Biohaven Presents Expanded EEG and Safety Data for BHV-7000 at the American Epilepsy Society Annual Meeting

December 1, 2023

- Biohaven reported full results from the BHV-7000 Phase 1 study examining doses up to 120 mg daily, demonstrating BHV-7000 was well-tolerated at all doses studied without the typical central nervous system (CNS) adverse effects associated with other anti-seizure medications (ASMs), such as somnolence and cognitive/mood disturbances.
- In a Phase 1 electroencephalogram (EEG) biomarker study, BHV-7000 demonstrated dose-dependent target engagement in the brain as measured by changes in EEG spectral power across all brain regions.
- Additional poster presentations at the American Epilepsy Society Annual Meeting will include: BHV-7000 preclinical data, health-related quality of life in patients with focal epilepsy, and functional impairments in patients with KCNQ2-associated developmental and epileptic encephalopathy (KCNQ2-DEE).

NEW HAVEN, Conn., Dec. 1, 2023 /PRNewswire/ -- Biohaven Ltd. (NYSE: BHVN) announced today that it is presenting expanded EEG and safety data for BHV-7000 at the 2023 American Epilepsy Society (AES) Annual Meeting, taking place December 1-5, 2023, in Orlando, Florida. The presentations include results from the BHV-7000 Phase 1 EEG biomarker study and additional BHV-7000 safety and tolerability data from Phase 1 single ascending dose (SAD) / multiple ascending dose (MAD) studies. Additional posters showcase BHV-7000's preclinical data, findings from a systematic literature review on health-related quality of life (HRQoL) in patients with focal epilepsy, and results from a cross-sectional survey assessing functional impairments in patients with KCNQ2-DEE.

Jason Lerner, M.D., Medical Director and Epilepsy Clinical Lead at Biohaven, commented "Selective Kv7 activators are one of the most exciting new drug targets for the treatment of epilepsy, and BHV-7000 has shown a favorable and differentiated profile in preliminary Phase 1 studies to date. We are pleased to see favorable safety and tolerability with BHV-7000 dosed up to 120 mg daily for 15 days, without the CNS adverse effects typically associated with other ASMs, such as somnolence. Together with the preclinical data showing BHV-7000 is a selective Kv7.2/7.3 channel opener lacking $GABA_A$ activation and the results from our Phase 1 EEG study confirming target engagement, we are excited to advance BHV-7000 into late-stage development in epilepsy patients."

Dr. Lerner added, "The robust BHV-7000 data presentations at the AES meeting underscore Biohaven's progress and commitment to developing novel, efficacious and well-tolerated therapies for people living with epilepsy."

In addition, both the systematic literature review and parental survey illustrated the importance of Health-Related Quality of Life issues among patients with focal epilepsy and developmental manifestations of KCNQ2-DEE that are relevant to parents, such as communication, eating abilities, and motor impairments.

Presentation Highlights:

Poster 2.510: Novel, Selective Kv7.2/7.3 Potassium Channel Activator, BHV-7000, Demonstrates Dose-Dependent Pharmacodynamic Effects on EEG Parameters in Healthy Adults

- In this Phase 1 study, pharmacodynamic activity of BHV-7000 in the brain of healthy adults was demonstrated by dose-dependent increases in EEG spectral power.
- Unlike prior reports where EEG effects of a Kv7.2/7.3 activator showed the greatest power increase in the delta frequency band (Biondi et al. 2022), the highest spectral power increases with BHV-7000 were seen in alpha, beta, and gamma frequency bands.
- While changes in spectral power were observed across all frequency bands with BHV-7000, the minimal impact on slower frequencies (i.e., delta) is consistent with the low incidence of CNS adverse events, in particular somnolence, seen in the BHV-7000 Phase 1 SAD/MAD studies.
- EEG delta activity is associated with somnolence, an undesirable CNS adverse event often seen with other ASMs.

Poster 3.265: A First in Human Phase 1 Study Evaluating the Safety and Tolerability of BHV-7000, a Novel, Selective Kv7.2/7.3 Potassium Channel Activator, in Healthy Adults

- BHV-7000 was safe and well-tolerated at single doses up to 100 mg and multiple doses up to 120 mg daily for 15 days
- No serious adverse events or severe treatment emergent adverse events were reported
- Adverse events typically associated with other ASMs, such as somnolence and cognitive/mood disturbances, were not reported

Poster 2.249: Characterization of BHV-7000: A Novel Kv7.2/7.3 Activator for the Treatment of Seizures

- BHV-7000 is a potent activator of Kv7.2/7.3 channels, impacting both deactivation kinetics and voltage dependence of activation
- BHV-7000 requires the Kv7.2 W236 residue for channel activity
- No significant activation of the $GABA_A$ receptor with BHV-7000
- BHV-7000 is potent in the maximal electroshock seizure (MES) test without impact on neurobehavior or motor (rotorod) behavior

Poster 1.487: Determinants of Health-Related Quality of Life of Patients with Focal Epilepsy: A Systematic Literature Review

- This systematic literature review identified multiple factors associated with lower HRQoL in patients with focal epilepsy
- Depression and anxiety were among the most significant and frequent determinants of HRQoL change
- Other relevant and frequent determinants of HRQoL change included cognition, ASM adverse events, seizure freedom, and employment
- A comprehensive understanding of the modifiable determinants of HRQoL is relevant to patient health and well-being and can inform clinical practice and observational/interventional studies

Poster 2.451: Functional Impairments in Patients with KCNQ2-DEE: Associations Among Key Clinical Features

- Data obtained from a cross-sectional survey (2018-2020) of parents of children aged ≥2 years with KCNQ2-DEE was analyzed
- Among individuals with KCNQ2-DEE, there is a hierarchy of impairments wherein communication is the most sensitive domain and is often affected in isolation from others
- Gross and fine motor skill impairments tend to be correlated
- Hand use impairment is closely correlated with multiple other functional impairments

Full posters will be available on the **Posters and Presentations** page at: **www.biohaven.com**.

Reference
Biondi A, et al. Sci Rep. 2022 Feb 4;12(1):1919.

About BHV-7000
BHV-7000, the lead asset from Biohaven's Kv7 platform, is a novel and selective activator of Kv7.2/Kv7.3, a key ion channel involved in neuronal signaling and in regulating the hyperexcitable state, that Biohaven is developing for the treatment of epilepsy and mood disorders. BHV-7000 was rationally developed as a potent activator of heteromeric Kv7.2/7.3 potassium channels, the molecular substrate that underlies the M-current (IKM). BHV-7000 is highly differentiated from ezogabine (known as retigabine in Europe), a Kv7 activator that was previously approved for adjunctive treatment of partial-onset seizures in adults. In comparison with ezogabine, BHV-7000 belongs to a significantly different structural class and differentiates from ezogabine in key properties, including pharmacology, plasma stability and stability to photooxidation. In addition, BHV-7000 does not exhibit $GABA_A$ receptor positive allosteric molecular activity as seen with ezogabine and similar compounds, which may contribute to the poor tolerability of ezogabine. This lack of $GABA_A$ receptor activity potentially gives BHV-7000 a wide therapeutic window which, based on dose-dependent clinical responses seen in other ASM clinical trials, should translate to improved efficacy without the typical dose dependent side effect profile often seen in patients receiving ezogabine and other anti-seizure medications.

About Biohaven
Biohaven is a global clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of life-changing therapies to treat a broad range of rare and common diseases. Biohaven's experienced management team brings with it a track record of delivering new drug approvals for products for diseases such as migraine, depression, bipolar and schizophrenia. The company is advancing a pipeline of therapies for diseases, many of which have limited or no treatment options, leveraging its proven drug development capabilities and proprietary platforms, including Kv7 ion channel modulation for epilepsy and neuronal hyperexcitability, glutamate modulation for obsessive-compulsive disorder and spinocerebellar ataxia, myostatin inhibition for neuromuscular diseases and metabolic disorders, and brain-penetrant TYK2/JAK1 inhibition for neuroinflammatory disorders. Biohaven's portfolio of early- and late-stage product candidates also includes discovery research programs focused on TRPM3 channel activation for neuropathic pain, CD-38 antibody recruiting, bispecific molecules for multiple myeloma, antibody drug conjugates (ADCs), and targeted extracellular protein degradation platform technology (MoDE™) with potential application in neurological disorders, cancer, and autoimmune diseases.

Forward-looking Statements
This news release includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. The use of certain words, including "continue", "plan", "will", "believe", "may", "expect", "anticipate" and similar expressions, is intended to identify forward-looking statements. Investors are cautioned that any forward-looking statements, including statements regarding the future development, timing and potential marketing approval and commercialization of development candidates, are not guarantees of future performance or results and involve substantial risks and uncertainties. Actual results, developments and events may differ materially from those in the forward-looking statements as a result of various factors including: the expected timing, commencement and outcomes of Biohaven's planned and ongoing clinical trials; the timing of planned

interactions and filings with the FDA; the timing and outcome of expected regulatory filings; complying with applicable U.S. regulatory requirements; the potential commercialization of Biohaven's product candidates; the potential for Biohaven's product candidates to be first in class therapies; and the effectiveness and safety of Biohaven's product candidates. Additional important factors to be considered in connection with forward-looking statements are described in Biohaven's filings with the Securities and Exchange Commission, including within the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations". The forward-looking statements are made as of the date of this news release, and Biohaven does not undertake any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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