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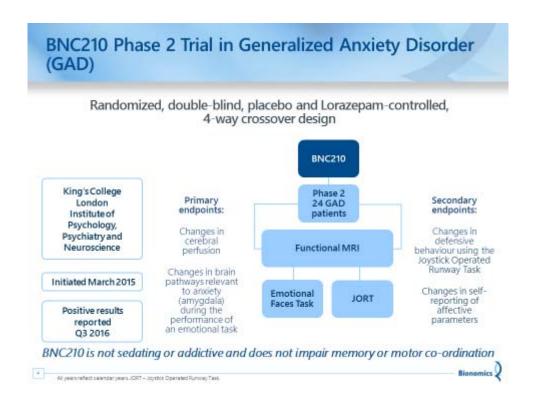
ASX ANNOUNCEMENT 8 November 2016

# CEO & MANAGERING DIRECTOR'S REPORT TO SHAREHOLDERS

I am pleased to report that Bionomics has taken some great strides this year in our long term goal of developing better treatments for cancer and disorders of the central nervous system.

Our great strength is the depth and breadth of our drug development pipeline which gives us multiple shots on goal.

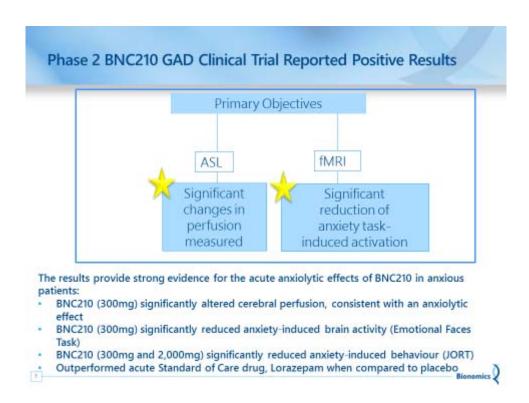
I firstly want to spend some time discussing in some depth the recent Phase 2 clinical trial results achieved by our drug candidate BNC210.



As you are no doubt aware, BNC210 not only met its two primary endpoints in treating Generalized Anxiety Disorder (GAD), it also outperformed the current standard of care Lorazepam when compared to placebo in reducing anxiety as measured by both imaging and behavioural read-outs.

The results of the trial are particularly important when you consider that BNC210 has not produced any signs of sedation, memory impairment, addiction or loss of motor co-ordination, side effects which can occur with the use of benzodiazepines such as Lorazepam.

This was a double-blinded, placebo-controlled and Lorazepam-controlled, 4-way cross-over phase 2 trial in 24 patients with untreated GAD. This is a very powerful trial design because each patient is their own control, receiving each of the different treatments under evaluation. It is also an efficient trial design because it considerably reduces the number of patients needed to achieve statistical significance.



It is also worth noting that these trial results showed that BNC210 caused significant changes to cerebral perfusion and reduced amygdala activation in response to fearful faces – both measures of anti-anxiety activity.

BNC210 treatment significantly reduced anxiety related defensive behaviour in the Joystick Operated Runway Task, again out-performing Lorazepam relative to placebo.

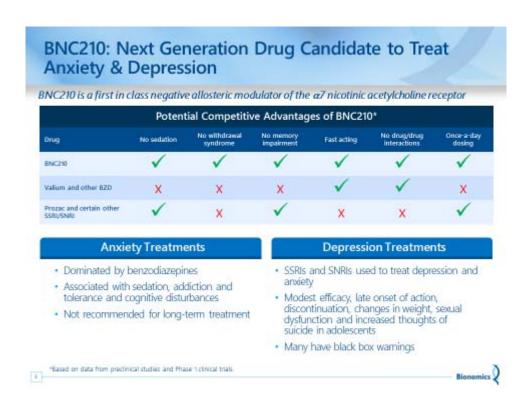
This means that BNC210 has now shown good results in both behavioural and neuroimaging tests – which adds another layer of confidence to these trial results.

An interesting observation from the trial is that the lower dose of BNC210 performed better than the higher dose of BNC210. In other words - more BNC210 is not necessarily better. This finding might be mirroring some of our observations from preclinical studies where lower doses of BNC210 were highly effective is models of stress. It is certainly worthy of further investigation.



A Channel 7 news story from 7 November 2016 can be viewed by placing the following in your web browser https://au.news.yahoo.com/video/watch/33130838/new-melbourne-drug-could-take-edge-off-anxiety-sufferers/#page1

Bionomics received considerable press coverage following the release of the Phase 2 GAD clinical trial results. Our PR advisors are continuing their outreach to secure additional coverage for this story and yesterday whilst at our Symposium Channel 7 interviewed Professor Young, with the story airing last night.

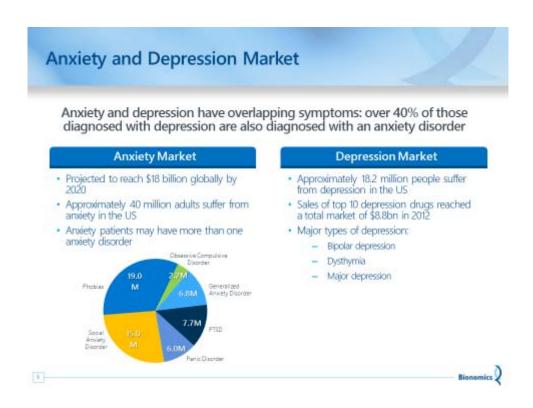


BNC210 is a novel, first in class negative allosteric modulator of the *a*7 nicotinic acetylcholine receptor.

It has so far been shown to be safe and well tolerated, non-sedating with no adverse effects on cognition, motor co-ordination, emotional stability or potential for addiction. These features represent part of the compelling advantage that BNC210 has over current medications for anxiety disorders – the benzodiazepines such as Valium and Iorazepam and the anti-depressants such Prozac and Effexor.

As our principal investigator Professor Allan Young, director of the Centre for Affective Disorders at King's College in London said after seeing the latest phase 2 results, BNC210 heralds a potential paradigm shift in the treatment of anxiety disorders.

These excellent results are obviously not the end of the drug development pathway but they reduce risk and enhance our confidence in BNC210. The results have strengthened the licensing package and significantly boosted partnering prospects for this drug candidate.



In this context, it is worth remembering the size of the anxiety disorders market, with 40 million adults in the United States sufferers, some 6.8 million of them with chronic GAD.

Every year in Australia, about 14 per cent of the population or one in seven people experience an anxiety disorder, with 2.7 per cent experiencing GAD.

Nearly 6 per cent of the Australian population will suffer from GAD in their lifetime.

The anxiety disorders market is projected to reach US\$18.2 billion by 2020, which highlights the significant market opportunity for BNC210 and the potential to make a positive contribution to expanding treatment options in the future.

The market for anti-depressant drugs such as Prozac and Effexor currently sell around US\$5-7 billion annually.

There are also under served parts of this market for disorders such as Post-Traumatic Stress Disorder, which is very poorly addressed by current medications.



PTSD is unfortunately very common and causes a significant economic and societal burden. There is a high prevalence of PTSD worldwide and it is a condition receiving greater attention. Patients are not well served with current medications and there is high off-label usage with unproven or contraindicated treatments. BNC210 may represent a potential opportunity to displace current therapies and expand market.

Only two drugs, the antidepressants paroxetine (such as Paxil) and sertraline (such as Zoloft) are approved for the treatment of PTSD but they have not been shown to address the full range of PTSD symptoms and complete remission of symptoms is rare. There is some evidence that they may be of limited benefit. The prescribing of benzodiazepines for people with PTSD is actively being discouraged in the US because these drugs are associated with a higher risk of unexplained death.

# Phase 2 Trial in Post Traumatic Stress Disorder (PTSD) Initiated in **Q2 2016 - Ongoing restore** Subjects 160 PTSD Patients Double-blind, placebo controlled, multi-center 1 week placebo run-in, 12 week treatment phase (placebo or Protocol BNC210) 2 arms, 1:1 randomization To determine whether BNC210 causes a decrease in symptoms of Primary Objective PTSD as measured by CAPS-5 To determine the effects of BNC210 on anxiety (HAM-A), Secondary & depression (MADRS) and cognitive functions Exploratory **Endpoints** Correlation of genotype and imaging pharmacodynamics markers PTSD is a risk factor for depression, alcohol or substance abuse, absenteeism/unemployment, homelessness, violent acts, suicidal thoughts and suicide

We are currently recruiting for a phase 2 clinical trial which is evaluating the effectiveness of BNC210 in treating PTSD and if we achieve good results in this trial, it would significantly expand the potential applications for the drug.

With the results of the GAD trial now available – and with the suggestion that lower doses of BNC210 may be more effective –Bionomics has been evaluating an expansion of the current PTSD trial to ensure that a broader range of BNC210 doses are evaluated. To accommodate an increase in the number of patients to be recruited without an extended timeline to data read-out in this trial we are also considering bringing US sites into the trial. We want to maintain the robustness of the trial but we do not want recruitment to lag and risk losing valuable time to commercialisation. Over the next few months we will update on trial design and our guidance on the anticipated timeline to complete recruitment and for data read-out.

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

Current estimates are that eight million Americans or 3.5 per cent of the population suffer PTSD in any year and that 12 per cent of Australians will experience PTSD in their lifetimes.

The innovation within our drug discovery processes have consistently produced drug candidates that are designed to address unmet needs in areas with large market opportunities where there exists "blockbuster" sales potential.

# Merck Partnerships: Technical Validation

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

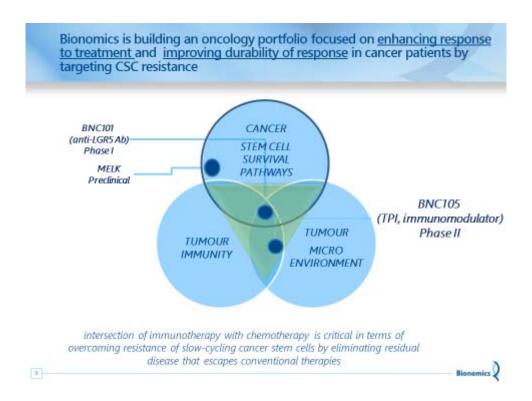


For example, our ion channel platform ionX and our MultiCore chemistry platforms combined have enabled us to accelerate the discovery of novel drug candidates that have the potential to significantly improve the lives of patients. This is evident with our recent BNC210 Phase 2 success. It has also been recognised by our strategic collaborator, Merck & Co., Inc. Kenilworth N.J., USA (known as MSD outside the US and Canada) during our cognition/Alzheimer's disease collaboration. Our relationship with MSD has been extremely beneficial to Bionomics and I am pleased to report that we made significant progress in our cognition/Alzheimer's disease collaboration, meeting important milestones on the path to a first clinical trial. We anticipate that MSD will initiate the first clinical trial, thereby triggering a significant milestone payment to Bionomics under our 2014 License and Research Collaboration Agreement. As a reminder that agreement could see Bionomics receive up to US\$506 million in upfront, research and milestone payments in addition to royalties on net sales of licensed products. We hope that this first milestone will be the first of many!

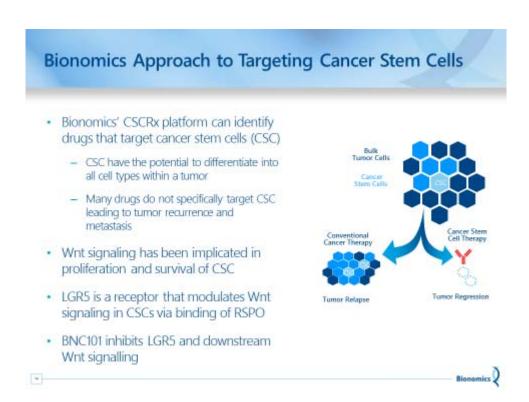
MSD has been an exemplary partner for Bionomics – a partner that has exceeded our expectations – as both companies have moved forward with a single focus.

The progress in the collaboration demonstrates that Bionomics is not only producing world class drug candidates but is progressing them with a major biopharmaceutical collaborator which has also become a Bionomics shareholder, investing US\$9 million in October 2015.

Now I will move on to report on some of this year's exciting developments in our oncology pipeline, where Bionomics is building an oncology portfolio focused on enhancing response to treatment and improving durability of response in cancer patients by targeting Cancer Stem Cell resistance.



# **BNC101**



Our cancer stem cell targeted treatment for solid tumours, BNC101, reached a significant milestone during the year with the acceptance of an investigational new drug (IND) application by the US Food & Drug Administration (FDA).

That allowed for the start of an open label Phase 1 trial to demonstrate that BNC101 is safe and well tolerated and is able to modulate the activity of its target LGR5 in colon cancer patients.

Cancer stem cells are the seeds of cancer. They are responsible for cancer initiation, recurrence and spread and they are very difficult to kill by chemotherapy and radiation therapy. Specifically targeted treatments such as BNC101 are desperately needed.

BNC101 is a first in class drug candidate which inhibits a process promoting cancer stem cell survival and proliferation called Wnt signaling. BNC101 reflects our philosophy to develop 'first in class' drugs – in this case, a promising therapeutic antibody against an established cancer stem cell target. With BNC101 we are aiming not just to stop the progression of cancer, but to prevent tumours from recurring.

Once the Phase 2 recommended dose is determined, it is intended that the trial will then move to the next stage of evaluating the combination of BNC101 and chemotherapy.



Colorectal cancer is the second most prevalent cancer type but overall survival lags behind other high incidence cancers with the five year survival rate for metastatic disease just 12 per cent. Whilst our initial focus in the development of BNC101 is on colon cancer, BNC101 has the potential to target other LGR5 positive solid tumour types including pancreatic, breast lung and liver cancer.

## **BNC105**

Another drug in our oncology pipeline is the vascular disrupting agent BNC105. BNC105 has now demonstrated multiple modes of action.

# BNC105 exerts direct anti-cancer efficacy through multiple modes of action in both solid and blood borne tumors BNC105 induced tumour vasculature destruction, tumour hypoxia and necrosis leads to changes in the tumour microenvironment and the surrounding immune 'landscape' Proposed mechanism of anti-tu induced by BNC105 Re-awakening the immune system contributes to the changes seen in the tumor microenvironment via: · an efflux of immune presenting tumour antigens via tumour disruption/necrosis · enhanced maturation of dendritic cells into antigen presenting cells · release of pro and antiinflammatory cytokines Tubulin polymerization inhibitors (TPI) induce functional maturation of dendriticaells (Mullar, Oncolmmunalogy 2014) TPIs program dendritic calls toward enhanced enti-turnor immunity (Martin, Canper Immunology Immunotherapy 2014)

New clinical and pre-clinical data on the effects of BNC105 on tumour immunity has highlighted the strong, synergistic anti-tumour activity of BNC105 when combined with checkpoint inhibitors.

Re-awakening the immune system contributes to the changes seen in the tumour microenvironment via:

- an efflux of immune presenting tumour antigens via tumour disruption/necrosis
- enhanced maturation of dendritic cells into antigen presenting cells
- release of pro and anti-inflammatory cytokines

Bionomics continues to work towards partnership opportunities for BNC105, with the ability to prime tumours for a more robust immune response opening up new avenues for development in combination with immuno-oncology drugs such as Opdivo, Keytruda and Yervoy.

Bionomics is collaborating with the Olivia Newton-John Cancer Research Institute to enable the comprehensive evaluation of BNC105 effects on immune cell subsets within tumours.

# **BNC105**: New Developments

- Investigator-initiated clinical trial evaluating BNC105 monotherapy and in combination with ibrutinib in patients with relapsed Chronic Lymphocytic Leukemia (CLL)
  - Expected to be initiated in early 2017 at the Norris Cotton Cancer Centre, New Hampshire, USA
  - Ibrutinib (Imbruvica, marketed by AbbVie, predicted to have sales of US\$5 billion in 2020)
- Novartis has approved funding for biomarker study to evaluate the ability of tumour gene expression analysis to predict the activity of BNC105 in patients with metastatic renal cell cancer.
  - Study will be conducted by Dr Guru Sonpavde at the University of Alabama Comprehensive Cancer Centre.



In a new development, an investigator-initiated study evaluating BNC105 monotherapy and in combination with ibrutinib (Imbruvica, marketed by AbbVie and predicted to have sales of US\$5 billion in 2020) in patients with relapsed Chronic Lymphocytic Leukemia (CLL) at the Norris Cotton Cancer Centre, New Hampshire, USA is proceeding. After scientific and institutional review board assessment and approval, the study is expected to be initiated in early 2017.

In a further new development Novartis has approved funding for a retrospective biomarker study to evaluate the ability of tumour gene expression analysis to predict the activity of BNC105 in patients with metastatic renal cell cancer. The study will be conducted by Dr Guru Sonpavde at the University of Alabama Comprehensive Cancer Centre. The study will follow-up biomarker data from Bionomics Phase 2 clinical trial in renal cancer trial.

## **Financials**

Bionomics is in a very strong position to execute its clinical and drug discovery programs with \$39.015 million in cash and cash equivalents at the end of September 2016 plus the R&D tax incentive refund of \$8m received in October 2016.

Revenue through the financial year was more than \$21.7 million and included payments under our agreement with MSD and contract services provided by our subsidiaries Neurofit SAS and Prestwick Chemicals SAS.

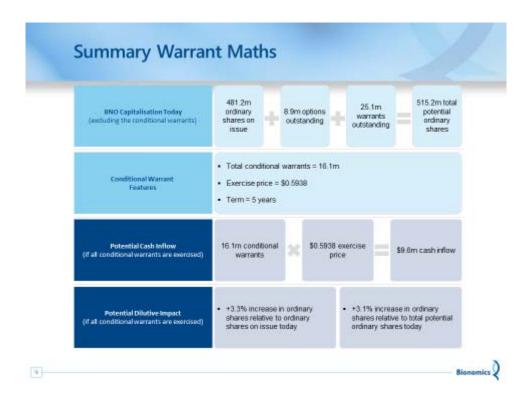
It also included US\$736,815 as our share of a US\$15 million upfront payment of a licensing agreement between MSD and the Australian Cooperative Research Centre for Cancer Therapeutics. Bionomics may benefit from future milestone and royalty payments from this program.

The after tax loss of \$16.6 million reflected investment in the clinical development of BNC210 and BNC101 and research on our other pipeline programs.

# **December 2015 Capital Raising**

As you know, in December 2015 Bionomics undertook a share placement to a set of new US based investors. As part of the placement, it was agreed that the new investors would receive warrants, although part of the warrant issuance would be, at least from a timing perspective, subject to shareholder approval. This approval was not forthcoming, and we recognise that shareholders clearly signalled their perspective on the situation as at the time of the vote.

While we still are required to either issue the remaining warrants or cash settle the obligation by 15 December 2016, Bionomics is firmly committed to acting in shareholders' best interests within the contractual framework.



Under the warrant alternative, Bionomics would issue 16.1m warrants with a strike price of c. \$0.59. The warrants would have a five term, and if exercised the Company would receive \$9.6m in cash and the new shares would account for 3.1% of total issued shares plus existing options and warrants outstanding.

Under the cash settlement alternative, which cannot be definitively calculated until next month, Bionomics would have to pay the higher of the value of the warrants in December 2015 – which is \$4.3m – or the value of the warrants on the same date in December 2016. The valuation methodology is based upon the Black Scholes formula.

At the current share price, all other things being equal, issuing the warrants would be less dilutive to shareholder value per share than returning the cash. For this reason, among others, as the Chairman has indicated, Bionomics currently believes it is likely to be in the best interests of shareholders to issue the warrants when the time comes. The funds thus retained will be deployed to build on the success of our BNC210 program.



Having said that, it is important to emphasise that no formal decision has been made. The Board has developed a framework for its decision making which takes into account a range of factors, including strategic flexibility.

We will maintain optionality and ensure the outcome, whether cash settlement or issuance, is in the best interest of all shareholders.

While this is a matter that will be determined by the Board, we do welcome and encourage any shareholder feedback regarding the two alternatives. Investor views will certainly be part of the range of qualitative and quantitative factors, which the Board and management will consider carefully.

## **Outlook**

# Outlook

- Results from Phase 1 BNC101 trial in patients with colon cancer in Q2,2017 and further data in Q3, 2017.
  - Recommended Phase 2 dose level
  - Data from expanded patient cohort
- Continue to recruit patients into the ongoing clinical trial of BNC210 in patients with PTSD.
  - Whilst we will aim to complete recruitment into the expanded trial by the end of 2017 we will provide guidance once our plans are confirmed with respect to dosing and overseas trial sites.
- Explore both partnership options and pathways for broader Phase 2 development of BNC210.
- Work closely with MSD, enabling MSD to reach milestones and demonstrate Bionomics strength in drug discovery.
- · Add to our strategic partnerships



Bionomics is eagerly awaiting clinical trial results in the coming year with first data expected from the BNC101 trial in patients with colon cancer in Q2,2017 and further data in Q3, 2017. We will continue to recruit patients into the ongoing clinical trial of BNC210 in patients with PTSD. Whilst we will aim to complete recruitment into the expanded trial by the end of 2017 we will provide guidance once our plans are confirmed with respect to dosing and overseas trial sites.

In parallel we will explore partnership opportunities for BNC210 whilst continuing to evaluate broader Phase 2 development.

We will also continue to work closely with MSD, enabling MSD to reach milestones and demonstrate the company's strength in drug discovery and development.

We are also working on additional strategic partnership opportunities.



I thank our Board and Management and our devoted staff for their support and hard work during a very successful year. Thank you to our shareholders for your support during 2016 and I look forward to sharing news of future progress with you all.

Dr Deborah Rathjen, CEO & Managing Director

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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 (α7) nicotinic acetylcholine receptor. The Company is also developing BNC101, its lead humanized 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 strategic partnerships with Merck & Co., Inc (known as MSD outside the United States and Canada) in pain and cognition.

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.

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 announcement.