Global leader in drug discovery and development

Deborah Rathjen | CEO & Managing Director

March 2015

**Bionomics** 





### 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' development candidates BNC105, BNC210, BNC101 and BNC420, its licensing agreements with Merck & Co, the acquisitions of Eclipse Therapeutics and Prestwick Chemical, drug discovery programs and pending patent applications 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 risks related to our available funds or existing funding arrangements, a downturn in our customers' markets, our failure to introduce new products or technologies in a timely manner, regulatory changes, risks related to our international operations, our inability to integrate acquired businesses and technologies into our existing business and to our competitive advantages, as well as other factors. Results of studies performed on competitors products 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.



## **BNO Value Proposition**



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

- Three Proprietary Technology Platforms: Unique and rigorous drug discovery platforms provide a pipeline of compelling drug candidates which exhibit characteristics with potential for development and commercialisation.
- 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.
- Broad and deep portfolio: Our pipeline of drug candidates has a series of near-term catalysts in both clinical progress and partnering opportunities.
- Strong cash position and growing revenue: Cash balance of A\$38.4m (at December 2014) supports rapid and unencumbered investment in development programs.



## Company Overview

- Leader in the discovery, development & strategic partnering of innovative biopharmaceuticals for cancer & central nervous system disorders.
- Operations in Australia, US and Europe, global presence built through acquisitions including Eclipse Therapeutics (2012) & Prestwick Chemical (2014).
- Robust pipeline and business model with multiple revenue generating streams through strategic partnering including two strategic collaborations with Merck & Co:
  - Cognition in neurodegenerative diseases (Alzheimer's, Parkinson's), U\$\$506m in upfront and milestone payments plus royalties on product sales
  - Pain, option and license agreement, US\$172m in fees and milestones payments plus royalties on product sales

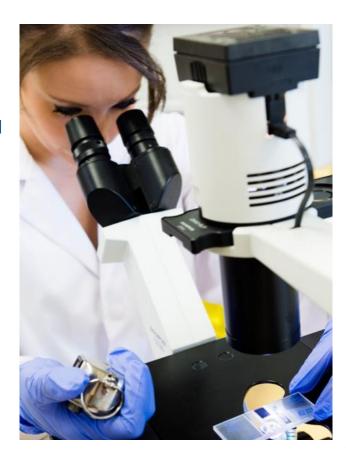




## **Company Overview**

## Broad and deep portfolio of clinical and preclinical drug candidates with near-term catalysts:

- **BNC210:** negative allosteric modulator of α7 nAChR in development for anxiety and depression with clinical trial readouts expected in 2015 and 2016.
- BNC101: monoclonal antibody targeting Cancer Stem Cells (CSC), entering clinic in 2015 (colon, pancreatic cancer);
- BNC105: A cancer treatment that disrupts tumour blood vessels and activates tumour cell death pathways, high response rate observed in ovarian cancer in combination with chemotherapy, biomarker driven development strategy; and
- BNC420: modulator of VEGFR3 in preclinical development for treatment of melanoma and breast cancer, expected IND filing in 2016.





## **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®	A set of novel technologies for the identification of drugs targeting ion channels for diseases of the central nervous system
CSC Rx Discovery™	Identifies antibody and small molecule therapeutics that inhibit the growth of cancer stem cells





### De-Risked Business Model



### DRUG DISCOVERY

- Rigorous selection of drug candidates
- Focus on oncology and neuroscience
- Build pipeline with multiple and diverse commercial opportunities

### DRUG DEVELOPMENT

- Identify drug candidates for partnering
- Clinical trials to validate efficacy and safety
  - Maximise value and commercial options

## STRATEGIC PARTNERING

- Share drug development risk with partner
  - Receive upfront payments
  - Generate multiple revenue streams in different markets
  - Future royalty revenue streams



## 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



## Merck Partnerships: Technical Validation

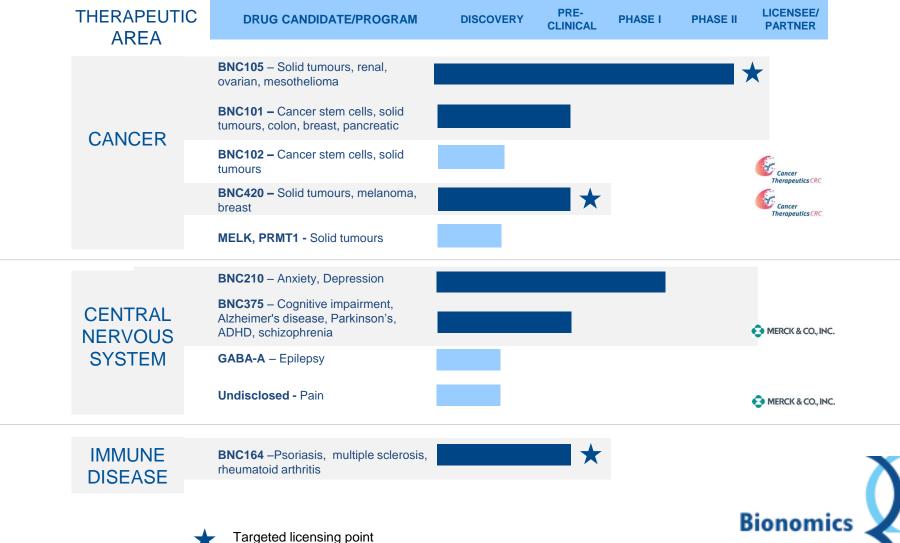


Merck Partnerships	PAIN	COGNITION & MEMORY
Target Indication	Treatment of chronic and neuropathic pain	Cognitive impairment – Alzheimer's, Parkinson's and other conditions
Partnership Deal	Option & license agreement – US\$172m in option exercise fees, development/regulatory milestone payments plus royalties	Potential up to US\$506m payments to Bionomics, plus royalties and product sales Upfront payment of US\$20m
Estimated Market Size	Neuropathic pain segment expected to grow from US\$2.4Bn in 2010 to US\$3.6Bn by 2020	Alzheimer's Disease –~US\$10.B in 2012, Parkinson's disease – US\$3.5B in 2014



## Platform Technologies Deliver Multi-Product Pipeline





# Partnered Programs









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.

	<ul> <li>Covers Bionomics' research program on BNC375 and related compounds.</li> </ul>
Partnership Deal	<ul> <li>Potential for up to US\$506m in payments to Bionomics plus additional royalties on net product sales.</li> </ul>
	<ul> <li>Upfront payments of US\$20m.</li> </ul>
	Merck funds R&D.
Compound Target	<ul> <li>Targets cognitive impairment in Alzheimer's disease other conditions, targeting receptor critical to cognitive processes.</li> </ul>
Market Size &	<ul> <li>Significant market opportunity includes many neurodegenerative &amp; psychiatric disorders.</li> </ul>
Positioning	<ul> <li>By 2025 the number of Americans aged 65 and older with Alzheimer's is forecast to rise 40% to 7.1 million</li> </ul>
	DIOHOHICS



## 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	✓	*



<sup>\*</sup>Based on data from preclinical animal studies

<sup>+</sup>Published information & Bionomics' in-house data





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

#### **Alzheimer's Disease**



More than 5 million Americans are living with the disease



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



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



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

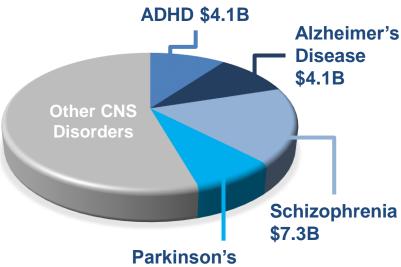


Alzheimer's disease is the 6th leading cause of death in the United States



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**



Disease \$3.2B

Source: Evaluate Pharma, 2013

Bionomics



## 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

Option & license agreement with Merck & Co.

• **US\$172M** in option exercise fees, development/regulatory milestone payments, **plus** additional royalties on net sales.

#### **TREATMENT**

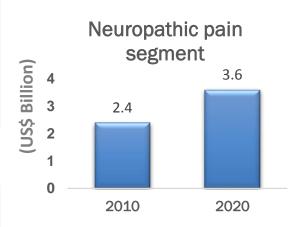
#### Chronic & neuropathic pain.

**Market Size & Positioning** 

- Pain market: ~US\$22b sales in 2010.
- Current medications have limited effectiveness:
  - Side-effects e.g. drowsiness, somnolence & dizziness.



Estimated 1 in 4 patients achieve >50% reduction in pain levels



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> <li>Anxiety – global sales of US\$5-7B annually.</li> <li>Depression – global sales US\$11B in 2008.</li> </ul>
CLINICAL / REGULATORY	<ul> <li>Phase I trial program - BNC210 prevented panic attack and reduced panic attack symptoms.</li> <li>BNC210-related changes in human brain activity observed, indicative of efficacy in absence of sedation.</li> <li>Excellent safety profile</li> </ul>



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	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
VALIUM	×	×	×	$\checkmark$	$\checkmark$	$\checkmark$
PROZAC	$\checkmark$	×	$\checkmark$	×	×	$\checkmark$



<sup>\*</sup>Based on data from preclinical animal studies and Phase I clinical trials



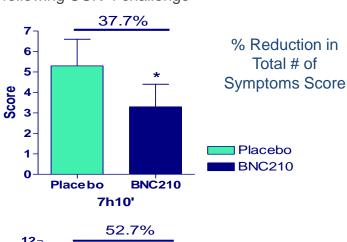
## BNC210: Key Findings from Phase I Trials

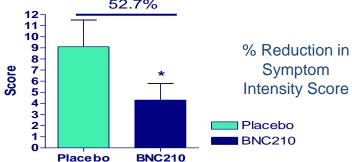


Double-blinded, placebo controlled Phase I trials have provided indicators of BNC210 efficacy in humans and strong data supporting its safety.

#### Subjects treated with BNC210 experienced:

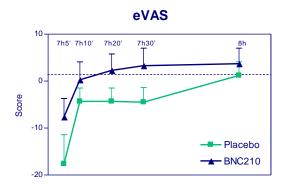
 A reduction in number and intensity of panic symptoms on the Panic Symptoms Scale scores following CCK-4 challenge





7h10'

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



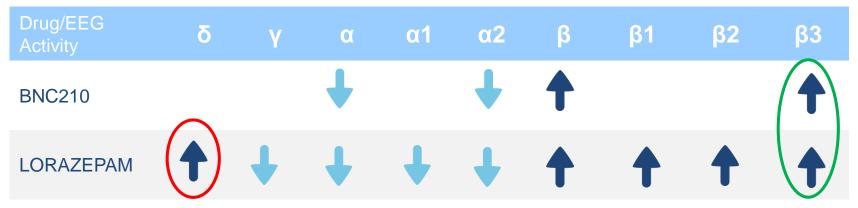




## Induced EEG Changes in Brain Activity

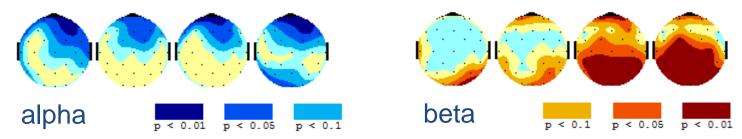


#### BNC210.003



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





## BNC105: "Best in Class" Tubulin Targeting Agent with Unique Mechanism of Action



TREATMENT	Solid and blood cancers: New paradigm with blockbuster potential.
MARKETS	<ul> <li>&gt;US\$10b current market size in solid tumours.</li> <li>Renal cancer market size &gt;US\$2.5b; includes TKIs Sutent (Pfizer), Nexavar (Bayer/Onyx), Afinitor (Novartis).</li> <li>Ovarian cancer market size ~US\$2.2b; includes carboplatin (BMS), gemcitabine (Gemzar, Eli Lilly).</li> <li>Chronic Lymphocytic Leukemia (CLL) market ~US\$1.4b in 2013</li> </ul>
BENEFITS	<ul> <li>Targets both solid tumours and blood cancers (CLL)</li> <li>Multi Action – selectively targets both tumour blood vessels (solid tumours) and cancer cells (solid tumours and blood cancers)</li> <li>Enhances Effectiveness of Other Cancer Treatments – delivers synergistic anti-cancer effects in numerous combinations</li> </ul>





## 10 of 12 patients achieved positive response in combination study of BNC2015 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/m² in combination with carboplatin and gemcitabine.

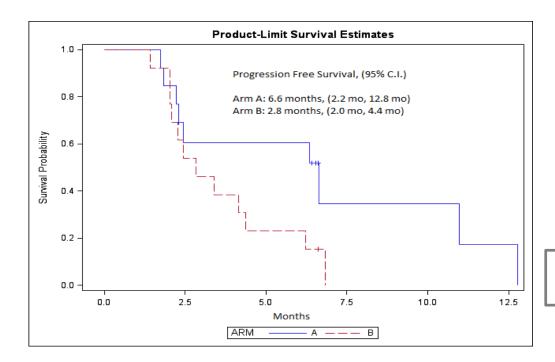




## DISRUPTOR-1 Phase II Trial in Renal Cancer Patients



- · Primary endpoint not met
- Patients with liver metastasis treated with BNC105+Afinitor experience 3.8 month increase in Progression Free Survival compared to patients treated with Afinitor alone.



**Arm A**: BNC105+Afinitor; N=13 **Arm B**: Afinitor only; N=13





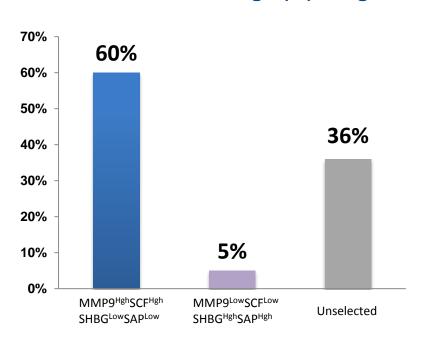
### **DISRUPTOR-1**:

## Static and Dynamic Biomarker Signatures Correlated with Patient Benefit

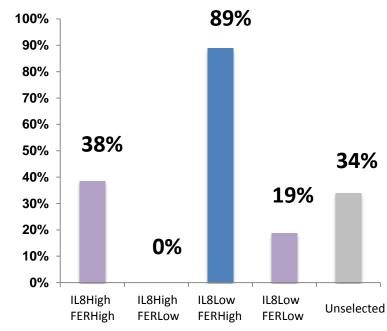


A prospective biomarker-driven study examining Afinitor + BNC105 with patients selected by baseline markers is in development.

#### Percentage (%) Progression Free Survival at 6 months



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



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





## BNC105 Potential in Chronic Lymphocytic Leukemia (CLL)

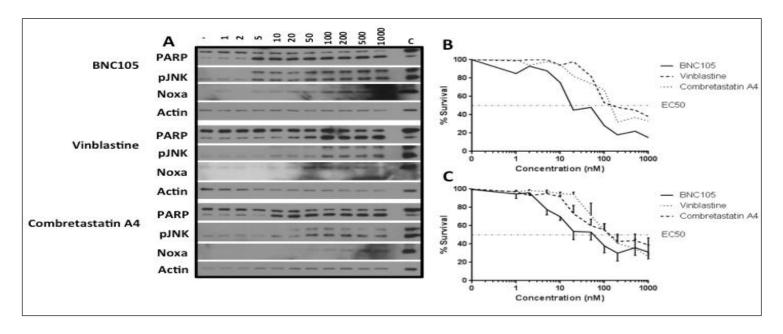


#### **Chronic Lymphocytic Leukemia:**

- Most common type of adult leukemia, affects mostly males over 50 years of age (typically around 70 years).
- In US ~15,720 new cases and 4,600 deaths from CLL predicted for 2014.

#### **BNC105 and CLL:**

BNC105 kills CLL cells through activation of death proteins pJNK and Noxa.





## BNC101: Targeting Cancer Stem Cells in Solid Tumours



TREATMENT	Solid tumours; colon & pancreatic are priority indications.	
MECHANISM OF ACTION	<ul> <li>Humanised monoclonal antibody.</li> <li>BNC101 binds selectively to LGR5; which marks tumour-initiating High expression of LGR5 in colon cancer has been linked to tumour recurrence &amp; poor prognosis in colon &amp; gastric cancer.</li> <li>LGR5 highly overexpressed in colon, ovarian, liver, breast, lung &amp; other solid tumours.</li> </ul>	
	<ul> <li>High expression of LGR5 in colon cancer has been linked to tumour recurrence and poor prognosis</li> </ul>	
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.	
	Inhibition of tumour recurrence.	
BENEFITS	Specific targeting of cancer stem cells which are not killed by chemotherapy or radiotherapy.	







## Suppressing Tumour Progression

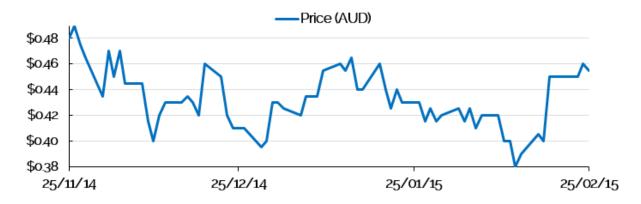
TREATMENT	Solid tumours; breast cancer & melanoma are priority indications.
MECHANISM OF ACTION	<ul> <li>Orally active, small molecule.</li> <li>Modulates activity of VEGFR3 receptor: <ul> <li>inhibits lymph vessel growth, key conduits promoting cancer spread; and</li> <li>Promotes re-activation of the anti-tumour immune response.</li> </ul> </li> </ul>
MARKET OPPORTUNITY	Melanoma market value growth predicted due to increasing patient numbers and market entry of novel pipeline therapies, expected US\$2.8b by 2021.  Breast cancer market projected to be US\$10.4b by 2019.
DEVELOPMENT STAGE	Preclinical.
BENEFITS	Inhibition of cancer spread.

Activation of the tumour immune response.

## **Strong Financial Position**



#### **BNO Share price performance in the last 3 months (AUD\$)**



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



## The Year Ahead: New Studies in Three Programs



#### **BNC 210 Clinical Development:**

- Initiation and completion of Phase Ib trial investigating target engagement, data anticipated Q3, CY2015
- Initiation of Phase II trial in patients suffering anxiety, Q1, CY2015, data anticipated Q2, CY2016

### **BNC105 Clinical Development:**

- Initiation of Phase II clinical trial in renal cancer patients, biomarker signatures will guide patient selection, in collaboration with global pharma company
- Initiation of clinical trial in patients with Chronic Lymphocytic Leukaemia, in collaboration with Dartmouth College (US)

### **BNC101 Development:**

IND filing and initiation of Phase I clinical trial in pancreatic and colorectal cancer patients

### Continued execution of Bionomics' partnership strategy



### Contact Us



## Deborah Rathjen

Chief Executive Officer & Managing Director



+61 8 8354 6101



drathjen@bionomics.com.au



www.bionomics.com.au

