

Bionomics



CREATING INNOVATIVE THERAPIES
FOR CNS DISORDERS.

BNC210 Update

BNO (Australia: ASX)

BNOEF (USA: OTCQX)

18 February 2019

Central Nervous System (CNS)

Safe Harbor Statement

Factors Affecting Future Performance

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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 Generalized Anxiety Disorder (GAD) patients reported in September 2016
 - Phase 2 trial in Post Traumatic Stress Disorder (PTSD) did not reach primary endpoint reported in October 2018 on a dosage basis
 - Additional work undertaken on a drug exposure-response analysis shows a statistically significant response of BNC210 in treatment of PTSD symptoms, as measured by CAPS-5 at 12 weeks
 - Phase 2 trial in Agitation ongoing in Australia with data anticipated in 2Q, 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
- Robust pipeline of first-in-class ion channel programs
- Financials: Cash at 31 December 2018 \$27.35M

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

- Anxiety, Depression and Agitation
- Potential for other CNS indications, including Autism Spectrum Disorder

Ongoing Clinical Trials

- Phase 2 multi-center trial (Australia) in Agitation, topline data 2Q, CY2019

Completed Clinical Trials

- 6 completed Phase 1 trials in > 200 healthy subjects
- 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
- Phase 2 in GAD patients met co- primary endpoints; low dose BNC210 outperformed Lorazepam, measured by cerebral perfusion and degree of amygdala activation
- Phase 2 in GAD patients met secondary endpoint; high and low dose BNC210 outperformed Lorazepam in an anxiety provoked behavioral task
- Phase 2 trial in Post Traumatic Stress Disorder (PTSD) did not reach primary endpoint reported in October 2018. Evidence of antidepressant and anxiolytic effects on components of CAPS-5

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
BNC210	✓	✓	✓	✓	✓
Valium and other BZD	✗	✗	✗	✓	✓
Prozac and certain other SSRI/SNRI	✓	✗	✓	✗	✗
Atypical Antipsychotics	✗	✗	✗	✓	✗

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

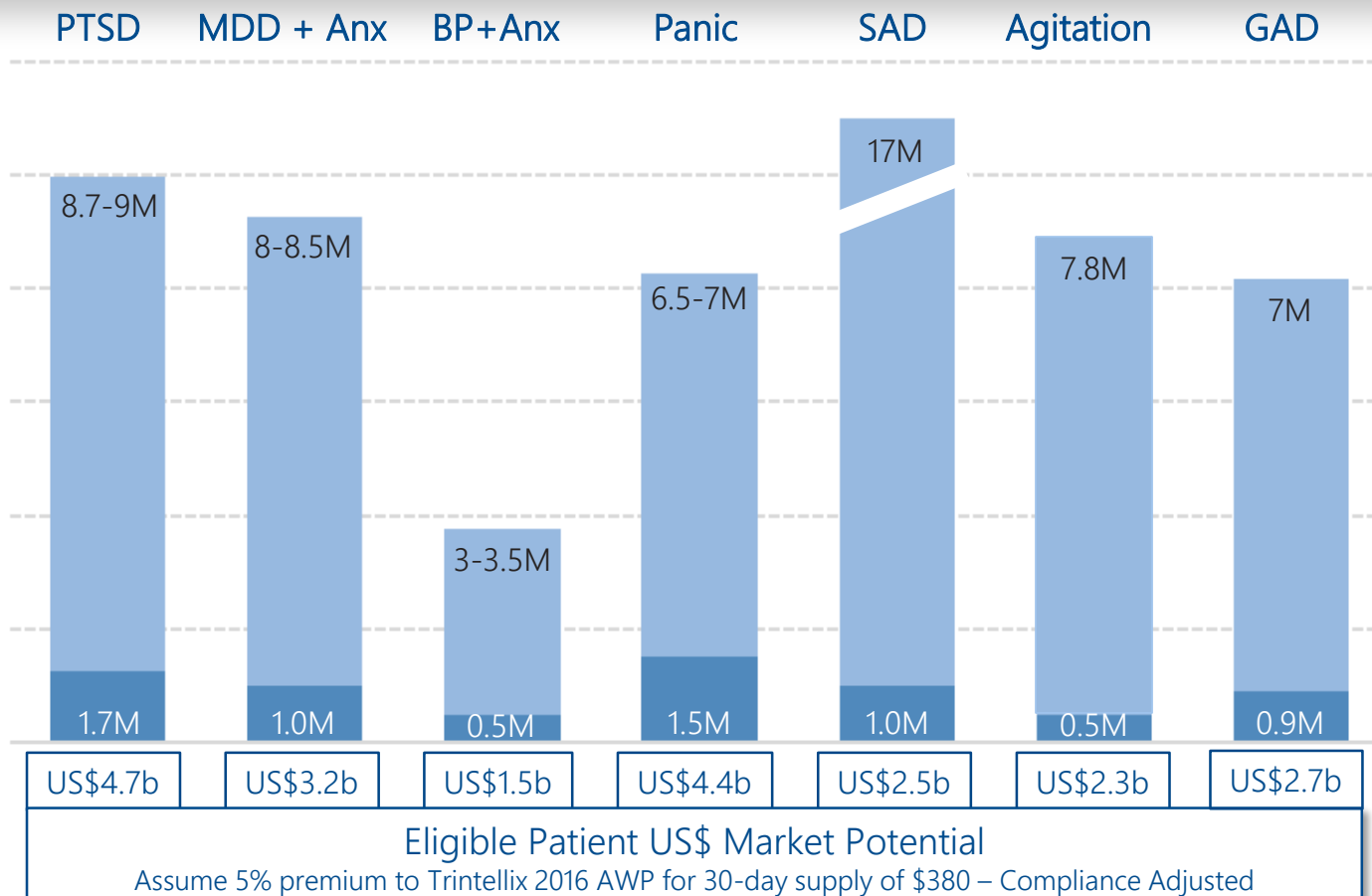
- Sertraline (Zoloft) and paroxetine (Paxil) are the only US FDA approved drugs for PTSD.
- Despite lack of efficacy, addictive potential and other harms associated with chronic use, BZDs are still over-prescribed.
- An estimated 2.8M scripts are written off-label for management of PTSD symptoms.
- VA/DoD '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)

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

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

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

BNC210.007: A Randomized, Double-Blind, Placebo-Controlled Phase 2 Study of BNC210 in Adults With Post-Traumatic Stress Disorder (PTSD)

Study Design

- 193 subjects
- Randomized to 4 treatment arms - placebo, 150 mg, 300 mg and 600 mg BNC210 (1:1:1:1)
- BNC210 or placebo in a liquid suspension is taken twice daily with food
- 3 week screening period
- 12 week treatment period
- 3 week follow up
- Multi-centre – Australia 6 sites / U.S. 20 sites

Key Patient Selection Criteria for Study Entry



INCLUSION CRITERIA

- A current diagnosis of PTSD as defined by CAPS-5 (Clinician-Administered PTSD Scale for DSM-5)
- Males and females between the ages of 18 - 70
- Concomitant use of current anti-depressant medication allowed [one anti-depressant only (SSRI or SNRI)]
- Rescue use of benzodiazepines allowed (not to exceed 2 days / week)
- Continuation/maintenance of long-term counseling support and /or behavior therapy allowed

EXCLUSION CRITERIA

- Subjects with severe depression were excluded
- Increased risk of suicidal behavior or suicidal ideation with intent
- Moderate to severe substance use disorder in the 2 months prior to study
- Patients with borderline personality disorder, bipolar disorder, psychotic disorders, and significant traumatic brain injury

Primary Objective

- To assess the effects of BNC210 on investigator-rated symptoms of PTSD measured by CAPS-5 scores

Secondary Objectives

- To assess effects of BNC210 on Individual Symptom Clusters in CAPS-5:
 - Intrusion
 - Avoidance
 - Negative alterations in cognition and mood
 - Arousal and reactivity
- To assess safety and tolerability of BNC210 in subjects with PTSD

Exploratory Objectives

- To assess the relationship between nicotine use and treatment effect of BNC210
- To assess the relationship between anti-depressant use and treatment effect of BNC210

Patient Demographics



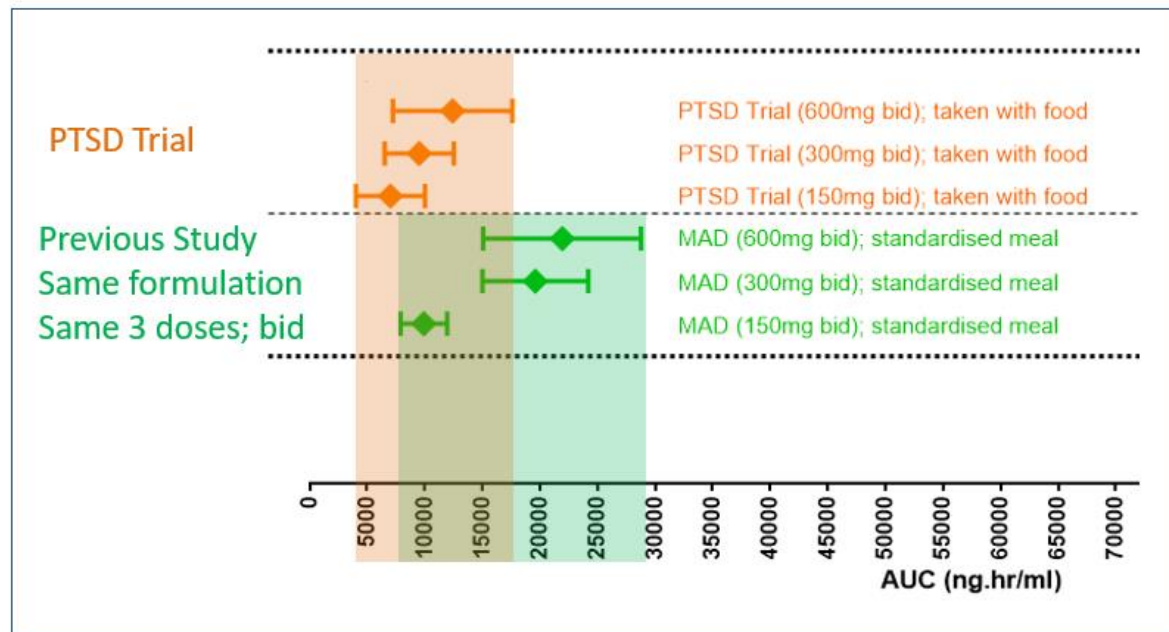
	Placebo	BNC210 150 mg b.i.d.	BNC210 300 mg b.i.d.	BNC210 600 mg b.i.d.
Age (years): Mean	41.1	41.1	43.6	42.2
Sex:				
Male	19	16	22	23
Female	30	31	26	25
Country:				
Australia	11	6	7	7
USA	38	41	41	41
Antidepressant use at baseline:				
Yes	11	8	9	12
No	38	39	39	36
Time since PTSD event (years): Mean	16.4	17.9	16.2	18.8
Nicotine Use:				
Before	11	7	10	9
Never	26	26	25	33
Ongoing	12	14	13	6
Baseline CAPS-5: Mean	35.3	36.5	34.9	29.4

BNC210 PTSD Clinical Trial Conclusions Based on Dose Response Analysis

- No overall effect on the primary endpoint (CAPS-5 total score at 12 weeks)
- Significant results obtained in CAPS-5 Criterion D (Negative Alterations in Cognitions and Mood) overall, and on specific items within the criterion, particularly in the BNC210 high dose group
 - D2: Persistent and exaggerated negative beliefs about oneself, others or the world
 - D4: Persistent negative emotional state
 - D7: Persistent Inability to experience positive emotions
- Evidence of anxiolytic effect
 - Trend towards improvement on CAPS-5 Criterion E (arousal and reactivity), question 3 (hypervigilance) in the total population
 - Trend towards improvement on CAPS-5 Criterion E, question 4 (exaggerated startle response) in the total population
- BNC210 was safe and well tolerated in 193 subjects with PTSD

BNC210 PTSD Clinical Trial Observations and Continued Data Analysis

- Analysis of data continues in line with the BNC210 PTSD Phase 2 clinical trial's predetermined statistical analysis plan in order to improve understanding of trial results
- Overall, blood levels of BNC210 in PTSD patients were variable and lower than were projected based on multiple ascending dose (MAD) studies previously carried out in healthy subjects with the liquid suspension of BNC210 administered in an in-clinic setting with a standardised meal



- Pharmetheus AB, an international pharmacometrics consulting company with extensive scientific and regulatory expertise, conducted pharmacometric analysis to quantify the level of efficacy of BNC210 on the overall CAPS-5 score related to exposure (blood levels) of BNC210

Overall Conclusions from the Trial



- No effect on primary CAPS-5 endpoint based on dosage response
- Additional data analysis conducted in Sweden by Pharmetheus AB showed a statistically significant response ($p < 0.01$) when drug exposure versus response was measured in the Phase 2 trial
- This analysis demonstrated reduction in total PTSD symptoms as measured by total CAPS-5, the endpoint mandated by the US Food & Drug Administration (FDA) for PTSD trials
- Mats O Karlsson, Professor in Pharmacometrics at Uppsala University, states:
“Exposure-response modelling has shown the potential for BNC210 to have significant benefit in PTSD provided that adequate blood levels are achieved. This analysis provides a basis for optimal design of future trials to demonstrate efficacy.”

A Solid Dose Formulation of BNC210 is Being Developed

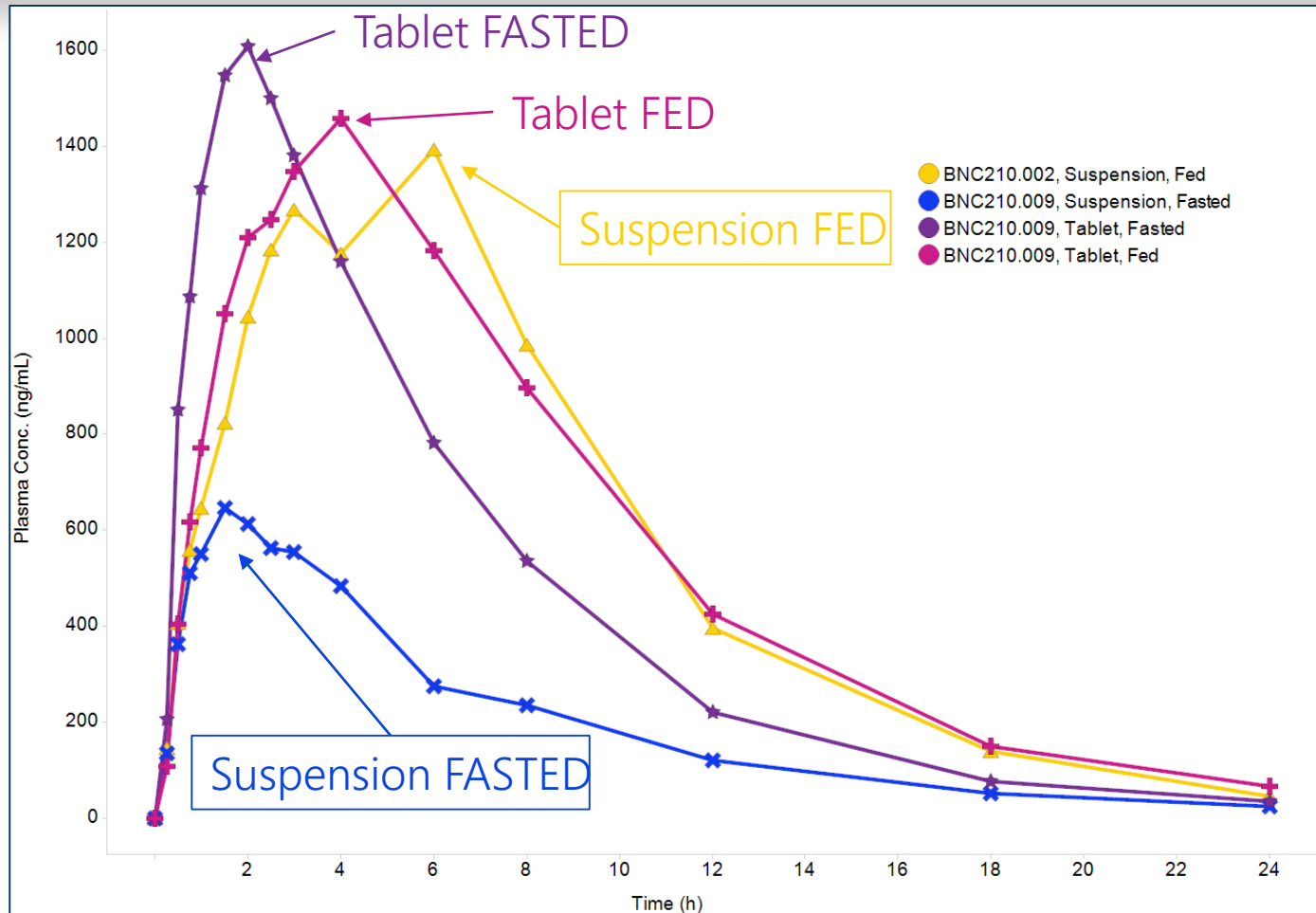
Rationale:

- A liquid suspension formulation was used in all BNC210 trials and administered with food to give best exposure
- PTSD trial results indicated that the liquid formulation did not give sufficient exposure in the ambulatory (out patient) setting

Solid Dose Formulation Work:

- Spray dry dispersion technology used
- 150 mg BNC210 tablets manufactured using an HPMCAS-M polymer in the spray dry dispersion
- Single doses of 300 mg BNC210 suspension and tablets have been evaluated in a pharmacokinetic clinical trial in healthy volunteers
- The effect of food on absorption of the solid form of BNC210 has been greatly reduced

Preliminary Data in Healthy Volunteers on Improved Solid Dose Formulation of BNC210 With Potential to Overcome “Food Effect” of Liquid Suspension Formulation Used in PTSD Trial



- The tablet, whether administered with food or not, was superior to the liquid suspension fasted, and comparable to the liquid suspension fed

Next Steps for BNC210

BNC210 PTSD	<ul style="list-style-type: none">▪ Seek FDA guidance on next steps for BNC210 for PTSD including the design of a further trial and whether BNC210 is eligible for Fast Track designation
BNC210 Formulation Development	<ul style="list-style-type: none">▪ Identified an improved solid dose formulation of BNC210 with potential to overcome the “food effect” of the liquid suspension formulation used in previous clinical trials
BNC210 Agitation	<ul style="list-style-type: none">▪ Data from the ongoing BNC210 trial in Agitation will be analysed by dose and by measures of exposure given the PTSD trial learnings▪ Consequently, this trial is anticipated to read out in Q2, 2019
Pipeline	<ul style="list-style-type: none">▪ Additional 1-2 therapeutic candidates prior to June 30 2019

- Validated Platform – Merck partnership and shareholding
 - We anticipate being able to update on progress of the therapeutic candidate in coming months
- Robust pipeline of first in class ion channel candidates addressing significant unmet need in Bionomics’ areas of strength in CNS disorders
- Bionomics will continue to evaluate partnership opportunities in parallel. These new data will also form part of the ongoing strategic review being conducted by Greenhill & Co.