Biohaven Acquires Exclusive License for Oral, Brain-Penetrant, Dual TYK2/JAK1 Inhibitor for Immune-Mediated Brain Disorders

March 22, 2023

- Novel first-in-class, brain-penetrant, dual inhibitor of TYK2/JAK1 offers wide therapeutic index with TYK2 inhibition and high selectivity for JAK1 inhibition without the severely limiting adverse class effects of JAK2/JAK3 inhibitors
- Exclusive license covers global rights excluding China region
- Biohaven anticipates initiating Phase 1 clinical development in 2023

NEW HAVEN, Conn., March 22, 2023 /PRNewswire/ -- Biohaven Ltd. (NYSE: BHVN) today announced that it acquired global rights, excluding China regions, for the development of an oral, brain-penetrant, dual inhibitor of Tyrosine Kinase 2 (TYK2) and Janus Kinase 1 (JAK1) for the treatment of brain disorders. BHV-8000 (previously TLL-041) was licensed from Hangzhou Highlightll Pharmaceutical Co. Ltd. (Highlightll) and Biohaven anticipates advancing the agent into a Phase 1 study in 2023.

Dysregulation of the immune system has been implicated in several neurodegenerative and neuroinflammatory disorders including Parkinson's Disease, Multiple Sclerosis, Alzheimer's Disease, Amyotrophic Lateral Sclerosis and Autoimmune Encephalitis. Over-active immune cells and microglia driving chronic neuroinflammation results in release of cytokines with activation of leukocytes and is thought to contribute to neuronal injury, death, gliosis, and demyelination. The TYK2 and JAK1 signal transduction pathways mediate highly complementary immune and inflammatory signaling events. Targeted, small-molecule therapies that inhibit TYK2 or JAK kinases have separately demonstrated robust efficacy in autoimmune, dermatologic and gastrointestinal disorders. TYK2 is a validated immune target as evidenced by a recent peripheral program that gained FDA approval, and there are multiple additional peripheral non-CNS programs in clinical development. Brain penetrant inhibitors of TYK2/JAK1 have the potential to bring this validated immune target to brain disorders.

There are currently no brain penetrant, selective, dual TYK2/JAK1 inhibitors approved for brain disorders.

Vlad Coric, M.D., Chairman and Chief Executive Officer of Biohaven, commented, "We have gained tremendous insight into the role of the immune system and critical inflammatory signaling pathways with events that drive the onset, propagation and relentless progression of neurodegenerative diseases. BHV-8000, with its blood-brain barrier penetrant activity and dual profile of TYK2/JAK1 inhibition, offers the potential for a unique and highly attractive therapeutic advancement for the treatment of brain disorders. Dual TYK2/JAK1 inhibition is a novel target combination and potentiates complementary activities that permit a graded degree of therapeutic immunomodulation specific to pathogenic neuroimmune pathways. We look forward to advancing BHV-8000 into clinical development and uncovering the potential of neuroimmunomodulation for severe neurological disorders in desperate need of novel treatment options."

Highlightll was founded by Chris Liang PhD and is focused on the research and development of small molecules for the treatment of autoimmune and inflammatory disorders. Dr. Liang is a Princeton trained chemist and seasoned drug developer who was an inventor of sunitinib and ensartinib. Dr. Liang oversaw the development of the licensed intellectual property, and the compound was designed to be brain penetrant while delivering dual selectivity for TYK2/JAK1 without the toxicity of JAK2/JAK3.

Chris Liang, Ph.D., Chairman and Chief Executive Officer of Highlightll, added, "Biohaven's proven track record in successfully innovating, developing, and commercializing neuroscience therapies makes them an attractive partner to help maximize the potential of BHV-8000. We have delivered what we believe is a best-in-class dual TYK2/JAK1 molecule and the team at Biohaven has the clinical development expertise to explore its utility in brain disorders. We look forward to working together to expedite development of this compound to improve outcomes for patients in need."

Dr. Coric added, "The addition of BHV-8000 expands our growing and diverse set of complementary neuro-immunomodulatory therapeutic approaches including selective extracellular degraders (commonly referred to as LYTACs or MoDEs™) against IgG, IgA, and antigen-specific targets in development at Biohaven. We are excited to work with Chris and the team at Highlightll to advance this novel and highly differentiated dual TYK2/JAK1 inhibitor in the treatment of brain disorders."

Terms of the Arrangement
Highlightll will receive $10 million in upfront cash and $10 million in BHVN equity, development and commercial milestone payments of up to $950 million, and tiered royalty payments ranging from mid-single digit to lower teens percentages. Biohaven and Highlightll will coordinate clinical development across global regions.

About BHV-8000
BHV-8000 (previously TLL-041) is a highly selective, brain-penetrant, dual TYK2/JAK1 inhibitor. TYK2 and JAK1 are STAT pathway activators addressing a range of proinflammatory cytokines; inhibition of these kinases may play a significant role in reducing inflammation in neurological disorders including Parkinson's Disease, Alzheimer's Disease, Amyotrophic Lateral Sclerosis, and Multiple Sclerosis. BHV-8000 has demonstrated high selectivity over JAK2, JAK3 and other kinases, potentially offering improved safety over less selective or non-selective JAK inhibitors. Mechanistic proof of concept for BHV-8000 has been demonstrated in multiple preclinical models.

About Hangzhou Highlightll Pharmaceutical Co. Ltd.
Hangzhou Highlightll Pharmaceutical Co. Ltd. is an innovative drug development company focused on the research and development of small molecules for the treatment of autoimmune/inflammatory diseases and central nervous system diseases. The company's lead project, a peripheral TYK2/JAK1 dual inhibitor, is being evaluated in clinical trials in the US and China for immunological disorders.

About Biohaven
Biohaven is a global clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of life-changing therapies for people with debilitating neurological and neuropsychiatric diseases, including rare disorders. 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 with little 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 and myostatin inhibition for neuromuscular diseases. 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 extracellular target degrader platform technology (bispecific MoDE degraders) with potential application in neurological disorders, cancer, and autoimmune diseases. More information about Biohaven is available at www.biohaven.com.

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 Food and Drug Administration; the timing and outcome of expected regulatory filings; complying with applicable U.S. regulatory requirements; the potential commercialization of Biohaven's product candidates; 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 new 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.

Biohaven Contact:
Jennifer Porcelli
Vice President, Investor Relations
jennifer.porcelli@biohavenpharma.com
201-248-0741

Media Contact:
Mike Beyer
Sam Brown Inc.
mikebeyer@sambrown.com
312-961-2502

View original content to download multimedia:https://www.prnewswire.com/news-releases/biohaven-acquires-exclusive-license-for-oral-brain-penetrant-dual-tyk2jak1-inhibitor-for-immune-mediated-brain-disorders-301778426.html

SOURCE BIOHAVEN LTD