NEWS RELEASE

BioVie Announces FDA Authorization of Investigational New Drug Application for Phase 2 Trial to Evaluate Bezisterim in Long COVID

2024-09-03

Authorization expands use of bezisterim in a Phase 2, placebo-controlled, multicenter trial assessing bezisterim's impact on neurological symptoms associated with long COVID

Key milestone reached ahead of schedule, with BioVie on track to receive additional $12.6 million of award from the U.S. Department of Defense and initiate the Phase 2 trial

Recent Centers for Disease Control and Prevention survey estimated over 5% of U.S. adults currently have long COVID, and ~3.6 million people reported significantly modifying their activities because of illness [1]

CARSON CITY, Nev., Sept. 03, 2024 (GLOBE NEWSWIRE) -- BioVie Inc. (NASDAQ: BIVI), ("BioVie" or the "Company"), a clinical-stage company developing innovative drug therapies for the treatment of neurological and neurodegenerative disorders and advanced liver disease, today announced that the U.S. Food and Drug Administration (FDA) has authorized the Company's Investigational New Drug ("IND") application to evaluate bezisterim for the treatment of neurological symptoms that are associated with long COVID. Receipt of this FDA authorization puts the Company ahead of schedule and on track to receive an additional $12.6 million in grant funding from the U.S. Department of Defense ("DOD") and initiate its Phase 2 trial.

"We are delighted to announce that the FDA has authorized our IND application for bezisterim, allowing us to study a novel, anti-inflammatory approach for the treatment of the debilitating neurocognitive symptoms associated with long COVID," said Cuong Do, BioVie's President and CEO. "A growing body of evidence points to inflammation as a key driver of long COVID, and we believe that bezisterim has shown promise in addressing these underlying mechanisms. This is a significant milestone that brings us closer to exploring how bezisterim could help patients with this debilitating condition."

The planned Phase 2 study is a randomized (1:1), placebo-controlled, multicenter trial in approximately 200 patients to evaluate the safety and tolerability of 3 months of treatment with bezisterim and the potential ability to reduce the neurocognitive symptoms associated with long COVID.

Long COVID is a condition in which symptoms of COVID-19, the acute respiratory disease caused by the SARS-CoV-2 virus, persist for an extended period of time, generally three months or more. The Centers for Disease Control recently reported that around 5.5% of adults in the U.S. currently have long COVID, and around 3.6 million people have reported significantly modifying their activities because of the illness. [1] Symptoms include cognitive dysfunction and fatigue and are debilitating. No therapies have proven effective for treatment to date. Chronic inflammation is one of the main hypotheses that researchers have proposed to explain the persistence of symptoms in long COVID. [3] Specifically in individuals with "brain fog," sustained systemic inflammation and persistent localized blood-brain-barrier (BBB) dysfunction are key physiological features. [5] Bezisterim permeates the BBB and has been shown to modulate inflammation via the activation of NF-kB, thus representing a novel oral treatment targeting a suspected underlying cause of long COVID symptoms.

Terms of the Department of Defense Award
The work is supported by the Assistant Secretary of Defense for Health Affairs endorsed by the Department of Defense, in the amount of $499,200 for the planning phase with the option, if approved, to receive an additional $12.6 million, to initiate a clinical trial once the planning phase has concluded and milestones have been met, through the Peer-Reviewed Medical Research Program (PRMRP) under Award No. HT9425-24-1-0113. Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the Assistant Secretary of Defense for Health Affairs or the Department of Defense.

About Long COVID
Long COVID is a condition in which symptoms of COVID-19, the acute respiratory disease caused by the SARS-CoV-2 virus, persist for an extended period of time, generally three months or more. Common symptoms include lingering loss of smell and taste, hearing loss, extreme fatigue, and "brain fog," though persistent cardiovascular and respiratory problems, muscle weakness, and neurologic issues have also been documented. The Centers for Disease Control recently reported that 5.5% of adults in the United States (more than 17 million individuals) currently have long COVID, and 18.3% have experienced it at some point. [1] With around 3.6 million people having reported significantly modifying their activities because of long COVID, the loss in quality of life and earnings and increased medical costs has an enormous economic impact estimated to be $3.7 trillion. [1, 2] To date there are no non-pharmacological or pharmacological therapies proven effective for treatment of long COVID.

Chronic inflammation is one of the main hypotheses that researchers have proposed to explain the persistence of symptoms in long COVID. [3] The expression of proteins associated with inflammation (LGALS9, CCL21, CCL22, TNF,

CXCL10 and CD48) and immune regulation (IL1RN and CD22) have been shown to be elevated in individuals with long COVID versus full-recovered individuals. [4] Specifically in individuals with "brain fog," sustained systemic inflammation and persistent localized blood-brain-barrier (BBB) dysfunction are key physiological features. [5] Thus, drugs modulating inflammation, and that work to regulate the BBB integrity, could represent potential therapeutic mechanisms for treating neurological symptoms of long COVID.

About Bezisterim

Bezisterim (NE3107) is an orally bioavailable, BBB-permeable, insulin-sensitizer that is also anti-inflammatory. In addition, it is not immunosuppressive and has a low risk of drug-to-drug interaction. Bezisterim has the potential to reduce symptoms of long COVID, including fatigue and cognitive dysfunction. Persistently circulating viral spike proteins are believed to trigger TLR-4 driven activation of NFkB and the subsequent expression of inflammatory cytokines (IL-6, TNF, IFNg). NE3107 has been shown to modulate the activation of NFkB and thus modulate inflammation.

Bezisterim is also being investigated for Alzheimer's disease ("AD") and Parkinson's disease ("PD"). BioVie has conducted and reported efficacy data on its Phase 3 randomized, double-blind, placebo-controlled, parallel-group, multicenter study to evaluate bezisterim in patients who have mild-to-moderate AD (NCT04669028). Results of a Phase 2 investigator-initiated trial (NCT05227820) showing bezisterim-treated patients experienced improved cognition and biomarker levels were presented at the Clinical Trials on Alzheimer's Disease (CTAD) annual conference in December 2022. An estimated six million Americans suffer from AD. A Phase 2 study of bezisterim in PD (NCT05083260) has been completed, and data presented at the AD/PD™ 2023 International Conference on Alzheimer's and Parkinson's Diseases and related neurological disorders in Gothenburg, Sweden in March 2023 showed significant improvements in "morning on" symptoms and clinically meaningful improvement in motor control in patients treated with a combination of bezisterim and levodopa vs. patients treated with levodopa alone, and no drug-related adverse events.

About BioVie Inc.

BioVie Inc. (NASDAQ: BIVI) is a clinical-stage company developing innovative drug therapies for the treatment of neurological and neurodegenerative disorders and advanced liver disease. In neurodegenerative disease, the Company's drug candidate bezisterim inhibits inflammatory activation of ERK and NFkB (e.g., TNF signaling) that leads to neuroinflammation and insulin resistance, but not their homeostatic functions (e.g., insulin signaling and neuron growth and survival). Both are drivers of AD and PD. In liver disease, the Company's Orphan drug candidate BIV201 (continuous infusion terlipressin), with FDA Fast Track status, is being evaluated and discussed with guidance received from the FDA regarding the design of Phase 3 clinical testing of BIV201 for the treatment of ascites due to chronic liver cirrhosis. The active agent is approved in the U.S. and in about 40 countries for related complications of advanced liver cirrhosis. For more information, visit www.bioviepharma.com.

Forward-Looking Statements

This press release contains forward-looking statements, which may be identified by words such as "expect," "look forward to," "anticipate" "intend," "plan," "believe," "seek," "estimate," "will," "project" or words of similar meaning. Although BioVie Inc. believes such forward-looking statements are based on reasonable assumptions, it can give no assurance that its expectations will be attained. Actual results may vary materially from those expressed or implied by the statements herein due to the Company's ability to successfully raise sufficient capital on reasonable terms or at all, available cash on hand and contractual and statutory limitations that could impair our ability to pay future dividends, our ability to complete our pre-clinical or clinical studies and to obtain approval for our product candidates, our ability to successfully defend potential future litigation, changes in local or national economic conditions as well as various additional risks, many of which are now unknown and generally out of the Company's control, and which are detailed from time to time in reports filed by the Company with the SEC, including quarterly reports on Form 10-Q, reports on Form 8-K and annual reports on Form 10-K. BioVie Inc. does not undertake any duty to update any statements contained herein (including any forward-looking statements), except as required by law.

References

[1] U.S. Census Bureau. Household Pulse Survey, 2022-2024. **https://www.cdc.gov/nchs/covid19/pulse/long-covid.htm** .

[2] Cutler, David M. 2022 The economic costs of Long COVID: An update. **long_covid_update_7-22.pdf (harvard.edu)**

[3] Evans RA, Leavy OC, Richardson M, et al. Clinical characteristics with inflammation profiling of Long-COVID and association with one-year recovery following hospitalisation in the UK: a prospective observational study. The Lancet Respiratory Medicine . 2022;10(8):761-775.

[4] Yin K, Peluso MJ, Luo X, et al. Long COVID manifests with T cell dysregulation, inflammation and an uncoordinated adaptive immune response to SARS-CoV-2. Nature Immunology . 2024;25:218-225.

[5] Greene C, Connoly R, Brennan D, et al. Blood–brain barrier disruption and sustained systemic inflammation in individuals with long COVID-associated cognitive impairment. Nature Neuroscience . 2024;27:421-432.

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