

Bionomics



ersonal use only



CREATING INNOVATIVE THERAPIES FOR CNS DISORDERS.

Corporate Presentation

BNO (Australia: ASX); BNOEF (USA: OTCQB)

November 2020

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.

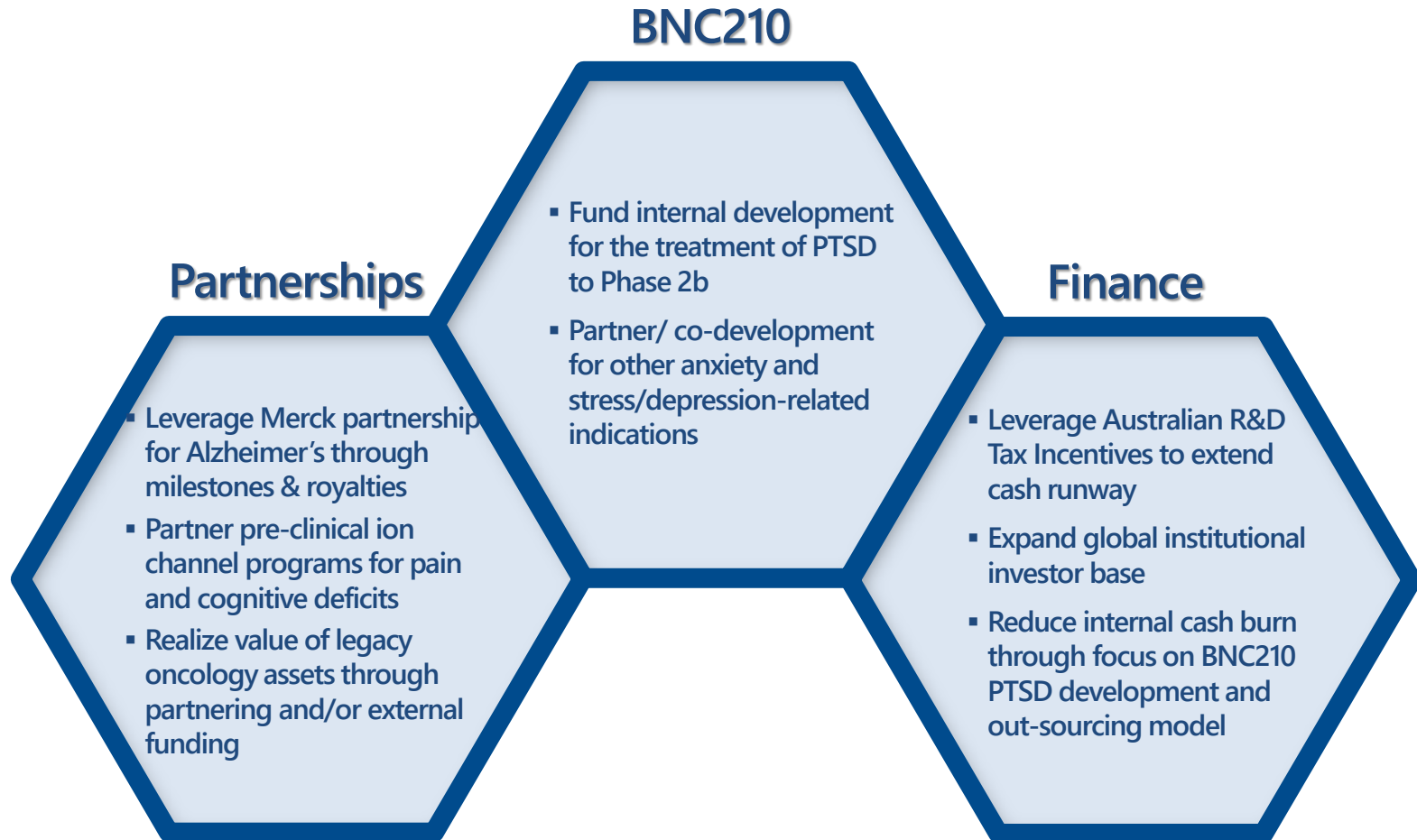
There are a number of important factors that could cause actual results or events to differ materially from those indicated by these forward-looking statements, including unexpected safety or efficacy data, unexpected side effects observed in clinical trials, risks related to our available funds or existing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

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

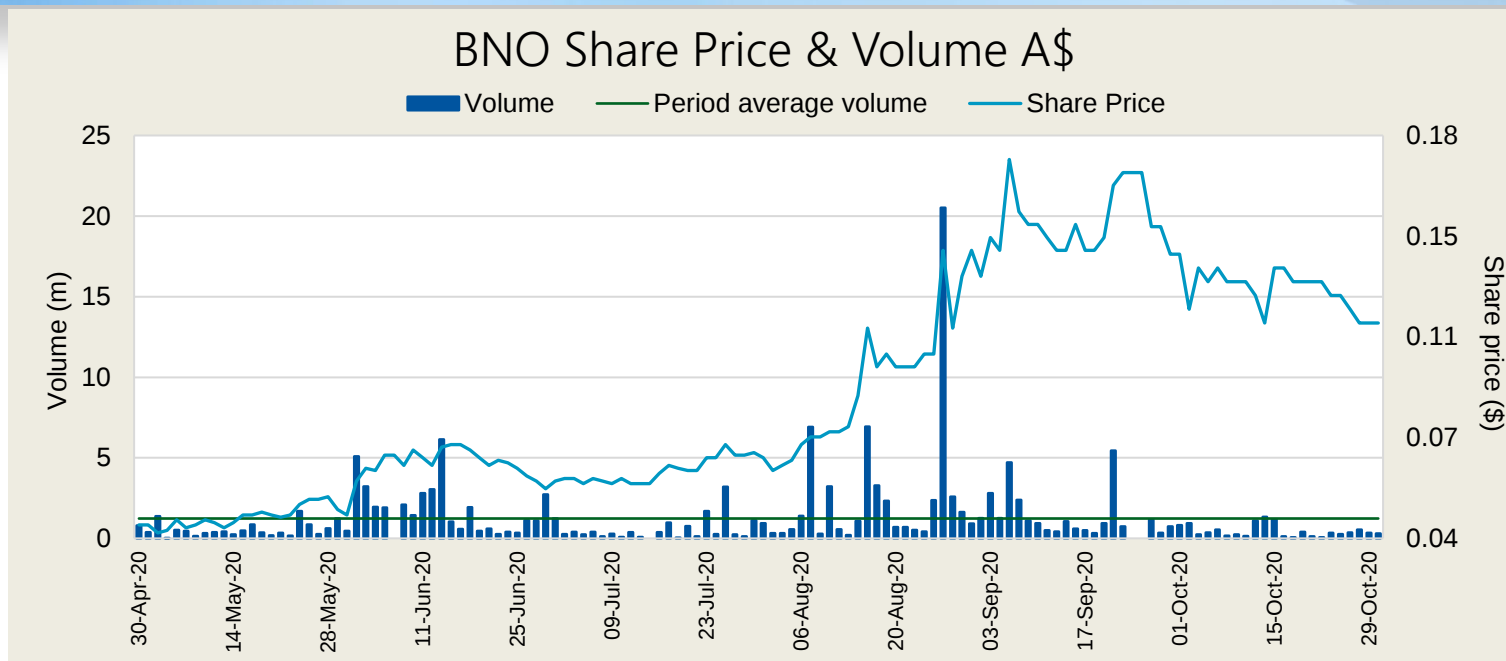
Bionomics Investment Highlights

- Global, clinical stage biopharmaceutical company developing a pipeline of novel drug candidates targeting ion channels in Central Nervous System (CNS) disorders
- Lead clinical candidate BNC210 in Phase 2 with Fast Track designation from FDA for treatment of Post-Traumatic Stress Disorder (PTSD)
- Strategic partnership with Merck & Co., with multiple therapeutic candidates in clinical development for treatment of cognitive impairment in Alzheimer's Disease
- Emerging CNS partnering pipeline of ion channel candidates for treatment of pain and cognitive deficits
- Additional value in non-core Phase 1-2 oncology assets through external funding and partnering
- Experienced Management and Board of Directors
- Strong international investor base
- Financials: Market Capitalization (range in September 2020) of ~ A\$100 MM – A\$130 MM; Cash at 30 Sept 2020: A\$4.26 MM; ~A\$15 MM in committed and underwritten funding

Bionomics' Strategy and Value Proposition



Bionomics Stock & Financial Information

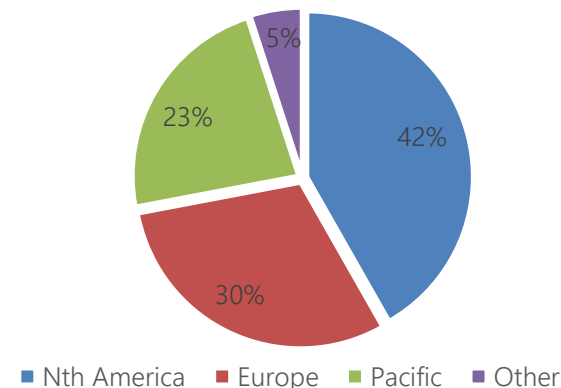


Cash at September 30, 2020: A\$4.26MM
 Share Register Issued Capital 735,247,550 shares
 Market capitalization of ~A\$84.5MM *(as at 30 Oct 2020)*

Significant Investors

- Apeiron Investment Group Ltd.
- Biotechnology Value Fund
- Thiel Capital
- Galaxy Investment Partners (M Novogratz)
- Merck & Co.

Global Distribution



Management Team



Errol De Souza PhD
Executive Chairman

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



**Jack Moschakis BEc, DIPLaw (BAB) NSW,G
DipBA, FCIS,FGIA**
Legal Counsel & Company Secretary

- Over 26 years experience as a legal practitioner
- Joined Bionomics in 2015
- Held senior Legal / Company Secretary roles in the Energy and Resources sectors
- Extensive experience in commercial, contractual and regulatory related legal matters



Adrian Hinton BAEC, FCA
Acting Chief Financial Officer

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



Liz Doolin MSc
VP Clinical Development

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

Bionomics' CNS Focused Pipeline

Program	Pre-IND	Phase 1	Phase 2a	Phase 2b
BNC210 $\alpha 7$ nAChR Negative Allosteric Modulator (NAM)	PTSD study, 193 pts, results released October 2018			
	Agitated Elderly in Hospital Setting, exploratory study, 38 pts, results released June 2019			
	GAD study, 24 pts, results released September 2016			
	Panic - CCK panic model in 15 healthy volunteers			
	Nicotine-induced EEG changes in 24 healthy volunteers			
Merck & Co. Collaboration $\alpha 7$ nAChR* Positive Allosteric Modulator (PAM)	Two candidates in development Phase 1 studies ongoing			
PAIN Nav1.7/Nav1.8 Inhibitors	Candidate			
COGNITION Kv3.1/3.2 Activators	Series Lead			

BNC210: Next Generation Drug Candidate with Potential to Treat Anxiety, Depression, PTSD and other Stress-Related Disorders

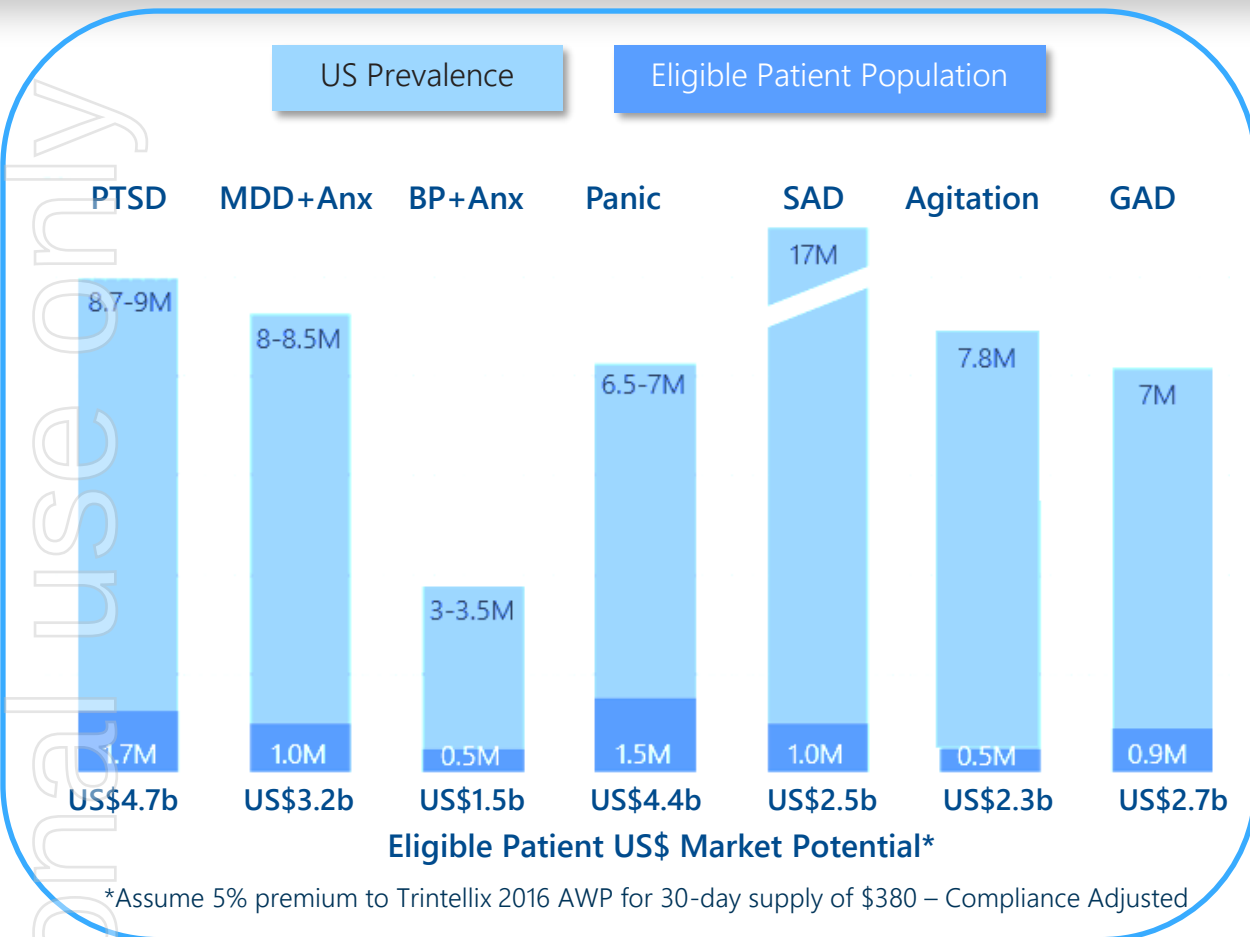
- Novel, orally-administered, first-in-class, negative allosteric modulator (NAM) of the $\alpha 7$ nicotinic acetylcholine receptor
- Large market potential for treatment of multiple psychiatric indications
- Strong safety database in humans – 11 trials with exposure in ~400 subjects
- Demonstrated nicotinic receptor target engagement in healthy subjects
- Proof of biology in healthy subjects (anti-panic) and in Generalized Anxiety Disorder patients (anti-anxiety)

Potential Competitive Advantages of BNC210*

Drug	No sedation	No withdrawal syndrome	No memory impairment	Fast acting	No drug/drug interactions
BNC210	✓	✓	✓	✓	✓
Valium and other benzodiazepines	X	X	X	✓	✓
Prozac and certain other SSRIs/SNRIs	✓	X	✓	X	X

*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

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

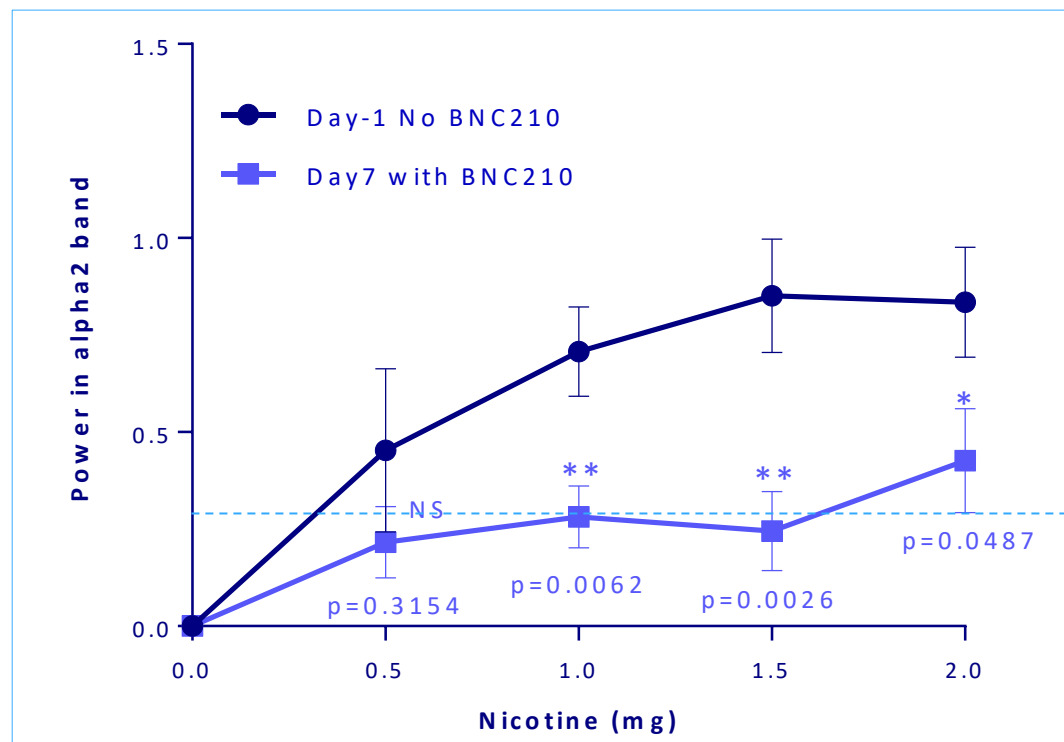
⁵ ~6.8% prevalence, 15-20% diagnosed and treated

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

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

BNC210 Treatment Reduced Nicotine-Induced EEG Responses: Demonstration of Target Engagement in Humans

- The EEG response to nicotine is achieved through activation of nicotinic receptors in the brain. The major populations targeted are $\alpha 4\beta 2$ and $\alpha 7$ receptors.
- Oral dosing with 2000 mg BNC210 for 7 days reduced nicotine-induced EEG power in the $\alpha 2$ band.

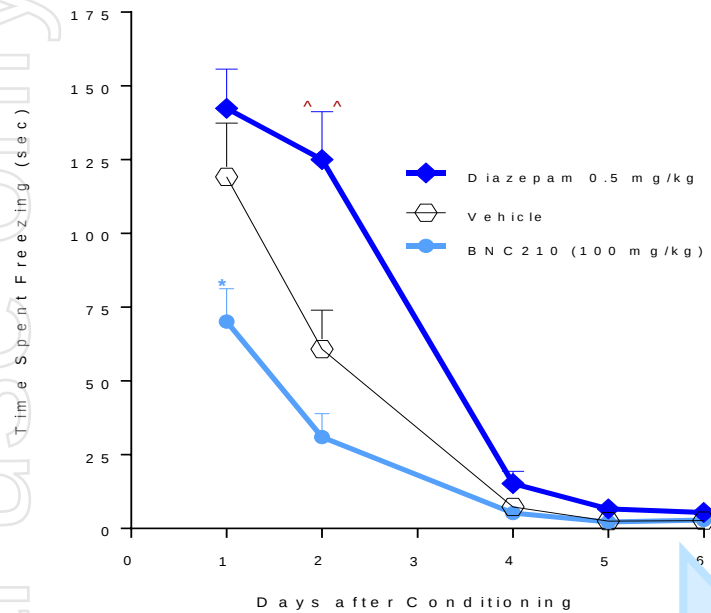


n= 24 healthy volunteers

Reduction in the EEG response is due to negative allosteric modulation of the $\alpha 7$ receptors by BNC210

BNC210 Enhanced Fear Extinction in Mice - This Translated to Rapid Improvement Following a CCK-4-Induced Panic Attack in Healthy Subjects

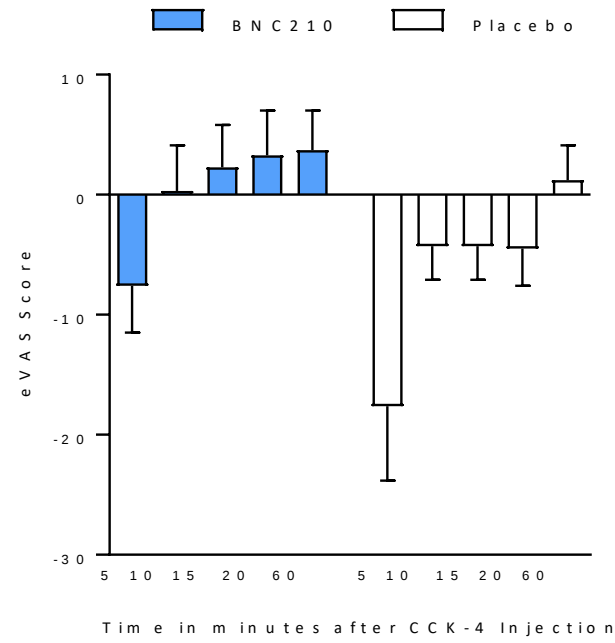
Conditioned Fear Extinction Model



MICE

BNC210 enhanced fear extinction following conditioned stimulus training

Emotional Visual Analog Scale (eVAS)

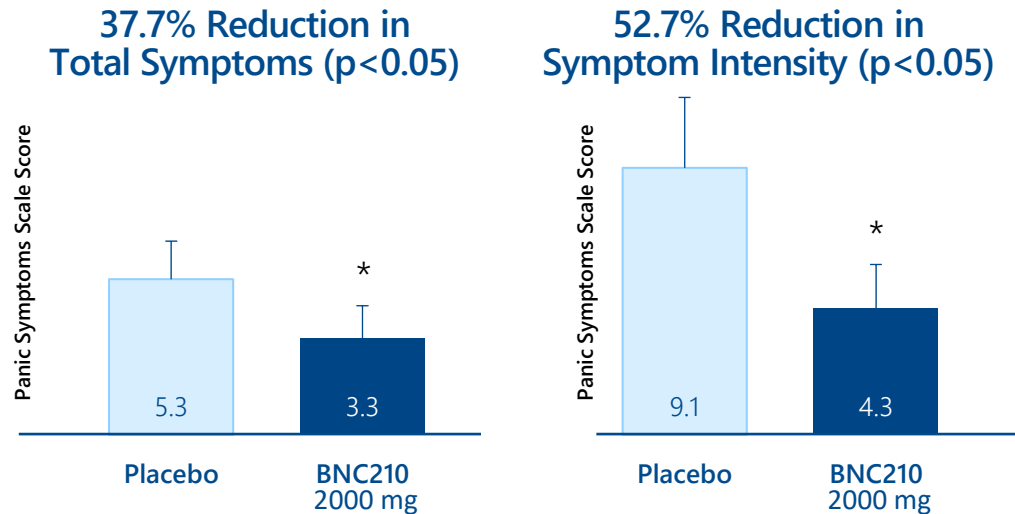


HUMANS

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

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

BNC210 Significantly Reduced Cholecystokinin 4 (CCK4)-Induced Panic Symptoms in Humans



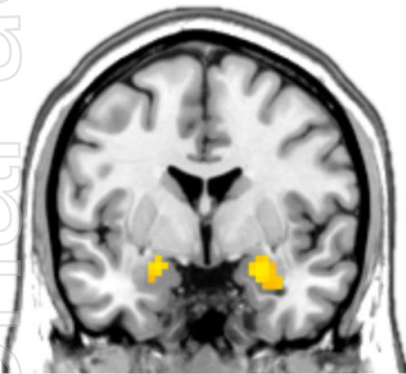
Panic Symptom Scale:
BNC210 resulted in a significant reduction in the total number of panic symptoms and the panic symptom severity

Evaluation conducted in 15 healthy volunteers who experienced a CCK4-induced panic attack

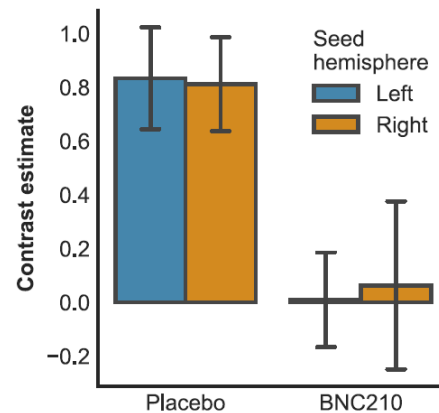
BNC210 Phase 2 Trial in Generalized Anxiety Disorder (GAD) Demonstrated Acute Anxiolytic Activity

- Two single doses of BNC210 (300 and 2000 mg), lorazepam (1.5 mg) and placebo were administered to GAD patients
- 24 subjects received all treatments (4-way crossover study)
- Patients were exposed to 'fearful faces' while in a Magnetic Resonance Imaging (MRI) machine and also performed a behavioral task called the Joystick Operated Runway Task (JORT)

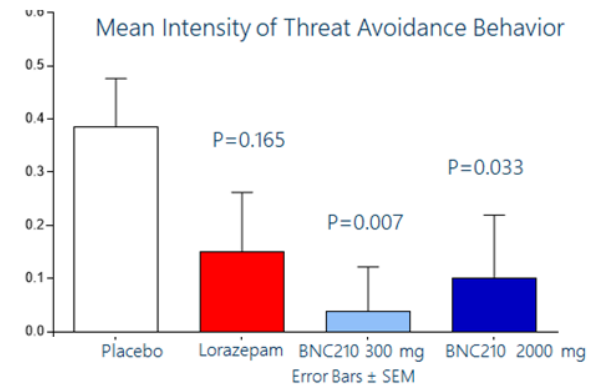
Viewing fearful faces caused activation of the L & R amygdala which was significantly reduced by administration of BNC210 (300 mg) ($p < 0.001$)



BNC210 (300 mg) significantly reduced connectivity between the amygdala and ACC while viewing fearful faces ($p < 0.05$)



BNC210 (300 & 2000 mg) significantly reduced threat avoidance behaviour of anxious subjects in the JORT behavioural task



Wise T. et al., *Biological Psychiatry* 2020 (<https://doi.org/10.1016/j.biopsych.2019.12.013>)

- Amygdala activation is an imaging surrogate for anxiety
- Connectivity between the amygdala and anterior cingulate cortex (ACC) is very strong in high anxiety

Phase 2 Trial of BNC210 in Adults with Post-Traumatic Stress Disorder (PTSD)



Study Design

- Multi-center, randomized, double-blind, placebo-controlled
- BNC210 150 mg, 300 mg, 600 mg and placebo (1:1:1:1) (liquid suspension formulation taken twice daily, b.i.d.)
- 12-week treatment period
- 193 participants
- 20 US sites / 6 Australian sites

Key Selection Criteria

- Current diagnosis of PTSD as defined by CAPS-5 (Clinician-Administered PTSD Scale for DSM-5)
- Concomitant use of one anti-depressant medication allowed

Key Study Objectives

- To assess the effects of BNC210 on investigator-rated symptoms of PTSD measured by CAPS-5
- To assess the safety and tolerability of BNC210 in subjects with PTSD

BNC210 PTSD Trial Overall Conclusions:



- **No overall effect on primary endpoint of CAPS-5 total severity score at 12 weeks**
- **Australian patients had a greater improvement over placebo than US patients**
 - ✓ CAPS-5 statistically significant at Week 4 in Australians ($p < 0.05$)
- **Evidence of antidepressant effect in high dose treatment group in the total population**
 - ✓ CAPS-5 Criterion D overall (negative alterations in cognitions and mood) statistically significant at Week 1 ($p < 0.05$)
 - ✓ CAPS-5 Criterion D, Question 2 (persistent and exaggerated negative beliefs or expectations) statistically significant at Week 1 ($p = 0.001$)
 - ✓ CAPS-5 Criterion D, Question 4 (persistent negative emotional state) statistically significant at Weeks 4 and 8 ($p < 0.05$)
- **Evidence of anxiolytic effect in high dose treatment group in the total population**
 - ✓ Trend towards improvement on CAPS-5 Criterion E (marked alterations in arousal and reactivity), Question 3 (hypervigilance)
 - ✓ Trend towards improvement on CAPS-5 Criterion E, Question 4 (exaggerated startle response)
- **BNC210 was safe and well tolerated in patients with PTSD**
 - ✓ No trend for increased adverse events with treatment
 - ✓ No evidence of cognitive impairment
 - ✓ No evidence of suicidal ideation or behavior worsening

BNC210 Phase 2 Trial: Summary of Significant Clinical Trial Results & Trends

CAPS-5 Severity Scores – LSMean Changes from Baseline*

CAPS-5 Total	Australian cohort (n=31): Week 4 (300 mg, p=0.052^; 600 mg, p=0.013)^ Week 12 (600 mg, p=0.088)
Criterion B	
Criterion C	
Criterion D	Week 1: Overall Criterion D (600 mg, p=0.037) Week 1: Qu. D2 (300 mg, p=0.024; 600 mg, p=0.001) Week 4: Qu. D4 (600 mg, p=0.013) Week 8: Qu. D4 (600 mg, p=0.040)
Criterion E	Week 8: Qu. E3 (600 mg, p=0.073) Week 4: Qu. E4 (600 mg, p=0.063)

*MMRM with multiple imputation on ITT population; ^MMRM with observed data

CAPS-5 Total Score Remission Analysis* – Proportion of Patients With Loss of Diagnosis (CAPS-5 <12)

	Week 4	Week 8	Week 12
Group (b.i.d. dose)	%	%	%
Placebo	23	42	47
BNC210 150 mg	23	18	30
BNC210 300 mg	24	24	37
BNC210 600 mg	38 (p=0.063)	50	44

*ITT Completers at each time point; One-sided proportion analysis with z-test

CAPS-5 Total Score Responder Analysis* – Proportion of Patients Achieving Response Thresholds

	Week 4	Week 8	Week 12
Group (b.i.d. dose)	%	%	%
Threshold ≥30% improvement from baseline			
Placebo	55	69	67
BNC210 150 mg	51	50	70
BNC210 300 mg	51	55	66
BNC210 600 mg	71 (p=0.061)	74	72
Threshold ≥50% improvement from baseline			
Placebo	35	44	60
BNC210 150 mg	26	29	36
BNC210 300 mg	38	37	47
BNC210 600 mg	52 (p=0.056)	58	56

*ITT Completers at each time point; One-sided proportion analysis with z-test

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

- Inadequate overall blood exposure of BNC210
- BNC210 blood levels declined over 12-week period
- Placebo effect continued to increase from 4W to 12W

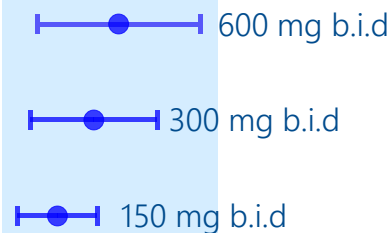
BNC210 PTSD Trial Conclusions: Analyses Performed on a Dosage Basis



Population pharmacokinetic (PK) modelling indicated that plasma levels of BNC210 were substantially lower than expected and declined over the 12-week period using the liquid suspension formulation in this out-patient trial setting

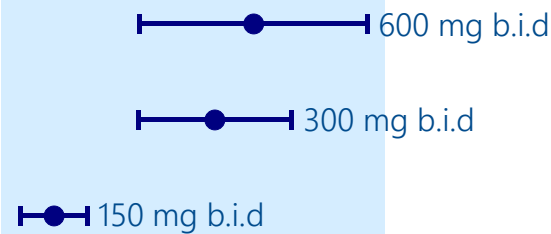
PTSD

PTSD Trial:
Out-patient
setting

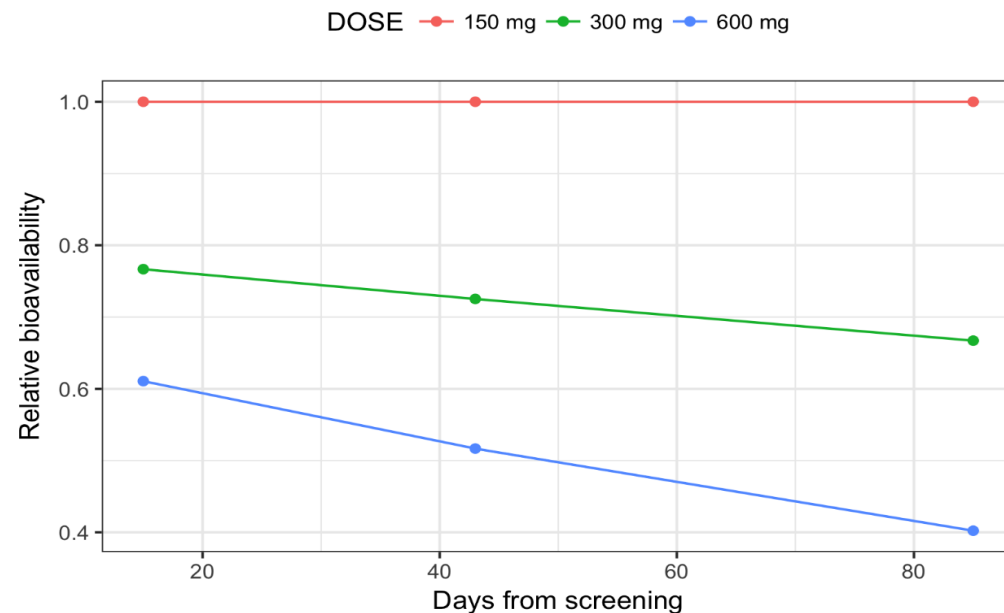


MAD

MAD Study:
Resident, healthy
volunteers



b.i.d. = administered twice daily; MAD = multiple ascending dose

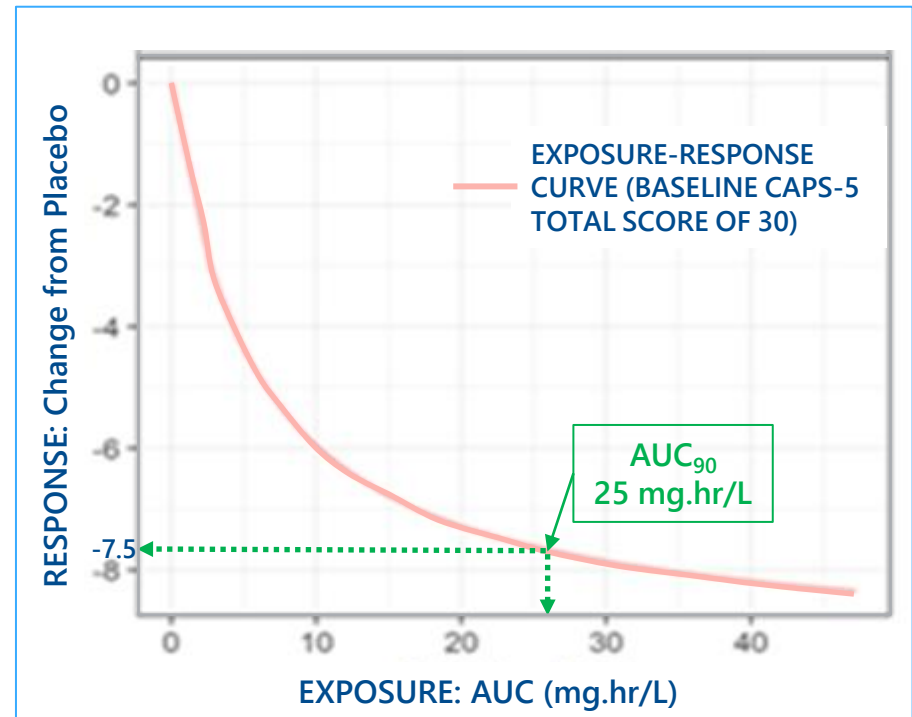


Exposure-Response Analysis Showed the Potential for a Significant Response when Adequate Drug Exposure is Achieved

- Pharmacometric analysis of the Phase 2 data established an exposure-response relationship for CAPS-5 total severity scores where higher AUC values (plasma exposure) were related to a larger effect ($p < 0.01$)

The figure shows the model-predicted exposure-response curve for a subject with a baseline CAPS-5 total severity score of 30 (this was the mean baseline score for the PTSD trial patients in the 600 mg b.i.d. BNC210 treatment group.)

~25 mg.hr/L is the model predicted AUC_{90} being targeted in future BNC210 trials in PTSD patients



AUC_{90} is the drug exposure giving 90% of the maximum drug effect

A Solid Dose Formulation of BNC210 is being Developed to Achieve Target Exposure in Clinical Trial Subjects

PTSD trial results indicated that the liquid suspension formulation of BNC210 did not achieve sufficient exposure in the out-patient setting

Benefits of a solid dose formulation (tablets):

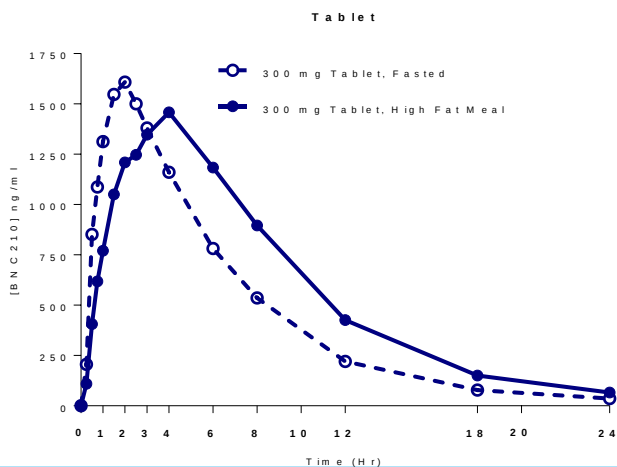
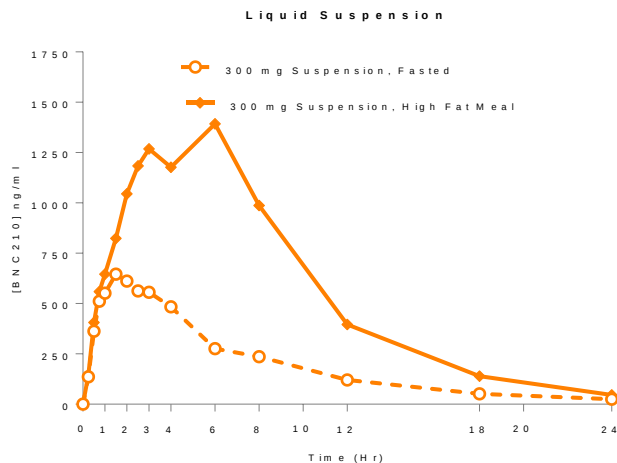
- Simple to administer with no need for thorough resuspension
- Formulated to overcome the need to take with food (the liquid suspension was administered with food to give best exposure)

Progress to date:

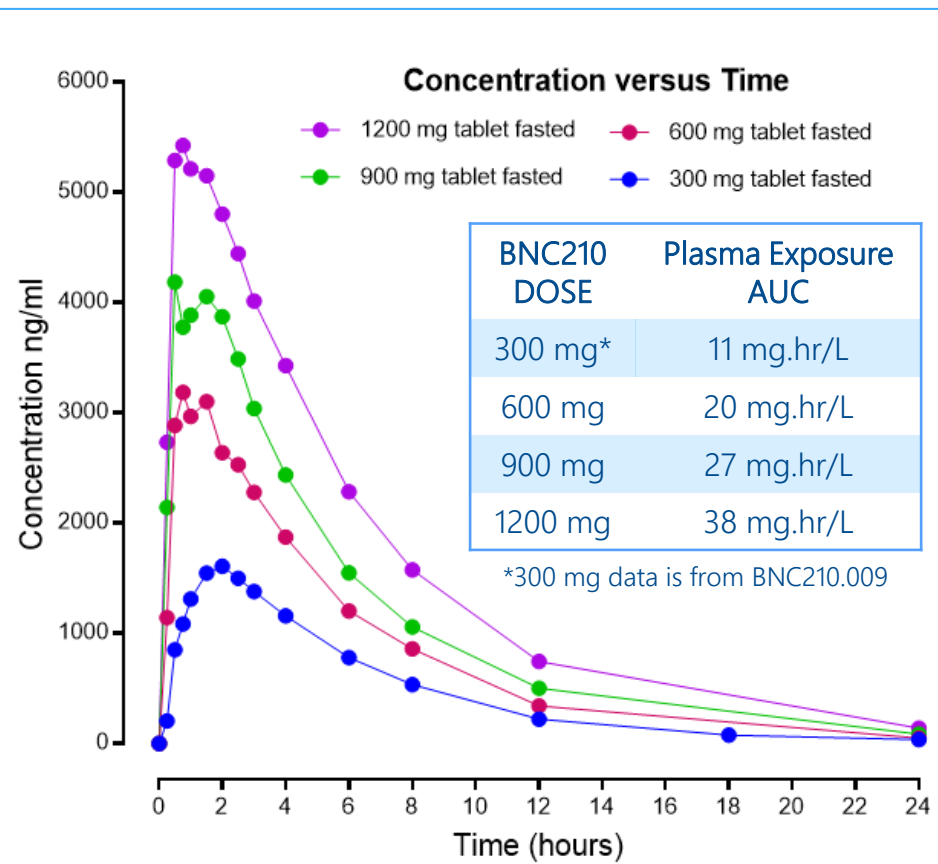
- Spray dry dispersion technology used to manufacture BNC210 tablets
- Human single dose PK studies completed

BNC210 Tablet Formulation Overcomes Food Effect of the Liquid Suspension and has Dose Linear Exposure

Trial BNC210.009: single 300 mg dose of BNC210 liquid suspension *versus* solid dose formulation (fed and fasted conditions)



Trial BNC210.010: single 600, 900 and 1200 mg doses of solid dose formulation in fasted subjects



AUC >25 mg.hr/L achieved at BNC210 tablet doses of 900 mg and higher in fasted subjects

Bionomics has Achieved Key Milestones Towards Continuing Development of BNC210 for the Treatment of PTSD

2019

- ✓ Pharmacometric analysis of the Phase 2 PTSD trial data showed that there is potential for significant patient benefit in future trials provided adequate drug exposure is achieved
- ✓ Successful development of a BNC210 solid dose formulation and evaluation in single dose PK studies achieved exposures adequate for future development
- ✓ FDA Type C Meeting provided positive feedback on the BNC210 development program for the treatment of PTSD
- ✓ FDA granted Fast Track designation to BNC210 for the treatment of PTSD

BNC210 is Back on Track to Leverage Large Opportunity for Treatment of PTSD

2020: Preparations for Phase 2b PTSD Trial

- Optimized and selected the tablet formulation for a Phase 2b clinical trial
- Manufacturing underway of BNC210 tablets for a multiple dosing PK trial in healthy volunteers scheduled for late Dec 2020/Jan 2021
- Large scale manufacture of BNC210 drug substance and tablets for Phase 2b trial have been contracted

2021 – 2022: Implementation of Phase 2b PTSD Trial

- Conduct a Phase 2b clinical trial in ~200 PTSD patients comparing one dose of BNC210 with placebo on the change in CAPS-5 total severity scores at 12 weeks – target start date of late 2QCY2021
- CAPS-5 is the FDA-accepted primary endpoint for PTSD clinical trials

Global License and Collaboration Agreement with MSD (Merck & Co.) in Cognition Provides Validation

- Partnership 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
- MSD (a tradename of Merck & Co., Inc., Kenilworth NJ USA) Collaboration Update:
 - Phase 1 safety clinical trials of the lead molecule in healthy subjects have been completed and there are ongoing plans for further biomarker studies
 - A backup molecule that showed an improved potency profile in preclinical animal models versus the current lead molecule is advancing into Phase 1 clinical trials



MERCK
PARTNERSHIP

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

Emerging CNS Pipeline for Partnering

- Small molecule Kv3.1 / Kv3.2 potassium ion channels activators
 - Kv3.1 / Kv3.2 activators represent a promising therapeutic strategy for improving cognitive dysfunction and negative symptoms in schizophrenia and other illnesses such as Autism Spectrum Disorder and Alzheimer's Disease
 - ~600 compounds synthesized; 3 chemical series developed and 2 series patented
 - Lead compound BL-76 fully reverses PCP-induced cognitive deficit in mice in the T-maze test
- Small molecule pan Nav inhibitors for treatment of chronic pain
 - Gain and loss-of-function mutations in Nav1.7, 1.8 and 1.9 have been associated with human pain
 - 1000+ compounds synthesized; 3 chemical series developed and patented
 - Bionomics' pan Nav inhibitors with functional selectivity for voltage gated sodium channels Nav1.7, Nav1.8 and potentially Nav1.9 offer potential to develop non-addictive therapeutics for chronic pain with less side effects

Value in Non-Core Phase 1-2 Oncology Assets Leveraged Through External Funding and Partnering

- BNC105 - a Multi-Modal Small Molecule Tubulin Polymerization Inhibitor has completed four Phase 1 and Phase 2 clinical trials
 - Two externally-funded investigator-initiated clinical trials are in progress:
 - Phase 2 trial of BNC105 in combination with nivolumab (Opdivo) for the treatment of metastatic colorectal cancer sponsored by the Australasian Gastro-Intestinal Trials Group (AGITG) and funded by BMS; patient enrolment at 16 sites across Australia is complete with final results projected for early 2023
 - Phase 1 trial of BNC105 in combination with ibrutinib (Imbruvica) for the treatment of chronic lymphocytic leukemia funded by the Leukemia & Lymphoma Society (US)
- BNC101 - a First-in-Class Humanized Monoclonal Antibody to LGR5, a Cancer Stem Cell Receptor
 - BNC101 clinical dose and schedule were established in a Phase 1 trial in patients with metastatic colorectal cancer - the recommended Phase 2 dose was identified
 - Phase 2 ready: BNC101 in combination with standard of care treatment for gastro-intestinal cancers overexpressing LGR5
 - Potential for BNC101 to be developed as an Antibody-Drug-Conjugate (ADC) therapeutic or in combination with CAR-T being explored

Bionomics Outlook

- **Balanced business model with potential for short term milestones to drive shareholder value:**
 - Internal development of BNC210 is back on track with a solid dose formulation to achieve the blood exposure required for future PTSD trials, along with positive feedback from the FDA and Fast Track designation provide a promising opportunity for the company in 2020 and beyond
 - Strengthened strategic investor base with committed funding for BNC210 development
 - We continue to pursue licensing and partnering possibilities for our core CNS pain and cognition programs and have an ongoing collaboration with Merck & Co.
 - Maximize the value and partnering potential of legacy oncology assets through external funding of clinical programs
 - Cost cutting measures implemented in 2019 along with leveraging Australian R&D Tax Incentive Refund allow us to extend cash runway with non-dilutive funding

Bionomics



Personal use only



CREATING INNOVATIVE THERAPIES
FOR SERIOUS HUMAN DISEASES.

Appendix

Board of Directors



Errol De Souza PhD
Executive Chairman

- More than 35 years experience in Biotech, Big Pharma and Academia
- Previous President & CEO of multiple public (Biodel, Synaptic) & private (Neuropore, Archemix) biotech Companies
- Founder of Neurocrine Biosciences
- Previous SVP Aventis Pharmaceuticals
- Previous Head of CNS Diseases, DuPont Merck
- Multiple public and private Boards



David Wilson

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



Jane Ryan PhD

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



Alan Fisher

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

Board of Directors



Srinivas Rao

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



Aaron Weaver

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



Mitchell Kaye

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

Our Proprietary Platform Technologies and CNS Therapeutic Focus

ionX

Ion channel drug discovery capabilities
Ligand- & voltage-gated channels
Proprietary cell lines
Multiple screening platforms
In vivo models to measure target biology & safety

MultiCore

A diversity orientated chemistry platform for the discovery of small molecule drug candidates
Scaffold-hopping synthetic approach rapidly creates diversity in focused libraries
Parallel, differentiated chemical series

Therapeutic Areas

PTSD
Anxiety
Agitation
Depression
Cognitive Impairment
Pain

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

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

Bionomics



Personal use only



CREATING INNOVATIVE THERAPIES
FOR SERIOUS HUMAN DISEASES.

Emerging CNS Pipeline For Partnering

Small Molecule Kv3.1 / Kv3.2 Ion Channels Activators for Treatment of Cognitive Dysfunction & Negative Symptoms

Kv3.1 / Kv3.2 activators represent a promising therapeutic strategy for improving cognitive dysfunction and negative symptoms in schizophrenia and other illnesses such as Autism Spectrum Disorder and Alzheimer's Disease

~600 COMPOUNDS
SYNTHESIZED

3 CHEMICAL
SERIES DEVELOPED

2 SERIES PATENTED

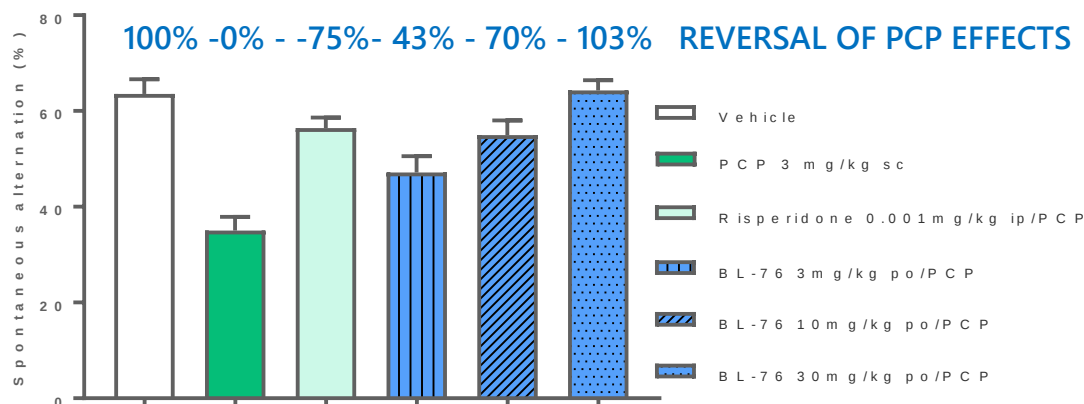
Lead
Compound
BL-76

Back-up
Compounds

2 Patents Published

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

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



Pan Nav Inhibitors Offer Potential to Develop Non-Addictive Therapeutics for Chronic Pain with Less Side Effects

Disease-Related Genomics

Gain & Loss-of-function mutations in Nav1.7, 1.8 and 1.9 have been associated with human pain syndromes where extreme pain or no pain is experienced.

Bionomics' Pan Nav inhibitors are small molecules with functional selectivity for voltage gated sodium channels: Nav1.7, Nav1.8, hERG and potentially Nav1.9

1000+ COMPOUNDS
SYNTHESIZED

3 CHEMICAL
SERIES DEVELOPED

3 SERIES PATENTED

Lead Compound
BL-017881

Back-up
Compounds

3 Patents Published

Lead Candidate
Identified

BL-017881

- ✓ 100% pain reduction (100 mg/kg)
- ✓ No side effects (300 mg/kg)
- ✓ 40x selectivity over hERG
- ✓ CNS penetrant

Bionomics



Personal use only



CREATING INNOVATIVE THERAPIES
FOR SERIOUS HUMAN DISEASES.

Oncology Assets: Build Value Through External Funding

Bionomics' Oncology Assets

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

BNC105 - a Multi-Modal Small Molecule Tubulin Polymerization Inhibitor

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

Two externally-funded investigator-initiated clinical trials are in progress:

- Microsatellite stable refractory colorectal cancer:
 - Phase 2 trial of BNC105 in combination with nivolumab (Opdivo)
 - The trial is sponsored by the Australasian Gastro-Intestinal Trials Group (AGITG) and funding support is provided by BMS
- Chronic lymphocytic leukemia:
 - Phase 1 trial of BNC105 in combination with ibrutinib (Imbruvica)
 - Funding support is provided by the Leukemia & Lymphoma Society (US)

BNC105 Clinical Development Summary

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

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

BNC101 - a First-in-Class Humanized Monoclonal Antibody to LGR5, a Cancer Stem Cell Receptor

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

Future development:

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