atai Life Sciences Company GABA Therapeutics Announces Positive Final Results from Phase 1 Single and Multiple Ascending Dose Trial of GRX-917

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- GRX-917 (deuterated etifoxine) was well-tolerated with no dose-limiting toxicities and only mild adverse effects comparable to that of placebo in both single and multiple ascending doses, as previously announced as preliminary results during atai's R&D day.
- Final results demonstrate target engagement of GRX-917 via dose-related activation of quantitative electroencephalography (qEEG) frontal beta power, a biomarker for GABA-A receptor-associated anxiolytic activity, consistent with GRX-917's putative mechanism-of-action.
- Less frequent dosing is anticipated for GRX-917, versus the two-to-three times a day with non-deuterated etifoxine, due to marked improvements in pharmacokinetic properties.
- GRX-917 was well tolerated with sedation comparable to placebo noted over the entirety of the dose range explored.
- Initiation of a GRX-917 efficacy study is anticipated in H1 2023 with results expected in 2024.

NEW YORK and BERLIN, Jan. 09, 2023 (GLOBE NEWSWIRE) -- Today, atai Life Sciences N.V. (Nasdaq: ATAI) ("atai" or "the Company"), a clinical-stage biopharmaceutical company aiming to transform the treatment of mental health disorders, and its subsidiary GABA Therapeutics, announced final positive results from a Phase 1 clinical trial of GRX-917 that were previously announced as preliminary results during atai's R&D day. The randomized, double-blind, placebo-controlled trial was designed to evaluate the safety, tolerability, and pharmacokinetic profile of single and multiple ascending doses of orally administered GRX-917.

Overall, compared to placebo, GRX-917 was well-tolerated and neither dose-related nor dose-limiting adverse events were observed. There were no serious adverse events reported nor discontinuations due to drug administration. Furthermore, in contrast to current first-line anxiety disorder treatments such as benzodiazepines, sedation was found to be comparable to placebo.

Dose-dependent increases in qEEG beta power, a biomarker for GABA receptor activation, was demonstrated in subjects who received GRX-917 but not with those who received a placebo, providing evidence of target engagement consistent with GRX-917's putative mechanism of action.

GRX-917 is a deuterated version of etifoxine, which is an anxiolytic approved in France, with rapid onset and efficacy comparable to leading benzodiazepines like alprazolam and lorazepam that are currently considered the standard of care but is non-addictive with minimal side effects. Etifoxine is thought to achieve its anxiolytic activity by increasing endogenous production of brain neurosteroids like allopregnanolone. Dysregulation of neurosteroidogenesis has been implicated in a broad range of neuropsychiatric diseases including generalized anxiety disorder (GAD), anxious depression, social anxiety disorder (SAD), panic disorder, and postpartum depression.

"According to a World Health Organization report, the number of people living with anxiety disorders globally grew from 298 million people in 2020 to 374 million in 2021," said Florian Brand, CEO of atai. "Given the catastrophic effects of the pandemic on the mental health of people around the world, the need for a better tolerated, safer therapeutic for GAD and other anxiety disorders has never been more pronounced."

"We are very encouraged by the Phase 1 results for GRX-917," said Mario Saltarelli, MD, PhD, CEO and CMO of GABA. "Based on etifoxine's safety and efficacy profile, we believe GRX-917 will offer a differentiated treatment for GAD with fewer side effects—such as sedation, respiratory depression, and withdrawal."

Safety Data

In the single-ascending dose (SAD) portion of the trial, adverse events were observed in 53% (17/32) of GRX-917 treated subjects, comparable to 50% (5/10) observed in placebo-treated subjects. Adverse events related to GRX-917 specifically occurred in 25% (8/32) of subjects and were all mild in severity.

In the multiple-ascending dose (MAD) portion of the trial, adverse events were observed in 60.5% (26/43) of GRX-917 treated subjects, also comparable to 60% (9/15) observed in placebo-treated subjects. Adverse events related to GRX-917 specifically occurred in 32.6% (14/43) of subjects and were all mild in severity. The results of these two trial phases indicate that there were no dose-limiting adverse events in trial subjects at higher dosages and no benzodiazepine-like side effects, including sedation were observed.

Biomarker/Pharmacodynamic (PD) Data

Dose- and exposure-dependent increases in beta power were observed by quantitative electroencephalogram (qEEG) in healthy volunteers receiving single doses of GRX-917 but not in those who received a placebo. These results show that GRX-917 has measurable effects on the central nervous system and provide evidence of GABA receptor target engagement and mechanism of action.

About atai Life Sciences

atai Life Sciences is a clinical-stage biopharmaceutical company aiming to transform the treatment of mental health disorders. Founded in 2018 as a response to the significant unmet need and lack of innovation in the mental health treatment landscape, atai is dedicated to acquiring, incubating, and efficiently developing innovative therapeutics to treat depression, anxiety, addiction, and other mental health disorders.

By pooling resources and best practices, atai aims to responsibly accelerate the development of new medicines across its companies to achieve clinically meaningful and sustained behavioral change in mental health patients.

atai's vision is to heal mental health disorders so that everyone, everywhere can live a more fulfilled life. For more information, please visit www.atai.life.

About GABA Therapeutics

GABA Therapeutics, Inc. is a clinical stage biotechnology company focused on addressing the growing, unmet medical need in serious psychiatric and neurological disorders, including anxiety, depression, epilepsy, and rare diseases. GABA's flagship product, GRX-917, is a patent-protected, deuterated version of the approved French anxiety medication etifoxine. The company is a majority-owned subsidiary of atai Life Sciences. For more information, please visit https://gabarx.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. The words "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "expect," "initiate," "could," "would," "project," "plan," "potentially," "preliminary," "likely," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Forward-looking statements include express or implied statements relating to, among other things: statements regarding the trials and studies by GABA Therapeutics and future results and activities thereunder; the potential of GRX-917; the success, cost and timing of development of our product candidates, including the progress of preclinical and clinical trials and related milestones; our business strategy and plans; potential acquisitions; and the plans and objectives of management for future operations and capital expenditures. The forward-looking statements in this press release are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, many of which are beyond our control and which could cause actual results, levels of activity, performance, or achievements to differ materially from those expressed or implied by these forward-looking statements.

The forward-looking statements in this press release are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements. These forward-looking statements are subject to a number of risks, uncertainties, and assumptions that could cause actual results to differ materially from those expressed or implied by the forward-looking statements, including without limitation: we are a clinical-stage biopharmaceutical company and have incurred significant losses since our inception, and we anticipate that we will continue to incur significant losses for the foreseeable future; we will require substantial additional funding to achieve our business goals, and if we are unable to obtain this funding when needed and on acceptable terms, we could be forced to delay, limit or terminate our product development efforts; our limited operating history may make it difficult to evaluate the success of our business and to assess our future viability; we have never generated revenue and may never be profitable; clinical and preclinical development is uncertain, and our preclinical programs may experience delays or may never advance to clinical trials; we rely on third parties to assist in conducting our clinical trials and some aspects of our research and preclinical testing, and those clinical trials, including progress and related milestones, may be impacted by several factors including the failure by such third parties to meet deadlines for the completion of such trials, research, or testing, changes to trial sites and other circumstances; we cannot give any assurance that any of our product candidates will receive regulatory approval, which is necessary before they can be commercialized; third parties may claim that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and may prevent or delay our development and commercialization efforts; and a pandemic, epidemic, or outbreak of an infectious disease, such as the COVID-19 pandemic, may materially and adversely affect our business, including our preclinical studies, clinical trials, third parties on whom we rely, our supply chain, our ability to raise capital, our ability to conduct regular business and our financial results. These and other important factors described in the section titled "Risk Factors" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, filed with the Securities and Exchange Commission ("SEC"), our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K, as updated by our subsequent filings with the SEC, may cause our actual results, performance, or achievements to differ materially and adversely from those expressed or implied by the forward-looking statements. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change.

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