



Axalbion Announces Positive Findings from Phase 2 Clinical Study in Chronic Cough with AX-8, a Novel TRPM8 Agonist

AX-8 reduces cough frequency and improves patient-reported outcomes in patients with chronic cough

Manchester, UK and Mountain View, Calif, June 29, 2022 – Axalbion, a clinical-stage biopharmaceutical company focused on developing novel medicines to treat cough, today announced positive results from a Phase 2 proof-of-concept study (AX8-003) with its transient receptor potential melastatin 8 (TRPM8) agonist, AX-8, in patients with refractory or unexplained chronic cough.

The Phase 2 trial was a randomized, double-blind, placebo-controlled, crossover study that evaluated the efficacy and safety of AX-8 in 51 patients with refractory or unexplained chronic cough. Patients received 40 mg of the drug twice daily, eight hours apart, or matching placebo for two weeks, followed by a seven-day washout period before crossing over to the opposite treatment for two weeks. AX-8, a topically acting compound, is delivered as an orally disintegrating tablet (ODT) placed on the back of the tongue.

“We are pleased to report Phase 2 data showing that AX-8 reduced cough frequency in patients with chronic cough, particularly in the immediate post-treatment period, as well as improved key patient and clinician-reported outcomes,” said Michael Kitt, MD, chief executive officer. “As this was a proof-of-concept study evaluating a new mechanism of action, the endpoints chosen were exploratory. While the primary endpoint of cough reduction at eight hours did not reach statistical significance, there was a clear and immediate benefit after treatment with AX-8 in patients with chronic cough that warrants moving forward with clinical development.”

Results showed:

- Treatment with AX-8 40 mg BID compared to placebo showed a reduction in cough frequency within the first 15 minutes after treatment and lasting for more than 4 hours. This included a 44% reduction in cough frequency over two hours compared to 18% with placebo and a 35% reduction over 4 hours compared to 20% with placebo.
- Reduction in cough frequency was seen across patients in the study irrespective of high/low baseline cough frequency, duration of coughing, age or sex.
- In a pre-determined subset of patients with higher baseline throat discomfort, there was a statistically significant reduction of cough, including a 49% reduction over two hours compared to 8% with placebo and a 32% reduction over 24 hours compared to 13% with placebo.
- Overall improvements in patient- and clinician-reported outcomes over 14 days were observed in:
 - Leicester Cough Questionnaire (LCQ)
 - patient’s global impression of change (very much improved or much improved)
 - clinician’s global impression of change (very much improved or much improved)
- Good safety profile, with no serious adverse events

“With its rapid onset of action, AX-8 is an ideal candidate for the treatment of cough. Chronic cough is episodic by nature. Patients have cough bouts interspersed with periods of calm with reduced or no coughing. AX-8 as a standalone treatment or in combination with a P2X3 antagonist could significantly improve the quality of life of chronic cough patients,” said principal investigator Jacky Smith, MD, professor of respiratory medicine at the University of Manchester, UK.

Given these positive findings, the company plans to initiate a Phase 2 study examining more frequent dosing of AX-8 in the treatment of chronic cough patients in the first quarter of 2023.

About AX-8 and TRPM8

AX-8, a potent and selective transient receptor potential melastatin 8 (TRPM8) agonist, is in development for treatment of chronic cough. TRPM8 is expressed in many of the sensory fibers innervating the upper airways. Axalbion believes that activating TRPM8-expressing fibers with AX-8 will normalize the upper airway sensitivity in chronic cough patients, decreasing coughing (antitussive effect) and irritation of the throat (counterirritant effect). In a previous open-label pilot study in 12 patients with refractory/unexplained chronic cough, AX-8 appeared to reduce cough when given as a single 5 mg ODT ([EudraCT Number 2017-003108-27](#)).

The 2021 Nobel Prize in Physiology or Medicine was awarded to David Julius, PhD, and Ardem Patapoutian, PhD, for their discoveries of thermal and mechanical transducers, including the discovery of TRPM8. Since its cloning in 2002, extensive research has identified TRPM8 as a potential target to relieve symptoms or cure several diseases. Animal models have shown that activation of TRPM8-expressing fibers in the skin inhibits sensory hypersensitivity in peripheral neuropathy and inflammation, as well as itching. Additionally, activation of TRPM8 in corneal trigeminal fibers has been shown to increase basal tear secretion and relieve neuropathic ocular pain in patients with dry eye disease. AX-8 properties suggest that it could also be a promising drug candidate to treat dry eye.

About Chronic Cough

Chronic cough is defined as a cough lasting for more than eight weeks, often occurring in bouts. More than 80% of patients in tertiary cough clinics have throat irritation which triggers cough bouts, defining a population with oropharyngeal hypersensitivity potentially responding to a topical locally acting drug such as AX-8. After potential triggers such as gastro-intestinal reflux disease (GERD) and asthma have been excluded or treated, cough still remains a significant and common problem for many patients. Chronic cough has a substantial impact on quality of life with, for example, around half of female patients having urinary stress incontinence. There are no approved drugs for the treatment of chronic cough, making it a significant unmet need affecting more than 26 million people in the U.S. alone, with approximately three million having refractory or unexplained chronic cough lasting for more than a year and approximately six million having refractory or unexplained chronic cough lasting more than eight weeks and under one year.

About Axalbion

Axalbion is a privately held, clinical-stage biotechnology company developing novel medicines for the millions of patients who suffer from chronic cough and dry eye. The company, founded in December 2016, is based in Manchester, United Kingdom, a region known for its centers of excellence in respiratory research, with offices in Lausanne, Switzerland and Mountain View, CA. For further information, please visit www.axalbion.com.

Contacts:

Michael Kitt, MD
Chief Executive Officer
Axalbion Therapeutics Limited
investor@axalbion.com

or

Susan Kinkead
Kinkead Communications
susan@kinkeadcomm.com
(415) 509-3610