



## Altamira Therapeutics Announces Filing of Provisional Patent Application for OligoPhore Nanoparticles with siRNA Targeting p65 Protein in Treatment of Cancer and Inflammation

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- Continued expansion of IP portfolio related to RNA delivery
- Treatment of rheumatoid arthritis as one of the key therapeutic indications

HAMILTON, BERMUDA / May 1, 2024 / 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 announced that it has filed a provisional patent application with the United States Patent Office (USPTO) which covers nanoparticles comprising the Company's OligoPhore™ platform and siRNA targeting the p65 protein, a component of the NF-κB transcription factor.

The provisional patent application describes novel nanoparticle compositions based on OligoPhore, Altamira's peptide-based oligonucleotide delivery platform, or derivatives thereof in combination with siRNA sequences designed to silence p65. Activation of p65 has been observed in multiple types of cancer as well as in many inflammatory diseases and its function has been implicated in the pathogenesis of these diseases. For instance, p65 is a well-known key checkpoint in rheumatoid arthritis (RA) inflammation, and thought to regulate cell proliferation, cell death, and stimulate metastasis in cancer. The new filing is intended to extend Altamira's intellectual property related to its AM-411 development program for RA treatment, among others.

"We consider the treatment of arthritis one of the most promising applications of our OligoPhore RNA delivery platform," commented Covadonga Pañeda, Ph.D., Altamira Therapeutics' Chief Development Officer. "With our AM-411 program, we have demonstrated in vivo that we can deliver siRNA specifically to inflamed tissues, which in the case of RA is primarily the inflamed joints. The treatment is thus sparing non-inflamed tissues and avoiding the systemic side effects frequently observed with current treatment options. In addition, using siRNA to knock down the p65 protein allows to control a key inflammatory checkpoint, and promises not only potent treatment effects, but also a much-reduced risk of developing treatment resistance, another frequent issue with current treatment options."

### Rheumatoid arthritis is a major autoimmune disease

RA is a chronic inflammatory condition causing joint swelling and pain which may also affect other areas, including the skin, eyes, brain, and cardiovascular system. In the US, approximately 1.3 million adults suffer from RA; according to the World Health Organization (WHO), the autoimmune disease affects globally up to 14 million people. RA affects 1 in 28 women and 1 in 59 men during their lifetime. There is no cure for RA; current treatments seek to manage RA with biologic and non-biologic immunosuppressants, corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs). While useful, drug resistance occurs in up to 50% of patients and systemic adverse reactions are frequent, including rash, hair loss, altered liver function, low blood cell counts, nausea, increased infections and neuropathy. New biologics targeting JAK/interleukins have been issued black box warnings by the FDA. According to a market research study, the global anti-rheumatics market is expected to grow from \$57.9 billion in 2019 to \$62.9 billion in 2027, representing the second largest therapeutic area after oncology.

### Effective and specific suppression of inflammation in animal arthritis model

AM-411's therapeutic potential in RA was demonstrated in a study using a collagen antibody-induced arthritis model in mice, where OligoPhore nanoparticles with siRNA targeting NF-κB (p65) potently suppressed early inflammatory arthritis.<sup>1</sup> The treatment effectively reduced the expression of inflammatory cytokines and cellular influx into the joints, protected against bone erosions and preserved cartilage integrity. Importantly, the treatment did not affect p65 expression in off-target organs or elicit a humoral response after serial injections.

### Positive outcomes of NF-κB knock-down also in cancer animal models

In cancer, treatment with OligoPhore nanoparticles delivering p65 siRNA showed positive outcomes in animal models of melanoma lung metastasis and of Adult T-cell Leukemia Lymphoma (ATLL). Three-serial i.v. injections of nanoparticles retarded growth of lung metastasis within one week by 76% (p=0.003) as compared to saline control treatments.<sup>2</sup> In the second study, tumor size was significantly lower in treated mice compared to controls, tumor growth was reduced to near zero in the most aggressive tumors and late-stage ATLL tumors were sensitized to conventional chemotherapy.<sup>3</sup>

### About OligoPhore

OligoPhore is a versatile platform for safe and effective delivery of oligonucleotides such as siRNA (small interfering ribonucleic acid) into target cells. It is based on a proprietary 21-amino acid peptide that can engage any type of RNA in rapid self-assembly into a polyplex. The polyplex has a size, charge, and other physical features that allow it to escape hepatic clearance and thus to reach other target tissues than the liver. OligoPhore protects the RNA payload from degradation in the circulation and allows for rapid cellular uptake, while enabling pH-dependent nucleotide endosomal escape and cytoplasmic delivery. Effective delivery and positive treatment outcomes have been demonstrated in more than 10 murine models of disease for targets in the NF-κB family, various members of the ETS transcription factor family, and targets in the JNK and TAM pathways.

### 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](http://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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<sup>1</sup> Zhou et al. (2014), Peptide-siRNA nanocomplexes targeting NF- $\kappa$ B subunit p65 suppress nascent experimental arthritis, *J Clin Invest* 124(10):4363-74.

<sup>2</sup> Stansel et al. (2020), NF- $\kappa$ B Inhibition Suppresses Experimental Melanoma Lung Metastasis, *J Cancer Sci Clin Ther* 4(3):256-65.

<sup>3</sup> Rauch et al. (2021), Targeting NF- $\kappa$ B with nanotherapy in a mouse model of adult T-cell leukemia/lymphoma, *Nanomaterials* 11(6):1582.