NEWS RELEASE

BioVie Highlighted ADDRESS-LC Phase 2 Trial Design Exploring Bezisterim for the Treatment of Neurological Symptoms of Long COVID at Keystone Symposia on Long COVID and Other Post-Acute Infection Syndromes

2025-08-13

ADDRESS-LC trial is now enrolling patients with Long COVID-related fatigue and cognitive impairment at sites across the U.S.

CARSON CITY, Nev., Aug. 13, 2025 (GLOBE NEWSWIRE) -- BioVie Inc. (NASDAQ: BIVI) ("BioVie" or the "Company"), a clinical-stage company developing innovative drug therapies for neurological and neurodegenerative diseases, today announced that a poster highlighting the design and enrichment strategy of its ongoing Phase 2 ADDRESS-LC trial will be presented at the Keystone Symposia on **Long COVID and Other Post-Acute Infection Syndromes**, held August 10–13 in Santa Fe, New Mexico.

Long COVID is now recognized as a leading neurological condition that has affected an estimated 400 million individuals worldwide,[1,2.]The Centers for Disease Control has reported that 6.9% of adults in the United States (more than 18 million individuals) currently or previously had long COVID.[3] The neurological symptoms such as persistent cognitive dysfunction and fatigue can last for years and currently there are no FDA-approved treatment options.[2,4] ADDRESS-LC (NCT06847191; **www.addresslc.com**) is currently-enrolling participants for a phase 2, multicenter, double-blind, randomized, placebo-controlled, 16-week study evaluating the efficacy, safety, and tolerability of bezisterim in adult participants with Long COVID who are enriched for cognitive impairment and fatigue. The Phase 2 study is fully funded by a grant from the U.S. Department of Defense (DOD).

Bezisterim is an anti-inflammatory agent being developed for Long COVID and other neurodegenerative diseases including Alzheimer's disease (AD) and Parkinson's disease (PD), in which TLR-driven inflammation contributes to cognitive decline. It has been shown to inhibit both TLR4-induced signaling and inflammatory NF-κB signaling,[4] and

is orally available, not immunosuppressive, and crosses the blood-brain barrier.[5,6] In clinical trials of AD and PD, bezisterim has demonstrated a favorable safety and tolerability profile.

"The ADDRESS-LC trial was designed with input from Long COVID patients with the goal of helping to address the tremendous unmet needs of this community," said Penelope Markham, PhD, Senior Vice President of BioVie's Liver Disease and Long COVID Programs, who will be presenting the design. "Ongoing neuroinflammation has been observed in many patients with Long COVID, and BioVie leveraged its experience in studying other neurodegenerative diseases characterized by inflammation to create a unique trial that will both rigorously evaluate bezisterim in patients and add to our understanding of Long COVID pathology as a whole".

The ADDRESS-LC trial features a novel design informed by direct input from clinicians and patients, incorporating pragmatic elements to enhance relevance and feasibility. The study employs an enrichment strategy to increase the likelihood of signal detection and stratifies participants by symptom duration (<2 years or ≥2 years) to account for potential development of refractory symptoms, as well as by age (18–45 or 46–64) to address age-related differences in cognition. Key endpoints include the change in performance on a bespoke Cogstate Cognitive Battery, an objective tool designed to assess bezisterim's potential to improve neurocognitive symptoms such as cognitive impairment associated with Long COVID.

Details for the oral and poster presentations are as follows:

Oral Presentation and Poster Details:

Title: A Phase 2 Trial Designed to Enhance Signal Detection in an Evaluation of Bezisterim (NE3107) For the Treatment of Neurological Symptoms of Long COVID

Symposia Spotlight: 2:15pm-4:30pm (MT), Monday, August 11

Poster displayed from 7:30pm-10:00pm (MT), Tuesday August 12

Poster number: 2011

To learn more about ADDRESS-LC trial enrollment, visit **www.addresslc.com**.

About Bezisterim
Bezisterim (NE3107) is an orally bioavailable, blood-brain barrier (BBB)-permeable modulator of inflammation and insulin-sensitizer. In addition, it is not immunosuppressive and has a low risk of drug-drug interaction. By binding to ERK and selectively modulating NFκB activation and TNF-α production, BioVie believes that bezisterim may offer

clinical improvements in several disease indications, including Alzheimer's disease, Parkinson's disease and long COVID.

In Parkinson's disease, BioVie is currently enrolling patients in the Phase 2 **SUNRISE-PD** clinical trial evaluating the safety and efficacy of bezisterim on motor and non-motor symptoms in patients who have not been treated with carbidopa/levodopa, with topline data expected in late 2025 or early 2026. A previous Phase 2 study of bezisterim in Parkinson's disease (NCT05083260) completed in 2022, 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 versus patients treated with levodopa alone, and no drug-related adverse events.

In long COVID, bezisterim has the potential to reduce neurological symptoms including fatigue and cognitive dysfunction. Persistently circulating viral spike proteins are believed to trigger TLR-4 driven activation of NFκB and the subsequent expression of inflammatory cytokines (IL-6, TNF, IFNg). BioVIe's Phase 2 **ADDRESS-LC** study, is a randomized (1:1), placebo-controlled, multicenter trial in approximately 200 patients to evaluate the safety, tolerability and potential efficacy of 3 months of treatment with bezisterim to reduce the neurocognitive symptoms associated with long COVID, including difficulty concentrating or remembering things ("brain fog") and fatigue.

In Alzheimer's disease, BioVie 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 Alzheimer's disease (NCT04669028) in 2023. 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 Alzheimer's disease.

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, by a fully funded award in the amount of $13.13 million 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 BioVie Inc.
BioVie Inc. (NASDAQ: BIVI) is a clinical-stage company developing innovative drug therapies for the treatment of neurological and neurodegenerative disorders (Alzheimer's disease, Parkinson's disease and long COVID) and advanced liver disease. In neurodegenerative disease, the Company's drug candidate bezisterim inhibits

inflammatory activation of extracellular signal-regulated kinase and the transcription factor nuclear factor-κB, and the associated neuroinflammation and insulin resistance but not ERK and NFκB homeostatic functions (e.g., insulin signaling and neuron growth and survival). Both neuroinflammation and insulin resistance are drivers of AD and PD. Persistent systematic inflammation and neuroinflammation are key features in patients with neurological symptoms of long COVID. 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 reduction of further decompensation in participants with liver cirrhosis and ascites. 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. Avitzur O. President's Column, 2022. American Academy of Neurology. Accessed June 16, 2025. **https://www.aan.com/about-the-aan/presidents-column-advocating-post-acute-sequelae-covid**
2. Al-Aly Z, et al. Nat Med 2024;30:2148-2164. doi:10.1038/s41591-024-03173-6
3. Ford ND, Agedew A, Dalton AF, Singleton J, Perrine CG, Saydah S. Notes from the Field: Long COVID Prevalence Among Adults — United States, 2022. MMWR Morb Mortal Wkly Rep 2024;73:135–136. DOI: **http://dx.doi.org/10.15585/mmwr.mm7306a4**.
4. Davis HE, et al. EClinicalMedicine. 2021;38:101019. doi:10.1016/j.eclinm.2021.101019
5. Reading CL, et al. Neurodegener Dis Manag. 2021;11(4):289-298. doi:10.2217/nmt-2021-0022

6. Ahlem CN, et al. Int J Clin Exp Med. 2011;4(2):119-135.

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Source: BioVie, Inc.