

# Bionomics



CREATING INNOVATIVE THERAPIES  
**FOR SERIOUS HUMAN DISEASES.**

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CEO & Managing Director

May 2016

# Safe Harbor Statement

## Factors Affecting Future Performance

This presentation contains "forward-looking" statements within the meaning of the United States' Private Securities Litigation Reform Act of 1995. Any statements contained in this presentation 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.

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# Bionomics Overview

- Global, clinical stage biopharmaceutical company leveraging proprietary platform technologies to discover and develop a deep pipeline of novel drug candidates focused on the treatment of serious central nervous system disorders and on the treatment of cancer.
- Partnerships with Merck & Co. in cognition and pain - up to US\$658m combined future potential milestones plus additional royalties on net sales of licensed drugs
  - Merck & Co equity investment in October 2015
- Lead drug, BNC210, is a novel, orally-administered, first-in-class, modulator of  $\alpha 7$  nicotinic acetylcholine receptor, in development for the treatment of anxiety and depression
  - Ongoing Phase 2 trial in Generalized Anxiety Disorder patients, results expected Q3 2016 calendar year
  - Phase 2 trial in PTSD patients to be initiated in H1 2016 calendar year
- BNC101 is a first-in-class anti-LGR5 antibody targeting cancer stem cells, in development for the treatment on colon cancer and other solid tumors
  - LGR5 is a receptor that modulates Wnt signaling, a key proliferative pathway in cancer stem cells
  - Ongoing Phase 1 trial in colon cancer patients
- Financials: Market Cap \$152M, Cash (31 March 2016) \$51.1M, Receipts March qtr \$6.3M (\$10.8M YTD), Net cash outflow (March qtr) \$3.6M (\$9.3M YTD)

# 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

### 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

### 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

# 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




Validates ionX and MultiCore drug discovery platforms

Value creation through strategic partnering business model

Future success based revenue streams & royalties



# Bionomics Platform Technologies Deliver Broad Drug Pipeline

Drug Candidate	Indication(s)	Preclinical	Phase 1	Phase 2	Milestones (Calendar Year)
Central Nervous System (ionX and MultiCore)					
BNC 210	Generalized anxiety disorder				Results from P2 trial in Q3 2016
	Other indications including PTSD				Initiate P2 trial in PTSD H1 2016
Undisclosed	ADHD, Alzheimer's, cognition, Parkinson's, schizophrenia				
Undisclosed	Chronic and neuropathic pain				
Others	Pain, Parkinson's dyskinesia, epilepsy				
Cancer Stem Cells (CSCRx)					
BNC101	Colorectal cancer				Initiate P1 trial in Q1 2016
	Pancreatic cancer				
	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				

\* Maternal embryonic leucine zipper kinase

# BNC210 Overview: Novel, Best-in-Class Modulator of $\alpha 7$ Receptor

## Mechanism of Action

- Negative allosteric modulator of  $\alpha 7$  nicotinic acetylcholine receptor

## Target Indications

- Anxiety (Generalized Anxiety Disorder or GAD & Post Traumatic Stress Disorder or PTSD)
- Potential for other CNS indications

## Ongoing Clinical Trials

- Phase 2 trial in GAD patients, results expected Q3 2016 calendar year
- Phase 2 trial in PTSD anticipated to be initiated H1 2016 calendar year

## Completed Clinical Trials

- 6 completed Phase 1 trials in > 190 healthy subjects
- Demonstrated safety and tolerability
- Brain activity consistent with potential to reduce anxiety without typical side effects including sedation
- BNC210 significantly reduced CCK4-induced panic symptoms
- Evidence of BNC210 target engagement by measuring the effect of nicotine on brain EEG

# 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	✓	✓	✓	✓	✓	✓
Valium and other BZD	X	X	X	✓	✓	X
Prozac and certain other SSRI/SNRI	✓	X	✓	X	X	✓

### Anxiety Treatments

- Dominated by benzodiazepines
- Associated with sedation, addiction and 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, changes in weight, 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.

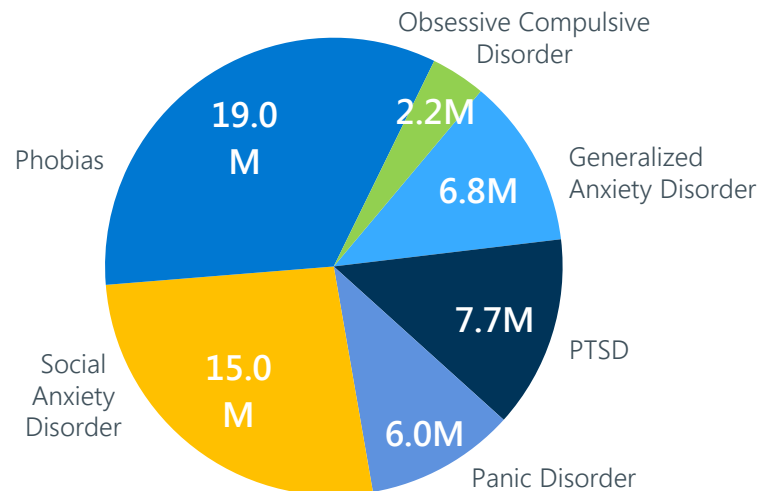


# Anxiety and Depression Market

Anxiety and depression have overlapping symptoms: over 40% of those diagnosed with depression are also diagnosed with an anxiety disorder

## Anxiety Market

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

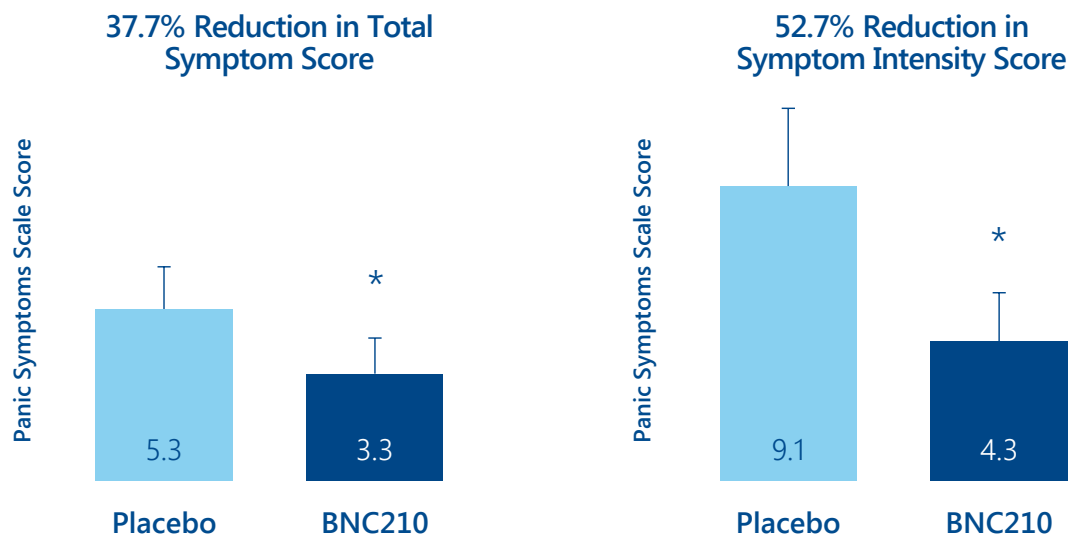


## Depression Market

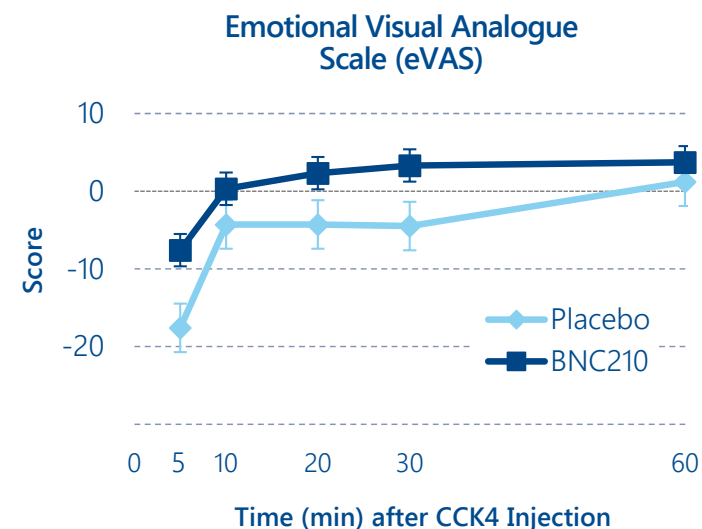
- Approximately 18.2 million people suffer from depression in the US
- Sales of top 10 depression drugs reached a total market of \$8.8bn in 2012
- Major types of depression:
  - Bipolar depression
  - Dysthymia
  - Major depression

# BNC210 Significantly Reduced CCK4-Induced Panic Symptoms

## % Reduction in Total Number of Symptoms & Symptom Intensity



## Emotional Visual Analogue Scale (eVAS)



## Subjects Experiencing Panic Symptoms When Treated with BNC210 Showed:

- Reduction in the number and intensity of panic symptoms compared to placebo
- More rapid return to baseline emotional stability compared to placebo

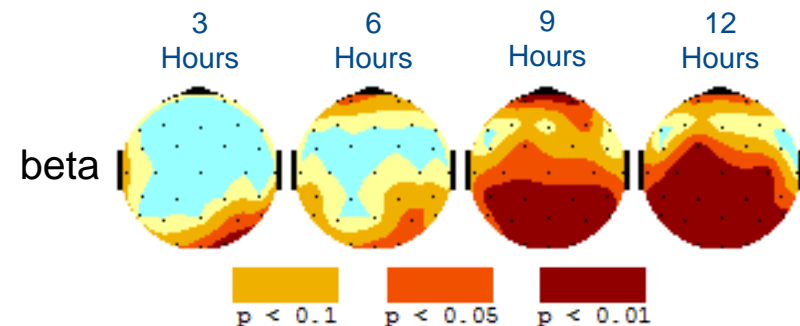
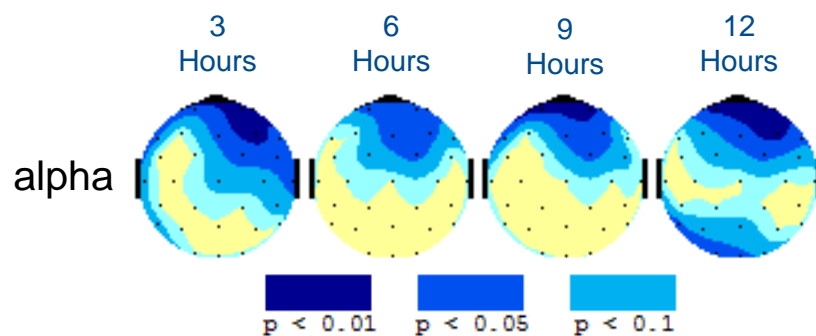
# BNC210-induced Changes on EEG Indicate Anxiolysis in the Absence of Sedation

Drug/ EEG Spectrum*	$\delta$	$\gamma$	$\alpha$	$\alpha 1$	$\alpha 2$	$\beta$	$\beta 1$	$\beta 2$	$\beta 3$
BNC210			↓		↓	↑			↑
Lorazepam	↑	↓	↓	↓	↓	↑	↑	↑	↑

*Increase in delta spectral power during vigilance control session is signature of Lorazepam-induced sedation*

*Increase in  $\beta 3$  spectral power is associated with the anxiolytic activity of Lorazepam*

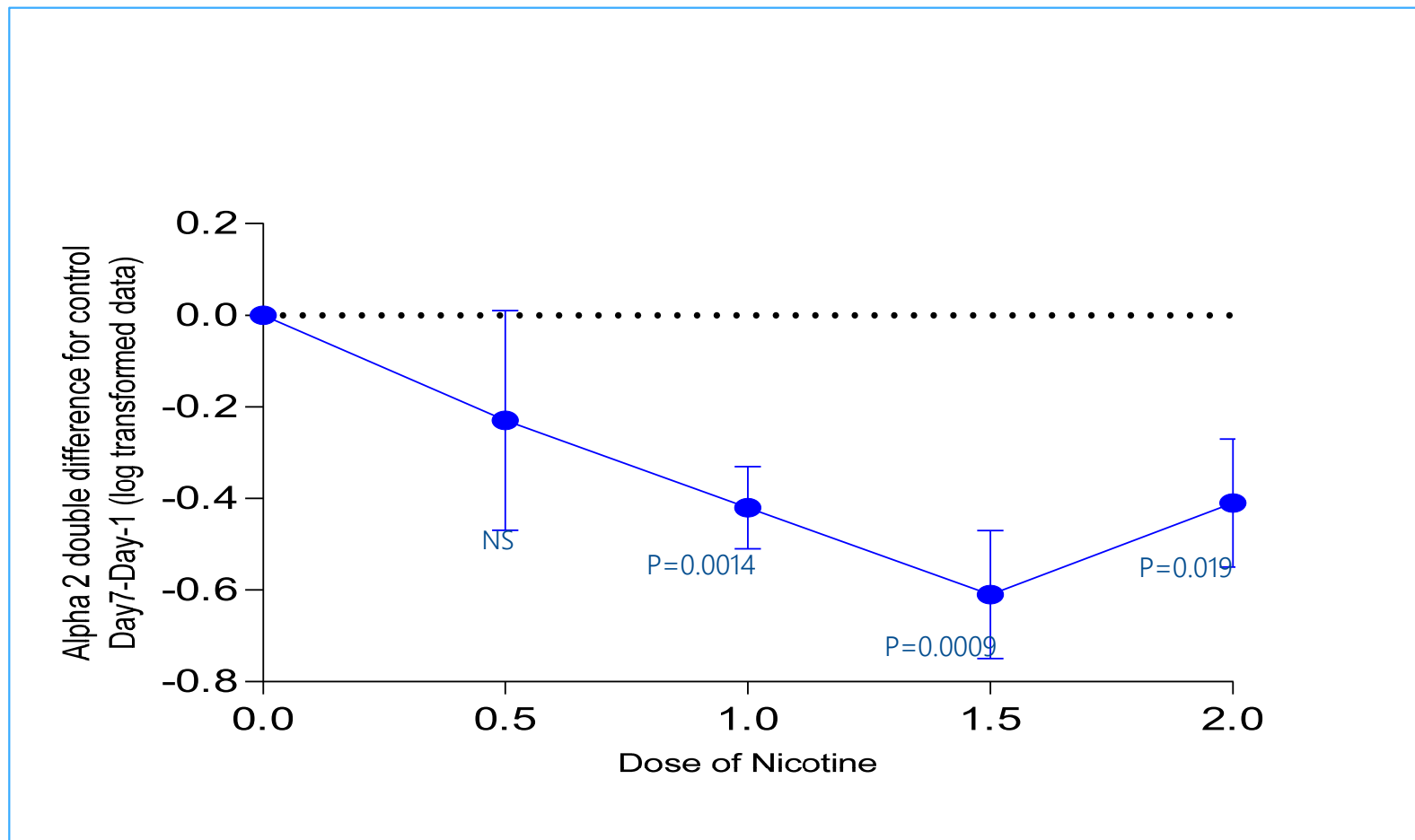
## Brain Maps showing temporal effect of BNC210 on $\alpha$ and $\beta$ frequency bands



\*Arrows represent statistically significant changes in spectral power ( $p < 0.05$ ) displayed over considerable surface or scalp regions measured at 6 hours (cMAX for Lorazepam and BNC210).

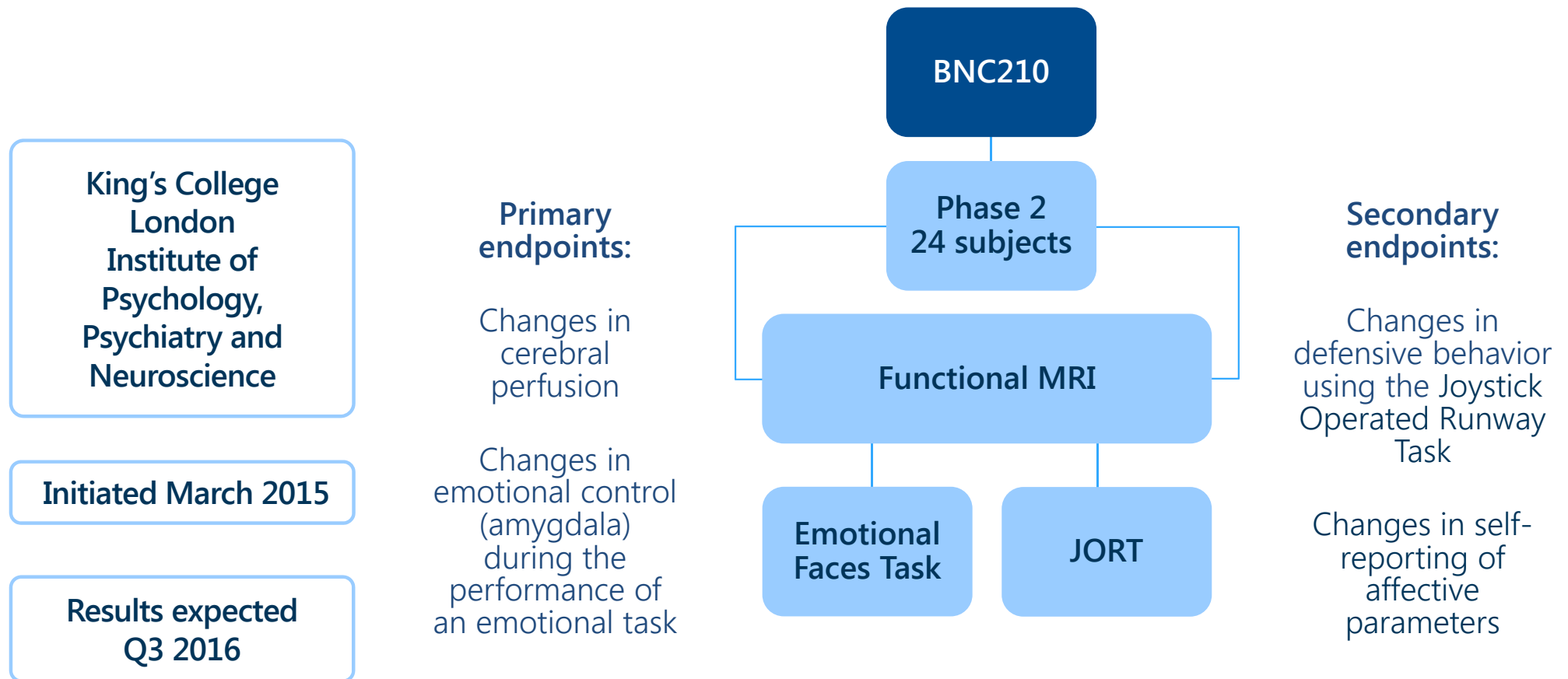
# BNC210 Treatment Reduced Nicotine-induced EEG Changes

The difference between nicotine-induced EEG changes with and without BNC210 (2,000mg)



# Ongoing BNC210 Phase 2 Trial in Generalized Anxiety Disorder (GAD)

Randomized, double-blind, placebo and Lorazepam-controlled,  
4-way crossover design

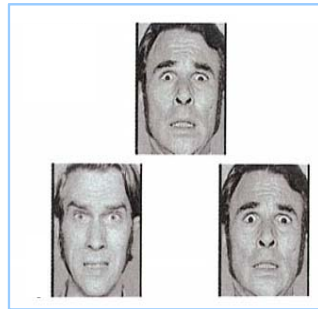


# Emotional Faces and Joystick Operated Runway Task (JORT)

We believe GAD patients treated with BNC210 will have reduced amygdala activity and less defensive behavior than placebo treated

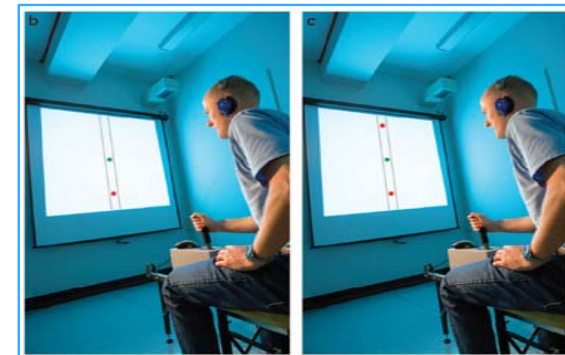
## Emotional Faces Task

- Primary Endpoint
- Evaluates activity in the amygdala via Functional MRI
- Several FDA-approved anxiety drugs reduce amygdala activation in the Emotional Faces Task



## Joystick Operated Runway Task

- Secondary Endpoint
- Computer simulation used to evaluate changes in defensive behavior including flight and risk taking behavior



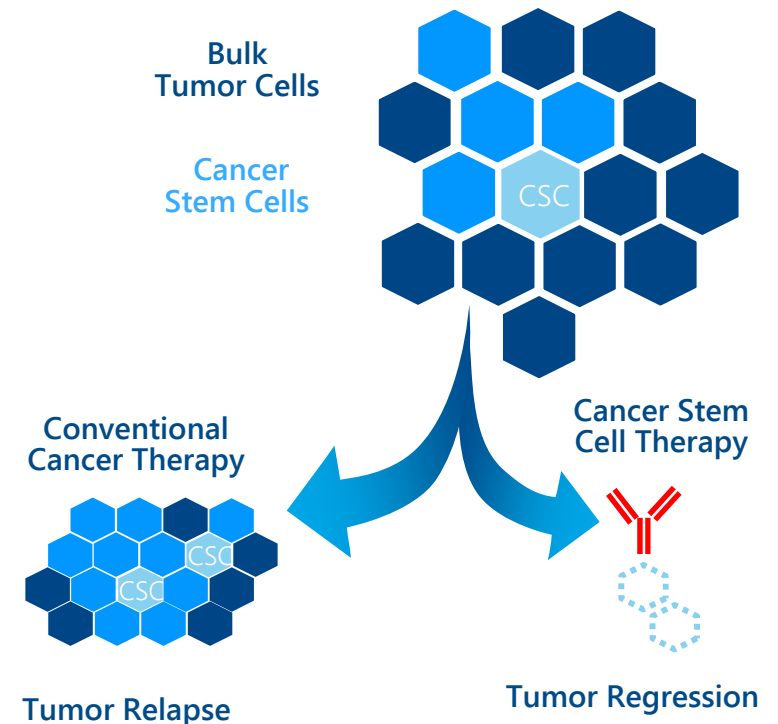


# Phase 2 Trial in Post Traumatic Stress Disorder (PTSD) to be initiated in H1 2016

<b>Subjects</b>	<ul style="list-style-type: none"><li>• Up to 200 PTSD Patients</li></ul>
<b>Protocol</b>	<ul style="list-style-type: none"><li>• Double-blind, placebo controlled, multi-center</li><li>• 1 week placebo run-in, 12 week treatment phase (placebo or BNC210)</li><li>• 2 arms, 1 : 1 randomization</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>

# Bionomics Approach to Targeting Cancer Stem Cells

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



# CSC technology = Commercially attractive assets

- On 28 April 2016, AbbVie announced acquisition of StemcenTrx in a Cash and Stock deal valued at US\$5.8 billion.
- US\$2 billion in Cash and US\$3.8 billion in stock
- Additional milestone payments of up to US\$4 billion
  - Approval of Rova-T (lead asset) in frontline SCLC could earn StemcenTrx shareholders US\$2B milestone from AbbVie
- US\$400m in cash held by StemcenTrx to be returned to StemcenTrx shareholders

**FORTUNE**

## AbbVie Buying Cancer Drug Startup Stemcentrx for \$10.2 Billion

by Dan Primack @danprimack APRIL 28, 2016, 7:29 AM EDT

### Market Exclusive

#1 Financial News & Analysis Website

AbbVie Inc (NYSE:ABBV) Buying StemcenTrx For \$5.8 Billion, Adding Key Drug Candidates

#### AbbVie joins wave of pharma moves with Stemcentrx deal

David Crow in New York

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PR Newswire  
A UBM plc company

**AbbVie to Expand Oncology Presence Through Acquisition of Stemcentrx and its Novel, Late-Stage Rova-T Compound for Small Cell Lung Cancer**

# BNC101 Overview: First-in-class LGR5 mAb Targeting Cancer Stem Cells

## Mechanism of Action

- Allosteric disruptor of LGR5/RSPO/ZNRF3 regulatory module Wnt signal strength
- Inhibition of cancer stem cell self-renewal and tumor initiating capacity

## Therapeutic Hypothesis

- A monoclonal antibody (mAb) that effectively targets LGR5 will eliminate a key pathway for CSCs
- Targeting both CSCs and the proliferate tumor bulk will prevent or significantly delay tumor recurrence and improve treatment outcomes and overall survival in cancer patients

## Target Indications

- Metastatic colorectal and pancreatic cancers
- Potential for other solid tumors including breast, lung, GI tract

## Clinical Development Plan

- Single agent dose escalation/expansion in 2<sup>nd</sup>/3<sup>rd</sup> line metastatic CRC (mCRC)
- Chemotherapy combination + BNC101
- Demonstration of safety and tolerability
- Exploratory Endpoints: OS, PFS, biomarkers

# BNC101 Market Opportunity

Currently approved therapies do not effectively address the underlying mechanism of tumor recurrence and metastasis

## CRC Therapeutic Market

- Projected to reach \$9B by 2020 in 8 Major Countries
- Colorectal Cancer (CRC) is the second most prevalent cancer type, yet overall survival lags behind other high incidence cancers
- Metastatic CRC incidence = >136,00 new cases in US in 2014
- In metastatic CRC, five year survival is just 12%

## Pancreatic Cancer Therapeutic Market

- Projected to reach \$5B by 2020 in 8 Major Countries
- Pancreatic Cancer remains a high unmet need due to lack of safe and highly efficacious products in the market
- Pancreatic cancer incidence = 46,420 new cases in US in 2014 (38,000 deaths)
- In Pancreatic Cancer, five year survival is just 6%

## Additional LGR5+ Solid Tumors

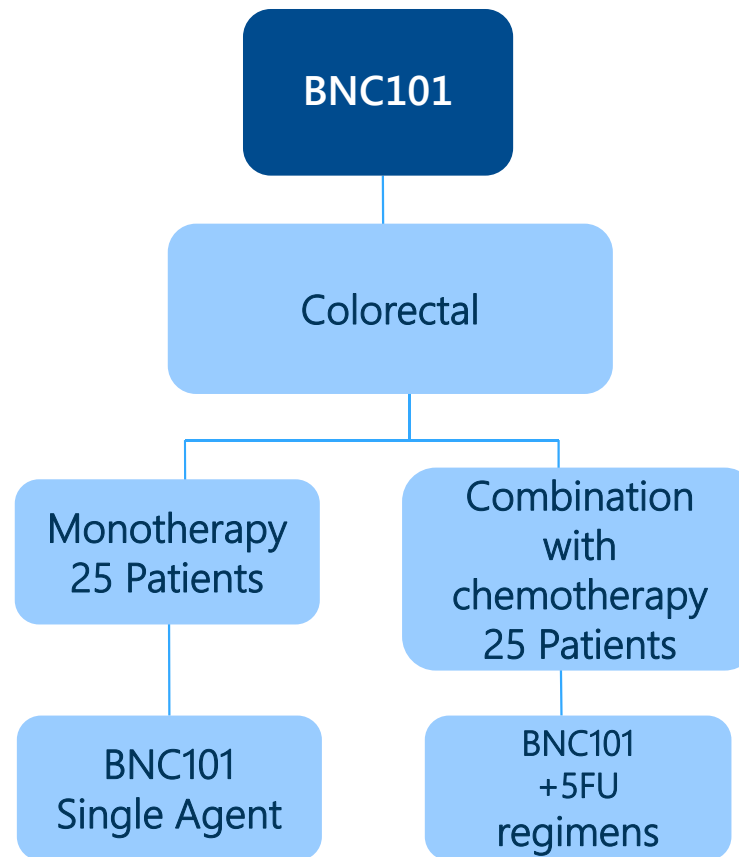
- Triple negative breast cancer therapeutic market est. \$6B by 2020
- Lung cancer therapeutic market est. \$4.5B by 2020
- Hepatocellular (liver) cancer therapeutic market est. \$1.5B by 2020

# BNC101 Phase 1 Clinical Trial

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

## Primary endpoints:

Safety and tolerability



## Other endpoints:

PFS, ORR, OS

Changes in biomarkers including circulating tumor cells and LGR5 expression as well as other disease-related biomarkers

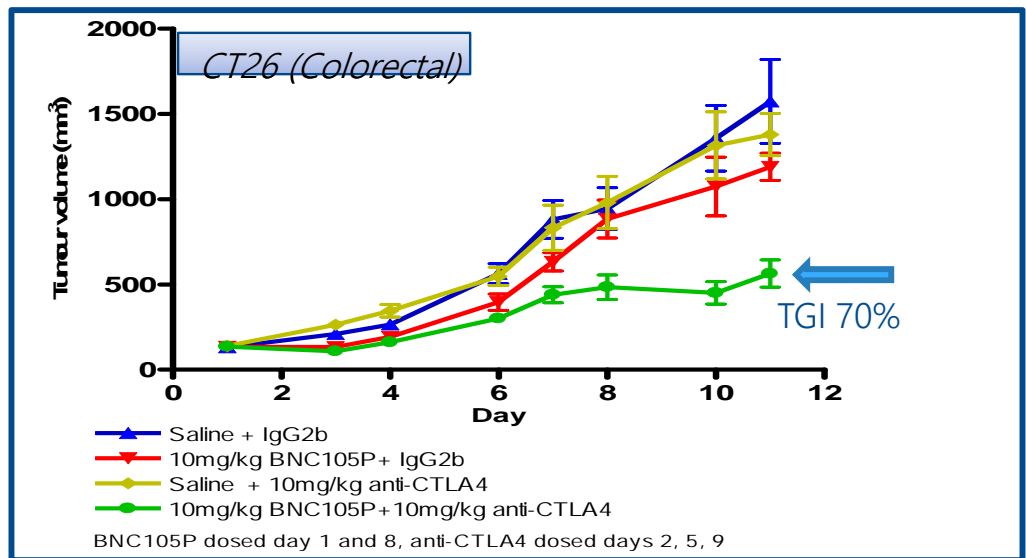
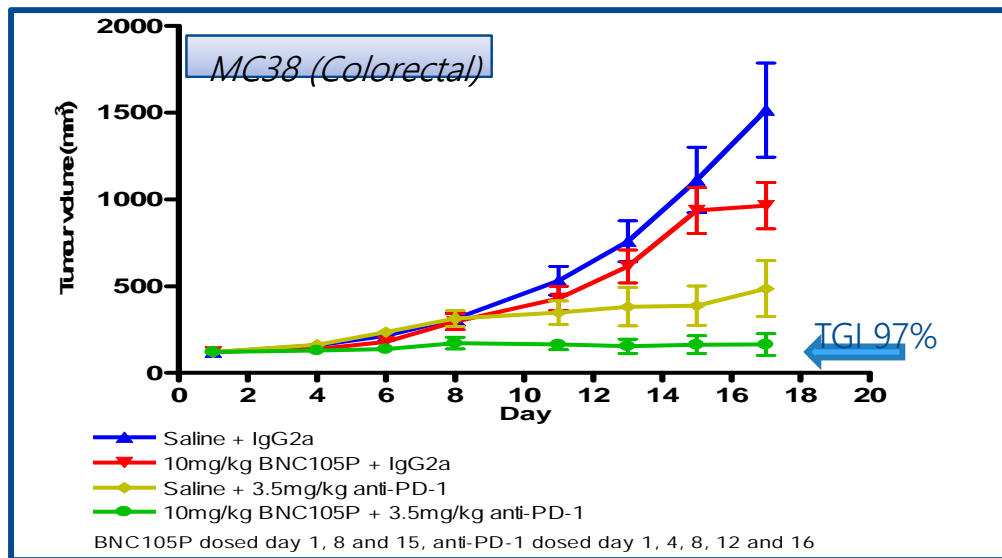
All dates reflect calendar years.



# Evolving context for BNC105, restoring immune activation within solid cancers

- BNC105 is a small molecule 2<sup>nd</sup>-generation Vascular Disrupting Agent (VDA)
  - Disrupts tumor blood vessels, kills tumor cells causing release of tumor antigens, promoting changes within the tumor microenvironment which stimulate the immune system
  - Excellent safety record in 183 treated patients
  - Overall 55% disease control rate in unselected patients – 1 complete response (CR), 12 partial responses (PR), 65 stable disease (SD)

*Combination of BNC105 with either PD-1 or CTLA4 inhibitors enhances anti-tumor activity*



*Sales of immuno-oncology agents are projected to reach US\$22B by 2020*

# Cognition Program: Partnership with Merck & Co.



Combines the platform expertise from ionX and MultiCore



## 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

# 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

# Milestones & Outlook

