

Global leader in drug discovery and development

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ASX Spotlight

May 2015



Safe Harbor Statement



Factors Affecting Future Performance

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BNO Value Proposition







Combining one of the world's most innovative drug discovery platforms with development of first-in-class and best-in-class therapies:

- **Broad and deep portfolio:** Our pipeline of drug candidates has a series of near-term clinical catalysts:
 - BNC210 for the treatment of anxiety & depression with anticipated Phase I/II data in 2015/2016
 - BNC101 targeting cancer stem cells entering Phase I in 2015 (colon and pancreatic cancers)
- **Three Proprietary Technology Platforms:** Unique and rigorous drug discovery platforms underpin this pipeline of compelling drug candidates.
- **De-risked Business Model:** Partnering for late stage development and commercialisation.
- **Technical Validation:** Two strategic collaborations with Merck & Co with up to US\$678m in potential future milestone and other payments.
- **Strong cash position and growing revenue:** Cash balance of A\$38.4m (at December 2014) supports rapid and unencumbered investment in development programs.



Platform Technologies Deliver Multi-Product Pipeline



Therapeutic Area	Drug Candidate/ Program	Discovery	Pre-Clinical	Phase I	Phase II	Licensee/ Partner
Central Nervous System	BNC 210 – Anxiety, Depression					 MERCK  MERCK
	Cognitive Impairment - Alzheimer's, Parkinson's, ADHD, schizophrenia					
	Pain					
	GABA-A - Epilepsy					
Cancer	BNC105 – Solid tumours, renal, mesothelioma					 <i>Cancer Therapeutics CRC</i>  <i>Cancer Therapeutics CRC</i>
	BNC101 – Cancer stem cells, solid tumours, colon, breast, pancreatic					
	BNC 420 – Solid tumours, melanoma, breast					
	BNC102 – Cancer stem cells, solid tumours					
	MELK, PRMT1 – Cancer stem cells, tumours					

Proprietary Technology Platforms



Drug discovery platforms focused on the creation of drug candidates across oncology and neuroscience pipeline.

Platform	Focus
MultiCore®	A diversity orientated chemistry platform for the discovery of small molecule drugs
ionX®	CNS: A set of novel technologies for the identification of drugs targeting ion channels
CSC Rx Discovery™	Cancer: Identifies antibody and small molecule therapeutics that inhibit the growth of cancer stem cells



Merck Partnerships: Technical Validation



Two major partnerships with Merck & Co – up to US\$678m combined future potential milestones plus additional royalties on product sales



Validates ionX® and MultiCore® drug discovery platforms



Value creation through strategic partnering business model



Future success based revenue streams & royalties secured



Partnered Programs





BNC375 Program: Partnership with Merck & Co.



The BNC375 program is developing small molecule therapeutics for the treatment of cognitive impairment in Alzheimer's disease, Parkinson's disease, ADHD, Schizophrenia and other conditions.

Partnership Deal	<ul style="list-style-type: none">• Covers Bionomics' research program on BNC375 and related compounds.• Potential for up to US\$506m in payments to Bionomics plus additional royalties on net product sales.• Upfront payments of US\$20m.• Merck funds R&D.
Compound Target	<ul style="list-style-type: none">• Targets cognitive impairment in Alzheimer's disease and other conditions, targeting a receptor which is critical to cognitive processes.
Market Size & Positioning	<ul style="list-style-type: none">• Significant market opportunity includes many neurodegenerative & psychiatric disorders.• By 2025 the number of Americans aged 65 and older with Alzheimer's is forecast to rise 40% to 7.1 million



BNC375 Program: Potential Competitive Advantages*



Demonstrated potent *in vivo* memory enhancing properties in animal models:

- Improvement in both episodic and working memory
- >100-fold therapeutic dose range & wide safety window

Characteristics	Bionomics BNC375	Competing Agents ⁺
Potent	✓	✓
Rapid onset of action	✓	✗
Potentiates endogenous receptor ligand	✓	✗
Preserve the normal signalling patterns of the receptor	✓	✗
Do not cause receptor desensitization	✓	✗
No potential for development of tolerance	✓	✗

*Based on data from preclinical animal studies

+Published information & Bionomics' in-house data





BNC375 Program: Market Potential



BNC375 market opportunity includes many neurodegenerative & psychiatric disorders with a significant need for new treatments:

Alzheimer's Disease

5 million

More than 5 million Americans are living with the disease



Every 67 seconds someone in the United States develops Alzheimer's

6th

Alzheimer's disease is the 6th leading cause of death in the United States



500,000

There are approximately 500,000 people dying each year because they have Alzheimer's



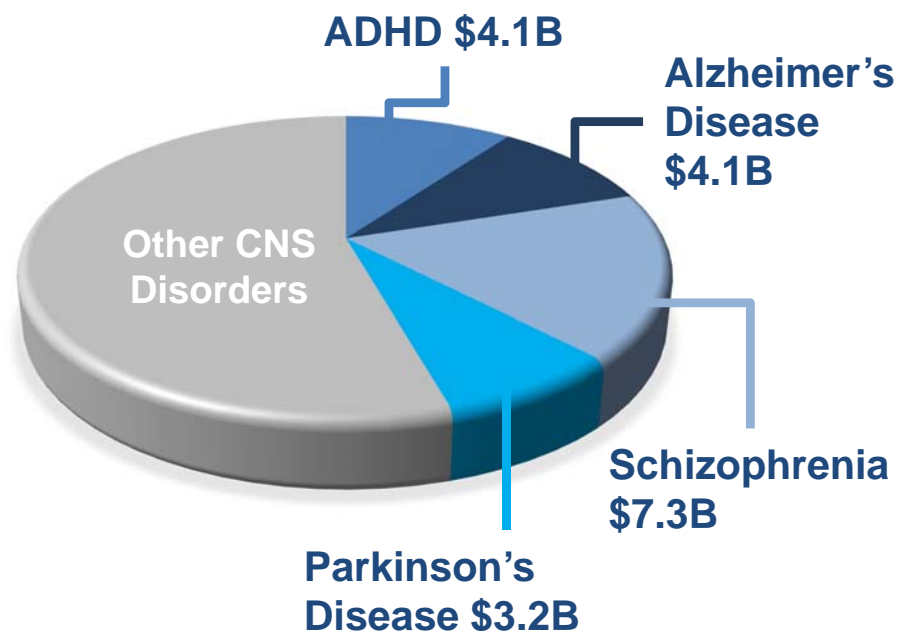
1 in 3

1 in 3 seniors dies with Alzheimer's or another dementia

\$220 billion

In 2013, 15.5 million caregivers provided an estimated 17.7 billion hours of unpaid care valued at more than \$220 billion.

Estimated 2017 CNS Global Sales



Source: Evaluate Pharma, 2013






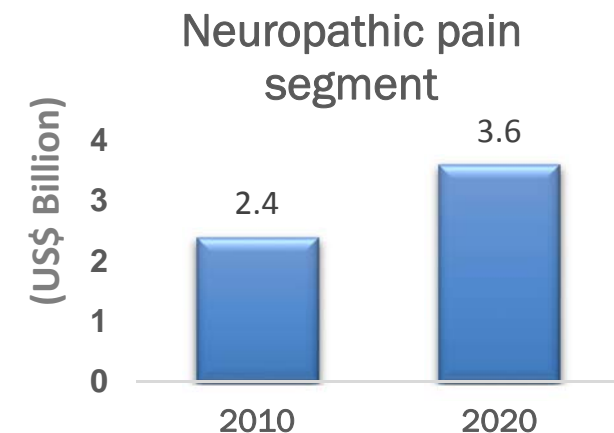
Pain Program: Partnership with Merck & Co



Further validates ionX® & MultiCore® drug discovery platforms.

Heterogeneity of pain requires a range of analgesics with different modes of action but there exists significant unmet needs.

Partnership Deal	<ul style="list-style-type: none">Option & license agreement with Merck & Co.US\$172M in option exercise fees, development/regulatory milestone payments, plus additional royalties on net sales.
TREATMENT	Chronic & neuropathic pain.
Market Size & Positioning	<ul style="list-style-type: none">Pain market: ~US\$22b sales in 2010.Current medications have limited effectiveness:<ul style="list-style-type: none">Side-effects e.g. drowsiness, somnolence & dizziness. <div><p>Estimated only 1 in 4 patients with neuropathic pain achieve >50% reduction in pain levels</p></div>



Neuropathic pain segment expected to grow from ~US\$2.4b in 2010 to ~US\$3.6b by 2020.



In-House Development Programs





BNC210: Next Generation Compound Potential to Treat Anxiety & Depression



TREATMENT	Anxiety and Depression.
MARKETS	<ul style="list-style-type: none">Anxiety – market US\$17.3B in 2014Depression – global sales US\$11B in 2008.
CLINICAL / REGULATORY	<ul style="list-style-type: none">Ongoing Phase II trial in anxiety patientsPhase I trial program - BNC210 prevented panic attack and reduced panic attack symptoms.BNC210-related changes in human brain activity observed, indicative of efficacy in absence of sedation.Excellent safety profile

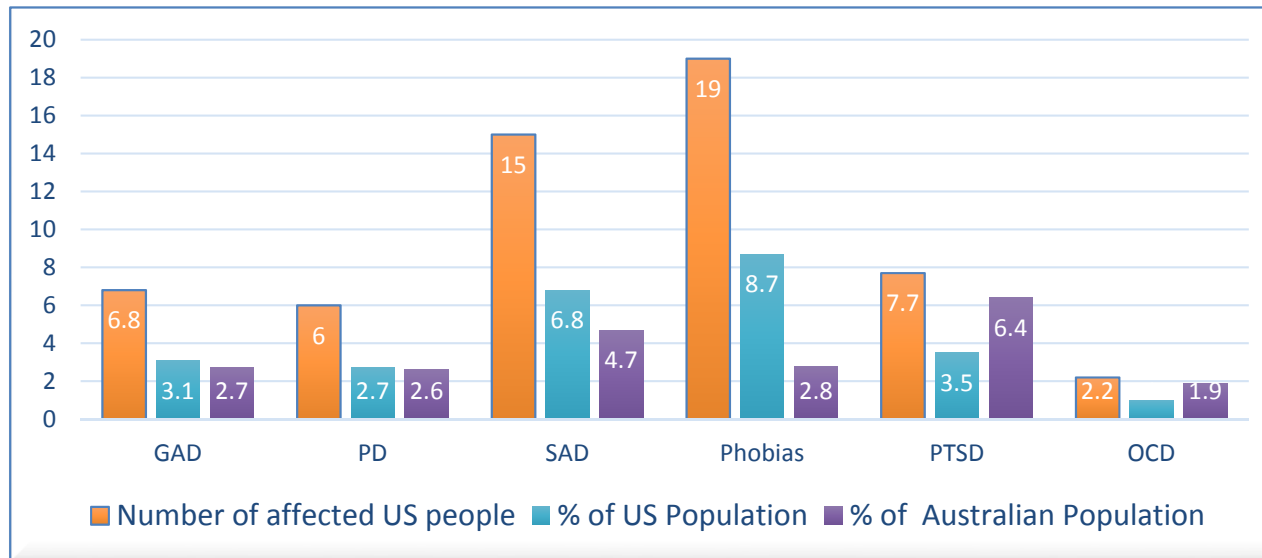


POTENTIAL COMPETITIVE ADVANTAGES OF BNC210*						
Drug	No sedation	No withdrawal syndrome	No memory impairment	Fast acting	No drug/drug interactions	Once-a-day dosing
BNC210	✓	✓	✓	✓	✓	✓
VALIUM	✗	✗	✗	✓	✓	✗
PROZAC	✓	✗	✓	✗	✗	✓



*Based on data from preclinical animal studies and Phase I clinical trials

The Prevalence of Anxiety Disorders



ANXIETY AND DEPRESSION
ASSOCIATION OF AMERICA

- Anxiety disorders affect ~40 million US adults ≥ 18 years (about 18%; ~ 14% Australians) in a given year
- Women are 60% more likely than men to experience an anxiety disorder
- ~ 8% of teens (13–18) have an anxiety disorder, symptoms often emerging around age 6.
- US ECONOMIC BURDEN of anxiety disorders estimated to be >\$46.6 billion p.a. (DuPoint,1996;Greenberg,1999).
- MARKET global anxiety disorders market ~US\$17.3 billion in 2014 (BCC Research)





BNC210: Key Findings from Phase I Trials

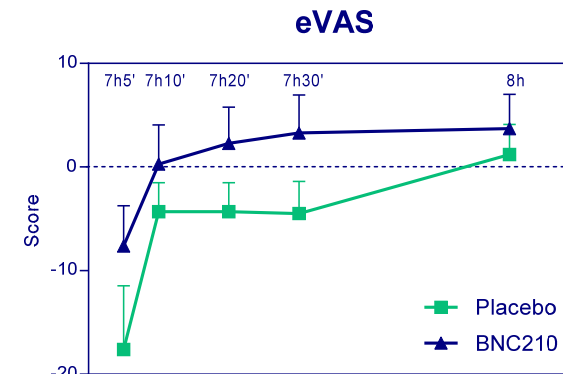
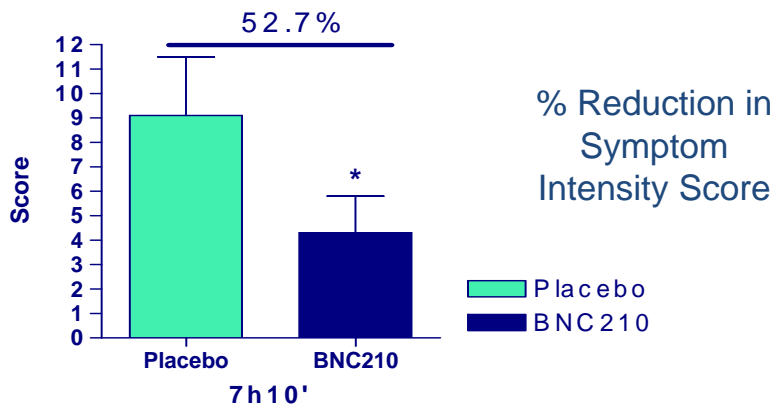
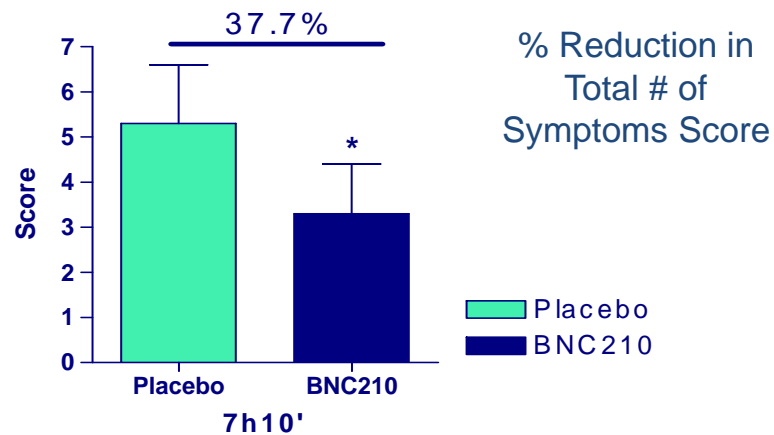


Double-blinded, placebo controlled Phase I trials have provided indicators of BNC210 efficacy in humans and strong data supporting its safety.

Subjects subject to an induced panic attack and treated with BNC210 experienced:

1. A reduction in number and intensity of panic symptoms on the Panic Symptoms Scale scores following CCK-4 challenge

2. A positive result on the emotional visual analogue scale following a CCK-4 challenge





BNC210: Induced EEG Changes in Brain Activity



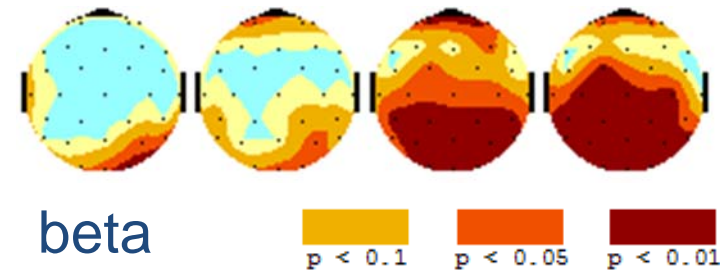
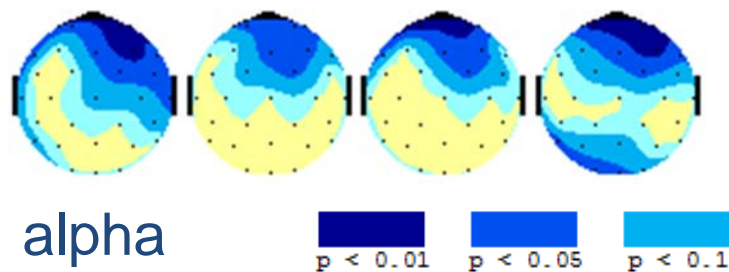
Induced EEG changes in brain activity associated with anxiolysis and the absence of sedation

BNC210.003

Drug/EEG Activity	δ	γ	α	$\alpha 1$	$\alpha 2$	β	$\beta 1$	$\beta 2$	$\beta 3$
BNC210			↓		↓	↑			↑
LORAZEPAM	↑	↓	↓	↓	↓	↑	↑	↑	↑

Arrows represent significant increases or decreases in spectral power displayed over considerable surface or scalp regions

Brain Maps showing BNC210 effect on alpha and beta frequency bands





BNC210: Current trials



Two clinical trials in progress:

1. PHASE I: Multiple Ascending Dose Study and Nicotine Shift Assay - France
 - Nicotine Shift assay performed with expanded group of subjects receiving highest dose
 - Nicotine shows dose response in alpha2 (10-12.5 Hz) frequency band on quantitative EEG
 - Nicotine shift assay evaluates effect of BNC210 on an EEG-measured nicotine dose response

2. PHASE II: Patients with Generalized Anxiety Disorder – UK
 - fMRI will be used to demonstrate the effects of BNC210 on anxiety-related changes in the brain
 - The amygdala is in the middle of the “emotional centre” of the brain
 - It plays a predominant role in fear conditioning and processing of facial and vocal signals of fear
 - In anxious and fearful situations, the amygdala is activated - this causes increased blood flow to the area which can be imaged using fMRI – anxiolytic drugs are known to reduce amygdala activation
 - In this trial, brain activation will be induced in anxious patients, while in an MRI machine, by viewing emotive images or performing tasks that generate anxiety



BNC210

Phase I: Multiple Ascending Dose Study



Title	Double-blind, placebo-controlled ascending multiple dose study of the safety, tolerability, pharmacokinetics and pharmacodynamics of BNC210 administered orally to healthy adult male subjects
Protocol #	BNC210.005
Phase	I
Study Centre	FRANCE
Design	Randomised, double-blind, placebo-controlled; b.i.d. dosing for 8 days
Population	Healthy adult male volunteers
Subjects/ Cohort	6 active+2 placebo for first 3 dose levels, expanded cohort for last dose level which includes nicotine shift assay (24 active+6 placebo)
Primary Objectives	<ul style="list-style-type: none">• Safety and tolerability of multiple ascending doses
Secondary Objectives	<ul style="list-style-type: none">• Pharmacodynamic profile on cognitive functions• Pharmacodynamic profile on nicotine shift assay (2000 mg dose level)• Pharmacokinetics of multiple ascending doses

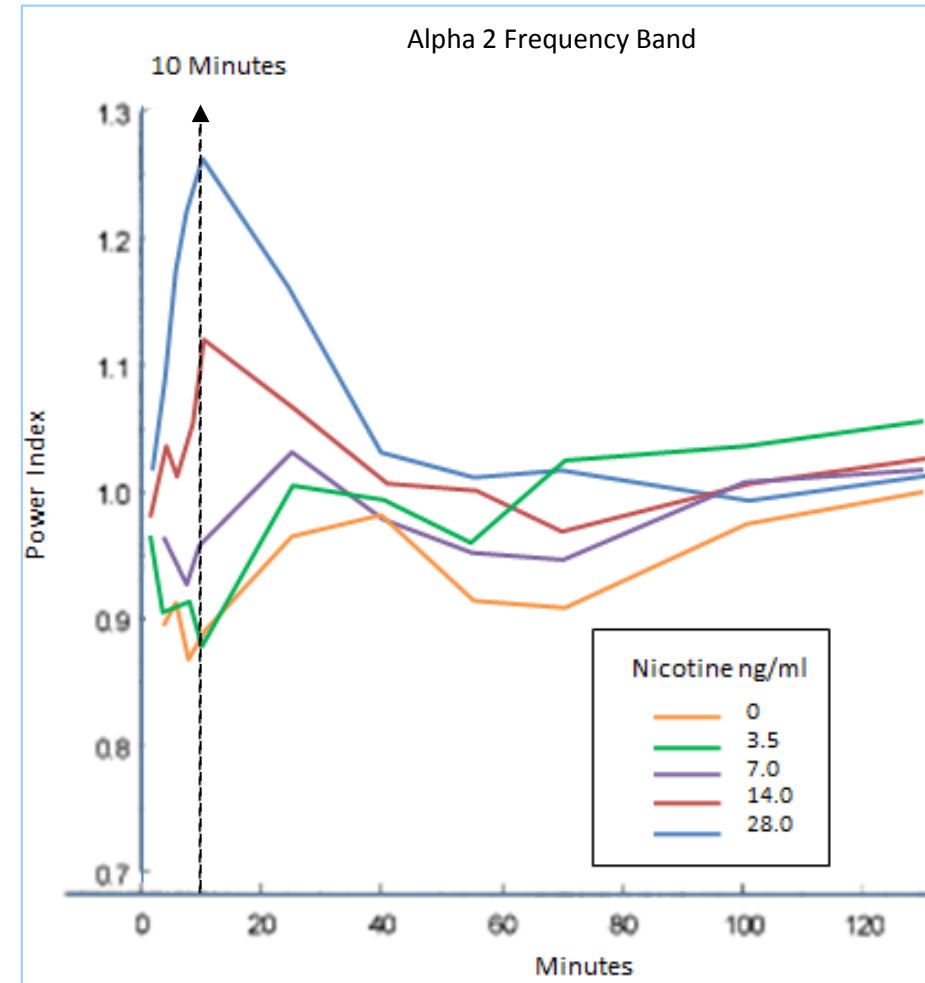


BNC210

Nicotine shift assay & target engagement



- Nicotine has a signature peak in the alpha2 (10-12.5 Hz) frequency band on qEEG
- T_{max} of the nicotine response occurs at 10 minutes
- Peak amplitude of the response is dose dependent = dose response
- Nicotine is administered using a nasal spray
- Subjects are non-smokers
- A change in the nicotine dose response in subjects treated with BNC210 indicates target engagement



Domino EF et al. Int J Psychophysiol. 2009 Dec;74(3):192-8.

Teter CJ, et al. Eur J Clin Pharmacol. 2002 Aug;58(5):309-14.

Lindgren M et al. Psychopharmacology (Berl). 1999 Aug;145(3):342-50.



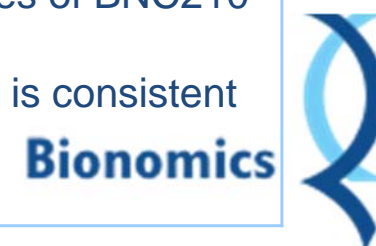


BNC210

Phase II: Proof of Biology Study



Title	A randomized, double-blinded, placebo & lorazepam-controlled, four-way crossover, Phase II study to evaluate the effects of single oral administration of BNC210 on brain activity changes captured by functional magnetic resonance imaging in adults with Generalized Anxiety Disorder
Protocol #	BNC210.006
Phase	II
Study Centre	UK
Design	Randomised, double-blind, placebo and Lorazepam-controlled, 4-way crossover
Population	Male or female volunteers with Generalized Anxiety Disorder who are un-medicated
Subject #	24
Primary Objectives	(A) To determine whether BNC210 causes significant changes in cerebral perfusion using Arterial Spin Labelling (ASL) in the resting state. (B) To determine whether BNC210 causes significant changes in task-related brain activity using the emotional faces task during fMRI.
Secondary Objectives	To determine the effect on defensive behavior of two different oral doses of BNC210 using the Joystick Operated Runway Task and fMRI. To determine whether BNC210 alters affective self report in a way that is consistent with reduced anxiety. To generate additional safety and tolerability information on BNC210.

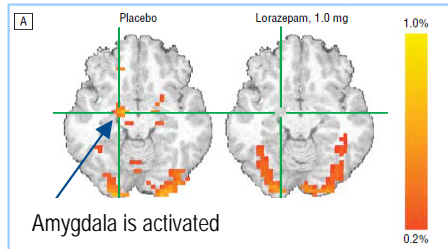




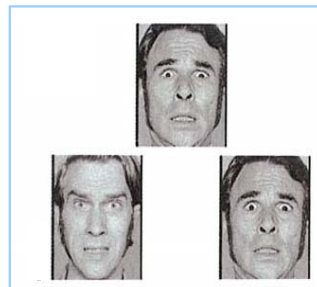
BNC210: Emotional Faces and Joystick Operated Runway Task (JORT)



- Human studies have identified the amygdala as a central component in processing threat-related stimuli



- It plays a predominant role in fear conditioning and processing facial signals of fear
- Angry faces also represent highly potent signals of threat, and are often rated as equally arousing and unpleasant as fearful faces
- Drugs used to treat anxiety reduce amygdala activation in the Emotional Faces task e.g., Lorazepam, Gabapentin, Citalopram, Escitalopram

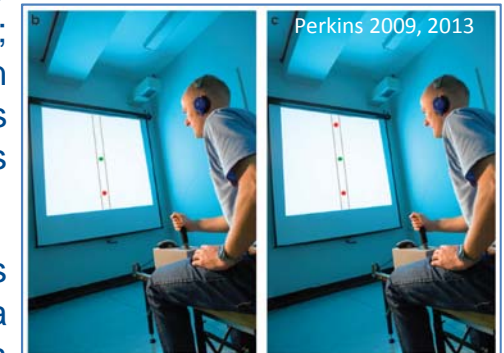


Hariri, 2009

- Clinically effective panic disorder drugs preferentially alter rodent **FLIGHT** behaviour and reduce departure from threat
- Clinically effective anxiety drugs preferentially alter rodent **RISK** assessment behaviour and allow cautious approach to threat
- Theory tested in humans - evaluating citalopram and lorazepam on the defensive behaviour of healthy adult male humans using the JORT

JORT: FLIGHT the green cursor is pursued by a single threat stimulus (red dot); Participants receive an unpleasant but harmless shock if the red dot collides with the green dot.

RISK A second red dot travels ahead of the green dot at a constant velocity, causing a goal conflict whereby the participant has to travel fast enough to avoid the pursuing threat, but not so fast that they collide with the leading threat stimulus.





BNC101: Targeting Cancer Stem Cells in Solid Tumours



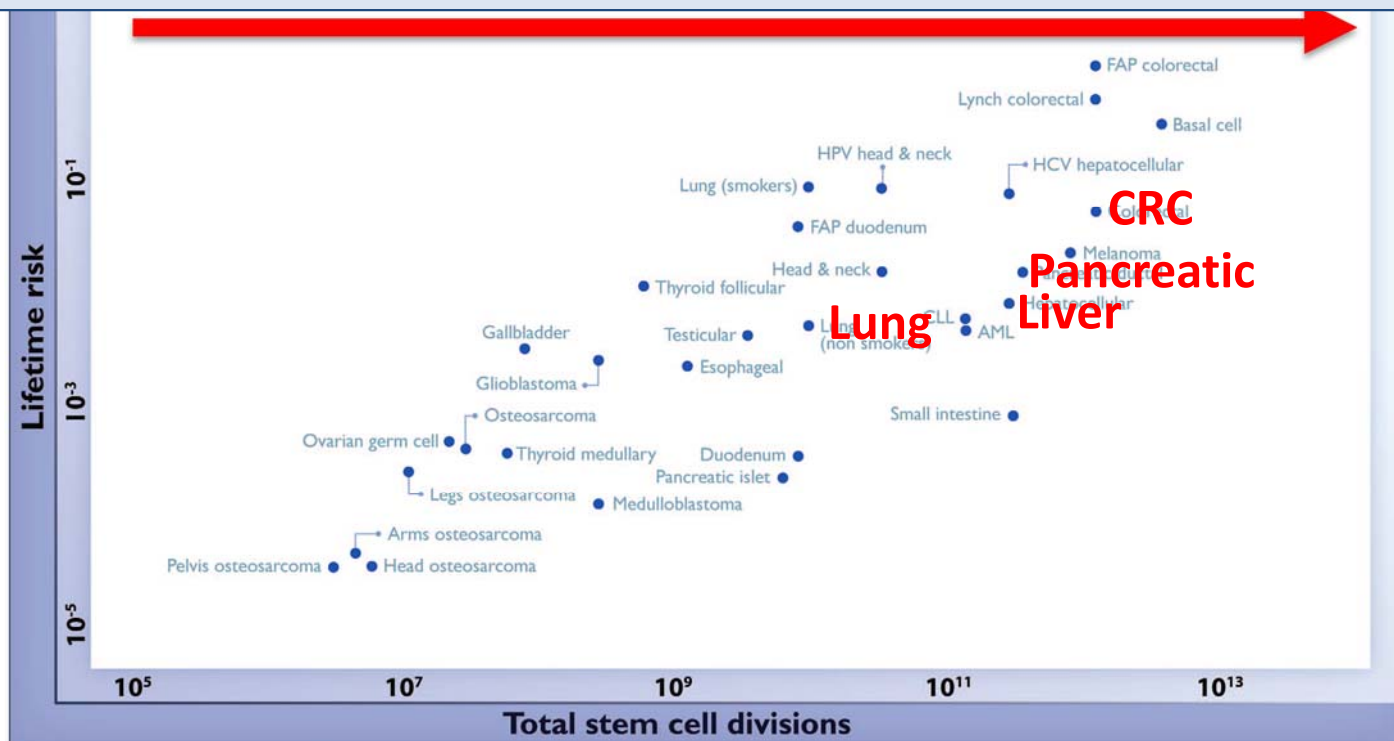
TREATMENT	Solid tumours; colon & pancreatic are priority indications.
MECHANISM OF ACTION	<ul style="list-style-type: none">• Humanised monoclonal antibody.• BNC101 binds selectively to LGR5; which marks tumour-initiating cells. High expression of LGR5 in colon cancer has been linked to tumour recurrence & poor prognosis.• LGR5 highly overexpressed in colon, gastric, ovarian, liver, breast, lung & other solid tumours.• High expression of LGR5 in colon cancer has been linked to tumour recurrence and poor prognosis
MARKET OPPORTUNITY	Market for cancer stem cell therapeutics estimated as US\$8b by 2018.
DEVELOPMENT STAGE	Targeting IND filing and Phase I clinical trials in 2015.
BENEFITS	<p>Inhibition of tumour recurrence.</p> <p>Specific targeting of cancer stem cells which are not killed by chemotherapy or radiotherapy.</p>



New Evidence That >60% of All Cancers Caused by Mutated Cancer Stem Cells



Increasing risk of cancer correlates with # of stem cell divisions



FAP = Familial Adenomatous Polyposis ♦ HCV = Hepatitis C virus ♦ HPV = Human papillomavirus ♦ CLL = Chronic lymphocytic leukemia ♦ AML = Acute myeloid leukemia

*From Science, Jan 2015
(Volgelstein)*

The New York Times
Cancer's Random Assault

By DENISE GRADY JAN. 5, 2015

- 2/3 cancers are not preventable, i.e. NOT due to environment or genetics
- Due to random mutations in tissue stem cells i.e. CSCs (CRC, panc, lung, liver)
- Secondary prevention strategies such as CSC targeting drugs necessary

LGR5 is a unique, common factor in these CSCs that can be targeted by BNC101 (vs. plethora of random mutations being targeted by investigational drugs)



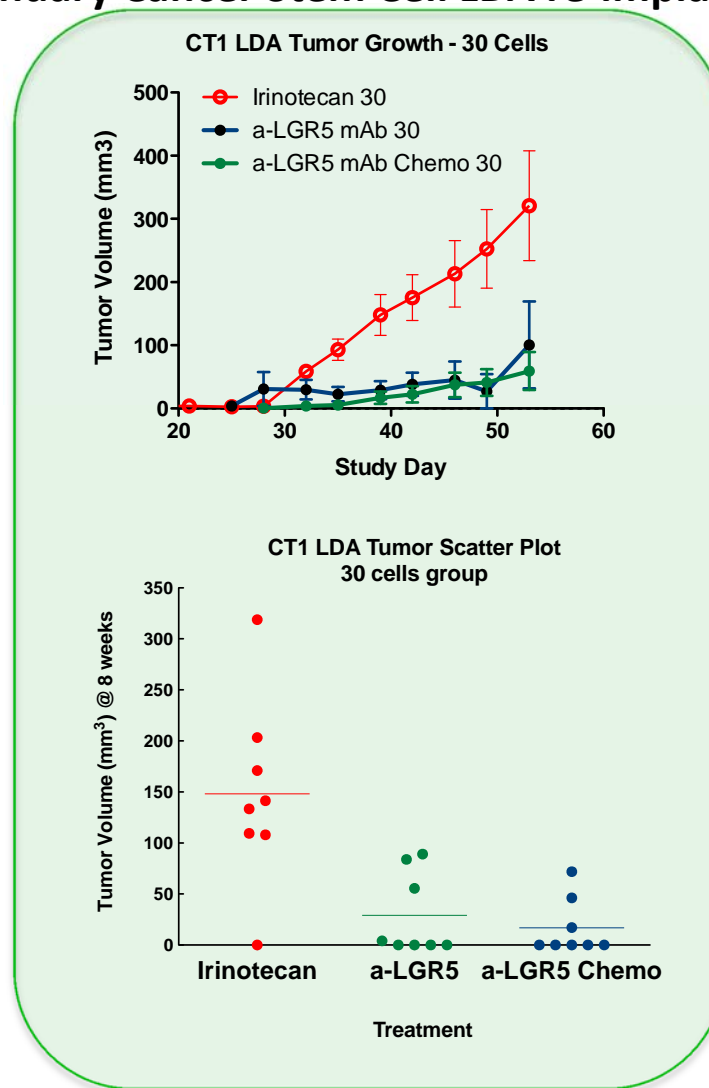


BNC101 is Active in Primary Colon Cancer Model



	Patient CT1
Histologic Type	Adenocarcinoma
Histologic Grade	Poorly differentiated
Stage	Invasive
Stage	IV
Mutations (Ion Torrent deep sequencing)	<ul style="list-style-type: none"> • K-Ras • PI3K • PTEN • p53
Notable	Patient had liver metastasis

Secondary Cancer Stem Cell LDA re-implant assay

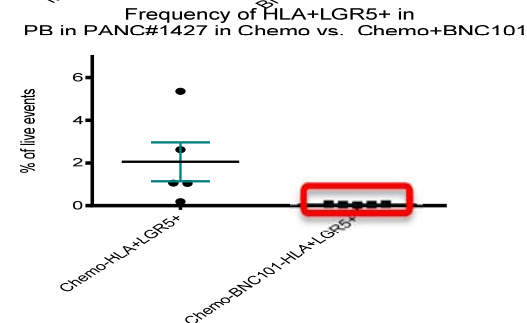
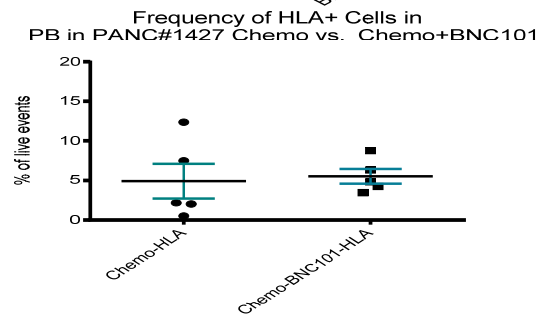
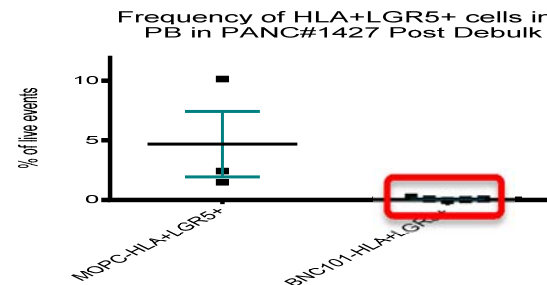
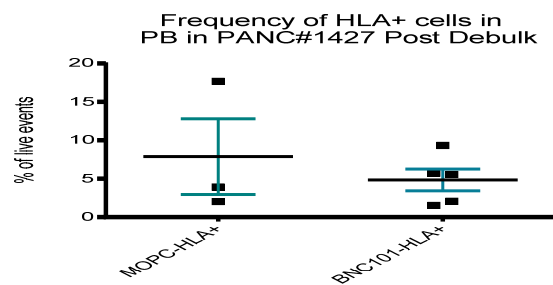
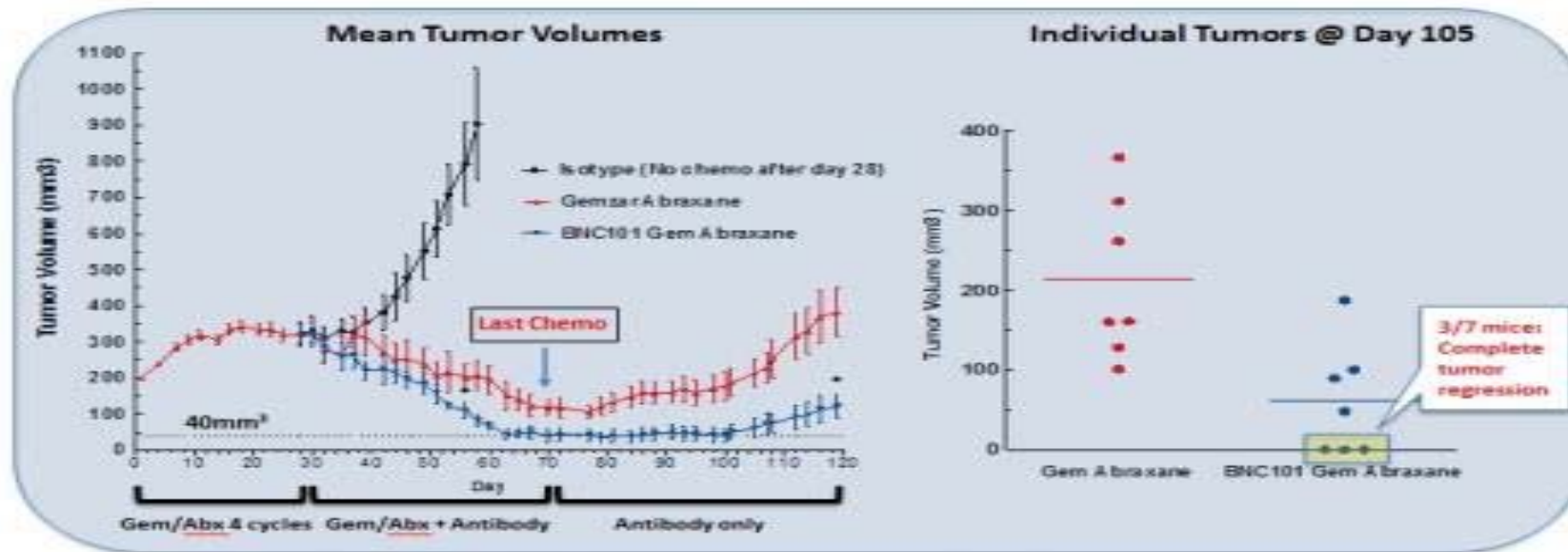


Bionomics



No Treatment in Secondary LDA Assay

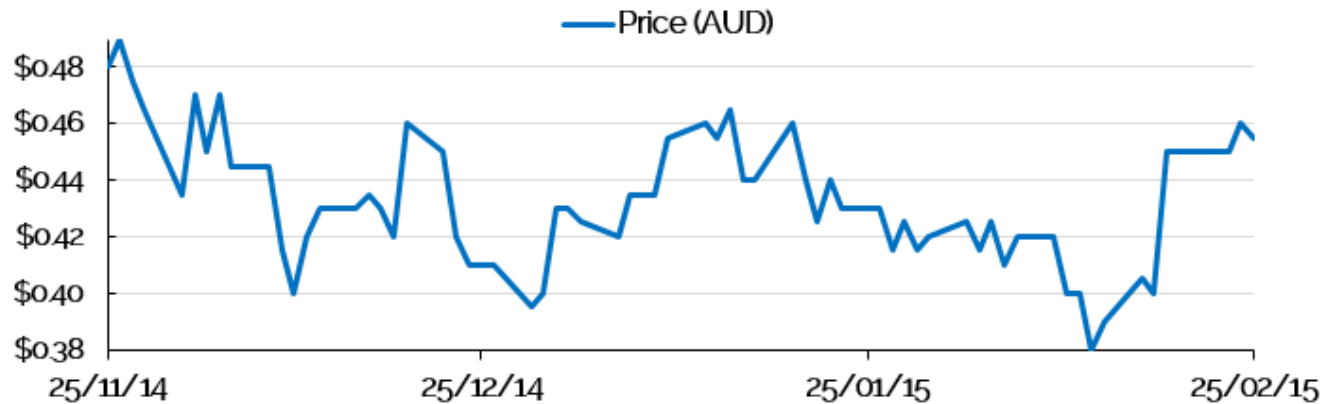
BNC101 Activity in Primary Pancreatic Cancer Models



Strong Financial Position



Recent BNO share price performance (AUD\$)



FY14 Results	First Half FY15 Results
Operating profit after tax: \$3.2m	Operating loss: \$5.68m
Revenue: \$27.5m	Revenue: \$7.33m
Cash at 31 December 2014: \$38.37m	

Milestones



BNC 210 Clinical Development:

- Initiation and completion of Phase Ib trial investigating target engagement, data anticipated Q3, 2015
- Initiation of Phase II trial in patients suffering anxiety, H1, 2015, data anticipated H2, 2016

BNC101 Clinical Development:

- IND filing (Q3, 2015) and initiation of Phase I clinical trial in pancreatic and colorectal cancer patients Q4, 2015

BNC105 Clinical Development:

- Further development to be pursued in collaboration - partnership

Continued execution of Bionomics' partnership strategy



Contact Us



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BNC105: “Best in Class” Tubulin Targeting Agent with Unique Mechanism of Action



TREATMENT	Solid and blood cancers: New paradigm with blockbuster potential.
MARKETS	<ul style="list-style-type: none">• >US\$10b current market size in solid tumours.• Renal cancer market size >US\$2.5b; includes TKIs Sutent (Pfizer), Nexavar (Bayer/Onyx), Afinitor (Novartis).• Ovarian cancer market size ~US\$2.2b; includes carboplatin (BMS), gemcitabine (Gemzar, Eli Lilly).• Chronic Lymphocytic Leukemia (CLL) market ~US\$1.4b in 2013
BENEFITS	<ul style="list-style-type: none">• Targets both solid tumours and blood cancers (CLL)• Multi Action – selectively targets both tumour blood vessels (inducing hypoxia in solid tumours) and cancer cells (in both solid tumours and blood cancers)• Enhances Effectiveness of Other Cancer Treatments – delivers synergistic anti-cancer effects in numerous combinations





BNC105:

Positive Phase I Ovarian Trial Results



10 of 12 patients achieved positive response in combination study of BNC105 and standard of care chemotherapy.

- Combination study (carboplatin + gemcitabine chemotherapy + BNC105) in partially platinum sensitive ovarian cancer patients in first or second relapse.
- 15 patients enrolled, 12 patients completed six cycles of combination therapy and commenced with BNC105 monotherapy.
- 10 patients achieved a positive response according to RECIST 1.1 and/or GCIG CA125 criteria.
- Side-effects related to gemcitabine and carboplatin treatment backbone; haematological origin.
- Recommended BNC105 Phase II dose: 12mg/m^2 in combination with carboplatin and gemcitabine.



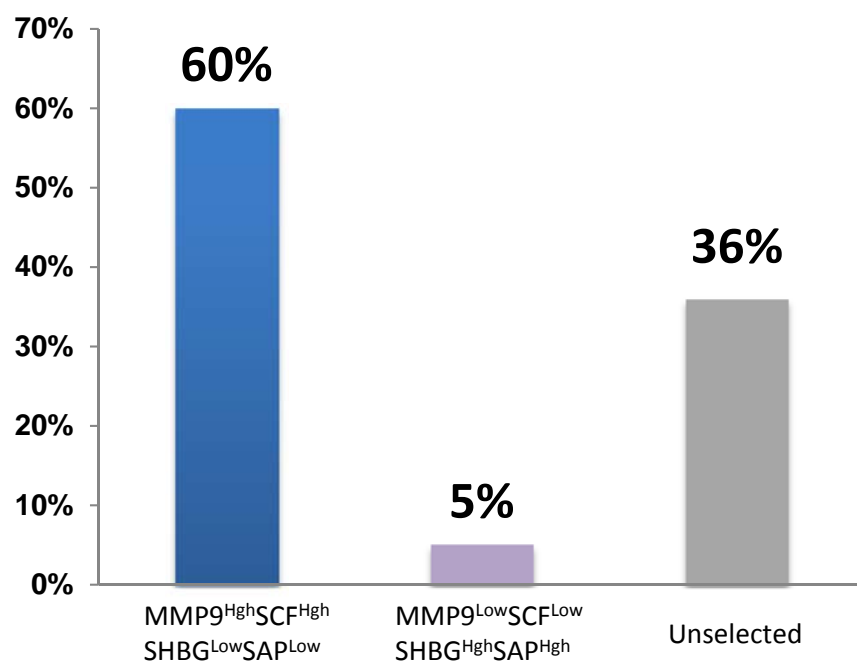
DISRUPTOR-1:

Baseline and Dynamic Biomarker Signatures Correlated with Patient Benefit

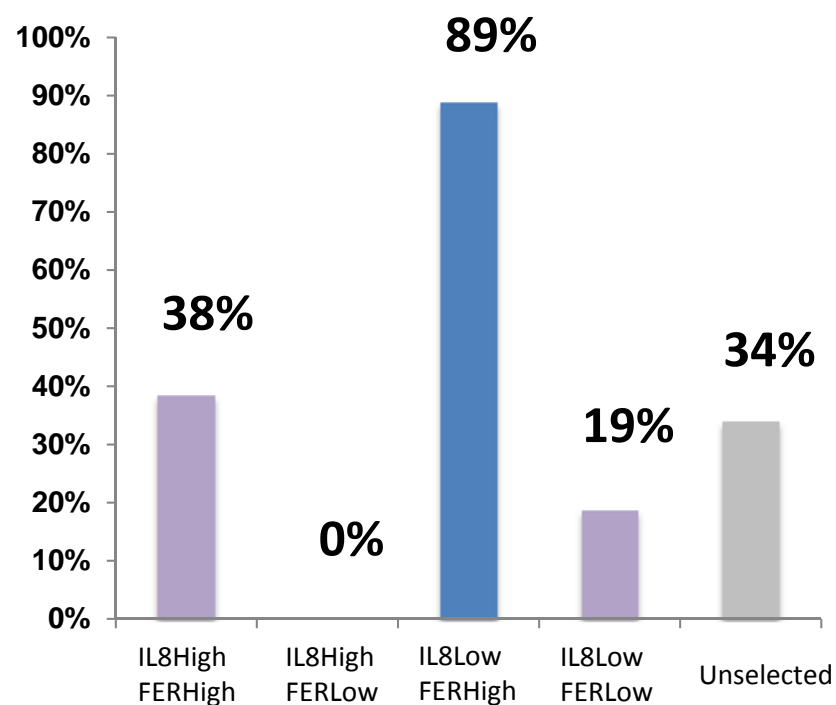


- Afinitor vs Afinitor + BNC105
- Randomized 2-arm study, 139 patients enrolled
- Primary endpoint not met – no PFS difference in unselected patient population.
- A prospective biomarker-driven study examining Afinitor + BNC105 with patients selected by baseline markers is in development.

Percentage (%) Progression Free Survival at 6 months



60% of patients displaying the dynamic biomarker signature were progression free at 6 months.



89% of patients displaying the baseline biomarker signature were progression free at 6 months.





BNC420: Suppressing Tumour Progression



TREATMENT	Solid tumours; breast cancer & melanoma are priority indications.
MECHANISM OF ACTION	<ul style="list-style-type: none">• Orally active, small molecule .• Modulates activity of VEGFR3 receptor:<ul style="list-style-type: none">• inhibits lymph vessel growth, key conduits promoting cancer spread; and• Promotes re-activation of the anti-tumour immune response.
MARKET OPPORTUNITY	<p>Melanoma market value growth predicted due to increasing patient numbers and market entry of novel pipeline therapies, expected US\$2.8b by 2021.</p> <p>Breast cancer market projected to be US\$10.4b by 2019.</p>
DEVELOPMENT STAGE	Preclinical.
BENEFITS	<p>Inhibition of cancer spread.</p> <p>Activation of the tumour immune response.</p>

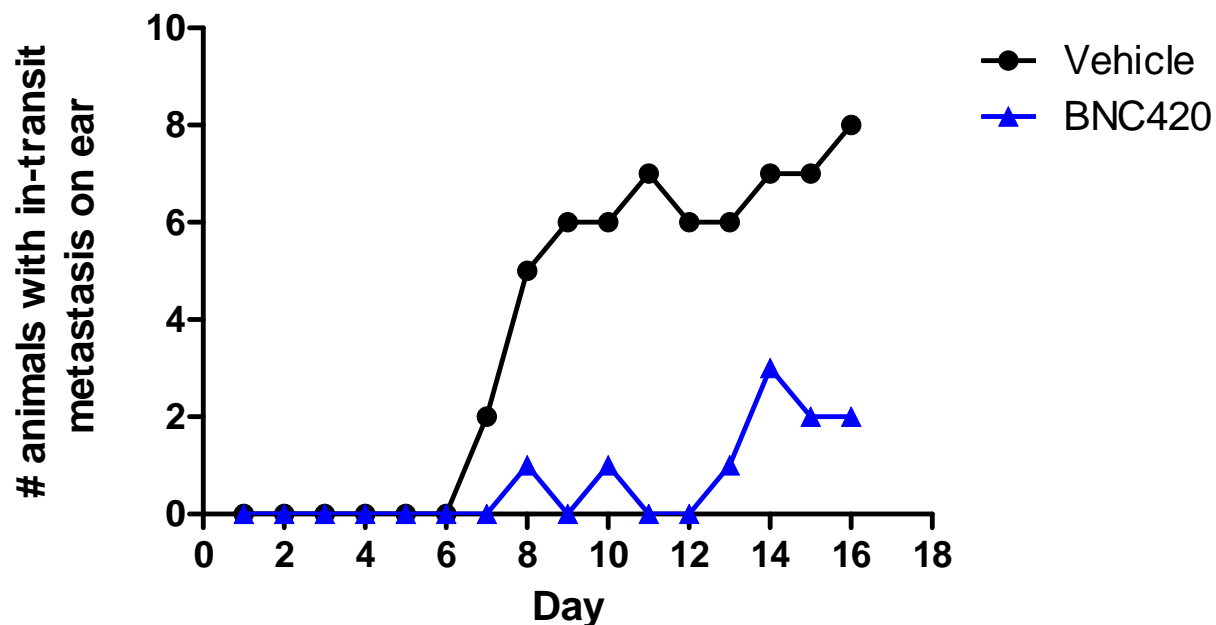




BNC420 Effectively Blocks Melanoma Progression in the B16F10 Model



Animals with in-transit metastasis on ear



Vehicle



BNC420 (75 mg/kg)

