Altamira Therapeutics Files Second Provisional Patent Application for OligoPhore Nanoparticles Targeting Different KRAS Mutations in Cancer Treatment

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- Altamira's *poly*KRAS^{mut} siRNA shown to knock down at least 65-91% of KRAS mutations in colorectal, non-small cell lung, and pancreatic cancer cell lines
- Fresh experimental data expected to strengthen Altamira's intellectual property around its AM-401 nanoparticles for the treatment of KRAS-driven cancers

HAMILTON, BERMUDA, Jan. 24, 2024 -- Altamira Therapeutics Ltd. (Nasdaq: CYTO) ("Altamira" or the "Company"), a company providing nanoparticle-based technology for efficient RNA delivery to extrahepatic targets, today announced that it has filed a second provisional patent application with the United States Patent and Trade Office (USPTO) to provide broad coverage of different KRAS mutations in human cancer treatment with nanoparticles comprising the Company's OligoPhore™ platform and a single siRNA sequence, *poly*KRAS^{mut}. The nanoparticles are developed by Altamira as AM-401.

The second provisional application contains *in vitro* data confirming the ability of *poly*KRAS^{mut} siRNA to knock down a broad range of KRAS mutations in cancer cell lines. These mutations include G12C, G12V, G12D, G12R, G12A, and A146T, which account for 90.9% of KRAS mutations reported in pancreatic ductal adenocarcinoma (PDAC), 65.3% in colorectal cancer (CRC) and 80.0% in non-small cell lung cancer (NSCLC).[1] In comparison, currently approved small molecule inhibitors target just one KRAS mutation (G12C), which represents 1.7%, 7.1% and 41.0% of total KRAS mutations in PDAC, CRC and NSCLC, respectively. Since *poly*KRAS^{mut} was tested against only a limited number of mutations, it may potentially knock down other, yet untested mutations.

"We are very pleased to observe the latest data on our *poly*KRAS^{mut} siRNA confirming its ability in knocking down several KRAS mutations known to drive some of the most severe types of cancer" commented Covadonga Pañeda, Ph.D., Altamira Therapeutics' Chief Operating Officer. "By combining the *poly*KRAS^{mut} siRNA with our OligoPhore platform we can direct its delivery to the tumor and tackle with one single compound many different KRAS mutations. This combination aims to not only treat cancers harboring different KRAS mutations but also addresses some of the escape mechanism developed by these tumors that make them less responsive to small molecule KRAS-directed therapies. Additionally, we expect that AM-401 will be better tolerated than small molecule-inhibitors as it specifically targets the tumor-affected organ without affecting healthy tissues. We are excited about advancing our AM-401 program to provide clinicians and patients with a comprehensive treatment option for KRAS-driven cancers."

Altamira expects the second provisional patent application to further strengthen its intellectual property around the AM-401 program, under which the Company is aiming to develop a treatment for KRAS-driven cancers. Previous *in vitro* and *in vivo* work demonstrated efficient uptake of OligoPhore nanoparticles with KRAS-targeted siRNA in CRC and PDAC cells, strong inhibition of KRAS expression, reduced viability of tumor cells, and significant reduction in tumor growth and volume.[2] Importantly, a murine model demonstrated the capacity of the OligoPhore platform to drive targeted delivery of the nanoparticles specifically to tumor cells. Altamira intends to file for an Investigational New Drug (IND) application with the FDA in 2025 and to partner the program upon an IND grant or following a phase 1 clinical trial.

The KRAS gene encodes one of the RAS proteins, that control – like an "on / off switch" – cell growth, maturation, migration, and death. Through mutations, the RAS proteins can be rendered persistently active, causing cancer cells to proliferate and spread in the body. Mutations of KRAS are associated with poor prognosis in several cancers, and there is a substantial body of evidence supporting the role of KRAS in the initiation and maintenance of cancer. Mutated forms of KRAS are found in one-fifth of all human cancers, including 32% of NSCLCs, 40% of CRCs and 85–90% of PDACs. According to the American Cancer Society, nearly 150,000 new cases of KRAS-mutated tumors are diagnosed annually in the United States across these three tumor types alone. It is estimated that KRAS mutations account for approximately one million deaths per year worldwide.[3]

Although the role of KRAS mutations in cancer has been known for decades, they have remained a challenging target for therapeutic interventions. KRAS was long considered undruggable, in part, because of the lack of obvious binding sites. Only recently, the FDA approved the first two treatments for KRAS-driven cancer: sotorasib and adagrasib, two small molecule inhibitors of G12C-mutated KRAS for the treatment of NSCLC.

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 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 (AM-125 nasal spray for vertigo; post Phase 2; Keyzilen® and Sonsuvi® for tinnitus and hearing loss; Phase 3). 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, 2022, 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] Based on Huang et al. (2021), KRAS mutation: from undruggable to druggable in cancer, Sig Transduct Target Ther 6: 386. https://doi.org/10.1038/s41392-021-00780-4

[2] Strand et al. (2019), Precision delivery of RAS-inhibiting siRNA to KRAS driven cancer via peptide-based nanoparticles, Oncotarget 10(46): 4761-75.

[3] Simanshu et al. (2017), RAS proteins and their regulators in human disease, Cell 170(1):17-33.

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