A global leader in drug discovery and development

**AGM 2015** 

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Bionomics







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### **Factors Affecting Future Performance**

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### **Company Overview**

- Deep understanding of ion channel physiology, CNS and cancer stem cells
- Three drug discovery platforms to support a robust pipeline
- Partnerships with Merck & Co. (MSD) in cognition and pain up to US\$658m combined future potential milestones plus additional royalties on net sales of licensed drugs
- Merck & Co now a 4.9% shareholder 8 Oct 2015 investment at a 29% premium
- Lead asset BNC210, is a novel, orally-administered, first-in-class, modulator of α7 nicotinic acetylcholine receptor
  - Ongoing Phase 2 trial in Generalized Anxiety Disorder (GAD) patients, results expected Q3 2016 calendar year
- BNC101 is a first-in-class anti-LGR5 antibody targeting cancer stem cells
  - IND submission accepted by the US Food and Drug Administration
- BNC105, a small molecule tubulin polymerization inhibitor targeting cancer cells and tumour vasculature with multiple modes of action – evolving positioning with immuno-oncology agents and hypoxia activated prodrugs (HAPs)
- Strong balance sheet





## **Our Proprietary Platform Technologies**

# Focused on discovery of drug candidates for CNS disorders and cancer

### ionX

- Identifies drug candidates targeting both ligand gated and voltage gated ion channels for CNS indications
- Proprietary cell lines and screening approaches
- Comprehensive in vivo models validate target biology

### **MultiCore**

- A diversity orientated chemistry platform for the discovery of small molecule drug candidates
- Computer aided pharmacophore modelling
- Scaffold hopping synthetic approaches rapidly create diversity in small, focused libraries
- Parallel, differentiated chemical series of potential drug candidates;

### **CSCRx**

- Identifies drug candidates that target cancer stem cells
- Enables dissection and validation of target biology
- Proprietary *in vitro* assays combined with *in vivo* assays



# Platform Technologies Deliver Broad Drug Pipeline



Drug Candidate	Indication(s)	Preclinica	al _	Phase 1	Pha	se 2	Milestones (Calendar Year)
Central Nervo	us System (ionX and MultiCore)						
BNC 210	Generalized anxiety disorder						Results from P2 trial in Q3 2016
	Other indications						
Undisclosed	ADHD, Alzheimer's, cognition, Parkinson's, schizophrenia			MERCK Re web	,		
Undisclosed	Chronic and neuropathic pain		MERCK				
Others	Pain, Parkinson's dyskinesia, epilepsy			Be well			
Cancer Stem	Cells (CSCRx)						
BNC101	Colorectal cancer						Initiate P1 trial in Q1 2016
	Pancreatic cancer						Initiate P1 trial in H1 2016
	Other solid tumors						
Cancer Stem Cells (CSCRx and MultiCore)							
MELK*	Solid tumors						
Others	Solid tumors						
Other Programs							
BNC105	Solid tumors, renal, ovarian, mesothelioma						
BNC420	Solid tumors, melanoma, breast						
BNC164	Psoriasis, uveitis						

<sup>\*</sup>Maternal embryonic leucine zipper kinase.







### **Drug Discovery**

**Drug Development** 



**Partnering** 



- Engine room delivering flow of new drug candidates
- Build pipeline with multiple shots on goal to manage risk

 Adding value through targeted clinical trials

- Lay off risk with experienced partners
- Generate revenue streams to support R&D





### **Strong Financial Position**

- Cash at 30 June 2015: \$26.6M
  - Boosted post 30 June 2015:
    - Merck investment US\$9M
    - Anticipated \$8.5M cash from Australian R&D
       Tax Incentive refund for FY15



# **Chemistry Capability Boosted Through Strategic Acquisition of Prestwick Chemical**

Prestwick is a premium provider of chemistry services to:

Big pharma





















- Mid-sized pharma: in France, Germany, Switzerland, USA ...
- Biotech firms: in Austria, Australia, France, Germany, Israel, Switzerland, USA ...











### **Milestones Achieved**

- Extension of pain program partnership with MSD
- US\$9M equity investment by MSD
- Initiated 2 clinical trials of BNC210 and secured project specific financing from Silicon Valley Bank
  - Phase 1b multiple ascending dose with assessment of target engagement
  - Phase 2 trial in patients with GAD
- Positive results from completed BNC210 Phase 1b clinical trial
  - All endpoints met
  - Significant data confirming target engagement
- Successful BNC101 FDA submission paving the way for clinical trials
- Enhanced commercial prospects for BNC105
  - Biomarkers associated with response across multiple tumour types
  - Synergy with immuno-oncology agents and HAPs



# Merck & Co US\$9M Investment Coverage



#### Canberra Times

The Age

Sydney Morning Herald

### US drug major Merck buys stake in researcher Bionomics

#### Biotechnology

**Brian Robins** 

The local biotechnology industry has received a significant boost to its international recognition with United States drug major Merck taking a direct slice of equity in Bionomics, a local drug developer.

The two groups are already partners in two research programs that could generate more than \$US670 million (\$931 million) of in-

come for Bionomics. Now, Merck has agreed to take up a direct 4.9 per cent shareholding in Bionomics, paying \$US9 million for 21.6 million shares in Bionomics at 59.38¢ a share.

Shares in Bionomics surged on the deal, rallying 18 per cent to close at 55¢, the day's high, but still

ceutical groups taking equity in local groups, since Celgene took up a 4.5 per cent slice of Mesoblast for \$58.5 million. It also follows a string of acquisitions, most recently the sale of the privately held Link Pharmaceutical for \$200 mil-

"It is more like a de-risking strategy," Bell Potter analyst Tanushree Jain said of the latest Bionomics deal with Merck.

"Any possible decision to buy [Bionomics outright] would come

Merck's acquisitions tend to be of companies with drugs in the later stage of development, which have less risk, she said.

Two years ago, Merck took a two-year option on the Bionomics pain treatment candidate, agreethis up last year with a deal cover-

ing Bionomics' Alzheimers treatment candidate in a deal worth up to \$US500 million.

Both of these agents are only in the early research stage and are vet to enter clinical trials.

The deal with Merck follows a steady strengthening of senior management at Bionomics with several appointments, analysts said. "The deal is further evidence that Merck likes Bionomics' drug discovery capability," Ms Jain said.

#### The Australian





Topics: Clinical trials | Partnering

### Australia's Bionomics gets more cash from Merck on pain, oncology, CNS bets

October 9, 2015 | By EJ Lane

SHARE Australia-listed biotech Bionomics has seen Merck (\$MRK) expand its interes act of benevolence to Bionomics broad pineline of candidates, buying pearly 5.3% of its outstanding ordinary shill.

### Bionomics (BNO) 55c

Big pharma companies aren't known for their philanthropy, but Merck's latest investment is as an Advertiser (Adelaide)

# Adelaide drug firm soars on **US deal**

### CAMERON ENGLAND

GLOBAL

company Merck and Co will buy more lion worth of Biores and extend a levelop pain treat-

> company will buy Bionomics shares e, which was a 29 mium to Bionomprice on Wednes-

based Bionomics are working todeveloping treatchronic and







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# Cost of ageing nation to hit \$80bn

#### EXCLUSIVE

#### SARAH-JANE TASKER

A global Alzheimer's expert warns the disease will cost the Australian economy about \$80 billion by 2050 unless a medical breakthrough is achieved in the interim.

Richard Hargreaves, from drug developer Biogen, said there would be almost one million Australians living with the disease by 2050, with 400 new cases diagnosed every week.

Dr Hargreaves, Biogen's vicepresident of discovery science, said the Alzheimer's epidemic was getting bigger with an increasingly ageing population.

He said there were not a lot of treatment options for Alzheimer's disease and the average lifespan was seven years after diagnosis.

"The cost of the disease to the USA is \$US200bn today and estimates are that worldwide there are around 44 million people with the disease and there is no means to treat the disease, only the symptoms," he said ahead of an Adelaide conference on Monday run jointly by Bionomics and US pharmaceutical giant Merck.

He will outline how cutting-

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benefit," Dr Hargreaves said.

Sydney-based Louise Brown understands the burden of Alzheimer's, having had to quit her job to move in and care for her father, who has lived with the disease for almost 10 years.

Ms Brown, who recently moved her father into care, said it was important carers were given support to help patients manage the disease. "There is a lot of potential to help people manage the disease but it needs a lot of resources, and support systems are needed to assist people who want to keep family members in a home environment." she said.

Frank Yocca, a senior vicepresident at BioXcel, said the challenge was to help families on whom the carer's role would increasingly fall.

"We need to say this is going to be a significant challenge for care-givers and patients in the not too distant future and the time might be right to start focusing on mechanisms and drug mechanisms that might alleviate this," Mr Yocca said.

Dohme (Australia)

# 3<sup>rd</sup> Annual Symposium Drug Discovery and Development for Cognition and Alzheimer's Disease

Crowne Plaza, Hindmarsh Square, Adelaide Monday 16 November 2015

Free registration (email Lauren Nicotra: Inicotra@bionomics.com.au)

Time	Speaker	Торіс			
9.30	TEA AND COFFEE				
	SESSION 1:				
10.00	Dr. Deborah Rathjen CEO & Managing Director, Bionomics	Welcome			
10.15	Dr. Darryle Schoepp Vice President & Therapeutic Area Head, Neuroscience, Merck Sharp & Dohme	Challenges in Neuroscience Discovery and Development: What has Changed and Where are we Headed			
10.50	Dr. Frank Yocca Senior Vice President, CNS Research and Development, BioXcel	Emerging Area for Drug Development: Psychiatric- based Symptoms of Neurodegenerative Disorders			
11.25	Prof. Christopher Rowe Director, Molecular Imaging Research, Austin Health	Imaging the Pathology of Alzheimer's Disease			
12.00	LUNCH				
	SESSION 2:				
12.45	Dr. Andy Stamford Executive Director, Discovery Chemistry, Merck Sharp & Dohme	Discovery of MK-8931 as a Disease Modifying Treatment for Alzheimer's Disease			
1.20	Prof. Philip Beart Neurodegeneration Divison Head, Florey Institute of Neuroscience	Autophagy Good and Bad: A Genuine Target for Rubbish Removal in Neuropathologies?			
1.55	Dr. Jens Mikkelsen Chief Scientific Officer, Bionomics	Heteromeric Nicotine alpha7 Acetylcholine Receptor in Humans: Implications for Drug Discovery			
2.30	AFTERNOON TEA				
	SESSION 3:	The second secon			
2.55	Dr. Jason Uslaner Director, In Vivo Pharmacology, Merck Sharp & Dohme	Using Non-Human Primates to Build More Predictive Tools for Treating Cognitive Disorders			
3.30	Prof. Paul Maruff Chief Science Officer, Cogstate	Using Cognition to Make Decisions about Drug Efficacy in Clinical Trials of Putative Cognitive Enhancing Drugs			
4.05	Dr. Richard Hargreaves Vice President, Discovery Science, Biogen Ideo	Use of Imaging for Neuroscience Drug Discovery and Development			
4.40	Dr. Susanne Fiedler Vice President & Managing Director ANZ, Merck Sharp &	Close			



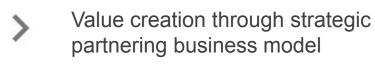


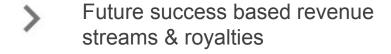
### **Merck Partnerships: Technical Validation**

Two major partnerships with Merck & Co – up to US\$658M combined future potential milestones plus additional royalties on net sales of licensed drugs











# Pain Program: Partnership with Merck & Co.



Combines the platform expertise from ionX and MultiCore



### **Scope / Market Opportunity**

- Target related to chronic and neuropathic pain
- Neuropathic pain market expected to grow to US\$3.6B by 2020
- Current medications have limited effectiveness and multiple side effects

### **Partnership Economics**

- Option and license agreement
- US\$172M in option exercise fees, development/regulatory milestone payments, plus potential royalties



# **Cognition Program: Partnership with Merck & Co.**



Combines the platform expertise from ionX and MultiCore

**Bionomics** 



### **Scope / Market Opportunity**

- Small molecule drugs for the treatment of cognitive impairment in ADHD, Alzheimer's disease, Parkinson's disease, Schizophrenia and other conditions
- Targeting cognitive impairment through a receptor critical to cognitive processes

### **Partnership Economics**

- Merck funds all R&D
- Upfront payments of US\$20M
- Up to US\$486M in future payments to Bionomics plus potential royalties



# **BNC210: Next Generation Drug Candidate to Treat Anxiety & Depression**



Potential Competitive Advantages of BNC210*						
Drug	No sedation	No withdrawal syndrome	No memory impairment	Fast acting	No drug/drug interactions	Once-a-day dosing
BNC210	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
Valium and other BZD	X	X	X	✓	✓	X
Prozac and certain other SSRI/SNRI	✓	X	<b>√</b>	X	X	✓

### **Anxiety Treatments**

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

### **Depression Treatments**

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

**Bionomics** 

<sup>\*</sup>Based on data from preclinical studies and Phase 1 clinical trials.

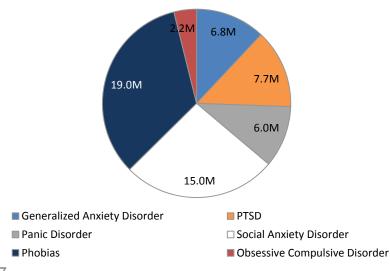


### **Anxiety and Depression Market**

# Anxiety & depression have overlapping symptoms: 40+% diagnosed with depression are also diagnosed with an anxiety disorder

### **Anxiety Market**

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



### **Depression Market**

- ~18.2M people suffer depression in the US
- Sales of top 10 depression drugs reached total of \$8.8B in 2012
- Major types of depression
  - Bipolar depression
  - Dysthymia
  - Major depression







Subjects	<ul> <li>54 healthy subjects</li> </ul>
Protocol	Double-blind, placebo controlled
	<ul> <li>Subjects received multiple ascending dose</li> </ul>
	<ul> <li>BID treatment for each of 8 consecutive days</li> </ul>
Primary Endpoints	<ul> <li>Safety and tolerability of multiple doses</li> </ul>
Secondary Endpoints	Changes in cognitive functions, mood and addictive potential
	<ul> <li>Reduction of nicotine-induced EEG changes (2,000mg level)</li> </ul>
	<ul> <li>Pharmacokinetics of multiple ascending doses</li> </ul>
Results	All primary and secondary endpoints met
	<ul> <li>no adverse effects on cognition or emotional stability and no abuse potential indicated</li> </ul>
	<ul> <li>BNC210 reduced the effect of nicotine, as measured by EEG, consistent with its mechanism of action</li> </ul>





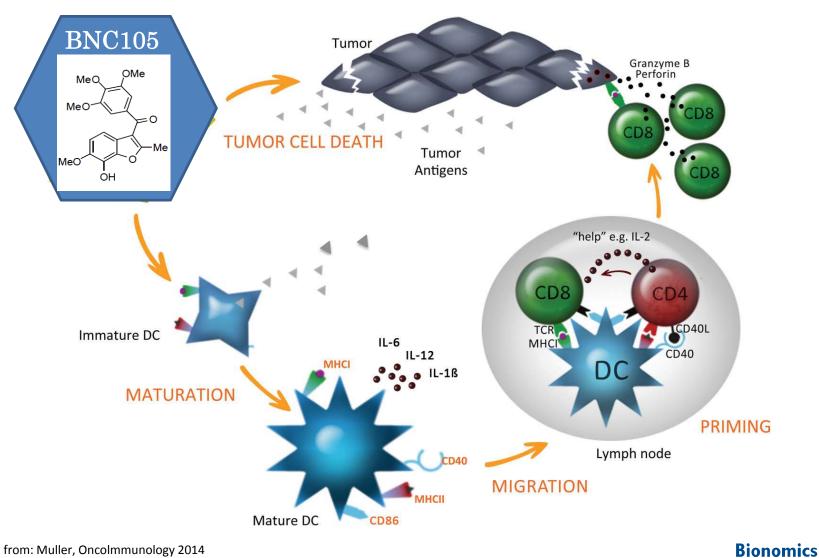


- BNC105 has demonstrated synergistic activity with checkpoint inhibitors in colorectal cancer (CRC) in a preclinical setting
- Therapeutic limitations still exist with immuno-oncology agents
  - Checkpoint inhibitor responses are durable; however, response rates are modest (15% to 20%) in unselected patients
- Different (combination) strategies are being explored to maximize the therapeutic potential of check point inhibitors
- Disruption of the tumour micro-environment may be required in addition to amplification of immune system response to differentiate a growing pipeline of check point inhibitors and broaden their utility
- Growing evidence indicates that approved check point inhibitors (PD-1, CTL-4) may have improved anti-tumour activity through:
  - Disruption of micro-environment (enhanced infiltration)
  - Changing nature of antigen presentation



# **Proposed Mechanism of Anti-Tumour Immunity Induced by BNC105**

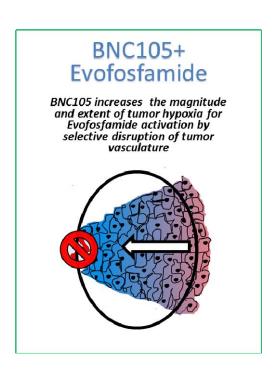








- Evofosfamide (TH-302) is a hypoxia activated prodrug (HAP)
  - TH-302 is cleaved in the presence of hypoxia to release a potent alkylating agent
  - Currently in two completed randomised Phase III trials (pancreatic cancer and soft tissue sarcoma)
  - Collaboration with Merck KGAa and Threshold Pharmaceuticals
- Strong scientific rationale to combine BNC105 + TH-302 to enhance the anti-tumour activity
  - BNC105 causes selective tumour vascular disruption leading to changes in the tumour microenvironment, acute hypoxia and tumour cell death





# **Expanded Therapeutic & Commercial Potential**



# COMBINATION WITH IO DRUGS

- NSCLC
  - Incidence: 228,000 (US)
- Ovarian
  - Incidence: 22,000 (US)
- RCC
  - Incidence: 65,000 (US),200,000 (WW)
- CRC
  - Incidence: 150,000 (US)

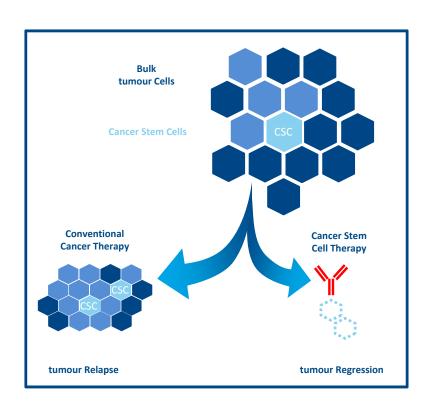
# COMBINATION WITH HAP MOLECULES

- Soft Tissue Sarcoma
  - 36,000 cases diagnosed pa (US & EU)
- Pancreatic
  - 277,000 cases diagnosed pa
- RCC
  - Incidence: 65,000 (US), 200,000 (WW)
- Breast
  - -232,000 cases diagnosed pa (US)



# **Bionomics Approach to Targeting Cancer Stem Cells**





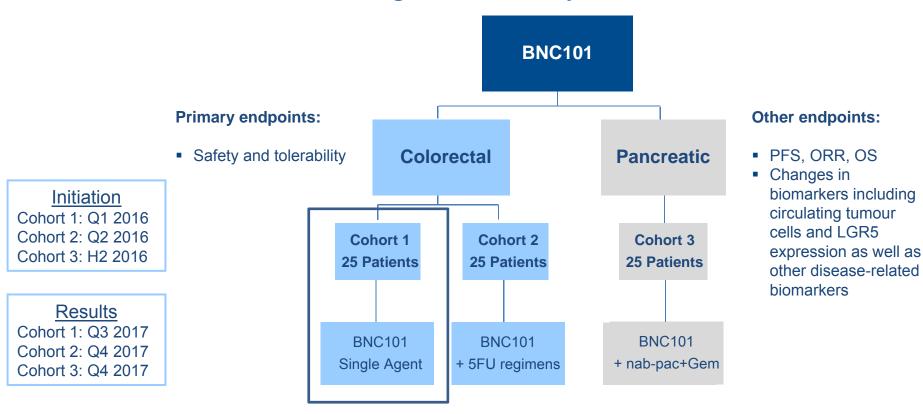
- Bionomics' CSCRx platform can identify drugs that target cancer stem cells
  - CSC have the potential to differentiate into all cell types within a tumour
  - Many drugs do not specifically target
     CSC leading to tumour recurrence and metastasis
- Wnt signaling has been implicated in proliferation and survival of CSC
- LGR5 is a receptor that modulates
   Wnt signaling in CSCs





### **BNC101 Phase 1 Clinical Trial**

# Ascending dose trial to examine safety, tolerability and preliminary signals of efficacy





### **Milestones**

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