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# BNC105 CANCER CLINICAL TRIALS REACH KEY MILESTONES CLINICAL PROGRAM TO BE EXPANDED

- Data from renal cancer trial supports progression of the trial:
  - Combination of Afinitor and BNC105 safe and well tolerated
  - Patient recruitment continuing
  - Strongly supported by preclinical data
- Mesothelioma interim analysis of 24 patients indicates:
  - o One patient with an objective response, remains on BNC105 treatment
  - o At least 5 patients with stable disease as measured by RECIST
  - o Enrolment into the trial will be discontinued
  - Further development in combination treatments with Alimta and cisplatin being considered through evaluation in preclinical models
- Ovarian cancer trial planned:
  - Randomised Phase I/II trial of BNC105 in combination with carboplatin and gemcitabine
  - Preclinical data support use of BNC105 in combination with platinum (cisplatin; carboplatin) based therapeutic regimens
  - Ovarian cancer is the fifth leading cause of cancer-related death among women.
- **3 August 2011; Adelaide, Australia:** Bionomics Limited (ASX: BNO; ADR: BMICY) today provided an update on the status of ongoing clinical trials of BNC105, its proprietary vascular disrupting agent (VDA) for the treatment of solid tumours.

## Clinical development strategy

The clinical development of BNC105 has undertaken a two-pronged approach involving the use of BNC105 either, in combination with other established methods of cancer treatment, or as a monotherapy.

The key objective of this approach is to consolidate the safety profile, obtain early evidence of efficacy and delineate the development path.

The first approach is evident in the clinical trial which is in progress in renal cell carcinoma where BNC105 is combined with the targeted therapy Afinitor. This approach is also seen in the planned clinical trial of BNC105 in women with ovarian cancer. The ovarian cancer trial will combine the use of BNC105 with cisplatin and gemcitabine. The second approach, evaluation as a monotherapy or single agent, was adopted in the mesothelioma trial.

Bionomics' CEO and Managing Director Dr Deborah Rathjen commented, "In our clinical development strategy for BNC105, Bionomics has tried to learn as much as possible about the effects of BNC105 in cancer patients in the most efficient way. Our two pronged strategy has helped enormously in this regard. The mesothelioma trial in particular has enabled the Company to quickly establish the safety and tolerability of BNC105 in a large patient group with one patient having a sustained, durable anti-tumour response to BNC105 and at least five other patients showing stable disease".

"The current renal cancer trial combines BNC105 with a drug which has broader application in the treatment of different cancer types beyond renal. It is pleasing that BNC105 in combination with Afinitor is safe and well tolerated with individual patients receiving at least 12 cycles of treatment."

"Our strategy has successfully defined the future development path for BNC105 in combination with established chemotherapy regimens and provided signals of efficacy."

Most cancer therapies are used in combination rather than as single agents which broadens both the potential application to different tumour types and the commercial potential of a new drug.

### US metastatic renal cell carcinoma (RCC) trial

Bionomics is conducting a US based multi-centre clinical trial of BNC105 in combination with Afinitor in patients with metastatic RCC. Afinitor is an mTOR inhibitor, which is used as a second line treatment after patients have failed first line therapy with Tyrosine Kinase Inhibitors (TKI). Afinitor, which was approved by the FDA in 2009, had sales of US\$192 million in the six months to 30 June 2011.

The BNC105 clinical trial design has two stages. The first stage involves dose escalation of BNC105 to assess the safety of combining BNC105 and Afinitor. The second stage of the trial is an efficacy evaluation where the therapeutic benefit of the combination is compared to the therapeutic benefit of Afinitor monotherapy.

The escalation stage has now successfully demonstrated that BNC105 at a dose level of  $12.6 \text{ mg/m}^2$  is well tolerated in RCC patients when administered in combination with Afinitor. To date individual patients have received 12 cycles or more of treatment with BNC105 in combination with Afinitor.

This is a key milestone for this trial as 12.6 mg/m² is a dose that gives rise to reduced tubulin polymerization, the therapeutic target of BNC105. Based on this, it is reasonable to anticipate that BNC105 attains blood exposure levels that would enable it to achieve therapeutic benefit. This warrants continuation of the renal cancer trial to complete evaluation of the 16mg/m² dose and into the efficacy evaluation stage.

Dr Thomas E Hutson of the Texas Oncology-Baylor Charles A. Sammons Cancer Center and Principal Investigator of this clinical trial commented "It is encouraging that to date BNC105 has shown an excellent safety profile when used in combination with Afinitor to treat patients with metastatic RCC".

"This clinical trial builds on our experience in the treatment of metastatic renal cancer with mTOR inhibitors and our preclinical data. It makes sense that the combination of BNC105 with an agent active against mTOR would cut off a tumour "survival" response and improve clinical outcome", Dr Hutson added.

Dr Deborah Rathjen commented "Today's announcement represents a positive and important step forward in the evaluation of BNC105 in patients with this form of kidney cancer. Bionomics continues to target the end of 2012 for completion of enrolment into this trial. With this in mind there are now nine clinical centres across the US actively recruiting patients with an additional 12 clinical sites to be initiated by October."

Bionomics presented preclinical data supporting the current trial in patients with renal cancer at the American Association for Cancer Research (AACR) in April 2011. The data demonstrated the potent VDA effects of BNC105 in two mouse models of renal cancer, including a model in which the cancer metastasizes to the lungs. BNC105 induced tumour blood vessel shutdown in both the primary tumour and the secondary lung metastatic lesions. Furthermore, BNC105 activity was shown to be comparable with the blockbuster drug Sutent, a tyrosine kinase inhibitor (TKI) used in first line therapy of renal cancer. Sutent had worldwide sales of US\$1.066 billion in 2010. Treatment options remain limited in progressive metastatic renal cell cancer for patients who no longer respond to TKI treatments such as Sutent. The BNC105 trial is being conducted in patients who have failed TKI therapy.

#### Australian mesothelioma trial

Bionomics has also been conducting a clinical trial of BNC105 as a second line treatment for metastatic mesothelioma, a cancer caused by asbestos exposure.

This single arm, Phase II trial included patients progressing after first line chemotherapy with pemetrexed (Alimta) and cisplatin. In accordance with the clinical trial protocol, an interim analysis of the safety, tolerability and response rate has now been completed on the first 24 patients enrolled in this study.

BNC105, at a dose of 16mg/m² has been well tolerated in the 24 patients evaluated. This is consistent with clinical experience in the first clinical trial of BNC105.

One patient showed a 57% reduction in tumour measurement, which was classified as an objective response. This patient remains on BNC105 treatment with a clear, durable response. At least five patients have been to date classified as having stable disease according to RECIST for mesothelioma. There is ongoing evaluation of patients continuing on treatment with BNC105. Based on this analysis there will be no further enrolment into the current trial.

Dr Anna Nowak, Professor at the Faculty of Medicine, University of Western Australia and consultant medical oncologist at Sir Charles Gairdner Hospital and Principal Investigator of the trial commented "There are several encouraging outcomes from this trial. The objective tumour response, safety profile and tolerability of BNC105 warrant further research into its integration with established chemotherapy regimens."

Dr Deborah Rathjen commented "This trial has yielded important information which will be valuable for future development partners of BNC105. Based on the findings of this trial and on our preclinical evidence of encouraging combination data with cisplatin, Bionomics is considering development of BNC105 for the treatment of mesothelioma as first line therapy in combination with Alimta and Cisplatin".

"We are extremely grateful to the patients who participated in this clinical trial and their families. We also appreciate the efforts of the Australasian Lung Cancer Trials Group and the NHMRC Clinical Trials Centre in the conduct of this trial."

## Clinical program for BNC105 to be expanded to include ovarian cancer trial

Bionomics is planning to evaluate BNC105 in combination with carboplatin and gemcitabine in a multi-centre randomised Phase I/II trial in women with ovarian cancer. Discussions are in progress with Australian and US based clinical networks on trial design. The trial will be undertaken in Australia and the US.

As reported at the AACR conference in April 2011 preclinical studies have demonstrated that the combination of BNC105 with gemcitabine or a platinum treatment results in increased therapeutic benefit for animals carrying subcutaneous solid tumours. The combination of gemcitabine with a platinum treatment (Cisplatin or Carboplatin) is standard of care chemotherapy in a number of

cancer indications including ovarian cancer. Bionomics plans to conduct a clinical trial in women with ovarian cancer combining BNC105 treatment with these agents.

Dr Rathjen commented "It has always been Bionomics' intention to initiate further clinical trials of BNC105 and the decision to undertake a clinical trial in women with ovarian cancer has followed extensive consultation with key opinion leaders in Australia and the US. The trial is anticipated to commence in the first half of 2012".

"The decision to undertake this trial has a sound scientific rationale and is supported by solid preclinical data on the combination of BNC105 with current chemotherapies. The Board of Bionomics has approved the funding required to undertake this trial."

Drugs used to treat ovarian cancer reported sales of approximately US\$3.6 billion in 2010.

Ovarian cancer is the fifth leading cause of cancer-related death among women. Ovarian cancer is often diagnosed at an advanced stage, after the cancer has spread beyond the ovary. In 2010 there were an estimated 21,880 new cases and 13,850 deaths from ovarian cancer in the US. It is estimated that approximately \$2.2 billion is spent in the US each year on treatment of ovarian cancer.

In 2006 in Australia 1,226 ovarian cancer cases were diagnosed. The number of ovarian cancer cases in Australia increased by 47% between 1982 and 2006. It is anticipated that the number of new cases will continue to increase, with an estimated 1,434 women expected to be diagnosed with ovarian cancer in 2015.

Encouraging data in a single arm Phase II ovarian cancer trial have previously been reported with the VDA Zybrestat. Based on Bionomics' extensive preclinical benchmarking, BNC105 is considerably more potent and more selective than Zybrestat.

#### Outlook

Commenting on the outlook for Bionomics, Dr Rathjen noted "Bionomics has achieved important milestones in the past few months with the results of clinical trials of BNC210, which is in development for the treatment of anxiety and depression, and the extension of our collaboration with global Pharma company Merck Serono. The clinical development of BNC105 will continue in renal cell cancer and a trial in women with ovarian cancer will be initiated. Bionomics has the resources and will continue to pursue its partnership strategies for BNC210 and BNC105".

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#### **About Bionomics Limited**

Bionomics (ASX: BNO) is a leading international biotechnology company which discovers and develops innovative therapeutics for cancer and diseases of the central nervous system. Bionomics has small molecule product development programs in the areas of cancer, anxiety, epilepsy and multiple sclerosis. BNC105, which is undergoing clinical development for the treatment of cancer, is based upon the identification of a novel compound that potently and selectively restricts blood flow within tumours. A clinical program is also underway for the treatment of anxiety disorders and depression based on BNC210 which has recently completed Phase Ib clinical trials. Both compounds offer blockbuster potential if successfully developed.

Bionomics' discovery and development activities are driven by its three technology platforms: Angene®, a drug discovery platform which incorporates a variety of genomics tools to identify and validate novel angiogenesis targets (involved in the formation of new blood vessels). MultiCore® is Bionomics' proprietary, diversity orientated chemistry platform for the discovery of small molecule drugs. ionX® is a set of novel technologies for the identification of drugs targeting ion channels for diseases of the central nervous system. These platforms underpin Bionomics' established business strategy and Bionomics is committed to securing partners for its key compounds.

For more information about Bionomics, visit 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 press release that relate to prospective events or developments 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 the clinical evaluation of either BNC105 or BNC210, 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. 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 press release.