

**ASX ANNOUNCEMENT**  
**15 November 2017**

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## **CEO & MANAGERING DIRECTOR'S REPORT TO SHAREHOLDERS**

I am delighted to report that the past year has been a particularly strong one for the Company with impressive, positive BNC210 clinical trial results, continued progress in our collaboration with MSD and greater recognition of our rich development pipeline from global investors.

### **STRATEGY**

### Strategic & Operational Changes

#### A Focused, Agile Organisation

- Operational Efficiencies
- Core Strengths and Competitive Advantage
- Focused Strategy
- Partnership Opportunities

- **Closure of operations in the US**
  - Operations closed in June this year
  - Reducing costs but not operational capability, with no loss of intellectual property
  - Essential operations in Australia and France remain strong
- **Core strength in ion channel biology and drug discovery**
  - Clinical oncology assets no longer on strategy
  - Actively seeking partnership opportunities to monetise BNC105 and BNC101
- **Focus on maturing BNC210 which has blockbuster potential**
  - Recruitment in Phase 2 PTSD clinical trial on track
  - Opportunities to maximise value through expanded development ahead of partnering
  - Seek partner to fully capture value across multiple therapeutic targets



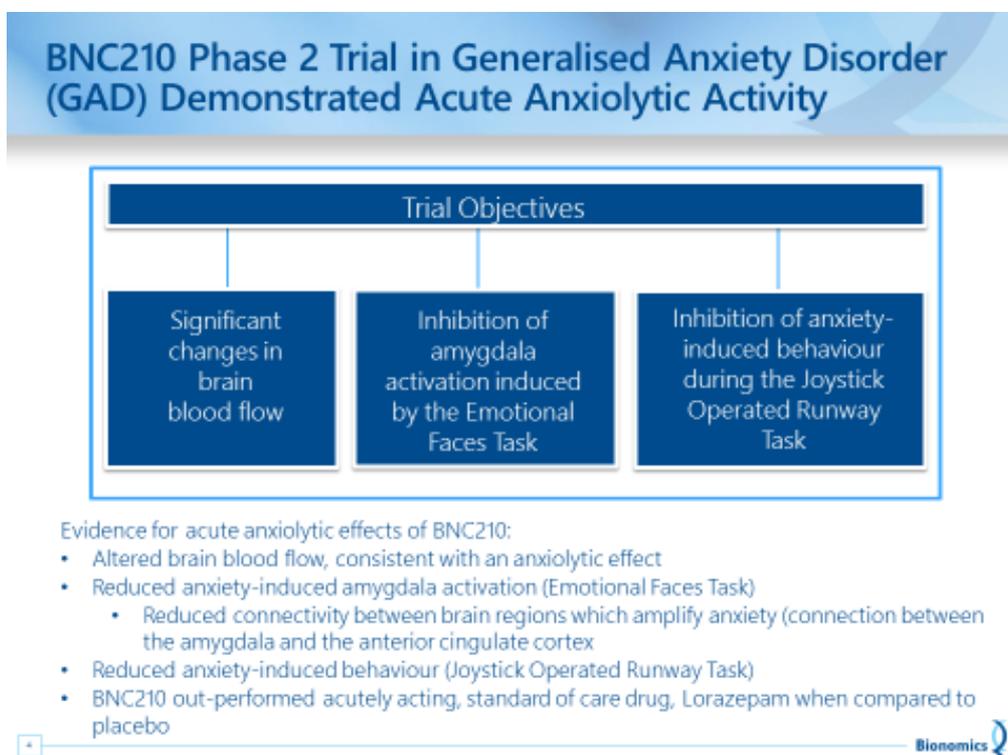
As part of our desire for continuous improvement Bionomics undertook a thorough review of its strategy and business operations with the result that some difficult decisions have been made to ensure that Bionomics remains an agile yet focussed organisation. In order to facilitate continued company success and extend our cash runway, Bionomics has closed its US operations. This decision has allowed us to focus on our essential operations in Australia and France, and resulted in

significant cost saving and increased efficiency for the Company, whilst ensuring that our core business remains strong.

The Company also underwent a strategic realignment to focus its capital on its ion channel assets. In focussing on our core strengths and strong competitive advantage in ion channel biology and drug discovery, we have recognised that our clinical stage oncology drugs BNC105 and BNC101 are no longer central to our strategy. Consequently, Bionomics is seeking to monetise both assets. A formal process for divestment, through partnering, licensing and other mechanisms, is underway.

While the depth and breadth of our pipeline has provided Bionomics with multiple shots on goal, as our clinical programs mature we must concentrate our resources on those therapeutic candidates addressing high unmet patient needs for safe and effective treatment, where there is limited competition and therefore high potential value, and which offer the greatest promise of generating returns for our shareholders. BNC210 – a first in class negative allosteric modulator of the  $\alpha 7$  nicotinic acetylcholine receptor – fits all of these criteria. In the coming year we are looking forward to results from the ongoing Phase 2 trial evaluating the effectiveness of this therapeutic candidate in treating Post-Traumatic Stress Disorder or PTSD. The Phase 2 clinical trial – known as the RESTORE trial - has been expanded as foreshadowed at last year's AGM to 192 patients across four treatment arms with 20 clinical trial sites in the US actively recruiting patients in addition to five trial sites in Australia. I am delighted to report that recruitment in the trial is on track.

## **BNC210: A NEXT GENERATION THERAPEUTIC CANDIDATE FOR THE TREATMENT OF ANXIETY, DEPRESSION AND STRESS AND TRAUMA RELATED DISORDERS**



It is worthwhile spending a few minutes on the impressive BNC210 Phase 2 trial results in Generalised Anxiety Disorder or GAD patients. As you will no doubt recall, BNC210 not only met its two co-primary endpoints in this trial, it also outperformed the current acute standard of care

Lorazepam when compared to placebo. It reduced anxiety as measured by both imaging and behavioural read-outs.

BNC210 caused significant changes to blood flow in the brain, reduced amygdala activation in response to an anxiety provoking task – the fearful faces task – and reduced anxiety-induced behaviour in the Joy Stick Operated Runway Task or JORT.

BNC210 has now achieved positive results in multiple clinical trials aimed at demonstrating its safety and tolerability, its lack of side-effects relative to currently marketed drugs for anxiety and depression, its ability to modulate its target the  $\alpha 7$  receptor and its ability to reduce the symptoms of panic attacks in addition to its usefulness in the treatment of GAD.

### BNC210: Next Generation Drug Candidate with Potential 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	✓	✓	✓	✓	✓	✓
Valium and other BZD	✗	✗	✗	✓	✓	✗
Prozac and certain other SSRIs/SNRIs	✓	✗	✓	✗	✗	✓

#### Anxiety Treatments

- Dominated by benzodiazepines
- Associated with sedation, abuse liability, tolerance and cognitive disturbances
- Not recommended for long-term treatment

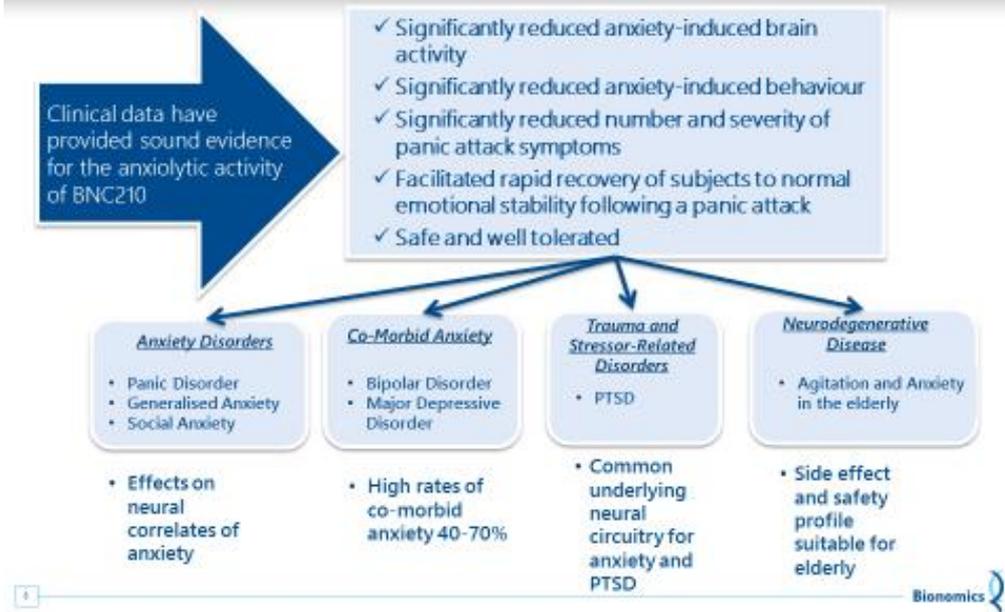
#### Depression Treatments

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

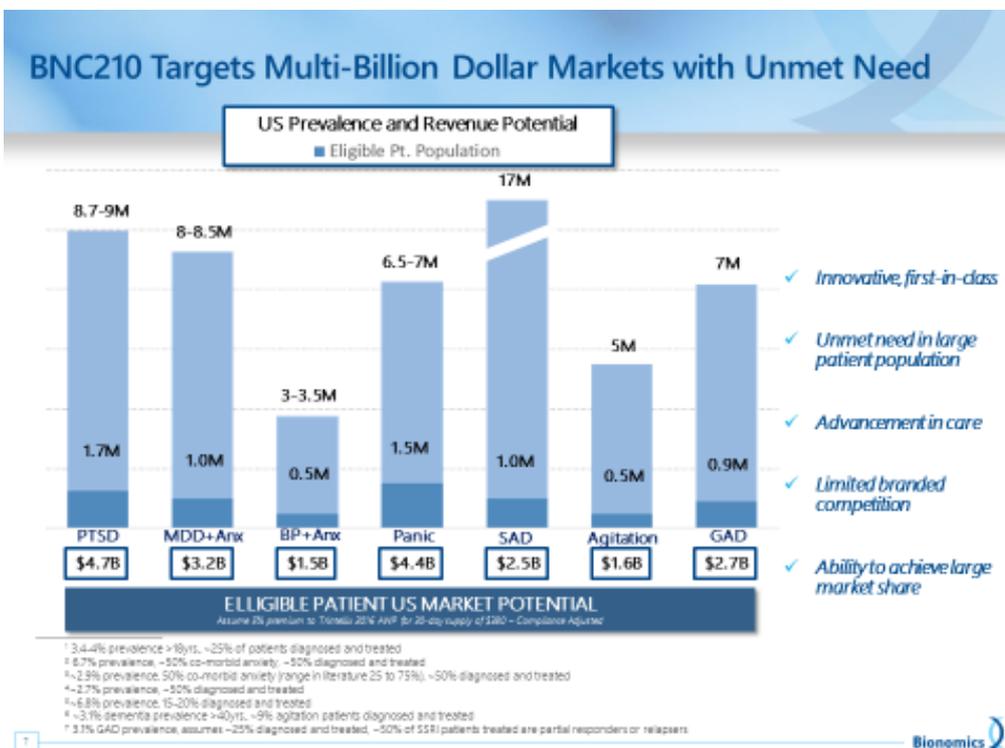
\*Based on data from preclinical studies and Phase 1 clinical trials.

We believe that BNC210 has a number of clear competitive advantages when it comes to side-effects. It is non-sedating, doesn't impair memory and current data indicates that it is non-addictive with no withdrawal syndrome. Yet BNC210 is fast acting in its anti-anxiety effects which adds to its attractiveness.

## A Next Generation Anxiolytic like BNC210 will have Broad Therapeutic Potential



Clinical data have therefore provided sound evidence for the anti-anxiety effects of BNC210. A next generation product like BNC210 could have broad therapeutic potential across a range of anxiety disorders including Panic Disorder and Social Anxiety Disorder in addition to GAD, depressive states where there is also anxiety such as major Depressive Disorder and Bipolar Disorder, trauma related disorders and potentially in neurodegenerative disorders for example in the treatment of agitation and anxiety in the elderly.



<sup>1</sup> 3.4-4% prevalence >18yrs, ~25% of patients diagnosed and treated

<sup>2</sup> 8.7% prevalence, ~50% co-morbid anxiety, ~50% diagnosed and treated

<sup>3</sup> 4.2-9% prevalence, 50% co-morbid anxiety (range in literature 25 to 75%), ~50% diagnosed and treated

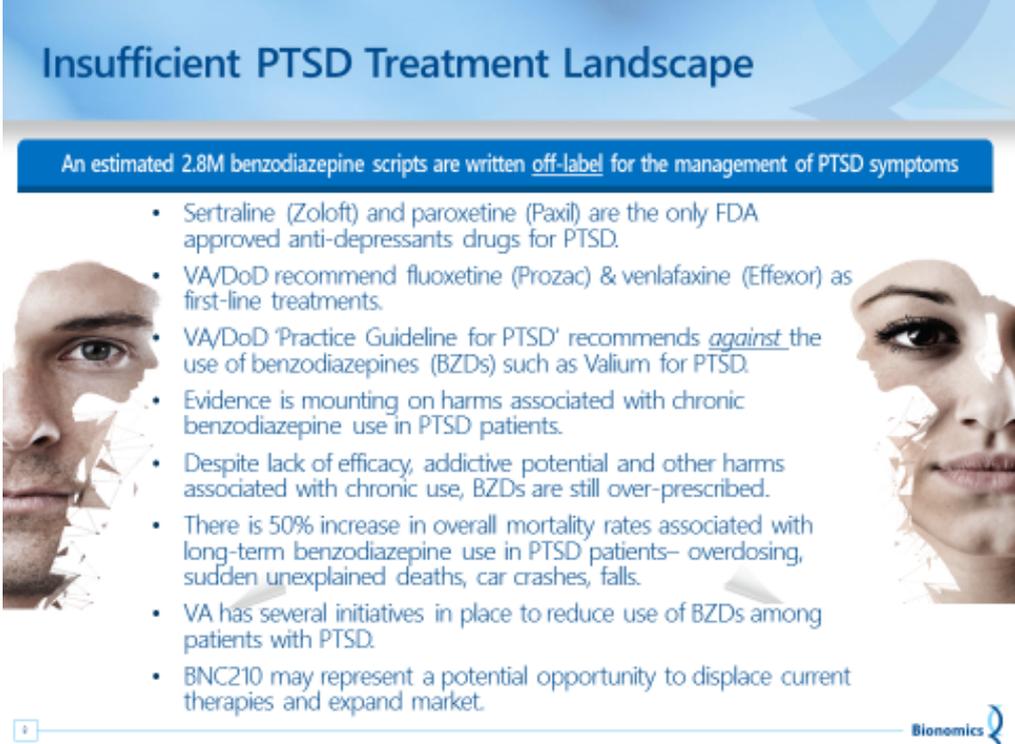
<sup>4</sup> 2-7% prevalence, ~50% diagnosed and treated

<sup>5</sup> 4-6.8% prevalence, 15-20% diagnosed and treated

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

<sup>7</sup> 3.1% GAD prevalence, assumes ~25% diagnosed and treated, ~50% of SSR patients treated are partial responders or relapsers

To assist us in the prioritisation of the path forward for BNC210 and also to better understand the US market potential, Bionomics commissioned independent market research from New York based Torrey Insights. The results indicated a much larger market opportunity for BNC210 than had previously been expected. Importantly it highlighted the market opportunity for BNC210 in PTSD as an innovative, first-in-class drug where there is an unmet need in a large patient population and where BNC210 could represent a major advancement in care.

The slide features a blue header with the title "Insufficient PTSD Treatment Landscape". Below the header is a blue box containing the text "An estimated 2.8M benzodiazepine scripts are written off-label for the management of PTSD symptoms". The main content is a bulleted list of seven points. The slide is flanked by two partial images of human faces, a man on the left and a woman on the right, both with a white, geometric, crystalline overlay on their faces. The Bionomics logo is in the bottom right corner.

## Insufficient PTSD Treatment Landscape

An estimated 2.8M benzodiazepine scripts are written off-label for the management of PTSD symptoms

- Sertraline (Zoloft) and paroxetine (Paxil) are the only FDA approved anti-depressants drugs for PTSD.
- VA/DoD recommend fluoxetine (Prozac) & venlafaxine (Effexor) as first-line treatments.
- VA/DoD 'Practice Guideline for PTSD' recommends against the use of benzodiazepines (BZDs) such as Valium for PTSD.
- Evidence is mounting on harms associated with chronic benzodiazepine use in PTSD patients.
- Despite lack of efficacy, addictive potential and other harms associated with chronic use, BZDs are still over-prescribed.
- There is 50% increase in overall mortality rates associated with long-term benzodiazepine use in PTSD patients– overdosing, sudden unexplained deaths, car crashes, falls.
- VA has several initiatives in place to reduce use of BZDs among patients with PTSD.
- BNC210 may represent a potential opportunity to displace current therapies and expand market.

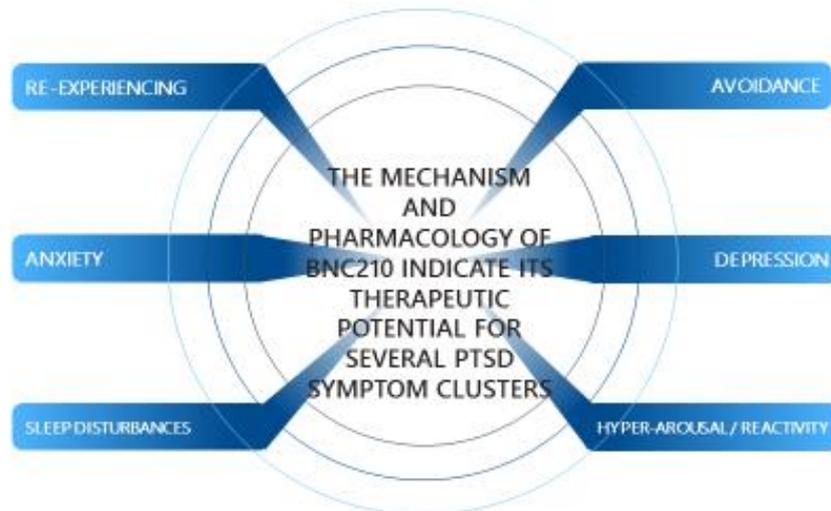
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Up to nine million Americans are estimated to suffer from PTSD and the Australian statistics are similarly sobering. Despite the high need, treatment of PTSD remains challenging and is lacking in treatment options. Only two anti-depressants are FDA approved for the treatment of PTSD with an additional two anti-depressants recommended by Veterans Affairs and the US Department of Defence.

Despite the increasingly recognised and politically sensitive harms that have been associated with the chronic use of benzodiazepines such as Valium, an estimated 2.8 million prescriptions are written off label each year in the US for the treatment of PTSD. There is a reported 50% increase in overall mortality rates associated with long-term benzodiazepine use in PTSD patients – and the efficacy of benzodiazepines in this patient population has been questioned. Despite their lack of efficacy in PTSD and their addictive properties this class of drug is still over-prescribed.

BNC210 may therefore represent a potential opportunity to displace current therapies and expand the already large PTSD market with a safe, non-addictive and effective therapy.

## BNC210 May Impact Multiple PTSD Symptoms



1

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What are our reasons to believe that BNC210 might be an effective treatment for PTSD? PTSD is a complex disorder with multiple symptom clusters. It can develop in some people who have been through a traumatic event such as combat, a natural disaster, a car accident or sexual assault, which threatened their life or safety or that of others around them. People who suffer from PTSD continue to experience memories and feelings of intense fear, helplessness or horror long after the trauma was experienced.

We believe that the way that BNC210 works – its mechanism of action and pharmacology – supports its potential effectiveness in treating several PTSD symptom clusters. These symptom clusters include anxiety, depression, re-experiencing and sleep disturbances.

Our market research indicates that clinicians find anxiety to be a persistent and difficult to treat symptom in PTSD patients. If you can reduce anxiety you may reduce its sleep disturbances. In addition to their anxiety PTSD, patients suffer from panic attacks as they re-experience the fear associated with their trauma. They also suffer from high rates of depression and we have preclinical evidence that BNC210 has anti-depressant activity as well as anti-anxiety effects.

In June this year Bionomics was invited to participate in and to present its' work at the *PTSD State of the Science Summit* hosted by the US Army Medical Research and Materiel Command. This invitation highlights Bionomics' position as a key subject matter expert in the development of more effective drug therapies for the treatment of PTSD.

**Phase 2 Trial in Post Traumatic Stress Disorder (PTSD) – Ongoing in Australia and US, Data Anticipated 2HCY18**



<b>Subjects</b>	<ul style="list-style-type: none"> <li>• 192 PTSD Patients</li> </ul>
<b>Protocol</b>	<ul style="list-style-type: none"> <li>• Double-blind, placebo controlled, randomized, multi-centre</li> <li>• 4 arms, 1 placebo, 3 BNC210 dose level treatment arms</li> <li>• 12 weeks, twice daily oral treatment</li> </ul>
<b>Primary Objective</b>	<ul style="list-style-type: none"> <li>• To determine whether BNC210 causes a decrease in symptoms of PTSD as measured by CAPS-5</li> </ul>
<b>Secondary &amp; Exploratory Endpoints</b>	<ul style="list-style-type: none"> <li>• To determine the effects of BNC210 on anxiety (HAM-A), depression (MADRS) and cognitive functions</li> <li>• Correlation of genotype and imaging pharmacodynamics markers</li> </ul>

*PTSD is a risk factor for depression, alcohol or substance abuse, absenteeism/unemployment, homelessness, violent acts, suicidal thoughts and suicide*

10



This next slide indicates some of the details of our robust Phase 2 clinical trial of BNC210 in patients with PTSD. The trial is actively recruiting in the US and Australia with recruitment on target. It is noteworthy that Bionomics now has two separate BNC210 Investigational New Drug (IND) applications accepted by the US Food and Drug Administration (FDA) and that one of these is specifically directed to the treatment of PTSD.

PTSD, relative to some other potential applications, is considered to be a faster path to market, one which may be able to take advantage of the FDA's Breakthrough Designation after completion of the current trial. This designation would be extremely valuable and highly attractive from a licensing perspective.

**POST TRAUMATIC STRESS DISORDER**

**IT BEGINS WITH A STORY...**

A story that is unique to you. One that has shaped your world in ways that people may not understand. It's a story full of twists and turns, especially if current treatments don't provide the relief you need. But every story has chapters – each building on the last. We may be able to help you write those next chapters.

Ask your doctor about the RESTORE Study, a potential new approach to managing PTSD. It is evaluating an experimental medication compared to placebo to see if it may help to reduce the symptoms of PTSD.

**Don't let PTSD have the last word. Speak with us today.**

**restore**  
A research study in PTSD

**restore**  
Bionomics

I would like to share with you some of the advertising for the PTSD trial across multiple platforms that is assisting our recruitment efforts. It includes leaflets such as those shown here

## Social Media and Trial Specific Websites for Global Recruitment

Australian Facebook Advertising

US StudyKik Advertising

Australian Clinical Trial Website

Don't let PTSD have the last word.

POST-TRAUMATIC STRESS DISORDER  
IT BEGINS WITH A STORY...

San Antonio, TX  
N/A  
(210) 941-3391

POST-TRAUMATIC STRESS DISORDER  
IT BEGINS WITH A STORY...

restore  
Bionomics

It also includes social media sites such as the Australian Facebook site, dedicated clinical trial web sites and the US specific StudyKIK advertising. Top line data from the trial is anticipated in CY2018. I look forward to updating you when the new data are available.

## STRATEGIC COLLABORATION WITH MERCK & CO (MSD)

## Clinical Progression of Cognition Drug Candidate in Merck Collaboration Provides Technical Validation

Partnership with Merck & Co in cognition 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

Validates ionX and MultiCore drug discovery platforms

Value creation through strategic partnering business model

Future success based revenue streams & royalties

MERCK PARTNERSHIP

Bionomics

Our ionX ion channel and MultiCore chemistry platforms enable us to accelerate the discovery of novel therapeutic candidates that have the potential to substantially improve outcomes for many patients.

This is evident with the Phase 2 success of BNC210 and the strength of these two platforms has also been recognised by our collaborator, MSD. Earlier this year we were very pleased to announce the attainment, by MSD, of the first clinical milestone in our collaboration to develop novel candidates for cognitive dysfunction associated with Alzheimer's disease.

The first administration of a candidate therapy in a clinical trial resulted in a US\$10 million milestone payment to Bionomics by MSD. As a reminder Bionomics is eligible to receive up to US\$506 million from MSD comprised of the upfront payment, research payments and milestones under our agreement. MSD is responsible for all investment into the program. Our agreement also includes eventual undisclosed royalties on product sales. We hope that this milestone payment will be the first of many!

MSD has been an exemplary partner for Bionomics – a partner that has exceeded our expectations – as both companies have moved forward with a single focus and a shared commitment.



Aside from its 4.5% equity stake in Bionomics, MSD supports our collaboration through the annual Bionomics – MSD Frontiers of Neuroscience Symposium. The 5<sup>th</sup> Symposium was held here in Adelaide last month as a satellite event of the annual AusBiotech industry association national conference. The Symposium has grown in both size and stature and it has become a feature of the neuroscience agenda in Australia. It attracts a high calibre audience from academia with its stellar list of speakers with this year's speakers from Harvard Medical School, Kings College London, MSD, Celgene and Adelaide University.

I will now briefly report on some of this year's developments in our clinical stage oncology pipeline.

## BNC101: First-In-Class Therapeutic Candidate for the Treatment of Colon Cancer and other Solid Tumour Types

- BNC101 is a humanised antibody that seeks out and inhibits the growth cancer stem cells
- It aims to prevent or delay tumour recurrence by inhibiting the activity of LRG5, a marker that is highly expressed in metastatic colon cancer, pancreatic cancer and other solid tumour types
- Safe and well tolerated in patients with metastatic colon cancer
- Engages LGR5 within patients tumours and induces changes consistent with its mechanism of action and data indicating that BNC101 increases the cancer fighting immune response within solid tumours

*Data supports both continued development and our ongoing partnering activities*

The 8 major markets for colorectal cancer treatments is estimated to reach US\$11 billion by 2025 (GlobalData)

The global pancreatic cancer treatment market estimated to reach US\$4.2B in 2025 (Grand View Research, Inc)

**Bionomics**

### BNC101

Despite promising data from the Phase 1 clinical trial Bionomics has initiated a formal process of partnering BNC101 to focus our resources on BNC210 and our ion channel core. This year's excellent progress in the BNC101 development program was marked by completion of patient enrolment in the clinical trial together and important, key data to support further development of BNC101 as well as our ongoing monetisation process.

## BNC105: Novel Vascular Disrupting Agent (VDA) for Cancer Treatment

- Multiple modes of action:
  - disrupts the blood vessels that nourish solid tumours.
  - Direct anti-cancer action extends potential use to blood cancers
  - New data on the effects of BNC105 on tumour immunity has highlighted the strong, synergistic anti-tumour activity of BNC105 when combined with checkpoint inhibitors

### Investigator Initiated Clinical Trials

Peter MacCallum Cancer Centre and Olivia Newton-John Cancer Wellness & Research Centre awarded \$2.25M grant to fund a BNC105 trial in patients with advanced melanoma in combination with Pembrolizumab (Keytruda)

Norris Cotton Cancer Centre, New Hampshire, USA evaluating BNC105 as both a monotherapy and in combination with ibrutinib in patients with relapsed Chronic Lymphocytic Leukemia (CLL)

Novartis approved funding for a biomarker study in BNC105 at the University of Alabama Comprehensive Cancer Center for patients with metastatic renal cell cancer

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## BNC105

As with BNC101, BNC105 is now in a formal partnering process. This process has been helped by a number of new data sets that became available throughout 2017, including positive data supporting the use of BNC105 in combination with a relatively new class of anti-cancer agent, the checkpoint inhibitors such as MSD's Keytruda and also exciting new data supporting the use of BNC105 for the treatment of blood cancers. This very focused work has been funded primarily through non-dilutive financing and is extremely supportive of both the ongoing partnering process and the continued development of BNC105.

Bionomics strongly believes in the therapeutic potential of both BNC101 and BNC105 however the level of investment required for both assets to reach the next value inflection point is significant in terms of financial and human resources. Divestment extends our cash runway and allows us to focus on generating value from BNC210 and our ion channel core.

### Strong Financial Position – FY17 Results

- Cash at 30 June 2017 A\$42.87M
- FY17 revenue and other income A\$28.25M
- Operating loss after tax A\$6.75M (30 June 2017)
- US\$10M milestone payment from MSD
- R&D tax incentive refund of A\$8M received in October 2016
- After tax loss reflects investment in development of BNC210 and BNC101

**We are well funded to complete BNC210 PTSD clinical trial**



## FINANCIALS

I am pleased to report that Bionomics is in a very strong position to complete the BNC210 PTSD clinical trial with \$42.87 million in cash and cash equivalents at the end of June 2017, which includes the milestone payment of US\$10 million from MSD plus the R&D tax incentive refund of \$8m received in October 2016.

Revenue and other income for the FY17 financial year was more than \$28.2 million.

The after tax loss of \$6.8 million reflected investment in the clinical development of BNC210 and BNC101 and continued research on our other pipeline programs.

## Outlook

- Continue recruitment in Phase 2 trial of BNC210 in PTSD patients
  - Data expected in 2H CY18
  - Explore partnership options and pathways for broader development of BNC210
- Work closely with MSD, enabling MSD to reach milestones and demonstrate Bionomics' strength in drug discovery
- Add additional strategic partnerships
- Monetise "off strategy" clinical stage oncology assets BNC105 and BNC101



## OUTLOOK

2017 has been an excellent year for Bionomics. We are well positioned to progress the development of BNC210 for the treatment of PTSD in the current Phase 2 trial. Bionomics is also in an excellent position to continue to support MSD to reach milestones and to provide further demonstration of the Company's strength in drug discovery and development.

We are working diligently on additional strategic partnership opportunities, including the monetisation of BNC101 and BNC105, to achieve our corporate objectives.

I believe that through the decisions taken in 2017, our renewed focus on our ion channel core, the potential for BNC210 to deliver value and the strength of our collaboration with MSD we have laid a solid foundation for success.

I thank our Board and Management and our entire team for their support and hard work during a very productive year. Thank you to our shareholders for your support during 2017 and I look forward to sharing news of future progress with you all as we continue to implement our strategy and demonstrate both our agility and our focus in the coming 12 months.

Thank You for your Continued Support in 2017



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**About Bionomics Limited**

Bionomics (ASX: BNO) is a global, clinical stage biopharmaceutical company leveraging its proprietary platform technologies to discover and develop a deep pipeline of best in class, novel drug candidates focused on the treatment of serious central nervous system disorders and on the treatment of cancer. Bionomics' lead drug candidate BNC210, currently in Phase 2 for the treatment of generalized anxiety disorder and for post-traumatic stress disorder, is a novel, proprietary negative allosteric modulator of the alpha-7 ( $\alpha 7$ ) nicotinic acetylcholine receptor. The Company is also developing BNC101, its lead humanised monoclonal antibody targeting a key receptor on cancer stem cells that is overexpressed in metastatic colorectal cancer, metastatic pancreatic cancer and many other solid tumours; BNC101 entered clinical trials in the first quarter of 2016. Bionomics has a strategic partnership with Merck & Co., Inc (known as MSD outside the United States and Canada).

[www.bionomics.com.au](http://www.bionomics.com.au)

**Factors Affecting Future Performance**

This announcement contains "forward-looking" statements within the meaning of the United States' Private Securities Litigation Reform Act of 1995. Any statements contained in this announcement that relate to prospective events or developments, including, without limitation, statements made regarding Bionomics' drug candidates (including BNC210 and BNC101), its licensing agreements 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.