Bionomics

Corporate Presentation

SEPTEMBER 2022

Improving the Lives of Patients with Serious CNS Disorders



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Bionomics Highlights



(G Targeting Social Anxiety Disorder (SAD), Post-Traumatic Stress Disorder (PTSD) and cognitive dysfunction associated with Alzheimer's disease, schizophrenia and other CNS conditions

Lead Asset BNC210: Potential for \$1.7B Peak Sales in SAD¹ and \$2.6B Peak Sales in PTSD¹

✓ IP coverage for BNC210 extending to late 2030s

BNC210 (negative allosteric modulator of the α 7 nicotinic acetylcholine receptor)

- ✓ Clinical proof of concept in Generalized Anxiety Disorder (GAD²) and panic attack model
- ✓ In Phase 2 PREVAIL trial with FDA Fast Track designation for acute treatment of SAD
- ✓ In Phase 2b ATTUNE trial with FDA Fast Track designation for treatment of PTSD

Partnerships & Collaborations

- ✓ Strategic partnership with Merck for treatment of cognitive deficits in Alzheimer's and other CNS disorders
- ✓ MOU with EmpathBio for feasibility assessment of EMP-01 (MDMA derivative) & BNC210 for PTSD treatment

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✓ Pipeline of partnering candidates targeting potassium (Kv) and sodium (Nav) ion channels

Cash runway beyond multiple near-term catalysts

CNS = Central Nervous System MOU = Memorandum of Understanding

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1. Bluestar BioAdvisors

2. Wise et al 2020, Biological Psychiatry; Perkins et al 2021, Molecular Psychiatry

Focused CNS Pipeline with Multiple Catalysts on the Horizon

Program	Indication	Pre-Clinical	Phase 1	Phase 2	Phase 3	Status
	Social Anxiety Disorder (SAD)		PREVAIL			Study underway Topline Data: YE 2022
BNC210Post-Traumatic Stressα7 receptor NAMDisorder (PTSD)		ATTUNE W				Study underway Topline Data: mid 2023
EmpathBio	+MDMA derivative EMP-01 (PTSD)	MOU to explore combination treatment regimen				Feasibility assessment
Collaboration α7 receptor PAM	2 candidates for Cognitive Deficit in Alzheimer's					Phase 1 safety & biomarker studies ongoing
Nav1.7/1.8 Inhibitors Series Lead	Chronic Pain					Partnering Asset
Kv3.1/3.2 Activators Series Lead	Cognitive Dysfunction in Schizophrenia, Alzheimer's					Partnering Asset



Acetylcholine Neurotransmitter and α7 Nicotinic Acetylcholine Receptor Imbalance Leads to Serious CNS Disorders



Cholinergic = System associated with memory, selective attention, and emotional processing cognitive functions PTSD = Post-Traumatic Stress Disorder CIAS = Cognitive Impairment Associated with Schizophrenia ADHD = Attention Deficit Hyperactivity Disorder ACh = Acetylcholine

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Allosteric Modulation of α 7 Nicotinic Acetylcholine Receptors: Potential to Enhance Efficacy and Minimize Side Effect Profile

a7 Nicotinic Acetylcholine Receptor

- Validated target for treatment of cognitive deficits; however, direct agonists desensitize receptor and side effects led to discontinuation of previous drugs in Phase 3 trials
- A novel target for anxiety rationalized by effects of ACh on amygdala, hippocampus and cerebral cortex
- Allosteric modulation has potential for minimal side effects



Normalizing Effect Utilizing Allosteric Modulation



Bionomics Clinical Assets Restore Neurotransmitter Balance Through Allosteric Modulation of the α7 Nicotinic Acetylcholine (nACh) Receptor



Cholinergic = System associated with memory, selective attention, and emotional processing cognitive functions PTSD = Post-Traumatic Stress Disorder CIAS = Cognitive Impairment Associated with Schizophrenia ADHD = Attention Deficit Hyperactivity Disorder ACh = Acetylcholine

BNC210 in Social Anxiety Disorder



Social Anxiety Disorder: Overview and Impacts

SAD Represents a Significant Unmet Need



Social Anxiety Disorder (SAD), or Social Phobia, is a significant and persistent fear of social and performance-related situations



Includes anxiety from everyday social situations; a reoccurring episodic disorder



Amongst the largest mental health conditions with lifetime prevalence affecting >31M Americans. Triggers that exacerbate anxiety can occur at any time

Work

Patients may orient their careers around a narrow set of potential occupations and may struggle with job performance

Relationships

Friendships, family relationships, and romantic partnerships are physically draining and stressful. Moderate to severe patients often live alone

Lifestyle

Activities like dining out, attending social events, and traveling, are often very distressful and/or avoided by SAD patients

Daily Activities

Normal parts of everyday life such as grocery shopping, calling a handyman, or picking up coffee can be very challenging for SAD patients

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9 Sources:

US Census Bureau. https://www.census.gov/library/stories/2021/08/united-states-adult-population-grew-faster-than-nations-total-population-from-2010-to-2020.html NIMH. "Social Anxiety Disorder" data from 2017 National Comorbidity Survey (NCS). https://www.nimh.nih.gov/health/statistics/social-anxiety-disorder.shtml Anxiety and Depression Association of America (ADAA). "Social Anxiety Disorder - Understand the Facts" https://adaa.org/understanding-anxiety/social-anxiety-disorder.

BNC210 Addresses the Shortcomings of Existing Social Anxiety Disorder Medications



FDA black box warning

See Appendix for references

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*Potential benefits based on analysis of data from separate studies and not on results that might have been obtained from head-to-head studies. Such data may not be directly comparable due to differences in study protocols, conditions and patient populations. Accordingly, cross-trial comparisons may not be reliable predictors of the relative efficacy or other benefits of BNC210 compared to existing therapies or other product candidates that may be approved or are in development for the treatment of SAD.

**Includes Valium and certain other benzodiazepines

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***Beta blockers address only the sequalae, e.g., physical symptoms such as blushing, increased heart rate, stammering of SAD but do NOT treat the underlying anxiety.

****Includes Prozac and certain other SSRIs (Selective Serotonin Reuptake Inhibitors) / SNRIs (Serotonin-Norepinephrine Reuptake Inhibitors)

Targeting a Large Segment of the Anxiety Market No FDA-approved fast-acting medications for as-needed treatment Projected BNC210 US Social Anxiety Disorder Sales (\$M) 31**M** \$2,000 12.1% of adults at some point in 1,662 \$1,750 their lives ~18M 1,506 \$1,500 \$1,250 1,092 ~7M \$1,000 36% of adults \$750 \$500 247 \$250 **Opportunity** \$0 for BNC210 2026 2029 2032 2035 BNC210 could achieve \$1.7B in US annual peak sales in SAD*

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Sources:

US Census Bureau. https://www.census.gov/library/stories/2021/08/united-states-adult-population-grew-faster-than-nations-total-population-from-2010-to-2020.html NIMH. "Social Anxiety Disorder" data from 2017 National Comorbidity Survey (NCS). https://www.nimh.nih.gov/health/statistics/social-anxiety-disorder.shtml Anxiety and Depression Association of America (ADAA). "Social Anxiety Disorder - Understand the Facts" <u>https://adaa.org/understanding-anxiety/social-anxiety-disorder</u> *Based on 3rd party (Bluestar BioAdvisors) independent market analysis

BNC210's Unique Profile is Well-Positioned for Acute Treatment of SAD

Rapid Onset of Action with BNC210 Formulation



45 – 105 min to reach maximum blood concentrations across dose range following oral administration of tablet



Well-suited for acute dosing – rapidly absorbed to high concentrations with coverage extending for several hours

Proof of Concept in GAD and Panic Attack Model

- SAD shares many characteristics with General Anxiety Disorder (GAD), including a common neural basis in amygdala hyperactivation expressed as excessive or unrealistic anxiety
- BNC210 clinically demonstrated its potential for reducing anxiety in acute treatment of GAD patients and following panic induction in healthy volunteers
- Observed acute anxiolytic efficacy of BNC210 similar to lorazepam without sedating properties or addiction liability
- Our studies also provide clear demonstration of efficacy using biomarker data including EEG and fMRI

BNC210 Reduces Anxiety and Panic Symptoms in Humans

Phase 1b placebo-controlled studyevaluating BNC210 in acute anxiety in15 healthy volunteers who experienceda CCK-4-induced panic attack

- Subjects assessed after a single dose of BNC210 as they would be in an acute SAD trial setting
- Proof of Principle in demonstrating anxiolytic activity



Phase 2 Study of BNC210 Assessing Acute Anxiolytic Activity in GAD



Joystick Operated Runway Task (JORT) -- a model used to measure anxiety-related threat avoidance

Wise T. et al., Biological Psychiatry 2020 (<u>https://doi.org/10.1016/j.biopsych.2019.12.013</u>); Perkins A. et al., Translational Psychiatry 2021 (https://doi.org/10.1038/s41398-020-01141-5) GAD = Generalized Anxiety Disorder SoC = Standard of Care JORT = Joystick Operated Runway Task

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BNC210 Reduces Acute Anxiety-Related Biomarkers in GAD Patients

Amygdala activation is an imaging surrogate for anxiety

BNC210 reduced activation of L & R amygdala caused by viewing fearful faces (L: p=0.011; R: p=0.006)

<image><image>

Connectivity between the amygdala and Anterior Cingulate Cortex (ACC) is very strong in high anxiety

BNC210 reduced connectivity between amygdala and ACC while viewing fearful faces (p=0.012)

BNC210 300 mg also significantly reduced self-reported state anxiety (p=0.003).

BNC210 300 mg reduced threat avoidance behavior of anxious subjects in the JORT behavioral task



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🔇 = BNC210

Wise T. et al., Biological Psychiatry 2020 (https://doi.org/10.1016/j.biopsych.2019.12.013); Perkins A. et al., Translational Psychiatry 2021 (https://doi.org/10.1038/s41398-020-01141-5) JORT = Joystick Operated Runway Task



BNC210 Phase 2 Social Anxiety Disorder Trial

Acute Social Anxiety Disorder Study Highlights

- Leveraging FDA-endorsed registration trial
 endpoint for SAD
- Cost-effective trial with an efficacy endpoint conducive to rapid data generation
- FDA Fast Track designation
- Phase 2 trial underway and will read out topline data by end of 2022



Compelling Rationale for BNC210 in Social and General Anxiety Disorders



BNC210 in Post-Traumatic Stress Disorder



PTSD: Overview and Impacts

A Chronic Psychiatric Disorder with Significant Morbidity and Mortality

PTSD Represents a Significant Unmet Need

A debilitating progressive disorder that leads to social, occupational and interpersonal dysfunction



PTSD involves flashbacks, intrusive thoughts and nightmares



PTSD causes changes in cognition, mood, arousal and reactivity



PTSD results from exposure to actual or threatened death, serious injury or sexual violence

Only 20-30% of PTSD patients achieve clinical remission on SoC SSRI therapy¹

Work

Patients may orient their careers around a narrow set of potential occupations and may struggle with job performance

Relationships

PTSD can impair trust, closeness, and communication, leading to difficulty maintaining family and romantic relationships

Lifestyle

PTSD-associated poor nutrition, reduced physical activity, and increased obesity and smoking, increase risk of cardiovascular and other diseases

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Daily Activities

PTSD patients avoid people, places, or environments which may trigger trauma, making daily living difficult

19 1. Lee DJ, et al. Psychotherapy versus pharmacotherapy for posttraumatic stress disorder: systemic review and meta-analyses to determine first-line treatments. Depress Anxiety. 2016;33(9):792–806.

PTSD Represents a Significant Unmet Need and Market Opportunity

No newly approved pharmacotherapy in almost two decades



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 Kilpatrick, D., Resnick, H., Milanak, M., Miller, M., Keyes, K. and Friedman, M., 2013. National Estimates of Exposure to Traumatic Events and PTSD Prevalence Using DSM-IV and DSM-5 Criteria. Journal of Traumatic Stress, 26(5), pp.537–547; 2 Mayo LM, Asratain A., Lindé J et al. Elevated Anandamide, Enhanced Recall of Fear Extinction, and Attenuated Stress Responses Following Inhibition of Fatty Acid Amide Hydrolase: A Randomized, Controlled Experimental Medicine Trial. Biol Psychiatry. 2020 Mar 15; 87(6): 538-54

2. Only 20 to 30% of PTSD patients achieve clinical remission on SSRI therapies.

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US Census Bureau. https://www.census.gov/library/stories/2021/08/united-states-adult-population-grew-faster-than-nations-total-population-from-2010-to-2020.html *Based on 3rd party market analysis

BNC210 Addresses the Shortcomings of Existing and Emerging PTSD Approaches

		BNC210's ADVANTAGES COMPARED TO CURRENT AND EMERGING THERAPIES*					
		No Withdrawal Syndrome	Neurotoxicity or other toxicity	No Cognitive or Memory Impairment	No Suicidal Ideation or increased suicide risk		
	BNC210	\checkmark	\checkmark	\checkmark	\checkmark		
1st line –	SSRIs / SNRIs	X ^{2,3}	\checkmark	\checkmark	X ⁶		
Emerging _	Ketamine	\checkmark	X ^{7,9}	X ¹¹	\checkmark		
	MDMA**	X ⁸	X ¹⁰	X ¹²	X ¹³		

See Appendix for references

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21 *Potential benefits based on analysis of data from separate studies and not on results that might have been obtained from head-to-head studies. Such data may not be directly comparable due to differences in study protocols, conditions and patient populations. Accordingly, cross-trial comparisons may not be reliable predictors of the relative efficacy or other benefits of BNC210 compared to existing therapies or other product candidates that may be approved or are in development for the treatment of PTSD or SAD.

** MDMA does not work as a monotherapy. MDMA has been explored in combination with CBT. BNC210 + MDMA combination therapy may reduce number of CBT sessions required during MDMA treatment.

BNC210 Promotes Fear Extinction in Animal and Human Models

People with anxiety disorders and PTSD have amplified fear responses to trauma- or stress-related stimuli and impaired fear extinction





*Time in minutes after CCK-4 injection CCK-4 = Cholecystokinin Tetrapeptide (a peptide that induces anxiety and panic symptoms) eVAS = Emotional Visual Analog Scale

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Phase 2 Study Determined Target BNC210 Blood Exposure for PTSD Pharmacometric (PMX) Analysis Target Exposure



PMX modelling on prior Phase 2 PTSD trial identified 25 mg.hr/L blood exposure target

Pharmacometric analysis identified a statistically significant exposure-response relationship for the CAPS-5 Total score (p value <0.01)

AUC Values (plasma exposure) CAPS-5 Score (PTSD symptoms)







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ATTUNE Study

BNC210 Phase 2b PTSD Trial Underway



symptoms of PTSD, changes in

anxiety and depression symptoms,

and global and social functioning;

Safety & tolerability endpoints

Investigator-rated PTSD symptoms on CAPS-5 Total Symptom Severity Scores in change from Baseline to Week 12 compared to placebo

Phase 2b

Single potential registrationalsupporting trial for monotherapy treatment in PTSD

KEY INCLUSION CRITERIA

Female and male (18 – 75 years) Current PTSD diagnosis CAPS-5 ≥ 30 (Screening & Baseline) (& ≤ 25% decrease Screening to Baseline)

~25 Sites

Fast Track designation from FDA



Topline data expected mid 2023



Compelling Rationale for BNC210 in PTSD



BNC210 "Pipeline in a Pill": Development Strategy Highlights



CNS-focused Collaborations

MDMA Derivative in combination with BNC210 for PTSD

Cognitive Impairment in Alzheimer's and other CNS disorders

Memorandum of Understanding with EmpathBio for BNC210 and MDMA Derivative for PTSD

MDMA-assisted therapy significantly reduced CAPS-V scores in PTSD patients (primary endpoint) ¹ (n=90)



Joint Feasibility Assessment

EMP-01 (3,4-Methylenedioxymethamphetamine) (MDMA) derivative BNC210 + EMP-01 could relieve the burden of pairing MDMA with CBT, potentially reducing the number of CBT sessions needed with MDMA treatment

MOU with EmpathBio's MDMA Derivative (EMP-01)

- Initial collaborative framework of preclinical studies to collectively explore a combination drug treatment regimen with BNC210 and EMP-01
- MDMA-assisted CBT has demonstrated significant symptom improvement in PTSD patients
- FDA has granted a Breakthrough Therapy designation to MDMA-assisted psychotherapy
- EmpathBio is developing MDMA derivatives that may permit the entactogenic effects of MDMA to be separated from some of the known adverse effects
- To explore the possibility of a combination treatment regimen warranting clinical evaluation

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28 1. Change in CAPS-V total severity score from T1 to T4 (P < 0.0001, d = 0.91, n = 89 (MDMA n = 46)), as a measure of the primary outcome. Primary analysis was completed using least square means from a mixed model repeated measure (MMRM) analysis model; (n=90) Mitchell et al., "MDMA-assisted therapy for severe PTSD: a randomized, double-blind, placebo-controlled phase 3 study" (2021) CBT = Cognitive Behavioral Therapy

Merck & Co Strategic Collaboration: Positive Allosteric Modulators (PAMs) of α7 Nicotinic Acetylcholine Receptor for Treatment of Cognitive Deficits

α7 Receptor PAMs correct hypocholinergic states in cognitive dysfunction and impairment

MSD Collaboration Overview



2014 agreement to develop α7 receptor PAMs targeting cognitive dysfunction associated with Alzheimer's disease, schizophrenia and other CNS conditions Merck funds all research and clinical development, and WW commercialization of any resulting products

Payments received: US\$20M upfront and US\$10M for Phase 1 milestone

Eligible to receive up to US\$465M in additional milestone payments plus royalties

Development Updates

PARTNERSHIP

Two α7 receptor PAM candidates in early-stage Phase 1 safety and biomarker studies for cognitive impairment

1st compound has completed Phase 1 safety clinical trials in healthy subjects and biomarker studies ongoing

In 2020, a second molecule with an improved potency profile in non-human primate models was advanced into Phase 1 clinical trials

29 Wang et al. J Pharmacol Exp Ther 373:311–324, May 2020 <u>https://pubmed.ncbi.nlm.nih.gov/32094294/</u> PAM = Positive allosteric modulator MSD = A tradename of Merck & Co., Inc., Kenilworth NJ USA





Financial Information & Investment Highlights



Stock, Financial and IP Snapshot



Bionomics Highlights



Balanced business model with multiple value-driving clinical milestones expected over the next 4 quarters



Lead Asset BNC210: Annual Peak Pales market opportunity of \$1.7B in SAD and \$2.6B in PTSD¹



BNC210's Phase 2 PREVAIL trial under way with Fast Track designation for acute treatment of SAD with topline data by YE 2022; Established clinical proof-of-concept

BNC210 Phase 2b ATTUNE PTSD study under way with Fast Track designation, topline data by mid 2023; Tablet formulation achieves blood exposure projected from pharmacometric analysis



Merck strategic partnership for treatment of cognitive impairment in Alzheimer's disease and Schizophrenia with two compounds in clinical development

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Well-capitalized balance sheet and experienced leadership







Pre-Clinical Assets

Kv3.1 / Kv3.2 Ion Channel Activators for Cognitive Dysfunction and Negative Symptoms in Schizophrenia and other Disorders

Nav1.7/1.8 Inhibitors: Potential Non-Addictive, Reduced Side-Effect Chronic Pain Therapies



Promising Therapeutic Strategy for Improving Cognitive Dysfunction and Social Withdrawal Symptoms

Kv3.1 / Kv3.2 Ion Channel Activators for treatment of Cognitive Dysfunction and Negative Symptoms

Potential in schizophrenia, Autism Spectrum disorders and conditions with cognitive impairments Bionomics' molecules target Kv3.1/3.2 ion channels on Parvalbumin (+), GABAergic interneurons in the PFC



Nav1.7/1.8 Inhibitors: Potential Non-Addictive, Reduced Side-Effect Chronic Pain Therapies

BNOX Pan Nav Inhibitors

Small molecules with functional selectivity for voltage gated sodium channels: Nav1.7, Nav1.8 and potentially Nav1.9

Disease-related genetics: Gain & Loss-of-function mutations in Nav1.7, 1.8 and 1.9. associated with human pain syndromes where extreme pain or no pain is experienced

Lead Candidate Identified: BL-017881

Observed to reverse pain in the formalin paw model in mice



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Arron Weaver Apeiron Nominee







Summary of BNC210 Clinical Trials

Phase	Description	Participants /Setting	Subjects Enrolled / Administered BNC210*	BNC210 Formulation and Doses	Location
1	Single Ascending Dose Safety and PK	Healthy volunteers / In-clinic	32/24	Suspension; single doses (5 to 2000 mg)	Australia
1	Single Ascending Dose Safety and PK; Food Effect	Healthy volunteers / In-clinic	4/3	Suspension; single doses (300 to 2000 mg)	Australia
1	Single Ascending Dose Safety and PK; Food Effect	Healthy volunteers / In-clinic	47/40	Capsule; single doses (300 to 3000 mg)	US
1b	Lorazepam Comparison	Healthy volunteers / In-clinic	24/22	Suspension; single doses (300 and 2000 mg)	France
1b	CCK-4 Panic Attack Model	Healthy volunteers / In-clinic	60/59	Suspension; single doses (2000 mg)	France
1b	Multiple Ascending Dose Safety and PK; Expanded Cohort for EEG Target Engagement	Healthy volunteers / In-clinic	56/44	Suspension; multiple doses (150 to 1000 mg twice daily for 8 days)	France
1	Suspension and Tablet Formulation PK Comparison	Healthy volunteers / In-clinic	6/6	Suspension and tablet; single doses (300 mg)	Australia
1	Single Ascending Dose Safety and PK	Healthy volunteers / In-clinic	5/5	Tablet; single doses (600 to 1200 mg)	Australia
1	Multiple Dosing Safety and PK	Healthy volunteers / In-clinic	10/10	Tablet; multiple doses (900 mg twice daily for 7 days)	Australia
2a	Imaging and Behavioral Study In Generalized Anxiety Disorder	Generalized anxiety disorder patients / In- clinic	27/25	Suspension; single doses (300 and 2000 mg)	UK
2a	Agitation in the Elderly in Hospital Setting	Agitated elderly patients / Hospital	38/18	Suspension; multiple doses (300 mg twice daily for 5 days)	Australia
2	Post-Traumatic Stress Disorder	Post-traumatic stress disorder patients / Out-patient	193/143	Suspension; multiple doses (150, 300 or 600 mg twice daily for 12 weeks)	Australia US
2b	Post-Traumatic Stress Disorder	Post-traumatic stress disorder patients / Out-patient	Ongoing	Tablet; multiple doses (900 mg twice daily for 12 weeks)	US
2	Social Anxiety Disorder	Social anxiety disorder patients / In-clinic	Ongoing	Tablet; single doses (225 and 675 mg)	US

40 * The number of enrolled subjects who were administered BNC210; other enrolled subjects were administered placebo only CCK-4 = Cholecystokinin Tetrapeptide. EEG = Electroencephalography. PK = Pharmacokinetic



Novel Proprietary BNC210 Tablet Formulation Achieves Pharmacometric Modeling Blood Exposure Target for PTSD and Eliminates Food Effect BNC210 Novel Spray- Dry Dispersion Formulation

BNC210 tablet formulation for PTSD

Novel spray-dry dispersion formulation used to produce a tablet with a favorable PK profile

Novel formulation achieves target AUC > 25 mg.hr/L blood exposure target with 900 mg dose b.i.d

Novel tablet alleviates food effect and has dose linear exposure



References for Comparative Analyses of BNC210 and SAD and PTSD Therapeutics: Slides 10 and 21

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