Biohaven Announces FDA Acceptance and Priority Review of Troriluzole New Drug Application for the Treatment of Spinocerebellar Ataxia

February 11, 2025

- *Spinocerebellar Ataxia (SCA) is a rare, genetic, life-threatening neurodegenerative disease with no available treatment.*
- *Troriluzole demonstrated a 50-70% slowing of SCA disease progression on the primary and secondary outcome measures at the 3-year endpoint in a real-world evidence (RWE) study.*
- *Troriluzole has a well-established safety profile and if approved, would be the first and only FDA-approved treatment for SCA; subject to receipt of FDA approval, Biohaven is prepared to commercialize troriluzole for SCA in the US in 2025.*

NEW HAVEN, Conn., Feb. 11, 2025 /PRNewswire/ -- Biohaven Ltd. (NYSE: BHVN) (Biohaven or the Company), today announced that the US Food and Drug Administration (FDA) has accepted for review the Company's New Drug Application (NDA) for troriluzole for the treatment of adult patients with spinocerebellar ataxia (SCA) and has granted Priority Review. This designation is assigned to applications for drugs that would offer a significant improvement over other available treatments for a given disorder or would provide a treatment option where none exists. In the case of SCA, a rare, genetic, neurodegenerative disease, troriluzole would be the first and only FDA-approved treatment for this life-threatening disorder. The FDA's decision regarding the NDA is expected within 6 months of filing (during 3Q2025). Based on FDA Priority Review timelines and if ultimately approved, Biohaven is prepared to commercialize troriluzole for SCA in the US in 2025.

Melissa Beiner, M.D., SCA Clinical Development Lead at Biohaven, commented, "Our NDA filing is the culmination of over 8 years of clinical research and represents an important collaboration across the SCA community. The troriluzole NDA reflects rigorous scientific collaborations between advocacy groups, patients and their families, clinical experts in SCA and Biohaven. The FDA decision to grant Priority Review demonstrates the extremely high unmet need in this rare neurodegenerative disease. Time is of the essence for patients with SCA, who are suffering relentless and irreversible functional decline including impairments in coordination and balance leading to falls, loss of ambulation, and difficulties with vision, speech and swallowing." Dr. Beiner added, "The robust clinical data presented in the NDA demonstrate sustained and compelling treatment benefit in SCA patients treated with troriluzole, a once-daily, oral pill. We look forward to working closely with the FDA throughout the review process to bring the very first treatment to patients and families suffering from SCA."

The NDA submission was based, in part, on positive topline results from Study BHV4157-206-RWE (NCT06529146), in which troriluzole 200 mg dosed orally in patients with SCA met the study's primary endpoint of change from baseline on the functional Scale for the Assessment and Rating of Ataxia (f-SARA), in all SCA genotypes, at 3 years compared to an external control arm. Troriluzole showed statistically significant superiority across 9 consecutive, prespecified primary and secondary endpoints with highly consistent, sustained, robust and clinically meaningful treatment effects. SCA patients treated with troriluzole showed a 50-70% slower rate of decline, representing 1.5-2.2 years delay in disease progression, over the 3-year study period (Figures 1-3 and Table 1). The NDA also includes confirmatory and supportive data from Studies BHV4157-201 and BHV4157-206, the first large, multi-center registrational trials in SCA. Notably, these data include disease stabilization in the SCA3 genotype (Figure 4) and a reduction in falls in all SCA genotypes (Figure 5), both compared to placebo over 48 weeks in Study BHV4157-206.

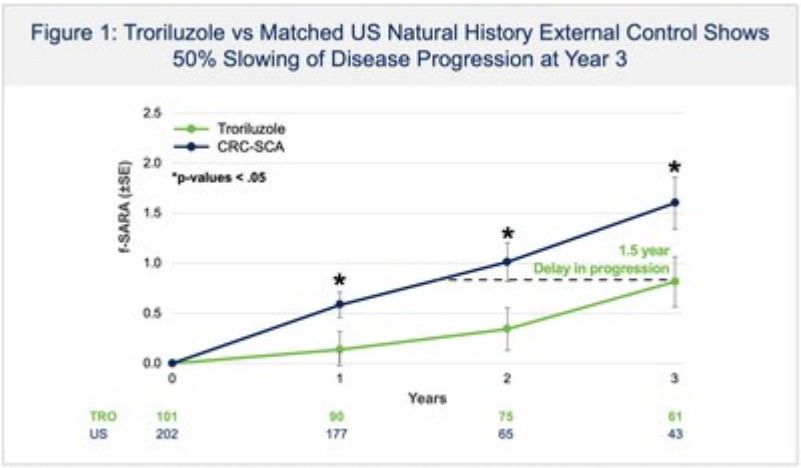

Figure 1: Change from baseline in f-SARA total ccore at 1-, 2-, and 3-years in troriluzole-treated subjects vs Untreated US External Control (Natural History Cohort: CRC-SCA) subjects in study BHV4157-206-RWE.

Figure 2: Troriluzole vs Independent Matched EU Natural History External Control Shows 70% Slowing of Disease Progression at Year 3

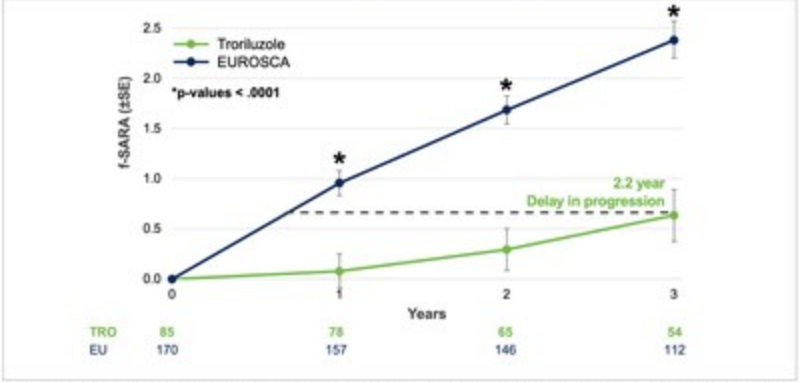

Figure 2: Change from baseline in f-SARA total score at 1-, 2-, and 3-years in troriluzole-treated subjects vs Untreated EU External Control (Natural History Cohort: EUROSCA) subjects in study BHV4157-206-RWE.

Figure 3: Troriluzole vs Matched Global Natural History External Control Shows 60% Slowing of Disease Progression at Year 3

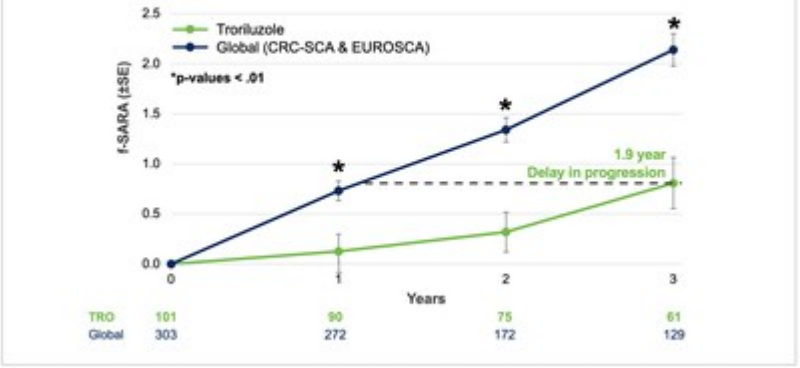

Figure 3: Change from baseline in f-SARA total score at 1-, 2-, and 3-years in troriluzole-treated subjects vs untreated Global External Control (Natural History Cohorts: CRC-SCA and EUROSCA) subjects in study BHV4157-206-RWE.

Table 1: Untreated SCA Patients Have Greater Risk of Significant Disease Worsening

	Odds Ratio of f-SARA ≥2-Point Worsening in Untreated	P-Value
US External Control vs. Troriluzole	**2.4**	0.0359
EU External Control vs. Troriluzole	**6.1**	<0.0001
Global External Control vs. Troriluzole	**4.1**	<0.0001

Table 1: Responder analysis of change from baseline in f-SARA total score at 3-years in troriluzole-treated subjects vs untreated external control arms (odds ratio of f-SARA ≥2-point change at 3 years representing a clearly defined worsening of SCA disease) in study BHV4157-206-RWE.

Jeremy Schmahmann, M.D., Professor of Neurology at Harvard Medical School and Founding Director of the Ataxia Center and the Martha and Robert Fogelman Endowed Chair in Ataxia and Cerebellar Neurology at Massachusetts General Hospital commented, "The FDA acceptance for review of this NDA represents a critical milestone for SCA patients. Since the discovery of the first gene for SCA in 1993, patients and families affected by SCA have watched generation after generation suffer severe, progressive disability and premature death with no treatment options. The need for an intervention that can slow disease progression and help patients maintain their independence is urgent. The delay in disease decline shown in the real-world evidence study is a watershed in the history of the SCAs. This is what patients have been waiting for. It is what the doctors who have been powerless, have been waiting for. Additionally, the importance of troriluzole's effects on reducing falls in this patient population cannot be overstated. I applaud the FDA for recognizing this urgency by granting a Priority Review and look forward to using troriluzole in the clinic if approved."

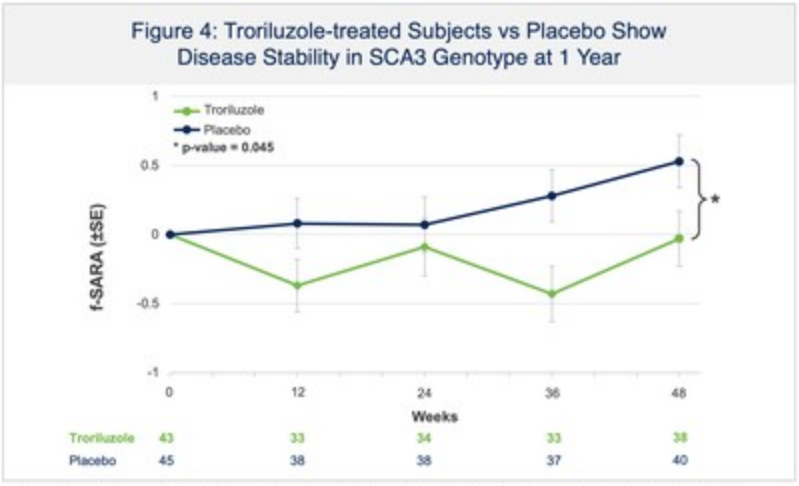

Figure 4: Change from Baseline in f-SARA total score at 1 year in in troriluzole-treated subjects vs placebo SCA3 subjects in study BHV4157-206.

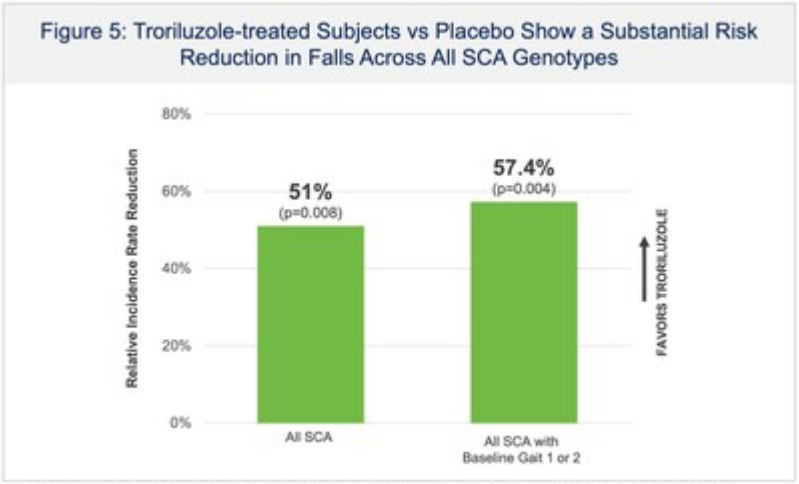

Figure 5: Reduction in falls in troriluzole-treated subjects vs placebo subjects at 1 year in Study BHV4157-206. Ambulatory subjects (defined as having baseline gait 1 or 2 on f-SARA gait item) demonstrated greater improvement.

Biohaven's troriluzole clinical development program in SCA collected data over 8 years, including a robust long-term safety profile, and was the first industry trial conducted in SCA. The external control arms used in Biohaven's BHV4157-206-RWE Study were provided from objective, third-party data gathered from two independent natural history cohorts: one in the United States and one in Europe (EUROSCA Natural History Study). The National Ataxia Foundation (NAF) sponsored the Clinical Research Consortium for the Study of Cerebellar Ataxia (CRC-SCA) that served as the basis for the US natural history cohort. The data from the CRC-SCA is managed by the University of South Florida Health Informatics Institute. A total of 35 clinical sites provided data in the US and European natural history cohorts that served as the external controls in BHV4157-206-RWE. As per instructions from FDA on the real-world evidence study design and statistical analysis plan, the external control arm was determined using a Propensity Score Matching (PSM) method to ensure that untreated subjects from the comparator natural history cohort were rigorously matched to treated subjects from the troriluzole arm of Study BHV4157-206. PSM was used on all prognostic, demographic, and baseline characteristics known to be associated with disease progression in SCA, including baseline f-SARA, age, sex, age at symptom onset, genotype, and trinucleotide repeat length (by genotype).

Andrew Rosen, Chief Executive Officer of the National Ataxia Foundation (NAF), stated, "Biohaven's SCA program reflects years of dedicated clinical research and collaboration with leading world experts and advocacy groups to advance the ataxia field. We are proud that our multi-year effort to fund and support the Clinical Research Consortium for the Study of Cerebellar Ataxia played such a critical role in providing the external control arm of Biohaven's study. The goal of CRC-SCA is to improve our understanding of SCA disease progression and to promote the development of disease-modifying therapies for SCA." Mr. Rosen added, "On behalf of patients and families, who have watched generations of family members succumb to this devastating disease and have been waiting for decades for a treatment that could slow disease progression, I thank the FDA for not only accepting this NDA for review, but recognizing the need for urgency for our community in the form of a Priority Review."

Biohaven previously received both Fast-Track and Orphan Drug Designation (ODD) from the FDA, and ODD from the European Medicines Agency, where a troriluzole MAA is currently under review.

An expanded access protocol (EAP) is currently enrolling patients with SCA who are eligible. EAPs are designed to give early access to potential therapies before they are approved by the FDA. More information about can be found at https://clinicaltrials.gov/study/NCT06034886.

About Spinocerebellar Ataxia (SCA)
Spinocerebellar ataxia is a group of dominantly inherited neurodegenerative disorders characterized by progressive loss of voluntary motor control and atrophy of the cerebellum and brainstem. SCA affects approximately 15,000 people in the United States and 24,000 in Europe and the United Kingdom. Patients experience significant morbidity, including impaired gait leading to falls, loss of ambulation and progression to a wheelchair, inability to communicate due to speech impairment, difficulty swallowing, and premature death. While signs and symptoms can appear anytime from childhood to late adulthood, SCA typically presents in early adulthood and progresses over a number of years. Currently, there are no FDA-approved treatments

and no cure for SCA.

About Troriluzole
Troriluzole is a new chemical entity (NCE) and third-generation novel prodrug that modulates glutamate, the most abundant excitatory neurotransmitter in the human body. The primary mode of action of troriluzole is reducing synaptic levels of glutamate. Troriluzole increases glutamate uptake from the synapse, by augmenting the expression and function of excitatory amino acid transporters located on glial cells that play a key role in clearing glutamate from the synapse. The glutamate modulating activity of troriluzole addresses the widely documented glutamate deregulation that underlies neurodegeneration and Purkinje cell dysfunction in patients with SCA. Troriluzole also has the potential to be developed in a number of other diseases associated with excessive glutamate. More information about troriluzole can be found at the Biohaven's website: https://www.biohaven.com/pipeline/clinical-programs/glutamate/.

About Biohaven
Biohaven is a biopharmaceutical company focused on the discovery, development, and commercialization of life-changing treatments in key therapeutic areas, including immunology, neuroscience, and oncology. The company is advancing its innovative portfolio of therapeutics, leveraging its proven drug development experience and multiple proprietary drug development platforms. Biohaven's extensive clinical and preclinical programs include Kv7 ion channel modulation for epilepsy and mood disorders; extracellular protein degradation for immunological diseases; TRPM3 antagonism for migraine and neuropathic pain; TYK2/JAK1 inhibition for neuroinflammatory disorders; glutamate modulation for OCD and SCA ; myostatin inhibition for neuromuscular and metabolic diseases, including SMA and obesity; antibody recruiting bispecific molecules and antibody drug conjugates for cancer. For more information, visit 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, , including the potential approval and commercialization of troriluzole for SCA, 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 approved 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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