



DELIVERING RNA – BEYOND THE LIVER

Investor Presentation

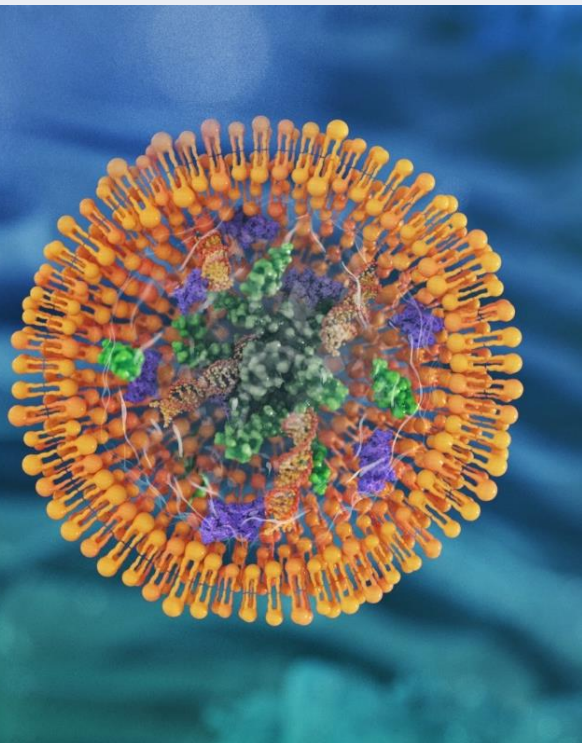
Summer 2024

Forward-Looking Statements



This presentation 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 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. 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.

Disruptive, Proprietary RNA Delivery Technology Platform



OligoPhore™ (siRNA) SemaPhore™ (mRNA)

- Proprietary 21 amino acid peptide (nanoparticles)
- Efficient delivery of RNA into extrahepatic target cells

RNA Market Taking Off

- Rapidly growing number of RNA therapeutics
- Active M&A, licensing environment

'Picks and Shovels' Platform Strategy

- Partner delivery platforms with pharma & biotech
- Initiated first collaborations

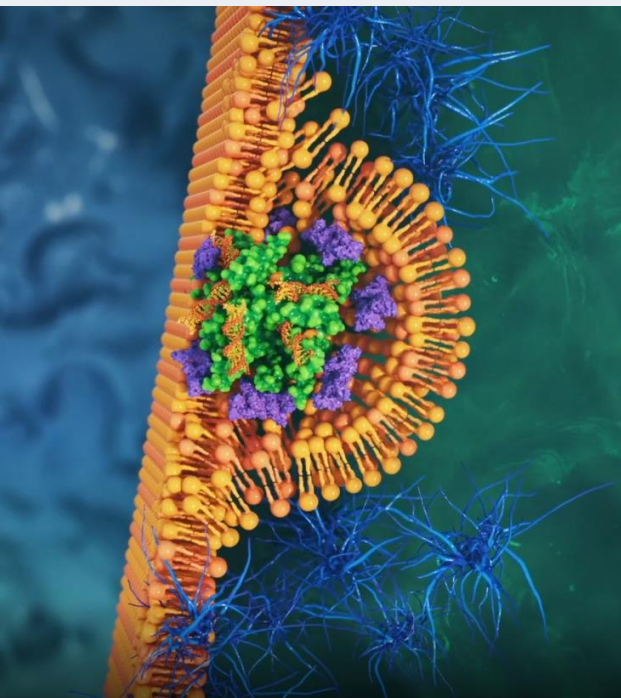
Two Flagship Programs for Demonstration

- KRAS-driven cancers (AM-401) - IND expected in 2026
- Rheumatoid arthritis (AM-411) - IND expected in 2026

Divesting / Partnering Legacy Assets

- Unlock intrinsic value of inner ear & OTC assets
- Extra, non-dilutive funding potential

OligoPhore/SemaPhore are nanoparticles comprising a **proprietary peptide + RNA payload** designed to enable safe and effective delivery by systemic administration.



Stability

RNA complexed in nanoparticle format and only released inside of cells after uptake

Extrahepatic delivery

Not sequestered in liver as is common with conventional RNA-based therapies; permeates inflamed pathological tissues (passive targeting)

Endosomal escape

Efficient release within target cell, about 10-fold increase over LNPs, the current industry standard

Selectivity

Acts on targets in diseased tissues only

Safety

No immune response to nanoparticle components or RNA after multiple serial doses, and no organ toxicities in mice

RNA Delivery is One of the Key Challenges

Exemplary listing of companies active in RNA therapeutics and delivery (list not exhaustive)

Silence gene expression	Promote protein expression	Deliver RNA therapeutic to target
<ul style="list-style-type: none"> • Short interfering RNA (siRNA) • Antisense oligonucleotides (ASOs) 	<ul style="list-style-type: none"> • Messenger RNA (mRNA) 	<ul style="list-style-type: none"> • Lipid nanoparticles • Virus-based vectors • Ligand conjugates • Peptide-based nanoparticles
		<p>\$32 million</p> <p>\$3.2 million</p> <p>\$723 million</p> <p>\$630 million</p> <p>\$3.3 billion*</p> <p>\$317 million</p>

*Represents valuation of the company derived from 2021 acquisition
 Figures are sourced from Yahoo Finance as of April 17, 2024



The Limitless Future of RNA Therapeutics

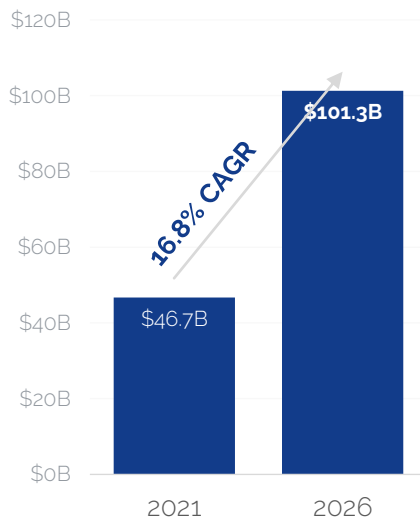
Tulsi Ram Damase¹, Roman Sukhovshin¹, Christian Boada², Francesca Taraballi^{3,4}, Roderic I. Pettigrew² and John P. Cooke^{1*}

Frontiers in Bioengineering
and Biotechnology,
March 2021

- ✓ High specificity
- ✓ Cost effective
- ✓ Relatively simple to manufacture
- ✓ Can target previously undruggable pathways
- ✓ Disruptive technology

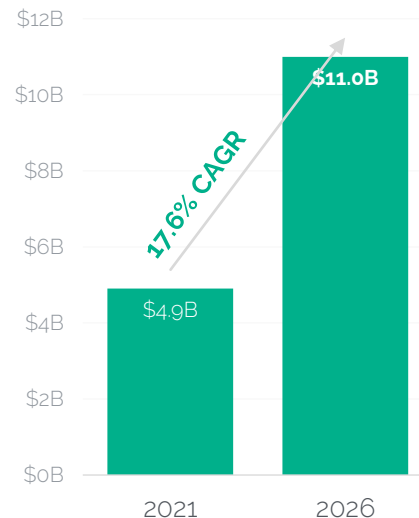
mRNA Vaccines & Therapeutics

Global Sales



siRNA Therapeutics

Global Sales



STRONG GROWTH—STARTING IN 2018
ONLY THE BEGINNING!

*Research and Markets; Allied Market Research

Strong strategy based on external collaborations and in-house programs

✓ Leverage versatility of technology

- Demonstrated to work in multiple disease areas (tested in 17 models...)
- Suitable for siRNA, mRNA, ASOs, circular RNA

✓ Particularly well-suited for indications in oncology and inflammatory disorders

✓ Selecting two therapeutic indications to showcase technology

- KRAS driven cancers – AM-401
- Rheumatoid arthritis – AM-411
- Partner upon IND or Phase 1

OligoPhore™ has been tested *in vivo*...

- Pancreatic and colorectal cancer (KRAS)
- Ovarian cancer (TAM: AXL)
- Lung cancer (ETV-2)
- Metastatic melanoma (NF-κB)
- Adult T cell leukemia/lymphoma (NF-κB)
- Sarcoma (MYCT-1)
- Sarcoma and breast cancer (MYCT-1)
- Necrotizing enterocolitis (NF-κB)
- Rheumatoid and osteoarthritis (NF-κB)
- Atherosclerosis (JNK2)
- Metabolic syndrome/Obesity (ASXL2)
- Aortic aneurysm (NF-κB)

SemaPhore™ has been tested *in vivo*...

- Osteoarthritis (WNT16)
- Osteoarthritis (DNMT3B)
- Atherosclerosis (p27^{Kip1})
- Tumor microenvironment (ZBTB46)
- Aortic aneurysm (SOD2)

Use Case: Enhancing the Potential of Anti-PD1 Therapy

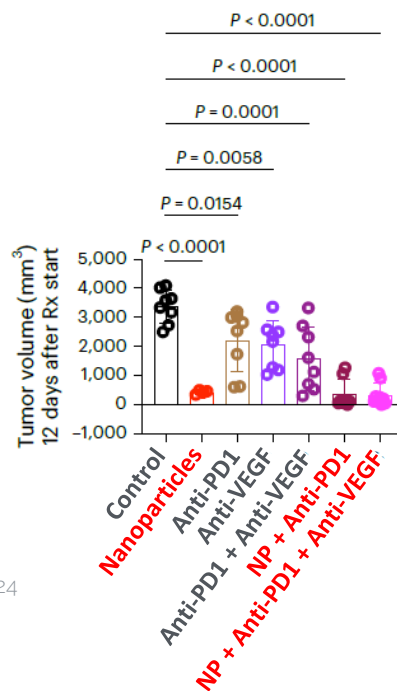
Delivering SemaPhore™ *Zbtb46* mRNA in sarcoma and metastatic breast cancer models.

- Work by Choi Lab at WashU
- Cancers form defective blood vessels that feed the tumor
- Defective vasculature blocks access to tumor infiltrating T cells
 - Limits effectiveness of anti-PD1 therapy
- *Zbtb46* mRNA nanoparticles normalized tumor vessels and enhanced antitumor immunity
 - Highly significant reduction in tumor growth ($p < 0.0001$)
 - Effects potentiated when combined with anti-PD1
- "Remarkably, *Zbtb46* nanoparticles induced dramatic anti-PD1 response in both anti-PD1-responsive [...] and anti-PD1-refractory [...] tumor models, generating long-term complete remission of tumor in many of the treated animals."

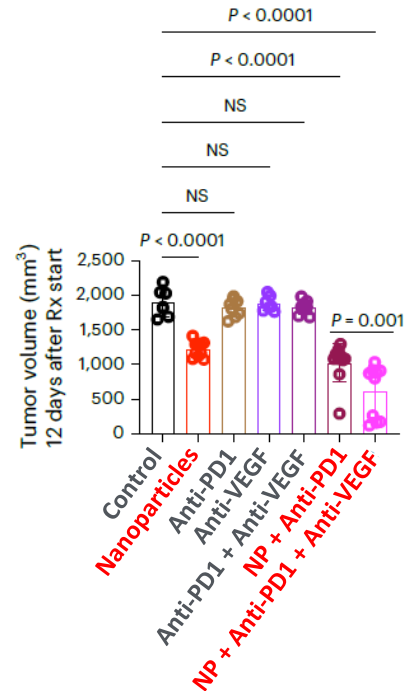
Kabir et al., 2024



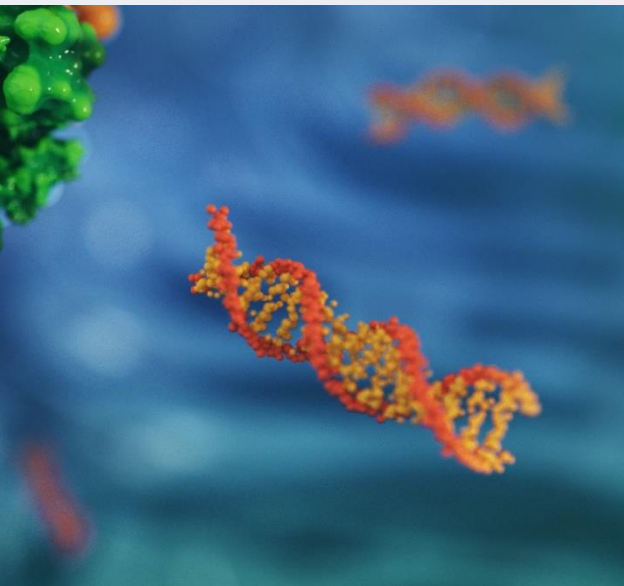
1956 Sarcoma



PyMT-BO1 Breast Cancer



License technology to biotechs / pharmas for use with their own RNA molecules



- Active business development program
- First two collaborators signed up



- Evaluate OligoPhore™ + certain non-coding RNAs in the regeneration of damaged heart tissue following myocardial infarction



- Evaluate SemaPhore™ + mRNA vaccine(s)
- Lower mRNA loss during cell entrance may allow for using lower doses and thus result in potentially more effective and efficient vaccines

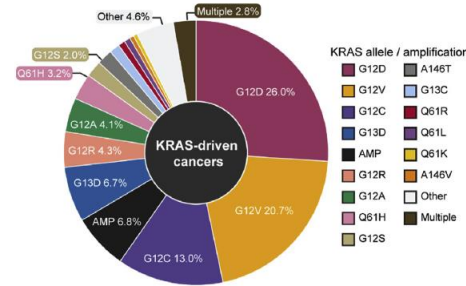
AM-401: Stop the “Beating Heart” of Tumors

Knock down various KRAS mutations with *polyKRAS^{mut}* OligoPhore nanoparticles

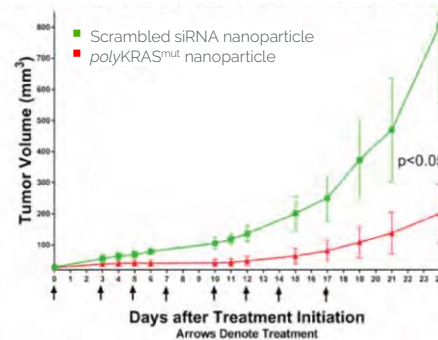
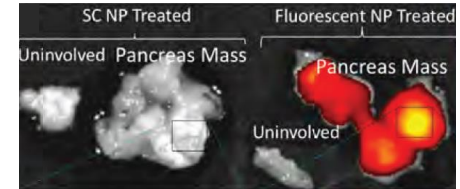
to inhibit cell proliferation in KRAS driven colorectal, pancreatic, or non-small cell lung cancer.

- Mutated KRAS may cause cancer to grow
- Found in 1/5 of all human cancers, particularly in:
 - Pancreatic cancer (85-90%)
 - Colorectal cancer (40%)
 - Non-small cell lung cancer (30-35%)
- 150,000 cases diagnosed in US p.a.
- ~1M deaths per year world-wide
- Considered “undruggable” for decades

Many mutations known, G12D, G12V, and G12C accounting for >50%



OligoPhore *polyKRAS^{mut}* siRNA transfects tumor cells, not healthy or uninvolved cells



OligoPhore *polyKRAS^{mut}* significantly reduces pancreatic tumor volume growth

KPC pancreatic tumor model in mice; Strand et al., 2019

AM-401

KRAS driven cancer
IND targeted for 2026

- ✓ High unmet medical need – most aggressive tumors
- ✓ Small molecule G12C inhibitors approved in NSCLC
 - Sotorasib (Lumakras, Amgen), Adagrasib (Krazati, Mirati)
- ✓ Multiple other small molecule inhibitors under development (G12C, G12D...), but few competing RNA projects (G12D or KRAS modulators)

AM-401 KEY DIFFERENTIATING FACTORS



*poly*KRAS^{mut} allows to target different mutations and is thus **polyvalent**
G12C, G12V, G12D, G12R, G12A, and A146T, covering 90.9% of KRAS mutations in pancreatic, 65.3% in colorectal, 80.0% in non-small cell lung cancer



Blocking production of KRAS by degrading mRNA to cause **less resistance** than inhibition of KRAS

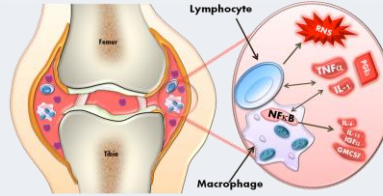


Small molecule inhibitors have significant side effects, particularly when combined with other agents
OligoPhore **targets specifically** tumor cells

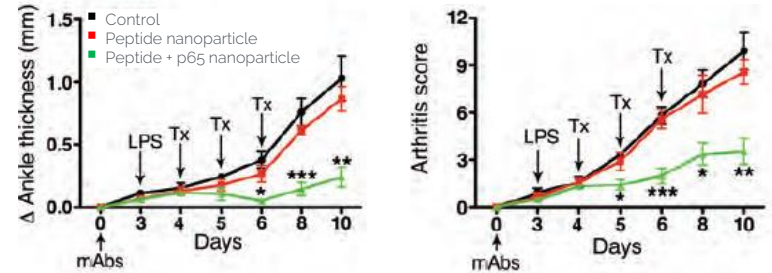
AM-411: Block Inflammation in Rheumatoid Arthritis

Knock down NF- κ B (p65), a key checkpoint in RA inflammation.

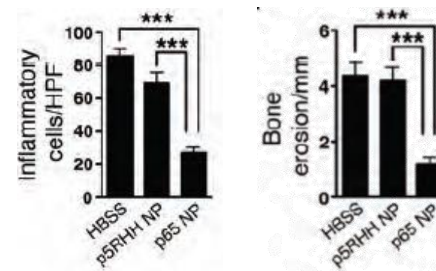
- Chronic autoimmune disease
- Causes joint swelling and pain
 - Reduced QoL and productivity
- Affects 1 out of 28 women / 59 men
- No cure available, but various treatment options:
 - Disease-modifying anti-rheumatic drugs (DMARDs)
 - Non-steroidal anti-inflammatory drugs (NSAIDs)
 - Corticosteroids
- Major shortcomings of therapies:
 - Drug resistance (up to 50% of patients)
 - Systemic adverse reactions (e.g., rash, hair loss, altered liver function, low blood cell counts, nausea, weight loss, increased infections, and neuropathy)



OligoPhore p65 stabilizes ankle swelling and reduces arthritis score



OligoPhore p65 reduces inflammation and protects against bone erosion



Collagen-antibody induced arthritis model in mice, Zhou et al., 2014.

AM-411

Rheumatoid arthritis
IND targeted for 2026



High unmet medical need



Global rheumatoid arthritis market = \$57.9 Billion in 2019 → \$62.9 Billion in 2027

- Expiration of patents, biosimilars arriving
- High hopes for novel Tx class of JAK inhibitors gave way to disappointment due to safety issues

AM-411 KEY DIFFERENTIATING FACTORS



Mediators of inflammation play many physiological roles in healthy tissues – AM-411 targets only inflamed tissues

Reduced systemic side effects



Blocking production of an NF- κ B component by degrading mRNA to cause less resistance than inhibition of NF- κ B

Less likelihood of resistance

(12) **United States Patent**
Wickline et al. (10) **Patent No.:** **US 9,987,371 B2**
 (45) **Date of Patent:** **Jun. 5, 2018**

(54) **COMPOSITIONS AND METHODS FOR POLYNUCLEOTIDE TRANSESECTION**
 (71) Applicant: **Washington University, St. Louis, MO (US)**
 (72) Inventors: **Samuel A. Wickline, St. Louis, MO (US); Kirk Hou, St. Louis, MO (US)**
 (73) Assignee: **WASHINGTON UNIVERSITY, Saint Louis, MO (US)**
 (*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **14/790,408**
 (22) Filed: **Jul. 2, 2015**
 (65) **Priority Publication Data**
 US 2015/0514013 A1 Nov. 5, 2015

Related U.S. Application Data
 (63) Continuation-in-part of application No. PCT/US2014/010212, filed on Jan. 3, 2014.
 (60) Provisional application No. 61/869,634, filed on Aug. 23, 2013, provisional application No. 61/873,187, filed on Sep. 3, 2013.

(51) **Int. Cl.**
C07K 19/00 (2006.01)
A61K 47/48 (2006.01)
A61K 31/713 (2006.01)
A61K 47/42 (2017.01)
C12N 15/11 (2006.01)
C12N 15/113 (2010.01)
C12N 15/87 (2006.01)
A61K 47/64 (2017.01)
A61K 33/00 (2006.01)

(52) **U.S. Cl.**
 CPC **A61K 47/48323** (2013.01); **A61K 31/713** (2013.01); **A61K 47/42** (2013.01); **A61K 47/6455** (2017.08); **C07K 19/00** (2013.01); **C12N 15/113** (2013.01); **C12N 15/111** (2013.01); **C12N 15/87** (2013.01); **A61K 33/00** (2013.01); **C12N 23/10/14** (2013.01); **C12N 23/10/35/13** (2013.01); **C12N 23/20/32** (2013.01); **H10T 42/8/292** (2015.01)
Field of Classification Search
 CPC — **C07K 14/00; A61K 47/48315; A61K 38/16**
 USPC **530/326**
 See application file for complete search history.

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(10) **Patent No.:** **US 9,987,371 B2**
 (45) **Date of Patent:** **Jun. 5, 2018**

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 (Continued)

Primary Examiner — Amber D Steele
 (74) **Attorney, Agent, or Firm** — Polsinelli PC

(57) **ABSTRACT**
 A pharmaceutical composition comprising a peptide-poly-nucleotide complex, and methods of use thereof.
15 Claims, 91 Drawing Sheets
(38 of 91 Drawing Sheets) Filed in Color

WORLDWIDE EXCLUSIVE LICENSE FROM WASHINGTON UNIVERSITY Patent covering OligoPhore™ / SemaPhore™ platform

- Compositions comprising a peptide-polynucleotide complex
- Methods for delivering such nanoplexes

Coverage until 2034 (+ potential extension)

Generating further IP (e.g. *polyKRAS*^{mut} and p65 – potential coverage until 2043/4)

Proprietary manufacturing process



Thomas Meyer, Ph.D.

CEO & CHAIRMAN

- Company founder
- Funded and grew Company since 2003
- 14 years with Disetronic Group including CEO and BoD member (>20% sales CAGR, \$3B market cap)



Covadonga Pañeda, Ph.D.

CHIEF OPERATING OFFICER

- Joined as CDO in 2022
- 18 years experience in FDA/EMA drug development
- Non-clinical and clinical study design and regulatory submissions
- 7 years in RNAi for ophthalmology



Marcel Gremaud, CPA

CHIEF FINANCIAL OFFICER

- Working for Company since 2013
- ~30 years experience in controlling and accounting
- International pharma companies and start-ups



Samuel Wickline, MD

CHIEF SCIENTIFIC ADVISER

- Joined in 2021 through acquisition of Trasir Tx
- Prof. of Cardiovascular Sciences, Molecular Physiology and Pharmacology at USF
- Former Prof. of Med., Physics, Biomedical Engr, Cell Biology and Physiology at Wash U

Bentrio® in Allergic Rhinitis

Protection Against Airborne Particles

- Drug-free, preservative-free formulation, applied as nasal spray
- Four clinical trials demonstrating safety and efficacy in allergic rhinitis
 - Efficacy: close to medicated sprays
 - Tolerability: close to saline sprays
- Commercialized through distributors
- Significant growth expected
 - Launch in additional countries / regions
- Advanced discussions on North America, Europe and other key markets



First Step in Transition Process

- Sale of 51% of Altamira Medica AG
 - Cash consideration about \$2.3 million
 - Buyer is Swiss private equity investor
 - CYTO retaining 49% of capital
- CYTO also entitled to 25% of:
 - Future license income
 - Medica's value appreciation in case of a sale
- CYTO's overall share of upside: 62%
- Financial gain CHF 5.2 million
- Going forward: reduction in Bentrio related expenditures



Become focused

"Pure play" RNA delivery company



Monetize legacy assets

through divestiture, out-licensing

AM-125 in Acute Vestibular Syndrome

- Rx product, applied as nasal spray
- Reformulation of oral betahistine
 - Global market \$450M (ex US) – standard of care for vertigo
 - Poor bioavailability
- Invested \$18 million to date
- Proof of concept in Phase 2, ready for Phase 3 trial
- No comparable product in US
- Structured partnering process initiated



Potential Other Indications

- Histamine plays important role in many behavioral and physiological functions:
 - Appetite, drinking, sleep, wakefulness, learning, attention and memory
- Clinical utility of betahistine shown, among others, in:
 - ADHD, cognitive function in dementia, memory loss, antipsychotic-induced weight gain
- Histamine as target, e.g.:
 - Narcolepsy, Tourette syndrome, Prader-Willi syndrome



RNA technology coming of age

- Disruptive potential in human medicine
- Rapidly growing # of RNA therapeutics



Altamira has unique, versatile RNA delivery technology platform

- Patented, under license from Wash U
- Suitable for different types of RNA molecules
- OligoPhore™ and SemaPhore™



Addressing major challenges in RNA delivery

- IV administration, reaching extrahepatic targets
- Strong endosomal release (10x compared to lipid nanoparticles)



Extensive proof of concept

- Successfully tested *in vivo* in 17 different disease models
- 30+ papers published



Flagship programs in oncology and rheumatoid arthritis

- First IND expected to be filed in 2026
- Technology platform out-licensing as business model



Divestiture/partnering of Legacy Assets

- Process started
- Unlock intrinsic value / non-dilutive funding

The logo features a stylized white icon on the left, resembling a hand or a series of horizontal bars that curve into a circular shape. To its right, the word "altamira" is written in a lowercase, bold, sans-serif font. Below "altamira", the word "therapeutics" is written in a lowercase, regular, sans-serif font.

altamira
therapeutics

DELIVERING RNA – BEYOND THE LIVER
