NEWS RELEASE

BioVie Announces Formation of Advisory Board for Bezisterim in Long COVID

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CARSON CITY, Nev., June 04, 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 the formation of a long COVID Advisory Board that will provide the Company with strategic guidance on the design and execution of a Phase 2b trial in patients with long COVID, with funding from the U.S. Department of Defense.

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 more than 17 million adults in the United States currently or previously had long COVID. [1] Symptoms, which include cognitive dysfunction and fatigue, are debilitating and to date there are no therapies proven effective for treatment.

The Advisory Board includes four of the leading experts in long COVID (Michael Peluso, MD, MHS and Steven Deeks, MD from the University of California, San Francisco; Sherry Chou, MD and Igor Koralnik, MD from Northwestern Feinberg School of Medicine in Chicago) and two industry experts in outcomes and neuropsychiatric clinical development (Cynthia Girman, Dr. PH, Founder and President of CERobs Consulting, Dr. Douglas Feltner, former Chief Medical Officer at Kisbee Therapeutics and Exicure Inc). Joseph Palumbo, MD, LFAPA, MACPsych, BioVie’s Chief Medical Officer and Head of Research and Development will chair the Advisory Board.

“We are gratified to have been selected and to have received funding from the DoD to evaluate our novel therapeutic bezisterim in patients with Long COVID,” said Dr. Palumbo. “Bezisterim is an anti-inflammatory and insulin-sensitizer that permeates the blood-brain barrier and could represent a novel oral treatment targeting an underlying cause of long COVID symptoms. Our Scientific Advisory Board will play a pivotal role in guiding and accelerating our program in the currently funded planning phase. We are pleased to have this esteemed group of scientists as collaborators to set science in motion."

Advisory Board

Michael Peluso, MD, MHS and Steven Deeks, MD are infectious disease clinical researchers at University of California, San Francisco. When the SARS-CoV-2 pandemic emerged, they led the efforts to implement the Long-term Impact of Infection with Novel Coronavirus (LIINC) study examining COVID's long-term effects on health. LIINC became one of the first studies focused on understanding the biological mechanisms that drive long COVID and has supported over 50 scientific collaborations. Dr. Peluso, Assistant Professor of Medicine, leads a long COVID clinical trial program within LIINC and also oversees the implementation of the NIH's RECOVER long COVID initiative at UCSF. Dr. Deeks, Professor of Medicine, was a co-organizer of the 2023 Keystone Symposia Meeting focused on long COVID pathogenesis and treatment.

Sherry Chou, MD and Igor Koralnik, MD from Northwestern Feinberg School of Medicine in Chicago are experts in the neurological sequalae of COVID infection and were the first to characterize the neurological complications in hospitalized COVID-19 patients in the U.S. Dr. Chou, who is the Chief of Neurocritical Care and Associate Professor of Neurology at Northwestern Feinberg School of Medicine, founded and leads the large Global Consortium Study on Neurological Dysfunction in COVID-19 (GCS-NeuroCOVID) and serves as an invited member to the World Health Organization forum on neurological impacts of COVID-19. Dr Koralnik, who is Chief of Neuro-infectious Disease and Global Neurology in the Department of Neurology at Northwestern Feinberg School of Medicine, created one of the first Neuro COVID-19 clinics in the country where he and his team investigate, diagnose and manage neurological symptoms of long COVID.

"Through the Northwestern Medicine Comprehensive COVID-19 Center, we have evaluated over 4,000 individuals with Long COVID and more than 2,500 at the NEURO-COVID-19 clinic and have documented the neurocognitive and other significant health challenges that remain without effective treatments" stated Dr. Koralnik. "I am excited to join my fellow colleagues to provide guidance to BioVie in the development of this important trial to assess the potential impact of bezisterim in the treatment of long COVID."

Cynthia Girman, Dr. PH, Founder and President of CERobs Consulting, has forty years of epidemiology and biostatistical experience in the pharmaceutical industry. She is an expert in study design and methodology for real world evidence, observational non-interventional studies as well as external control arms for clinical trials. Dr. Girman also provides expertise for endpoint strategies for clinical trials, including clinical outcome assessments and patient reported outcomes, and their justification to regulatory bodies. Previously, Dr. Girman served as Executive Director and Head of Data Analytics & Observational Methods in the Center for Observational & Real-World Evidence at Merck Research Laboratories, where she founded the Center of Excellence for Comparative & Outcomes Evidence and one for the Development, Validation, Standardization and Implementation of Endpoints

(DEVISE) for clinical trials. She is currently a member of the Methodology Committee for the Patient Centered Outcome Research Institute.

Dr. Douglas Feltner is a physician-scientist, with over 25 years of experience in clinical drug development and in translational medicine, primarily focused on neurology, psychiatry and neuroscience. Prior to recent positions as Chief Medical Officer at Kisbee Therapeutics and Exicure Inc., Dr. Feltner served as Vice President, Neuroscience Development, for AbbVie, Inc. and Vice President, Global Head of Translational Medicine for Pfizer, Inc. Dr. Feltner earned his M.D., with distinction in research, from the University of Michigan Medical School, did his residency in psychiatry at George Washington University, and was a postdoctoral fellow in the Lab of Mammalian Genes and Development at The National Institute of Child Health and Human Development.

"I am so delighted for our team to be working with and learning from our selected experts," said BioVie CEO Cuong Do. "The Advisory Board brings expertise to help us design the exploratory Phase 2b trial to assess how bezisterim may address the cognitive and fatigue symptoms of long Covid. Finalization of the protocol and obtaining the necessary regulatory approvals will trigger a milestone meeting with the PRMP programmatic panel that is required to allow us to exercise the award option of $12.6 million in the approved budget to conduct the clinical trial." 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.

The preliminary plan is to conduct a Phase 2b, randomized (1:1), placebo-controlled, multicenter trial to evaluate the safety and tolerability of 3 months of treatment with bezisterim and assess the ability of this treatment to reduce the neurocognitive symptoms that are associated with long COVID, in approximately 200 patients.

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 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 6.8% of adults in the United States (more than 17 million individuals) currently or previously have long COVID. [1] The loss in quality of life and earnings and increased medical costs has an enormous economic impact estimated to be $3.7 trillion. [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 NFκB and the subsequent expression of inflammatory cytokines (IL-6, TNF, IFNγ). NE3107 has been shown to modulate the activation of NFkB and thus modulate inflammation.

Bezisterim is 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 NFκB (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 U.S. Food and Drug Administration ("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] 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** .

[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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