Bionomics Reports Results of the Full Dataset Analysis from ATTUNE Phase 2b Trial of BNC210 in Patients with Post-Traumatic Stress Disorder

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BNC210 demonstrated a statistically significant improvement in post-traumatic stress disorder (PTSD) symptom severity with a clinically meaningful effect size suggesting a potential advantage over approved medications.

BNC210's emerging safety and tolerability profile continues to support its differentiation over approved, available, and experimental psychoactive treatments.

Bionomics will meet with the U.S. Food & Drug Administration (FDA) to discuss BNC210's registrational program in PTSD by end of the second quarter of 2024; Late-stage trial initiation is expected by the end of 2024.

ADELAIDE, Australia and CAMBRIDGE, Mass., March 21, 2024 (GLOBE NEWSWIRE) -- Bionomics Limited (Nasdaq: BNOX) (Bionomics or Company), a clinical-stage biotechnology company developing novel, first-in-class, allosteric ion channel modulators to treat patients suffering from serious central nervous system (CNS) disorders with high unmet medical need, today announced the release of the full dataset analysis from its Phase 2b ATTUNE trial in patients with post-traumatic stress disorder.

In September 2023, Bionomics reported the topline results for the Phase 2b ATTUNE trial of BNC210 in patients with PTSD demonstrating that the trial met its primary endpoint and several secondary endpoints, and that BNC210 was generally well tolerated. The full data analysis is detailed below and in an accompanying presentation of the results that is posted on the Company's website .

"The full results of the ATTUNE Phase 2b trial further strengthen, the already compelling, topline results and position BNC210 as a potential highly differentiated treatment with rapid onset and durable efficacy that could improve outcomes for patients with PTSD. There are over 13 million Americans adults suffering from PTSD, yet only 20%-30% of them are effectively treated with the currently approved selective serotonin reuptake inhibitors (SSRIs), which not only have slow onset of action but are also associated with many side effects," said Spyros Papapetropoulos, M.D., Ph.D., President and CEO of Bionomics. "BNC210 is the only non-psychedelic experimental therapeutic with a novel mechanism of action that has generated evidence of a clinically meaningful improvement in PTSD total symptom severity, with a favorable effect size compared to approved treatments, and a favorable safety and tolerability profile. We look forward to our discussion with the FDA in the second quarter of 2024 and preparing for initiation of a registrational late-stage trial in PTSD by the end of 2024."

ATTUNE Phase 2b Trial Efficacy Results

ATTUNE achieved its primary and several secondary endpoints highlighting the potential of BNC210 to address multiple key symptoms experienced by patients with PTSD. Effects were observed as early as Week 4 supporting potential for rapid onset of clinical efficacy compatible with BNC210's mechanism of action.

- The primary endpoint of mean change from baseline in Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) total symptom severity score was met showing that BNC210 led to a statistically significant improvement vs placebo ($p<0.05$) at Week 12 with an effect size of 0.40. The improvement in CAPS-5 score was observed as early as Week 4 ($p<0.05$, effect size 0.40) and continued through Week 8 ($p<0.05$, effect size 0.44) till the end of the treatment period, supporting a rapid onset and clinically meaningful and sustained effect of BNC210.
    - Within the CAPS-5 symptom clusters, statistically significant results at Weeks 4, 8 and 12 were achieved for intrusion symptoms, which is a crucial aspect of successful management of PTSD symptoms (Criterion B, $p<0.05$). Additionally, statistically significant results were achieved for negative alterations in cognitions and mood at Week 4 and Week 8 (Criterion D, $p<0.05$).
- Treatment with BNC210 led to statistically significant improvement ($p<0.05$) in the following secondary endpoints: depressive symptoms as measured by the Montgomery-Åsberg Depression Rating Scale (MADRS) at Week 12, and sleep as measured by the Insomnia Severity Index (ISI) at Weeks 4, 8 and 12.
- BNC210 treatment showed improvement trends ($p<0.1$) across visits in the other secondary endpoints including the clinical and patient global impressions severity scales (CGI-S, PGI-S), the Hamilton Anxiety Rating scale (HAM-A), and the Sheehan Disability Scale (SDS).

ATTUNE Phase 2b Trial Safety Results

Overall, BNC210 continued to demonstrate a favorable safety profile for a psychoactive experimental therapeutic.

- 66.7% of patients in the BNC210 arm and 53.8% of patients in the placebo arm reported at least one treatment-emergent adverse event (AEs). Most AEs were mild or moderate. No serious AEs were reported with BNC210. The most common (>5% of subjects in each group) reported AEs were headache, nausea, fatigue, and hepatic enzyme (ALT, AST) increases.

There were no reports in excess of placebo in sexual side effects (e.g., decreased libido, erectile dysfunction) that are commonly associated with SSRI treatment.
- The most frequent reasons for discontinuations were AEs (14.6%), withdraw of consent (9.9%) and lost to follow-up (10.4%). Overall, there were more discontinuations from AEs in the BNC210 group (19.8%) vs placebo (9.4%). Five patients in the BNC210 group (4.8%) and two patients in the placebo group (1.9%) discontinued treatment due to an increase in hepatic enzymes. These increases were not associated with liver injury or decompensation nor were there any elevations in bilirubin levels. There were no other system organ category (SOC) AE clusters or laboratory findings of note.
- Upon trial completion, there were no withdrawal symptoms reported, including no rebound anxiety that is common with treatment cessation of SSRIs and benzodiazepines.

Following the ATTUNE Phase 2b trial readout and based on a safety database of ~600 patients, BNC210 continues to demonstrate a non-sedating, non-habit forming, non-cognition impairing psychoactive profile.

ATTUNE Phase 2b Trial Pharmacokinetics Analyses

- BNC210's novel and proprietary solid tablet formulation (900 mg twice daily) delivered a predictable pharmacokinetic (PK) profile exceeding the projected therapeutic exposures for PTSD by ~2x based on a pharmacometrics model that was developed using data from completed studies prior to the initiation of the ATTUNE Phase 2b trial.
- The population PK and safety analyses revealed that the hepatic enzyme increases may be attributed to the high exposures achieved with 900 mg twice daily dose.
- In addition to the 900 mg twice daily dose, a lower BNC210 dose that may alleviate hepatic enzyme elevations will be tested in a subsequent late-stage clinical trial.

Based on these efficacy and safety observations, the Company plans to discuss the Phase 2b ATTUNE results with the FDA in the second quarter this year and proceed to a late-stage trial in the fourth quarter of 2024.

The full results of the Phase 2b ATTUNE trial together with prior datasets from other Phase 1b and Phase 2 clinical studies in social anxiety disorder, generalized anxiety disorder and panic attacks support BNC210's favorable efficacy, safety, and tolerability profile, especially over SSRIs, benzodiazepines and other available treatments for these disorders.

About ATTUNE

ATUUNE (NCT04951076) is a Phase 2b double-blind, placebo-controlled, randomized trial of 900 mg BNC210 given twice daily as monotherapy treatment for PTSD. Trial participants were randomized 1:1 to receive either placebo or BNC210. Key inclusion criteria include being 18-75 years of age, having a current PTSD diagnosis with a Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) total symptom severity score of ≥ 30 at screening and baseline, and ≤ 25% decrease in CAPS-5 score from screening to baseline. The primary endpoint is change in CAPS-5 total symptom severity scores from baseline to week 12 compared to placebo. Secondary endpoints include change from baseline to Week 12 compared to placebo on the PTSD-checklist (PCL-5), anxiety (Hamilton Anxiety Rating Scale, HAM-A), depression (Montgomery-Asberg Depression Rating Scale, MADRS), Clinician Global Impression (CGI), Patient Global Impression (PGI), sleep (Insomnia Severity Index, ISI) and disability (Sheehan Disability Scale, SDS). 212 participants have been enrolled at 27 sites in the United States and 7 sites in the United Kingdom

About Post Traumatic Stress Disorder

Post-Traumatic Stress Disorder (PTSD) is a psychiatric condition that may occur in people who have experienced or witnessed a traumatic event, series of events, or set of circumstances. People with PTSD have intense, disturbing thoughts and feelings related to their experience that persist long after the traumatic event has ended. They may relive the event through flashbacks or nightmares, may feel sadness, fear, or anger and may experience a sense of detachment or estrangement from others. As a result of these feelings, people with PTSD may avoid situations or people that remind them of the traumatic event, and they may have strong negative reactions to commonplace stimuli such as loud noises or an accidental touch.

About BNC210

BNC210 is a negative allosteric modulator of the α7 nicotinic acetylcholine receptor under development for the treatment of PTSD and Social Anxiety Disorder (SAD). BNC210 has been given the FDA Fast Track designation for treatment of PTSD and other trauma and stressor related disorders and for acute treatment of SAD and other anxiety related disorders. It should be noted that positive results in or from prior, current, or later clinical trials, studies and pre-clinical development may not provide positive data and/or similar results moving forward, as they are not a predictor or indicative of future results, success, or regulatory approval.

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About Bionomics Limited

Bionomics (NASDAQ:BNOX) is a clinical-stage biotechnology company developing novel, first-in-class, allosteric ion channel modulators to treat patients suffering from serious central nervous system ("CNS") disorders with high unmet medical need. Bionomics is advancing its lead drug candidate, BNC210, an oral, proprietary, selective negative allosteric modulator of the α7 nicotinic acetylcholine receptor, for the acute treatment of Social Anxiety Disorder (SAD) and chronic treatment of Post-Traumatic Stress Disorder (PTSD). Beyond BNC210, Bionomics has a strategic

partnership with Merck & Co., Inc. (known as MSD outside the United States and Canada) with two drugs in early-stage clinical trials for the treatment of cognitive deficits in Alzheimer's disease and other central nervous system conditions. Bionomics' pipeline also includes preclinical assets that target Kv3.1/3.2 and Nav1.7/1.8 ion channels being developed for CNS conditions of high unmet need. www.bionomics.com.au

Forward-Looking Statements

Bionomics cautions that statements included in this press release that are not a description of historical facts are forward-looking statements. Words such as "may," "could," "will," "would," "should," "expect," "plan," "anticipate," "believe," "estimate," "intend," "predict," "seek," "contemplate," "potential," "continue" or "project" or the negative of these terms or other comparable terminology are intended to identify forward-looking statements. These statements include the Company's plans to advance the development of its product candidates, the timing of achieving any development or regulatory milestones, and the comparability and potential of such product candidates, including to achieve any benefit or profile or any product approval or be effective. The inclusion of forward-looking statements should not be regarded as a representation by Bionomics that any of its plans will be achieved. Actual results may differ materially from those set forth in this release due to the risks and uncertainties inherent in the Company's business and other risks described in the Company's filings with the Securities and Exchange Commission (SEC), including, but not limited to, the Company's Annual Report on Form 20-F filed with the SEC, and its other reports. Investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and Bionomics undertakes no obligation to revise or update this news release to reflect events or circumstances after the date hereof. Further information regarding these and other risks is included in Bionomics' filings with the SEC which are available from the SEC's website (www.sec.gov) and on Bionomics' website (www.bionomics.com.au) under the heading "Investor Center." All forward-looking statements are qualified in their entirety by this cautionary statement. This caution is made under the safe harbor provisions of Section 21E of the Private Securities Litigation Reform Act of 1995.