



Altamira Therapeutics Highlights Newly Published Review Article Supporting Use of Betahistine in Vertigo Management

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- *Independent review discusses evidence supporting the use of betahistine to alleviate residual dizziness following physical repositioning procedures in benign paroxysmal positional vertigo (BPPV) patients*
- *Betahistine is marketed world-wide, except in the US, and considered standard of care treatment for dizziness / vertigo*
- *AM-125 is a nasal spray formulation of betahistine currently being developed by Altamira to overcome low bioavailability of oral formulation and make treatment option also available to US patients*
- *Altamira intends to partner or divest AM-125 as part of legacy assets in strategic pivot to RNA delivery technology*

Altamira Therapeutics Ltd. ("Altamira" or the "Company") (Nasdaq:CYTO), a company dedicated to developing and commercializing RNA delivery technology for targets beyond the liver, today highlighted the publication of an article describing the rationale for and use of betahistine in the treatment of residual dizziness following standard of care physical repositioning procedures for benign paroxysmal positional vertigo (BPPV). The peer reviewed article was published by an international group of medical and scientific experts in vestibular disorders in the journal *Frontiers in Neurology*¹ and reviews the potential causes of residual dizziness, which has been reported to occur in 31-61% of patients, and available treatment options.

BPPV is characterized by repeated episodes of vertigo produced by changes in the head position relative to gravity, e.g. when tipping the head backward. It is typically caused by dislodged inner ear particles (otoconia) in one of the semicircular canals, most often the posterior canal. The debris elicits unwanted vestibular stimulation and is often cleared through physical repositioning procedures such as the Epley maneuver, which is strongly recommended by the Clinical Practice Guideline of the American Academy of Otolaryngology–Head and Neck Surgery.

BPPV is the most common type of vertigo and accounts for 17 to 42% of all diagnosed cases; in the United States, healthcare costs associated with the diagnosis of BPPV alone approach \$2 billion per year. Patients suffering from BPPV experience significant inconveniences and disabilities during symptomatic episodes, as they interfere with day-to-day activities such as driving a car or climbing stairs. Almost 86% of BPPV patients suffer some interruption to their daily activities and lost days at work due to BPPV. The dysfunction generally emerges in the elderly with a peak onset in the 5th and 6th decade.

Even in case of a successful physical repositioning procedure, patients may experience residual dizziness. This may last for a few days up to several weeks and may affect quality of life and be of incapacitating nature. Residual dizziness may be due to, among others, remaining otoconia, incomplete vestibular compensation or microcirculation dysfunction. Based on their review of available treatment options, the authors of the publication suggest the use of vestibular habituation therapies and vestibular rehabilitation programs to facilitate vestibular compensation and treatment with betahistine for improvement of inner ear blood supply and promotion of vestibular compensation. An earlier publication by another research group had already shown in a meta-analysis that the combination of a common physical repositioning procedure with betahistine treatment resulted in a significantly greater reduction in dizziness handicap compared to the procedure alone ($p = 0.001$).²

"We welcome the additional research into residual dizziness after physical repositioning procedures in BPPV since this is a very common and oftentimes serious problem for patients", commented Thomas Meyer, PhD, Altamira's founder, chairman and CEO. "Treatment of BPPV is the single most important vestibular indication for betahistine, and we look forward to testing our AM-125, an intranasal formulation of the drug, specifically in this condition. AM-125 has a significantly higher bioavailability than the oral form of betahistine, which is currently marketed around the world, except for the US. As we are repositioning the Company around our RNA delivery technology, we are working towards the partnering of the program with one or several partners to take it forward and making betahistine ultimately also available to dizziness patients in the US."

About Betahistine

Betahistine, a small molecule structural analog of histamine, acts as an agonist at the H1 histamine receptor and as an antagonist at the H3 histamine receptor. Unlike histamine, it crosses the blood-brain-barrier. Betahistine is known to increase the release of histamine, acetylcholine, dopamine and norepinephrine in the brain. It increases cochlear, vestibular and cerebral blood flow and facilitates vestibular compensation and inhibits neuronal firing in the vestibular nuclei. Betahistine for oral administration is approved in about 115 countries (with the U.S. being a notable exception) for the treatment of vertigo and Meniere's disease. Despite its good safety profile, the clinical utility of orally administered Betahistine is limited due to poor bioavailability.

About AM-125

AM-125 is an intranasal formulation of betahistine. Because of its ability to circumvent first-pass-metabolism, AM-125 has been shown to have 5-to-29 times higher bioavailability than orally administered betahistine. Altamira Therapeutics is developing AM-125 for the treatment of acute vestibular syndrome (AVS). The investigational drug has been tested successfully in a Phase 2 clinical trial ("TRAVERS") with patients suffering from AVS following vestibular surgery: compared to placebo, AM-125 treatment helped accelerate vestibular compensation and alleviate signs and symptoms of

vestibular dysfunction.³

About Altamira Therapeutics

Altamira Therapeutics (Nasdaq: CYTO) is developing and supplying peptide-based nanoparticle technologies for efficient RNA delivery to extrahepatic tissues (OligoPhore™ / SemaPhore™ platforms). The Company currently has two flagship siRNA programs using its proprietary delivery technology AM-401 for KRAS driven cancer and AM-411 for rheumatoid arthritis, both in preclinical development beyond in vivo proof of concept. The versatile delivery platform is also suited for mRNA and other RNA modalities and made available to pharma or biotech companies through out-licensing. In addition, Altamira holds a 49% stake (with additional economic rights) in Altamira Medica AG, its commercial-stage legacy asset Bentrio®, an OTC nasal spray for allergic rhinitis. Further, the Company is in the process of partnering / divesting its inner ear legacy assets. Founded in 2003, Altamira is headquartered in Hamilton, Bermuda, with its main operations in Basel, Switzerland. For more information, visit: <https://altamiratherapeutics.com/>

Forward-Looking Statements

This press release may contain statements that constitute "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements are statements other than historical facts and may include statements that address future operating, financial or business performance or Altamira's strategies or expectations. In some cases, you can identify these statements by forward-looking words such as "may", "might", "will", "should", "expects", "plans", "anticipates", "believes", "estimates", "predicts", "projects", "potential", "outlook" or "continue", or the negative of these terms or other comparable terminology. Forward-looking statements are based on management's current expectations and beliefs and involve significant risks and uncertainties that could cause actual results, developments and business decisions to differ materially from those contemplated by these statements. These risks and uncertainties include, but are not limited to, the success of strategic transactions, including licensing or partnering, with respect to Altamira's legacy assets, Altamira's need for and ability to raise substantial additional funding to continue the development of its product candidates, the clinical utility of Altamira's product candidates, the timing or likelihood of regulatory filings and approvals, Altamira's intellectual property position and Altamira's financial position, including the impact of any future acquisitions, dispositions, partnerships, license transactions or changes to Altamira's capital structure, including future securities offerings. These risks and uncertainties also include, but are not limited to, those described under the caption "Risk Factors" in Altamira's Annual Report on Form 20-F for the year ended December 31, 2023, and in Altamira's other filings with the Securities Exchange Commission ("SEC"), which are available free of charge on the SEC's website at: www.sec.gov. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those indicated. All forward-looking statements and all subsequent written and oral forward-looking statements attributable to Altamira or to persons acting on behalf of Altamira are expressly qualified in their entirety by reference to these risks and uncertainties. You should not place undue reliance on forward-looking statements. Forward-looking statements speak only as of the date they are made, and Altamira does not undertake any obligation to update them in light of new information, future developments or otherwise, except as may be required under applicable law.

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¹ Özgirgin et al. (2024), Residual dizziness after BPPV management: exploring pathophysiology and treatment beyond canalith repositioning maneuvers, *Front Neurol* 15:1382196. <https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2024.1382196/full>

² Li et al. (2023), Efficacy of Epley's maneuver plus betahistine in the management of PC-BPPV - A systematic review and meta-analysis, *Medicine (Baltimore)* 102(13):e33421. https://journals.lww.com/md-journal/Fulltext/2023/03310/Efficacy_of_Epley_s_maneuver_plus_betahistine_in.34.aspx

³ Van de Heyning et al. (2023), Efficacy and safety of intranasal betahistine in the treatment of surgery-induced acute vestibular syndrome: a double-blind, randomized, placebo-controlled phase 2 study, *Otol Neurotol* 44(5):493-501. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10184813/>