatory neurotransmitters associated with hypercholinergic state; including NA, DA, GLUT, ACh – potential to reduce NA induced hyperarousal
Biological disturbances that have been proposed as causal for PTSD	
Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis	BNC210 shows clinical efficacy in CCK challenge, model of panic, elevated levels of ACh stimulate the HPA axis BNC210 treatment significantly reduced levels of ACTH in CCK study
The balance between excitatory and inhibitory brain neurocircuitry	α7 nAChR modulates gabaergic and glutamatergic interneurons in the amygdala

BNC210 as a potential therapy for PTSD Patients



	Day 1	Day 2
BNC210 vs **Vehicle**	*0.0318	0.06
BNC210 vs **Diazepam**	***0.0004	****0.0001
Vehicle vs **Diazepam**	NS	**0.01

Sertraline (Zoloft) and paroxetine (Paxil) are the only FDA approved drugs for PTSD.

The Veteran's Affairs/Department of Defence also recommend fluoxetine & venlafaxine (SNRI) as first-line treatments. Their 'Practice Guideline for PTSD' recommends against the use of benzodiazepines (BZDs) for PTSD.

Evidence is mounting on the harms associated with chronic benzodiazepine use in PTSD patients.

Despite their lack of efficacy, addictive potential and other harms associated with chronic use, BZDs are still over-prescribed

VA has several initiatives in place to reduce use of BZDs among patients with PTSD

There is a 50% increase in overall mortality rates associated with long-term benzodiazepine use in PTSD patients– overdosing, sudden unexplained deaths, car crashes, falls…..

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restore

BNC210 PTSD Study Overview

BNC210 PTSD Clinical Trial Overview

Overall Design:	• Randomized, double-blind, parallel, placebo-controlled, multi-center study in Australia and U.S. with a 12-week, 4-arm treatment phase (placebo, 150 mg, 300 mg and 600 mg BNC210 all twice daily). • 192 subjects. Randomization using a 1:1:1:1 ratio.
Study Duration:	• Treatment phase: 12-weeks of treatment, twice daily. • Target enrolment completed end calendar year 2017.
Study Primary Objectives:	• To assess the effects of BNC210 on investigator-rated symptoms of PTSD as measured by the CAPS-5 (Clinician-Administered PTSD Scale for the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5))
Study Secondary Objectives:	• To assess the effects of BNC210 on other psychiatric outcomes in subjects with PTSD including anxiety and depression • To assess the effects of BNC210 on global functioning and Quality of Life in subjects with PTSD • To assess the effects of BNC210 on patient-reported outcomes in subjects with PTSD • To assess the safety and tolerability of BNC210 in subjects with PTSD

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Dr. Deborah Rathjen

BNC210: A Potential Paradigm Shift in the Treatment of Anxiety and Depression

Novel

- Bionomics has broad IP protection and full freedom to develop compound

α7nAChR

- Unique mechanism targeting negative allosteric modulator of α7 nicotinic acetylcholine receptor, with demonstrated anxiolytic and antidepressant activity in animal models

Selective

- Selective for α7 nAChR, no activity seen at related ion channels or when evaluated for off target activity in over 700 assays

NAM

- Negative allosteric modulation (NAM) facilitates safety, selectivity and efficacy; binds to receptor at different site from agonists that activate the receptor (acetylcholine or nicotine), only active when agonists are bound

Efficacious

- Significantly reduced symptoms of anxiety in CCK-challenge model of panic; target engagement demonstrated; significantly reduces amygdala activity and avoidance behavior in GAD patients demonstrating rapid onset of action

Safe

- Safe and well tolerated in clinical studies in >200 subjects; no cognitive impairment, sedation or effects on motor coordination and no evidence of addiction

BNC210: Next Generation Drug Candidate to Treat Anxiety and Depression

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	✓

Anxiety Treatments

- Dominated by benzodiazepines
- Associated with sedation, addiction and tolerance and cognitive disturbances
- Not recommended for long-term treatment

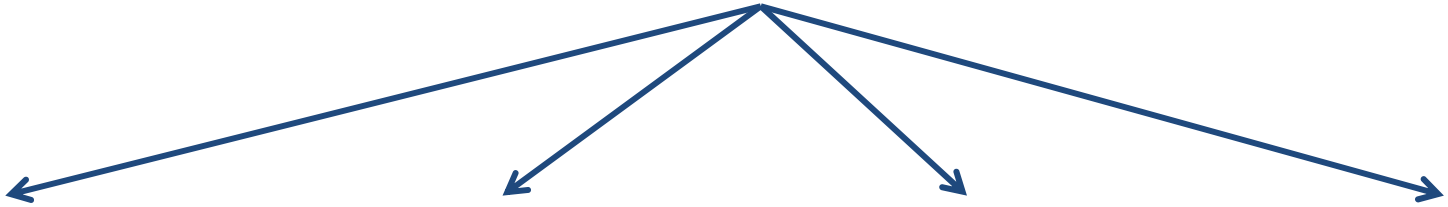
*Based on data from preclinical studies and Phase 1 clinical trials.

Depression Treatments

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

Mechanism of Action of BNC210 Supports Broad Commercial Opportunity

RESULTS OF GAD CLINICAL TRIAL PROVIDES PROOF OF BIOLOGY FOR ADDITIONAL INDICATIONS



Anxiety Disorders
- Panic Disorder
- Generalized Anxiety
- Social Anxiety

Co-Morbid Anxiety
- Bipolar Disorder
- Major Depressive Disorder

Trauma Related Disorders
- PTSD

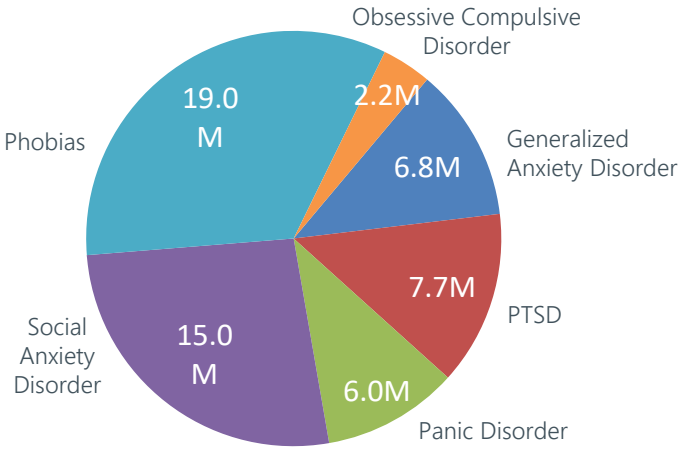
Neurodegenerative Disease
- Agitation and
- Anxiety

BNC210 is Uniquely Positioned to Address a Large and Underserved Market

Anxiety and depression have overlapping symptoms: 50-70% of those diagnosed with depression are also diagnosed with an anxiety disorder

Anxiety Market

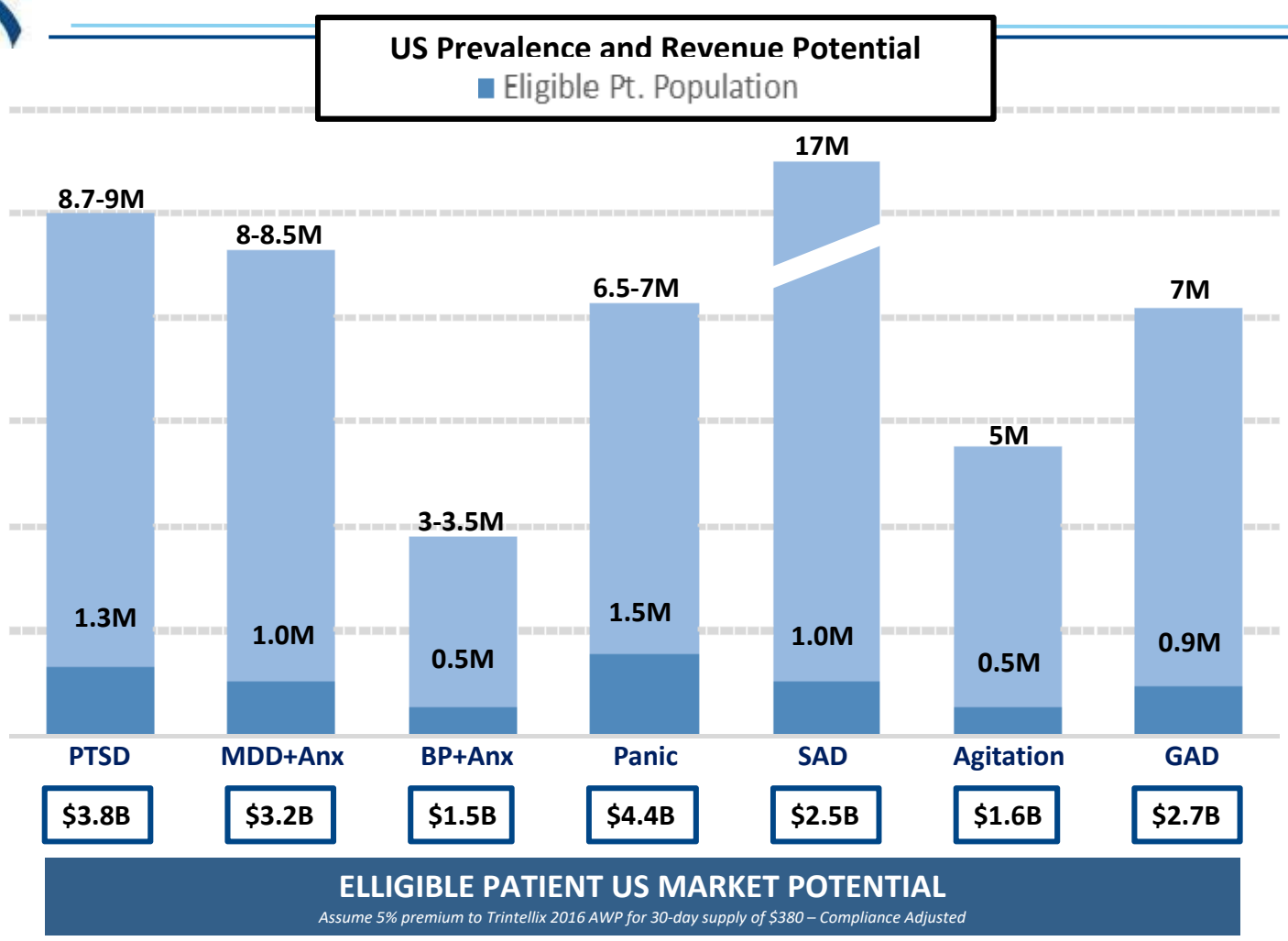
- Projected to reach $18 billion globally by 2020
- Approximately 40 million adults suffer from anxiety in the US
- Anxiety patients may have more than one anxiety disorder



Depression Market

- Approximately 18.2 million people suffer from depression in the US
- Sales of top 10 depression drugs reached a total market of $8.8bn in 2012
- Major types of depression:
  - Bipolar depression
  - Dysthymia
  - Major depression

BNC210, if Successfully Developed, may have Significant Revenue Potential



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

[1] 3.4-4% prevalence >18yrs., ~25% of patients diagnosed and treated
[2] 6.7% prevalence, ~50% co-morbid anxiety, ~50% diagnosed and treated
[3] ~2.9% prevalence, 50% co-morbid anxiety (range in literature 25 to 75%), ~50% diagnosed and treated
[4] ~2.7% prevalence, ~50% diagnosed and treated
[5] ~6.8% prevalence, 15-20% diagnosed and treated
[6] ~3.1% dementia prevalence >40yrs., ~9% agitation patients diagnosed and treated
[7] 3.1% GAD prevalence, assumes ~25% diagnosed and treated, ~50% of SSRI patients treated are partial responders or relapsers