Bionomics

CREATING INNOVATIVE THERAPIES
FOR CNS DISORDERS.

ANNUAL GENERAL MEETING
CEO PRESENTATION

BNO (Australia: ASX)
BNOEF (USA: OTCQX)

14 November 2018

Central Nervous System (CNS)

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, BNC105 and BNC101), its licensing agreement 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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Our Proprietary Platform Technologies and CNS Therapeutic Focus

ionX

Identifies drug candidates targeting both ligand gated and voltage gated ion channels

Proprietary cell lines and screening approaches

Comprehensive *in vivo* models validate target biology

MultiCore

A diversity orientated chemistry platform for the discovery of small molecule drug candidates

Computer aided pharmacophore modelling

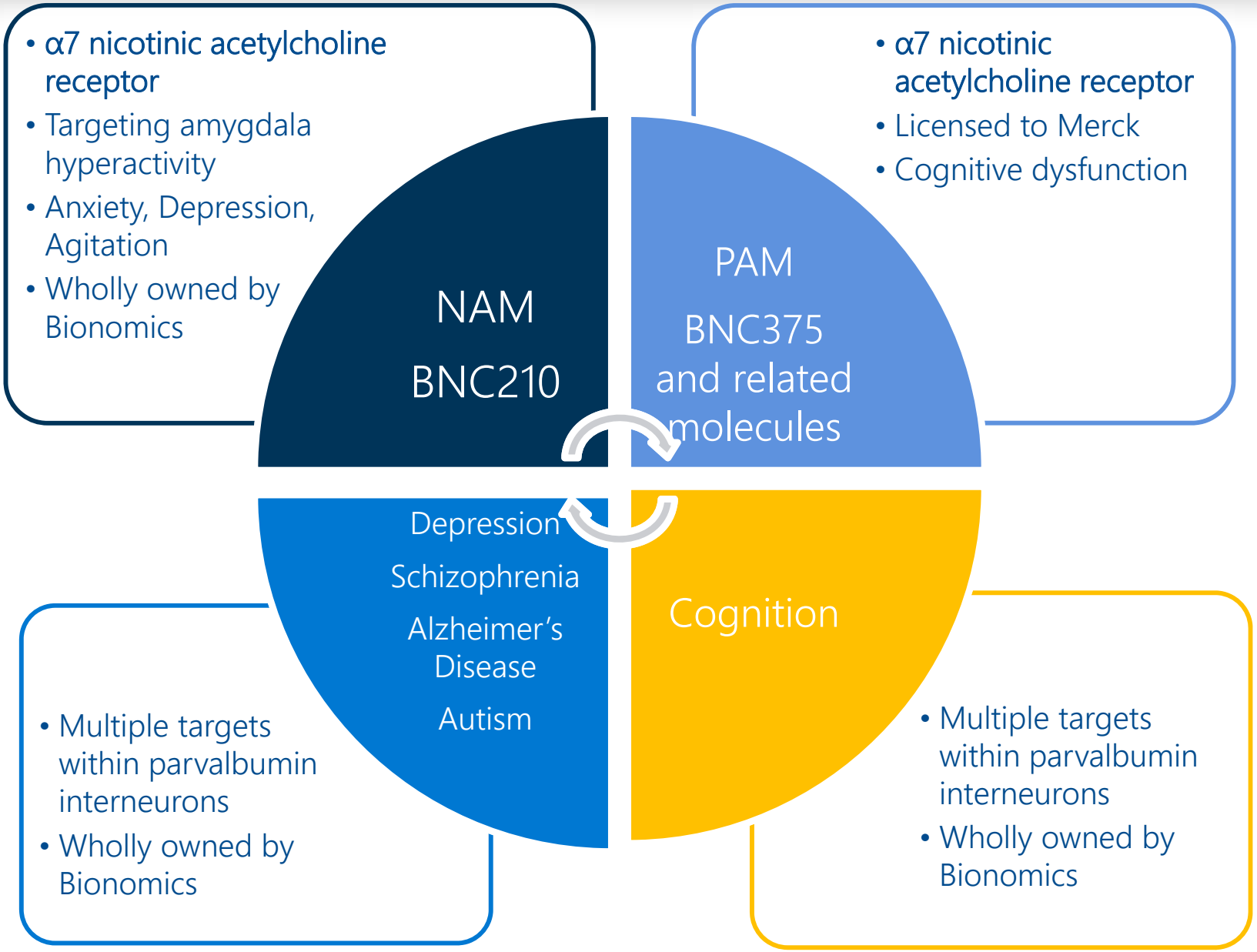
Scaffold hopping synthetic approaches rapidly create diversity in small, focused libraries

Parallel, differentiated chemical series of potential drug candidates

Therapeutic Areas

- Anxiety
- Agitation
- Depression
- Cognitive/Memory Deficits
- Pain

Bionomics' CNS Discovery Engine



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Bionomics' Pipeline

Program	Mechanism of Action	Indication	Pre-IND	Phase 1 / 2a	Phase 2b	Bionomics' Commercial Rights	Market Opportunity
BNC210	α7 nicotinic acetylcholine receptor NAM	PTSD	*Primary endpoint not met, October2018*			WW	▪ US$4.7B ▪ 3.4-4% prevalence >18 yrs ▪ ~25% of patients diagnosed and treated
		Agitation	*Phase 2 initiated Q2 2018; results expected Q1 2019*			WW	▪ US$1.6B ▪ ~3.1% dementia prevalence >40yrs ▪ ~9% agitation patients diagnosed and treated
		GAD	*Positive Phase 2a data*			WW	▪ US$2.7B ▪ 3.1% GAD prevalence ▪ ~25% diagnosed and treated ▪ ~50% of SSRI patients treated are partial responders or have relapsed
		Panic	*Positive CCK-4 induced panic data*			WW	▪ US$4.4B ▪ 2.7% prevalence ▪ ~50% diagnosed and treated ▪ Assumes 5% premium to Trintellix 2016 AWP for 30-day supply of $380 – compliance adjusted
MK#	α7 nicotinic acetylcholine receptor PAM	Alzheimer's, Parkinson's	*Phase 1 ongoing*			WW Merck Partnership	▪ US$506M total deal value including upfront and milestones payments ▪ Tiered royalties
Pain, Depression, Memory Enhancement	Undisclosed					WW	

Potential Competitive Advantages of BNC210*

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	✓
Atypical Antipsychotics	X	X	X	✓	X	✓

Anxiety Treatments

- Dominated by benzodiazepines (BZDs)
- 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

Agitation Treatments

- In addition to BZD, anti-psychotics are used to treat agitation and anxiety. They cause dizziness, sedation, weight gain, constipation, movement disorders and have black box warnings for use in elderly (stroke)

*Based on data from preclinical studies, Phase 1 & 2 clinical trials.

The Mechanism and Pharmacology of BNC210 Indicated Therapeutic Potential for Several PTSD Symptom Clusters

Four main PTSD symptom clusters (DSM-5 criteria)

Intrusive thoughts Nightmares

Avoidance

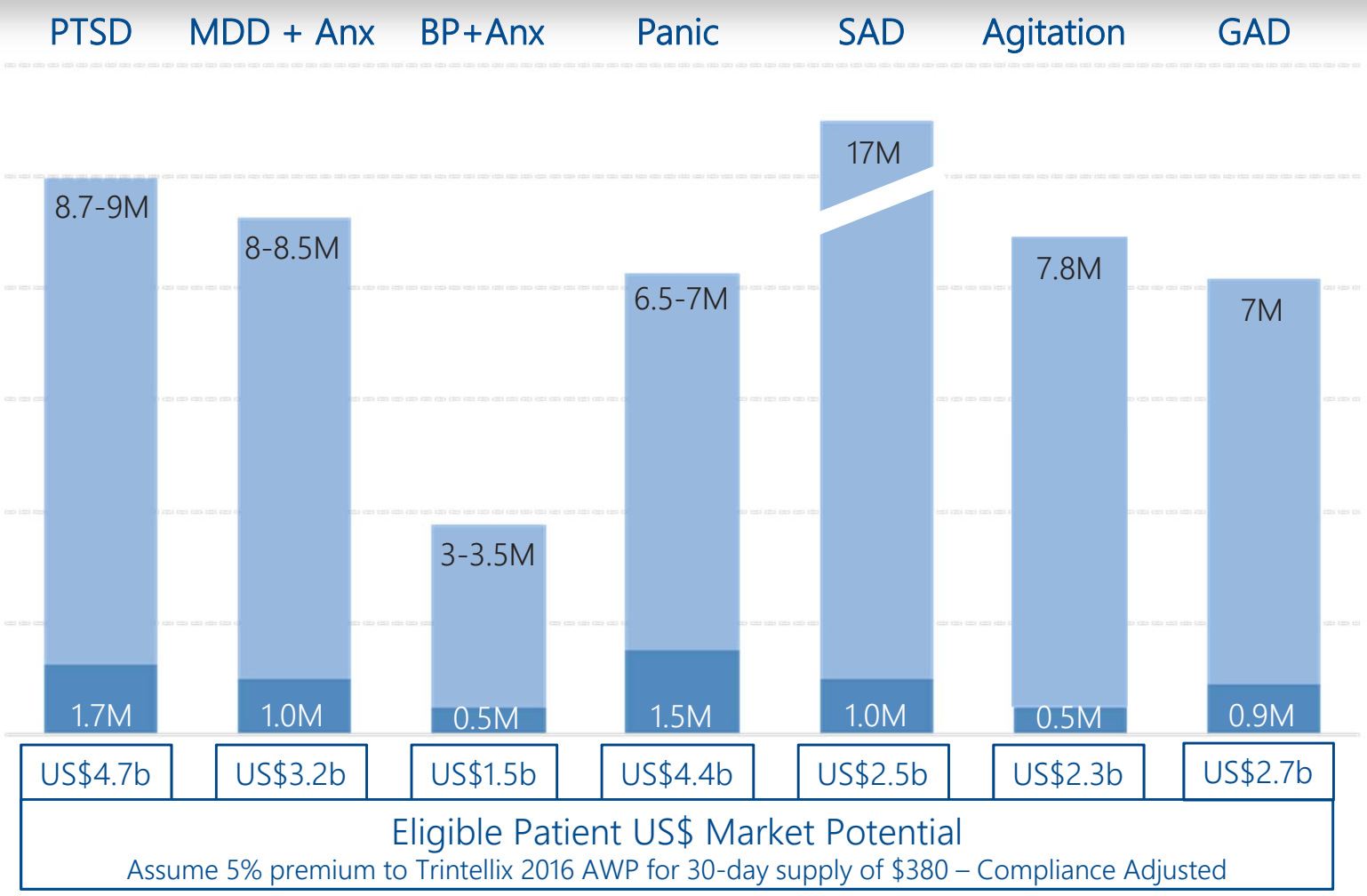
Negative alterations in cognition and mood.

Arousal and reactivity

- Anxiolytic in rodents and man
- Acute effects on neural circuitry associated with anxiety and PTSD in man
- Enhances fear extinction in mice and emotional recovery in man following panic attack
- Acute doses reduce defensive behavior in man
- Antidepressant effects in rats, acute efficacy which is enhanced with repeat dosing
- Promotes neurite outgrowth in primary neurons
- Reduces amygdala hyperactivity – a feature shared by anxious patients and PTSD patients
- Inhibition of a7 nAChR inhibits release of excitatory neurotransmitters associated with hypercholinergic state; including NA, DA, GLUT, ACh – potential to reduce NA induced hyperarousal
- Clinical efficacy in model of panic in HVs, elevated levels of ACh stimulate the HPA axis, BNC210 treatment significantly reduced levels of ACTH in CCK study
- α7 nAChRs modulate GABA and glutamate signaling in the amygdala and hippocampus

BNC210: US Market Potential

- ✓ *Innovative, first-in-class*
- ✓ *Unmet need in large patient population*
- ✓ *Advancement in care*
- ✓ *Limited branded competition*
- ✓ *Ability to achieve large market share*



US Prevalence	[1] 3.4-4% prevalence >18yrs., ~25% of patients diagnosed and treated [2] 6.7% prevalence, ~50% co-morbid anxiety, ~50% diagnosed and treated [3] ~2.9% prevalence, 50% co-morbid anxiety (range in literature 25 to 75%), ~50% diagnosed and treated [4] ~2.7% prevalence, ~50% diagnosed and treated [5] ~6.8% prevalence, 15-20% diagnosed and treated [6] ~3.1% dementia prevalence >40yrs., ~9% agitation patients diagnosed and treated [7] 3.1% GAD prevalence, assumes ~25% diagnosed and treated, ~50% of SSRI patients treated are partial responders or relapsers
Eligible Patient Population	

Major Depressive Disorder (MDD). Bipolar Disorder (BP). Social Anxiety Disorder (SAD). Generalized Anxiety Disorder (GAD).

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PTSD Clinical Trial Conclusions

- No overall effect on the primary endpoint (CAPS-5 total score at 12 weeks)
- Significant results obtained in CAPS-5 Criterion D (Negative Alterations in Cognitions and Mood) overall, and on specific items within the criterion, particularly in the BNC210 high dose group
  - D2: Persistent and exaggerated negative beliefs about oneself, others or the world
  - D4: Persistent negative emotional state
  - D7: Persistent Inability to experience positive emotions
- Evidence of anxiolytic effect
  - Trend towards improvement on CAPS-5 Criterion E (arousal and reactivity), question 3 (hypervigilance) in the total population
  - Trend towards improvement on CAPS-5 Criterion E, question 4 (exaggerated startle response) in the total population
- BNC210 was safe and well tolerated in 193 subjects with PTSD

Aggression, Agitation and Dementia in the Elderly

Agitation from sundown syndrome is a common cause of institutionalization of older patients suffering from dementia
Prevalence = 2.4% to 66%.

30% of caregivers rate stress associated with agitation / aggression as severely to extremely distressing

Disruptive Agitation in Alzheimer's Disease: Medication Treatment Murray A. Raskind, MD

- *#1 Anxiety, Agitation, Aggression*
- *#2 Pacing, wandering*
- *Resistance to redirection*
- *Confusion, Disorientation*
- *Mood swings*
- *Abnormally demanding, Suspicious*
- *Visual and auditory hallucinations*
- *Screaming, yelling*

Current treatments such as risperidone, olanzapine, aripiprazole, environmental interventions and behavioral modifications have had limited success

ISSUES WITH BZDs

- Most commonly prescribes meds for anxiety and insomnia in elderly, not good for chronic conditions with associated psychiatric comorbidity
- PK and PD for BZDs changes in elderly, therapeutic window reduced

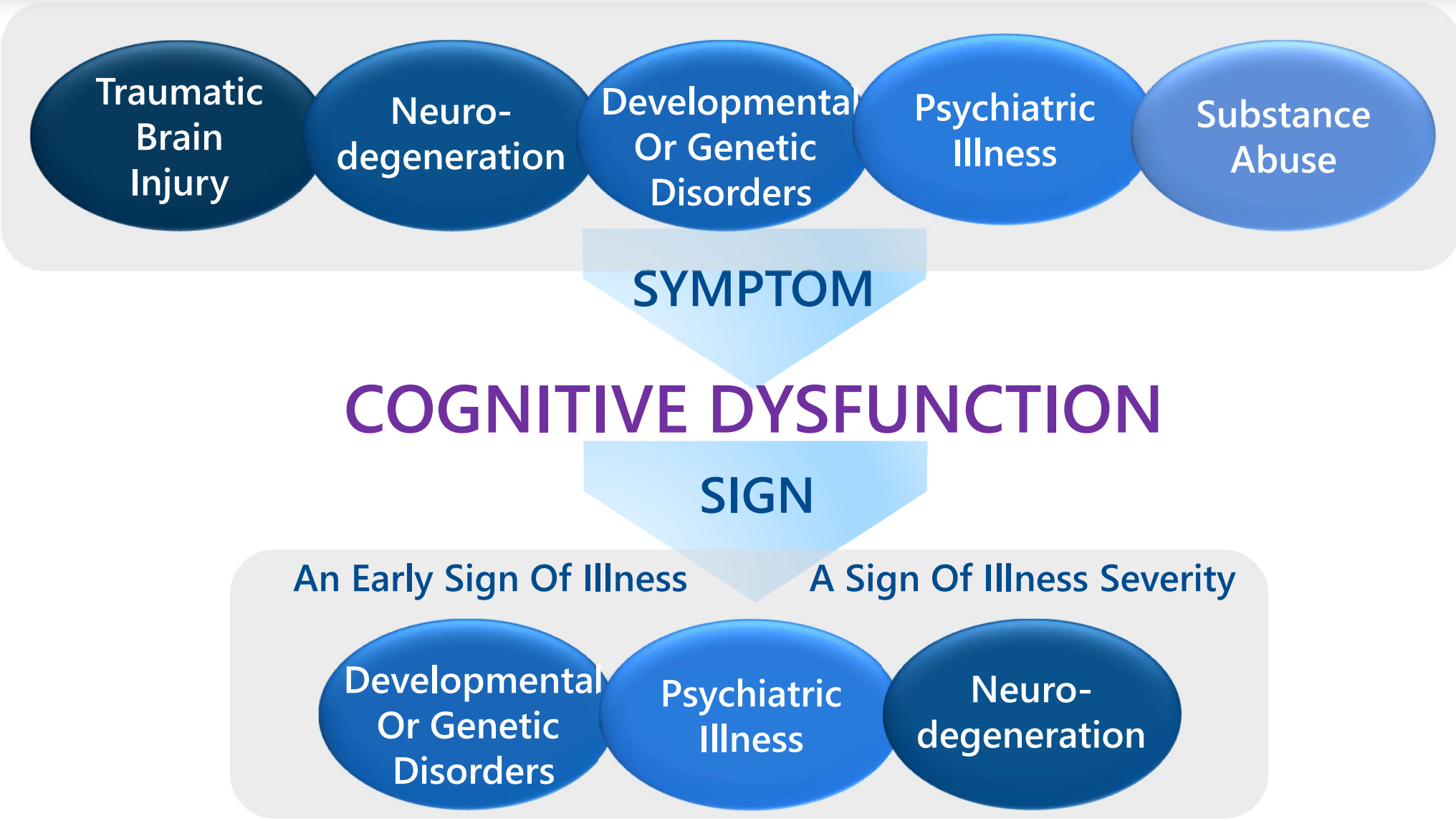
ISSUES WITH ANTIPSYCHOTICS

- Frequent non-responders
- Adverse effects: pseudoparkinsonism, sedation
- Increased risk of stroke and death - FDA have issued "Black Box Warning."

Phase 2 Clinical Trial to Assess the Efficacy and Safety of BNC210 in Hospitalised Elderly Patients with Agitation

Key Selection Criteria	• Hospitalised elderly patients under the care of a specialist Geriatrician • Presenting with agitation requiring intervention in addition to standard-of-care behavioural management
Design	• Randomized, double-blind, placebo controlled parallel dosing, 1:1 ratio • BNC210 300 mg and placebo (twice daily) • 5 days treatment; 2 days follow up • Approximately 40 participants
Objectives	• Primary: to compare the effects of BNC210 and placebo on the time to resolution of agitation as measured by the Pittsburgh Agitation Scale (PAS) • Secondary: to compare the effects of BNC210 and placebo on the change in global function as assessed by the Clinical Global Impression Scale (CGI-S/I) • Exploratory: to assess safety and tolerability of BNC210 in elderly patients with agitation

Cognitive Dysfunction



Harvey and Strassnig World Psychiatry 2012;11:73-79)

What is Cognition?

Cognition is defined as 'the mental process of acquiring knowledge and understanding through

- thought,
- experience,
- and the senses.'

Cognition refers to mental processes relating to the

- acquisition,
- storage,
- manipulation,
- and retrieval of information.

Good cognitive processes are necessary for general adjustment, emotional and social functioning, and well-being

There Are No Specific Treatments For Cognitive Dysfunction For Any Disorder Other Than Alzheimer's Disease

Condition	World Prevalence 2018	Age Range Included
Major Depression	46M	all
Bipolar Disorder	46M	≥13
Schizophrenia	14M	≥13
Autism	5M	0-19 years
Attention Deficit Hyperactivity Disorder	114M	≥3
Epilepsy	4M	all
Post Traumatic Stress Disorder	19M	all
Panic Disorder	14M	all
Generalised Anxiety Disorder	29M	all
Parkinson's Disease	5M	≥18
Alzheimer's Disease	27M	≥60
Fragile X Syndrome	0.5M	all
Down Syndrome	0.4M	In USA
Traumatic Brain Injury	69M	#per year!

#Dewan *J Neurosurgery* 2018 27: 1-18

https://pharma.globaldata.com/epidemiology/index

The Most Consistently Documented Cognitive Deficits In CNS Disorders Involve Executive Function

EXECUTIVE FUNCTION

1. INHIBITION

The ability to suppress one response in favor of another

2. WORKING MEMORY

The ability to maintain and manipulate multiple pieces of information at the same time

3. COGNITIVE FLEXIBILITY

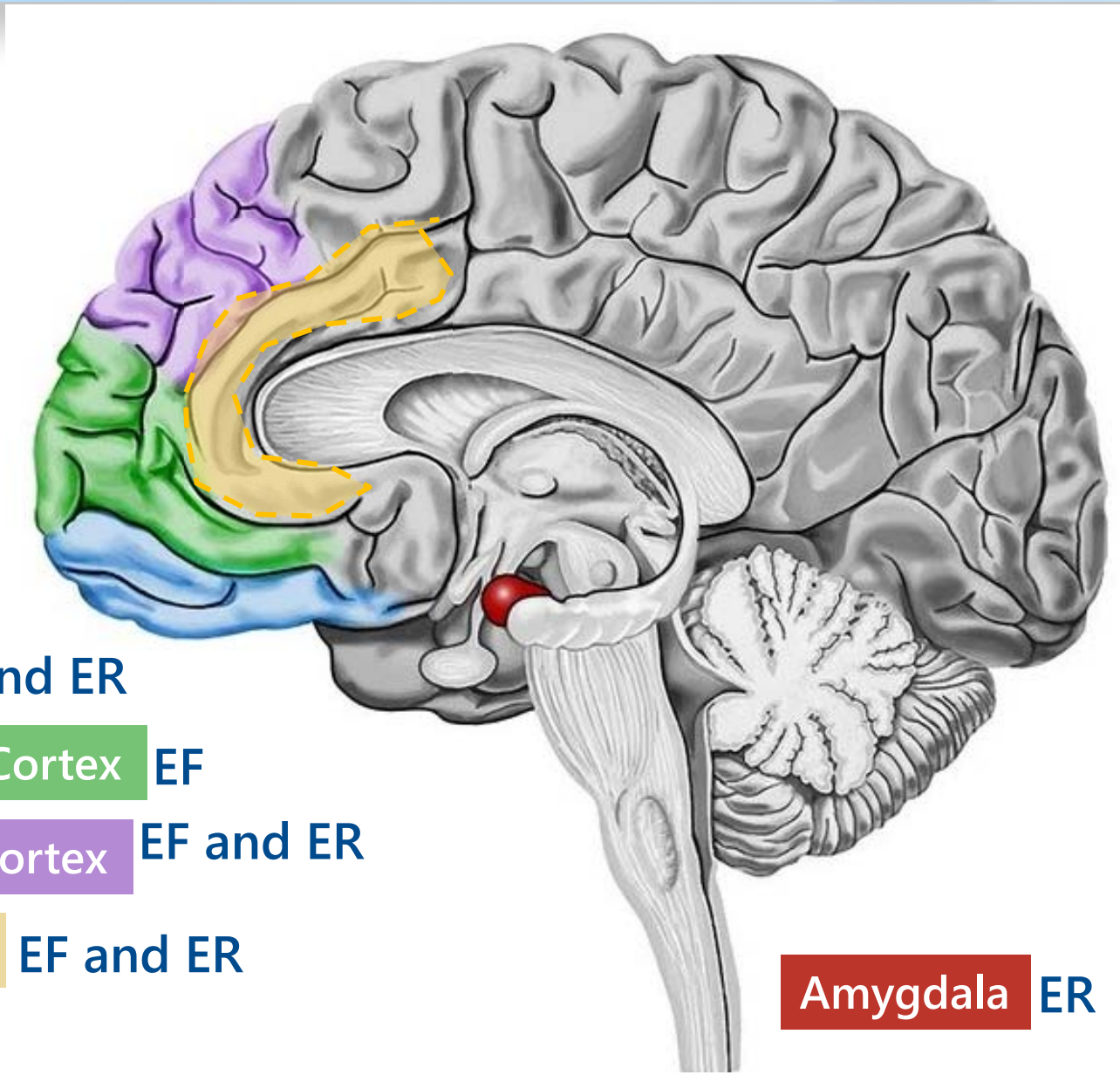
The ability to adjust response or attention quickly in the face of changing demands

From Miyake & Friedman *Cogn Psychol.* 2000;41:49-100 (in Etkin 2013 *Dialogues in Clinical Neuroscience* Vol 15 No 4)

The Prefrontal Cortex is the Home of Executive Function and Important for Emotional Regulation

Regions of the prefrontal cortex are involved in executive function and emotional regulation

Several Ion Channels are targets for improving cognitive function



Orbitofrontal Cortex EF and ER

Ventral Medial Prefrontal Cortex EF

Dorsal Medial Prefrontal Cortex EF and ER

Anterior Cingulate Cortex EF and ER

Amygdala ER

Compare, A. 2014 Cardiovascular Psychiatry and Neurology 2014(6):324374

Kv3.1 /2 Activators Represent a Promising Therapeutic Strategy for Improving Cognitive Dysfunction in Several CNS Disorders

- **Reasons why:**
  - High and selective expression in brain areas responsible for cognition
  - Potassium channel with special properties – Bionomics' speciality
  - Evidence for dysfunction of Kv3.1/3.2 in disorders with severe cognitive impairment including poor social cognition and social withdrawal:
    - Schizophrenia
    - Autism Spectrum Disorder
    - Major Depression

BNO teams are very experienced in drug discovery for ion channel targets and in targeting cognition

- Social withdrawal – becoming increasingly recognised as a consequence of cognitive dysfunction – Schizophrenia, Alzheimer's Disease, Autism…..
- Opportunity to address social withdrawal by improving cognitive dysfunction

- *Bionomics already has very promising compounds from the Kv3.1/3.2 program*

Global License and Collaboration Agreement with Merck & Co in Cognition Provides Validation

- Validates ionX and MultiCore drug discovery platforms
- 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

- Agreement covers research on BNC375 and related compounds
- BNC375 demonstrated potent memory enhancing properties in animal models – both episodic and working memory improved
- Targeting cognitive impairment in Alzheimer's and Parkinson's and other conditions

Thank You for your Continued Support in 2018