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ASX ANNOUNCEMENT

13 April 2018

Bionomics Presents BNC101 and BNC105 Data at the American Association for Cancer Research Conference

Bionomics Limited (ASX:BNO, OTCQX:BNOEF), a biopharmaceutical company has released new first-in-human data from the Phase I Clinical Trial of BNC101, its anti-LGR5 cancer stem cell drug candidate being developed to treat solid cancers. In addition, new data are also being presented on BNC105, its tubulin polymerization inhibitor, as a potent therapeutic for killing Acute Myeloid Leukemia (AML) cells and leukemic progenitor cells.

Bionomics is currently undertaking a formal process to partner both BNC101 and BNC105 as the company completes its transition to a focused Central Nervous System (CNS) disorders company. These new data are anticipated to assist that process.

The BNC101 data presented at the annual American Association for Cancer Research conference in Chicago, demonstrate:

- BNC101 target engagement with LGR5 for the first time in human tumour biopsies following treatment in the BNC101.001 Phase I clinical trial evaluation of BNC101 in patients with metastatic colorectal cancer (CRC).
- BNC101 co-localizes with LGR5 in patient metastatic CRC biopsies. This was evidenced using novel methodologies including LCMSMS and MALDI-MSI.
- A statistically significant decrease in the ratio of plasma levels of MMP-9 and TIMP-1 was observed in patients following treatment with BNC101 providing support for a potential pharmacodynamic effect. This change was seen especially in the mutational subset of patients that expressed the KRAS mutation, a finding that may be useful for patient selection in future clinical trials.
- BNC101 was shown to be safe and well tolerated, with no evidence of gut toxicity as measured by the biomarker Zonulin.

The BNC105 data demonstrate:

- BNC105 is a high potency inducer of apoptosis and cell death in patient-derived AML cells.
- BNC105 targets both peripheral acute leukemic and leukemic progenitor cell populations potentially reducing the potential for recurrence of AML.
- BNC105 was shown to be more potent than competing products in development.

Both poster presentations will be attended by Dr Tina Lavranos and Dr Dan Inglis of Bionomics.

Poster Presentation details:

1. BNC101 Poster

Title: *Characterization of BNC101 a humanized monoclonal antibody targeting the GPCR LGR5: First in human evidence of target engagement*

Session Title: Receptor Targeting and the Tumour Microenvironment
Session Date/Time: Tuesday, April 17, 2018, 8:00 am - 12:00 pm
Presentation Number: 3910
Poster Board Number: 10
Location: Poster Section 38

2. BNC105 Poster

Title: *The microtubulin-disrupting drug BNC105 is a potent inducer of apoptosis in AML patient samples*

Session Title: Experimental Agents and Combinations for Hematologic Malignancies 2
Session Date/Time: Monday, April 16, 2018, 8:00 am - 12:00 pm
Presentation Number: 1881
Poster Board Number: 12
Location: Poster Section 38

A copy of the both posters will be available at www.bionomics.com.au following the conclusion of the presentations.

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BNC101 Abstract

At the base of normal intestinal crypts, stem cells maintain the highly regenerative gut epithelium. These intestinal stem cells are well characterised for their high expression of the G coupled protein receptor LGR5 (also known as GPR49). Together with R-spondins, (potent Wnt signalling modulators) and stem cell growth factors, LGR5 forms part of a signalling cascade responsible for the regulation of cellular proliferation.

Key mutations in the APC or BRAF pathways of intestinal stem cells lead to lesions and metastatic colorectal cancer if not diagnosed and resected at an early stage. The majority of primary and metastatic tumours arising from these mutations over-express LGR5. It has been reported that metastatic colorectal cancer (CRC) patients expressing higher levels of LGR5 in tumour biopsies had increased rates of relapse.

BNC101 is a first-in-class anti-LGR5 humanized monoclonal antibody. Biacore analysis of BNC101 has demonstrated a high affinity to LGR5 (Kd=16nM) with no cross-reactivity to LGR4 or LGR6 receptors. Immunoprecipitation studies have also shown that BNC101 has no off-target binding. The murine equivalent of BNC101 has demonstrated anti-tumour activity in multiple CRC patient derived xenografts.

Flow cytometry studies on CRC cell lines have revealed that LGR5 is located intracellularly with a small fraction present on the cell surface. To better understand its mechanism of action, BNC101 was conjugated to Alexa Fluor 647 and incubated with human CRC cell lines. It was shown that BNC101 interacts with membrane bound LGR5 and is internalised within 5 minutes. Incubation of the cells for 24 hours at clinically relevant concentrations lead to accumulation of fluorophore conjugated BNC101 within the cell. This intracellular accumulation of BNC101 was further demonstrated with receptor recycling kinetic studies whereby only partial receptor recycling occurred which may be attributed to the large intracellular LGR5 pool. CHO cell lines overexpressing LGR5 with a GFP tag were used to determine co-localization of BNC101 with its LGR5 ligand.

BNC101 is currently in a safety and dose escalation Phase I clinical trial in patients with recurrent metastatic CRC. We were able to demonstrate BNC101 target engagement with LGR5 for the first time in tumour biopsies following treatment. Tumour biopsies were analysed by mass spectrometry together with Matrix Assisted Laser Desorption/Ionization, co-localisation of BNC101 with LGR5 was observed, providing us with evidence for the first time that BNC101 infiltrates the patient tumour and engages with the over-expressed LGR5 receptor.

BNC105 Abstract

BNC105 is a Phase II potent and highly selective disruptor of tumour micro-vasculature that causes the rapid onset of hypoxia and necrosis in solid tumours. BNC105 targets the colchicine-binding site on tubulin causing chronic disruption of adhesion molecules and was developed to be best-in-class with high specificity to actively dividing cells. It has one of the largest therapeutic windows of its class and has been shown to have direct cytotoxic activity on tumour cells. It is this highly tumour-specific mechanism of action that has positioned BNC105 as a therapeutic with high potential in the haematological cancer setting. Previous studies of BNC105 have shown that treatment with BNC105 results in the activation of c-Jun N-terminal kinase (JNK), phosphorylation of ATF2, and the induction of ATF3 and Noxa, leading to acute apoptosis in chronic lymphocytic leukemia (CLL) cells. These findings led to the commencement of a Phase 1/2 trial of BNC105 in patients with CLL.

The present study was designed to investigate the effect of BNC105 treatment on Acute Myeloid Leukaemia (AML), a disease that currently has limited treatment options. To assess the utility of BNC105 therapy in this setting, six AML cell lines representing different subtypes, including the high risk FLT3-ITD subtype, were initially used in proliferation and cytotoxicity assays. The production of reactive oxygen species (ROS), cell cycle distribution and cell signalling by western blot were all assessed after treatment. All tested AML cell lines were highly sensitive to treatment with BNC105 with an IC_{50} = 0.2nM to 1.3nM after 48h treatment. Analysis of apoptosis induction revealed cell line specific effects; however, a consistent dose-dependent increase in phosphorylation of JNK was observed across all cell lines.

AML patient samples obtained from the South Australian Cancer Research Biobank (SACRB) were exposed to BNC105 at clinically relevant doses for up to 72 hours and cellular viability and apoptosis induction were assessed by Annexin V/ 7AAD staining and caspase 3 and 7 activation measured. BNC105 induced caspase activity and significantly decreased viability in a dose and time dependent manner, including the FLT3 mutant subtype patient samples. In comparison, bone marrow mononuclear cells from healthy controls were much less affected by BNC105. Effects of BNC105 on the leukemic stem cell (LSC) phenotype population were also investigated. The LSC-containing population, measured by CD34/CD38 and GPR56 or CD93 staining, was targeted by BNC105 in all AML patient samples tested.

These results suggest that AML cells can be directly targeted by BNC105 at clinically relevant concentrations and hence further clinical investigation of BNC105 is warranted for AML treatment in a patient population with high unmet need.

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. 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. Bionomics has a strategic partnership with Merck & Co., Inc (known as MSD outside the United States and Canada).

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.