

Biohaven Achieves Positive Topline Results in Pivotal Study of Troriluzole in Spinocerebellar Ataxia (SCA)

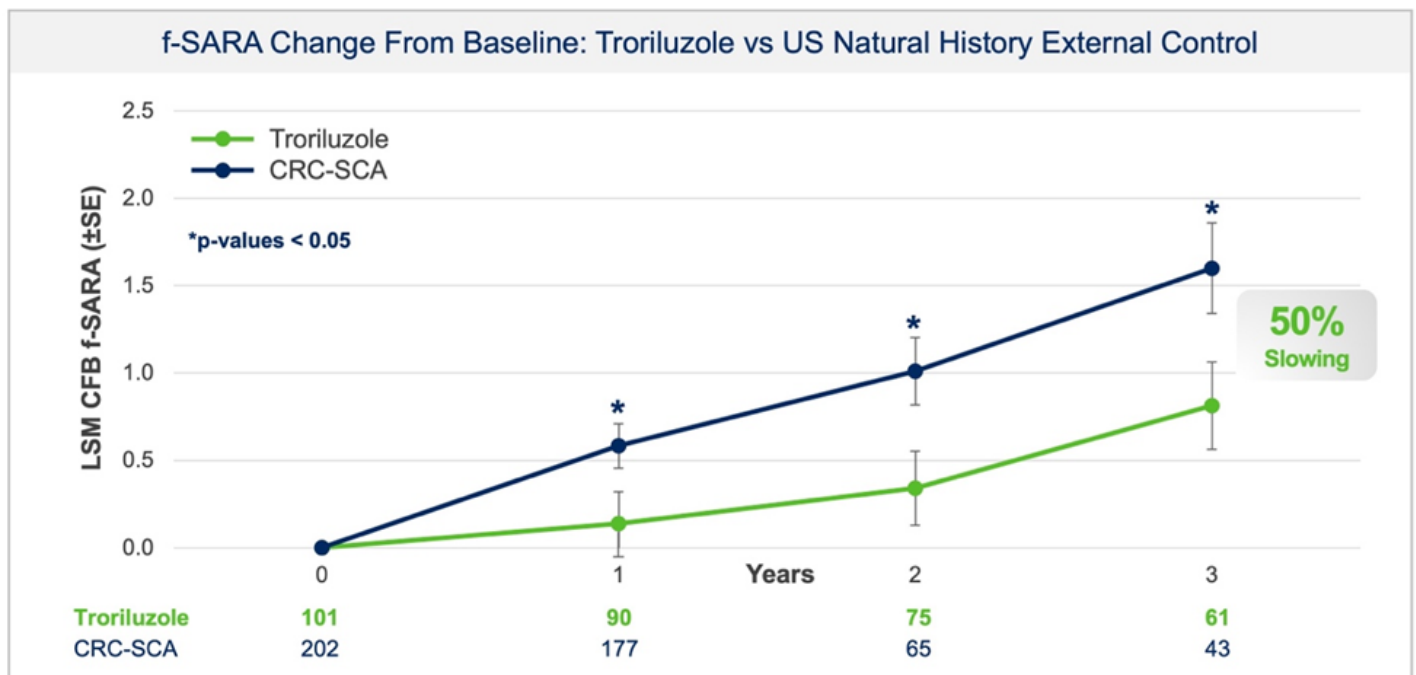
September 23, 2024

- Troriluzole 200 mg dosed orally, once daily, in patients with SCA met the study's primary endpoint on the change from baseline in the modified functional Scale for the Assessment and Rating of Ataxia (f-SARA) at 3 years in all study population genotypes.
 - Troriluzole also showed statistically significant superiority after both 1 and 2 years of treatment.
- Troriluzole achieved statistically significant superiority on 9 consecutive, prespecified primary and secondary endpoints.
- SCA patients treated with troriluzole showed a 50-70% slowing of disease progression, representing 1.5-2.2 years delay in disease progression over the 3-year study period.
- Biohaven plans to submit a New Drug Application (NDA) to the US Food and Drug Administration (FDA) for troriluzole in the treatment of all SCA genotypes in 4Q 2024. The application is eligible for a priority review given orphan drug and fast-track designations previously granted by FDA.
- Conference call and webcast to be held today at 8:30am ET

NEW HAVEN, Conn., Sept. 23, 2024 /PRNewswire/ -- Biohaven Ltd. (NYSE: BHVN) (Biohaven or the Company), today announced positive topline results from pivotal Study BHV4157-206-RWE (NCT06529146) demonstrating the efficacy of troriluzole on the mean change from baseline in the f-SARA after 3 years of treatment. The study achieved the primary endpoint and showed statistically significant improvements on the f-SARA at years 1 and 2 (Figure 1). SCA is a rare, progressively debilitating neurodegenerative disease that affects approximately 15,000 people in the United States and 24,000 in Europe and the United Kingdom. There are no FDA approved treatments for SCA.

Collectively, data across multiple analyses demonstrate a robust and clinically meaningful slowing of disease progression in SCA patients. These treatment benefits translate into a 50-70% slower rate of decline compared to untreated patients, representing 1.5-2.2 years delay in disease progression over the 3-year study period. Additionally, in a responder sensitivity analysis, disease progression when defined by a 2 point or greater worsening on the f-SARA at 3 years showed an odds ratio (OR) of 4.1 (95% CI: 2.1, 8.1) for the untreated external control arm versus troriluzole treated subjects ($p < 0.0001$; pooled analysis).

Dr. Susan Perlmán, Director of Ataxia Clinic and Neurogenetics Clinical Trials at the David Geffen School of Medicine at UCLA stated, "SCA is a debilitating, relentlessly progressive disease that destroys quality of life, leaving patients unable to care for themselves, walk, or speak. Troriluzole is the very first treatment to show a delay in disease progression that can give patients additional years of independence, where they can walk without assistance, continue to work, play with their children, and participate in daily activities. This is an exciting and hopeful moment for the SCA community."

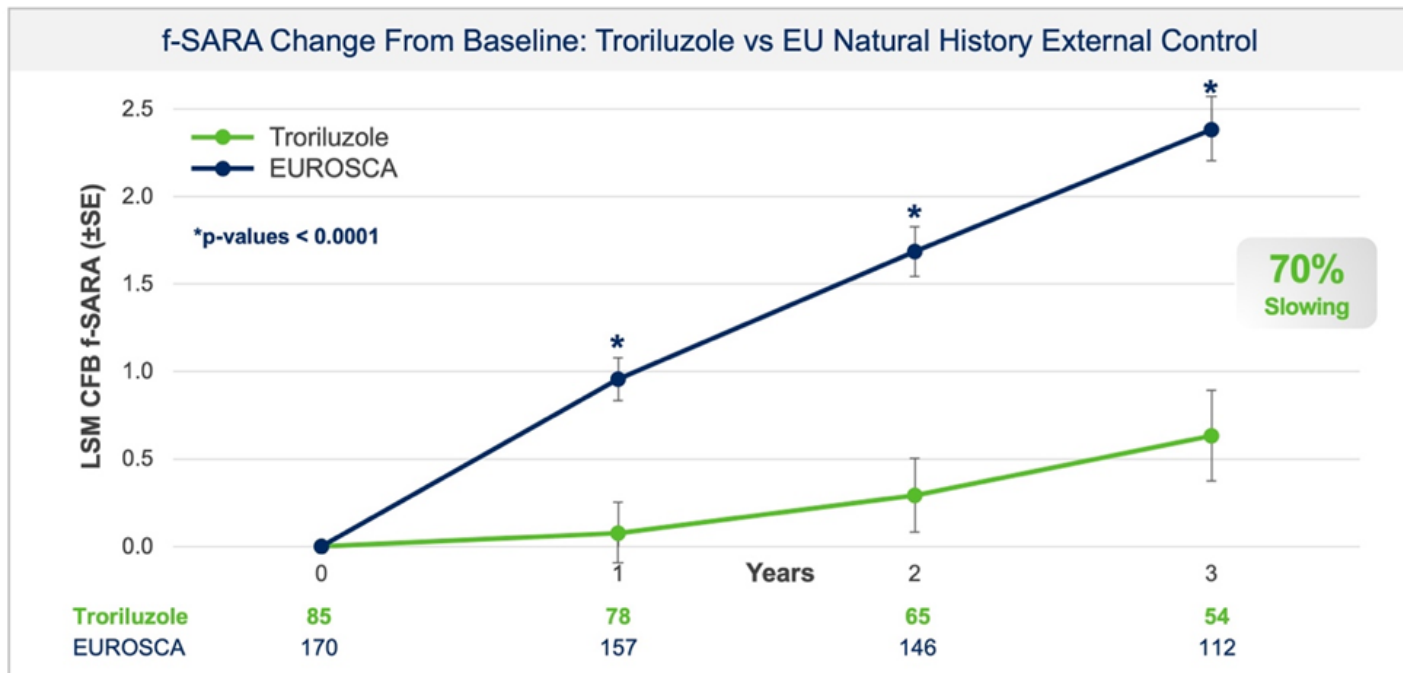


CRC-SCA, Clinical Research Consortium for SCA; EUROSCA, European registry of SCA; f-SARA, Functional Scale for the Assessment and Rating of Ataxia; LSM, least squares mean; PSM, Propensity Score Matching; CFB, Change from baseline

Figure 1: f-SARA Change from baseline demonstrating troriluzole reduced SCA disease progression vs US Natural History External Control

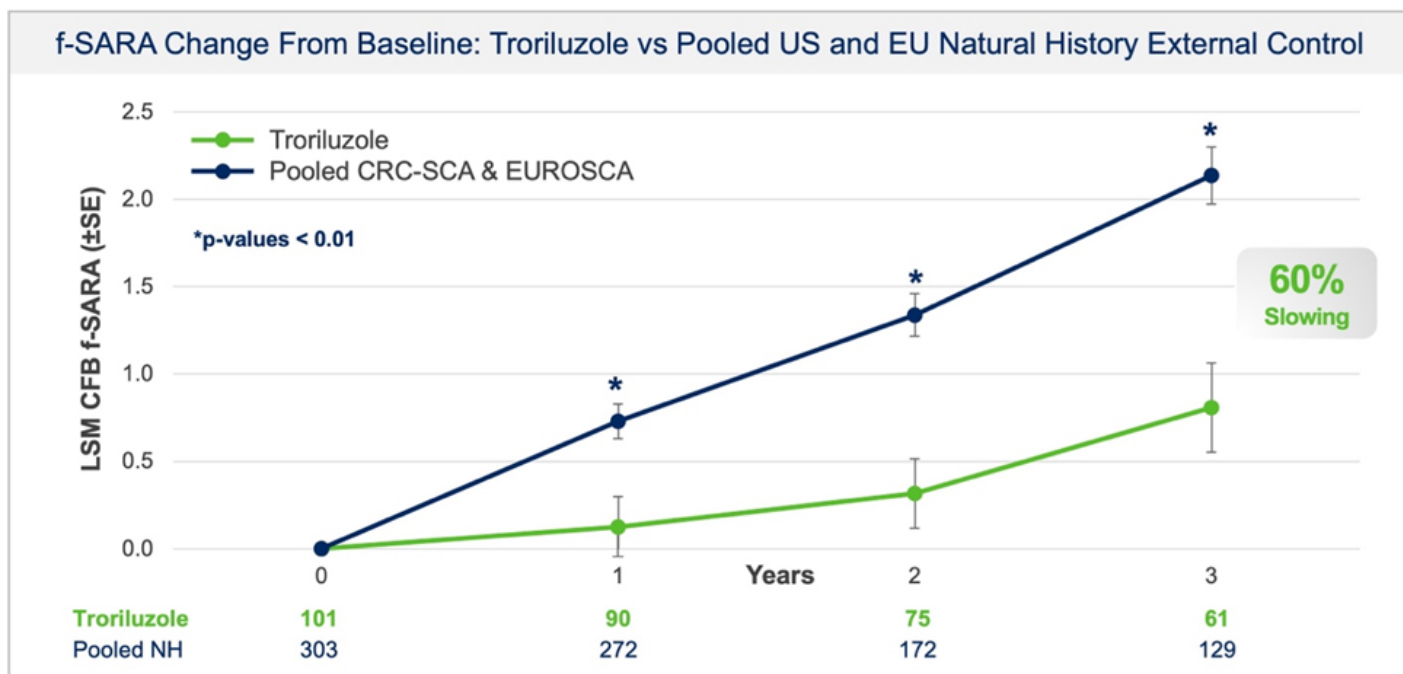
Study BHV4157-206-RWE was designed, in discussion with the US Food and Drug Administration (FDA), to assess the effectiveness of troriluzole in SCA after 3 years of treatment as measured by the change from baseline in the f-SARA. The study utilized Phase 3 data and an external control of matched, untreated SCA subjects from the US Clinical Research Consortium for the Study of Cerebellar Ataxia (CRC-SCA) in accordance with FDA's Guidance on Real-World Evidence (RWE) of effectiveness. All endpoints were prespecified, and both the study protocol and statistical analysis plan were submitted to, and reviewed by, FDA prior to topline data analysis. The new analysis doubled the previously available 3 year data with 63 subjects now completing 3 years of treatment with troriluzole and matched to the external control arm. Propensity Score Matching (PSM) was used to ensure that untreated patients from the CRC-SCA study were rigorously matched to treated patients from Study BHV4157-206 on baseline characteristics. The primary objective was to examine the treatment effects of troriluzole for up to 3 years, by comparing data on the f-SARA from patients treated with troriluzole in Study BHV4157-206 to untreated patients from the natural history study. Troriluzole-treated patients demonstrated statistically significant and sustained benefits at years 1, 2 and 3 on the f-SARA compared to a rigorously matched natural history control.

Additionally, prespecified analyses in the protocol employed a separate, independent natural history control from the European SCA natural history study (EUROSCA) for global regulatory purposes. Results using the EUROSCA patients, in addition to a pooled analysis using both CRC-SCA and EUROSCA patients, as the external controls were also statistically significant and consistent with the primary efficacy analysis at all timepoints (see Figure 2 and Figure 3). The addition of EUROSCA data increased the external control sample size and added to the robustness of the statistically significant treatment differences at years 1, 2, and 3, favoring troriluzole.



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Figure 2: f-SARA change from baseline demonstrating troriluzole reduced SCA disease progression vs Independent EU Natural History External Control



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Figure 3: f-SARA change from baseline demonstrating troriluzole reduced SCA disease progression vs Pooled US and EU Natural History External Control

Jeremy Schmahmann, M.D., Professor of Neurology at Harvard Medical School and Founding Director of the Ataxia Center at Massachusetts General Hospital commented, "The stabilization of SCA symptoms as reflected by the topline data at 3 years along with the previously reported reductions in falls show the therapeutic potential of troriluzole. I cannot underscore enough the impact of a potential treatment that can slow SCA disease progression and the effect on patients and caregivers who have helplessly watched generations of family members deteriorate and die from SCA. These new data provide support for troriluzole as a safe and effective once daily treatment for patients with SCA."

Spinocerebellar ataxia is a group of dominantly inherited neurodegenerative disorders characterized by progressive loss of voluntary motor control and atrophy of the cerebellum, brainstem and spinal cord. Patients experience significant morbidity, including progression to a wheelchair, impaired gait leading to falls, 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.

Vlad Coric, M.D., Chief Executive Officer and Chairman of Biohaven stated, "Advancing new therapies for patients with rare diseases is often a multiyear process of collaboration across academic, patient advocacy, regulatory and industry partners. The Biohaven team has always been committed to rigorously following the science in this area, and through our partnership with the National Ataxia Foundation and collaboration with leading SCA experts across the globe, our SCA development program has provided the first evidence of a clinically meaningful treatment benefit as well as slowing disease progression in SCA patients. We were excited to receive the positive topline results from Study BHV4157-206-RWE, which was designed with FDA input and pursuant to the principles outlined in the FDA's guidance for the use of real-world evidence. The need for treatments for this deadly neurodegenerative disease is urgent. As a company, we remain committed to developing novel therapies for patients living with rare disorders with no approved therapies, like SCA. We look forward to interacting with regulatory agencies to bring troriluzole to patients with SCA."

Andrew Rosen, Chief Executive Officer of the National Ataxia Foundation (NAF), shared, "Biohaven was the first company to join NAF's Drug Development Collaborative (DDC), a group of pharmaceutical

companies dedicated to bringing together advocates, clinicians, regulatory agencies, and the patient community to advance research and facilitate the development of therapies for ataxia. Today's topline results are the culmination of years dedicated to studying trilorizole as a treatment for SCA. Patients and families have been waiting for decades for a treatment that could slow disease progression in this devastating and relentlessly progressive disorder*.

Based upon the topline data from Study BHV4157-206-RWE, and previous safety and efficacy data from the trilorizole development program in SCA, Biohaven plans to submit a New Drug Application (NDA) to the FDA in Q4 2024. The trilorizole development program has generated the largest clinical trial dataset in SCA and now has follow-up in some patients treated with trilorizole for over 5 years. Biohaven has previously received both Fast-Track and Orphan drug designation (ODD) from the FDA, and ODD from the European Medicines Agency, for trilorizole in SCA. An NDA with ODD is eligible for priority FDA review. Biohaven will be prepared to commercialize SCA in the US in 2025, if ultimately approved, based on potential priority review timelines.

Conference Call and Webcast Details

Biohaven will hold a live conference call and webcast today at 8:30 a.m. Eastern Time. The webcast may be accessed via the Investor Relations portion of Biohaven's website at <https://ir.biohaven.com/events-presentations/events>. To participate in the live conference call via telephone, please register [here](#). Upon registering, a dial-in number and unique PIN will be provided to join the conference call.

About Trilorizole

Trilorizole 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 trilorizole is reducing synaptic levels of glutamate. Trilorizole 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. Trilorizole has the potential to be developed in a number of other diseases associated with excessive glutamate. More information about trilorizole can be found at the Company'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 (spinocerebellar ataxia); 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, including statements about Biohaven Ltd. and our planned and ongoing clinical trials, the timing of and the availability of data from those trials, the timing and our decisions to proceed with our planned regulatory filings (including our plans to submit a NDA to the FDA for trilorizole in the treatment of all SCA genotypes in 4Q 2024), the timing of and our ability to obtain regulatory approvals for our product candidates (including the timing of the regulatory approval for trilorizole in order to commercialize SCA in the United States in 2025), the clinical potential utility of our product candidates, alone and as compared to other existing potential treatment options, and the potential advancement of our early phase programs. 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 our 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, including the timing and outcome of the NDA for trilorizole; complying with applicable U.S. regulatory requirements; the potential commercialization of Biohaven's product candidates, including the commercialization of SCA in the United States in 2025; and the effectiveness and safety of Biohaven's product candidates. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation. Additional important factors to be considered in connection with forward-looking statements are described in the Company'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 presentation, 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. This presentation also contains market data and other information based on industry publications, reports by market research firms or published independent sources. Some market data and information is also based on the Company's good faith estimates, which are derived from management's knowledge of its industry and such independent sources referred to above.

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The logo for Biohaven, featuring the word "biohaven" in a lowercase, sans-serif font. The "bio" is in green and "haven" is in blue.

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