



DELIVERING RNA – BEYOND THE LIVER

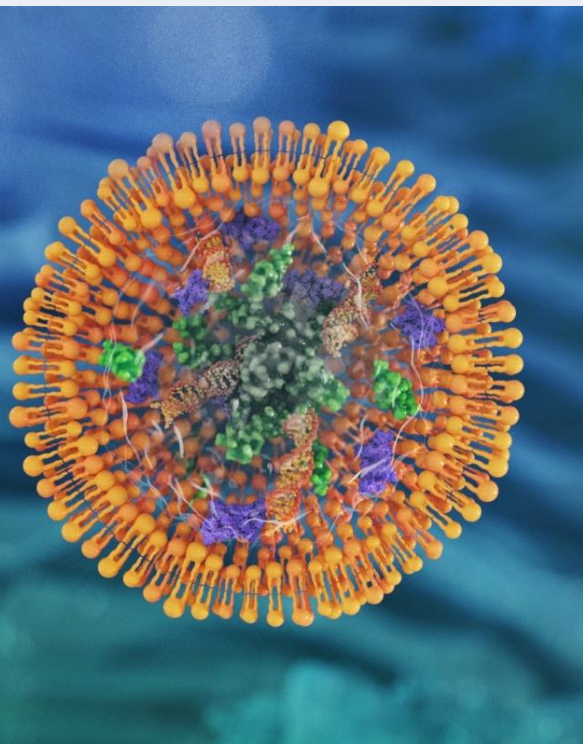
Company Presentation

Spring 2026

Forward-Looking Statements

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Disruptive, Proprietary RNA Delivery Technology Platform



OligoPhore™ (siRNA) SemaPhore™ (mRNA) CycloPhore™ (circRNA)

- 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

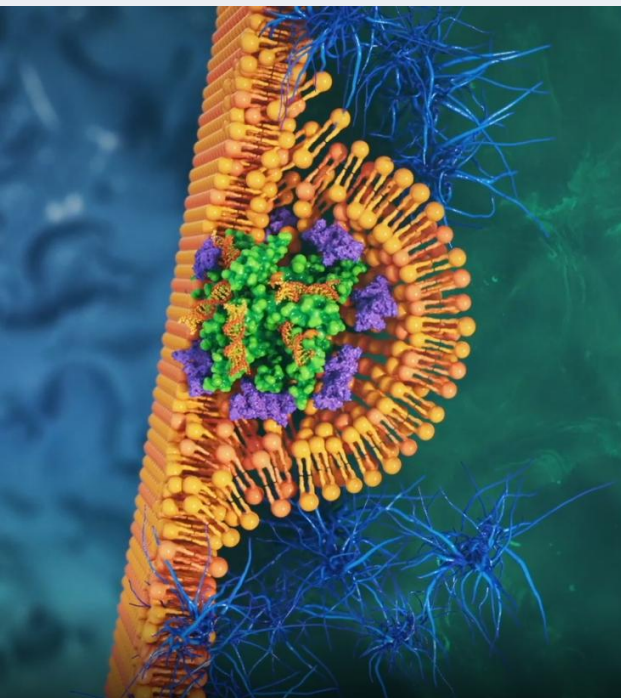
Two Flagship Programs for Demonstration

- 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/CycloPhore nanoparticles comprise 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



The Limitless Future of RNA Therapeutics

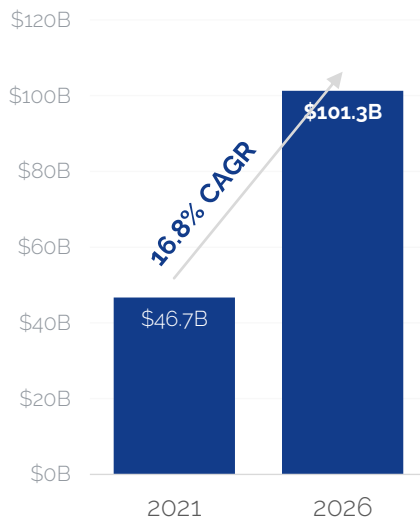
Tulsi Ram Damase¹, Roman Sukhovshin¹, Christian Boada², Francesca Taraballi^{3,4}, Roderic I. Pettigrew² and John P. Cooke^{1*}

Frontiers in Bioengineering
and Biotechnology,
March 2021

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

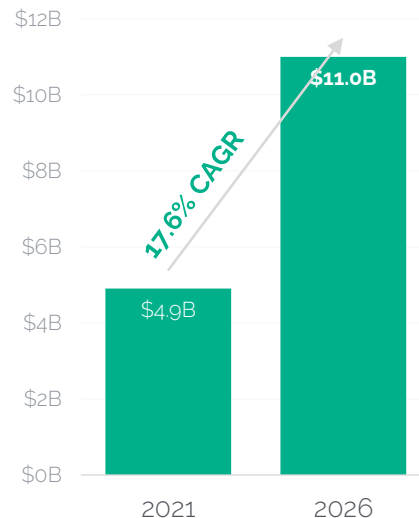
mRNA Vaccines & Therapeutics

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, circRNA, ASOs,

✓ 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*...

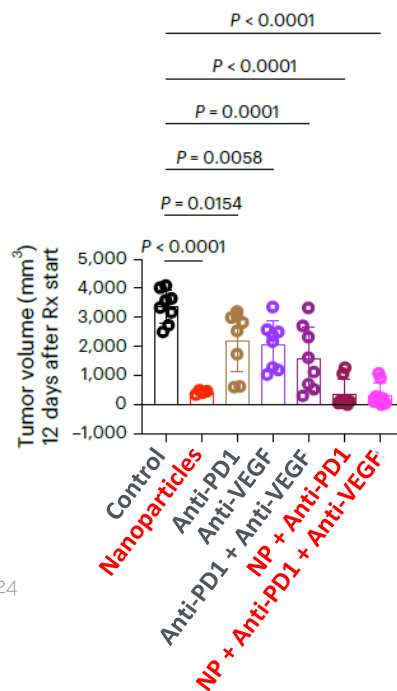
- Osteoarthritis (WNT16)
- Osteoarthritis (DNMT3B)
- Atherosclerosis (p27^{Kip1})
- Tumor microenvironment (ZBTB46)
- Aortic aneurysm (SOD2)

Use Case: Enhancing the Potential of Anti-PD1 Therapy

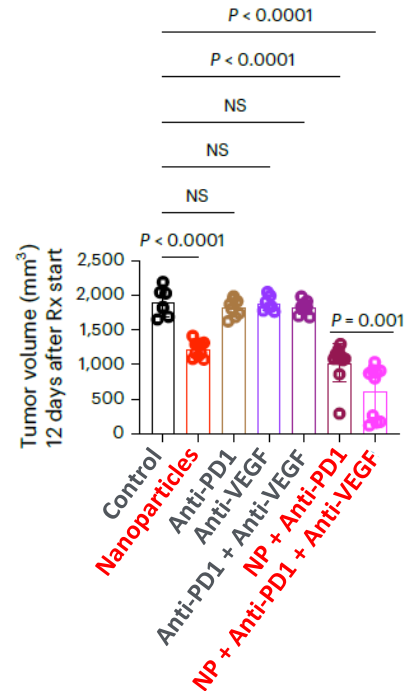
Delivering SemaPhore™ *Zbtb46* mRNA in sarcoma and metastatic breast cancer models.

- 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."

1956 Sarcoma



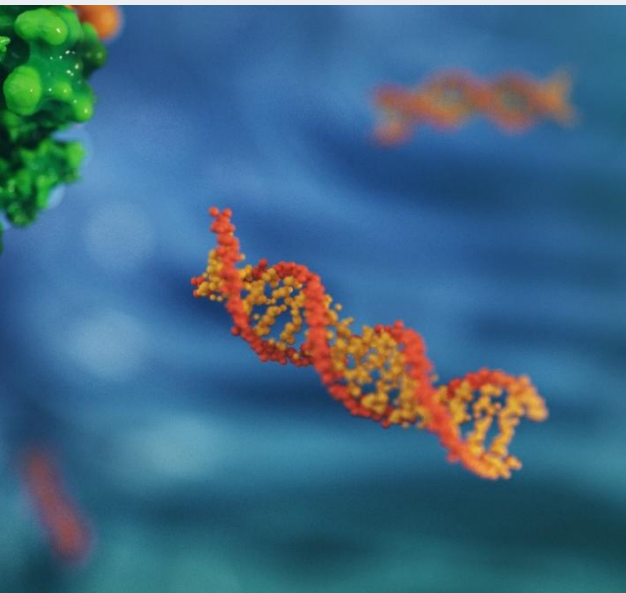
PyMT-BO1 Breast Cancer



Kabir et al., 2024



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



- 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

Undisclosed

- Evaluate RNA nanoparticles in conjunction with radiopharmaceutical cancer treatment

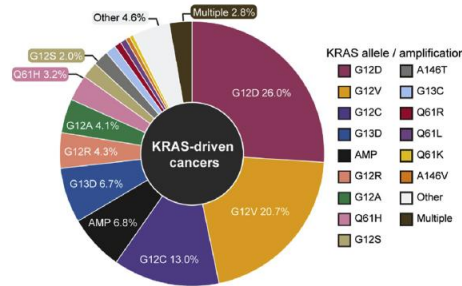
AM-401: Stop the “Beating Heart” of Tumors

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

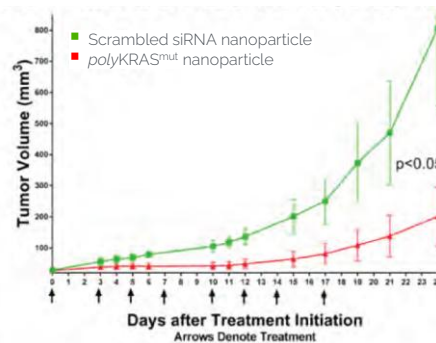
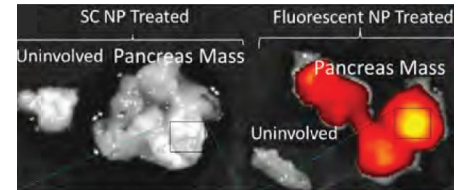
to inhibit cell proliferation in KRAS driven colorectal, pancreatic, or non-small cell lung cancer.

- 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



polyKRAS^{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

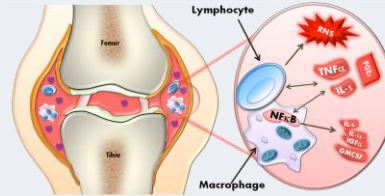


Small molecule inhibitors have significant side effects, particularly when combined with other agents
OligoPhore **targets specifically** tumor cells

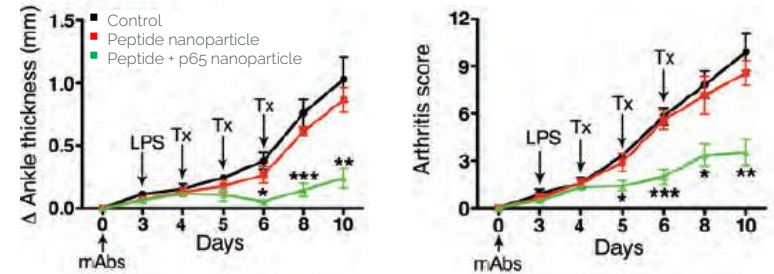
AM-411: Block Inflammation in Rheumatoid Arthritis

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

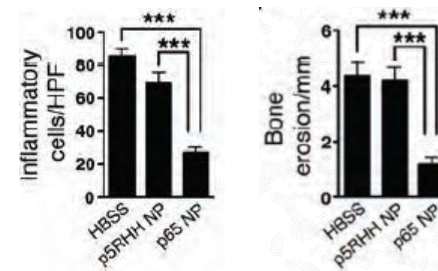
- Chronic autoimmune disease
- Causes joint swelling and pain
 - Reduced QoL and productivity
- Affects 1 out of 28 women / 59 men
- No cure available, but various treatment options:
 - Disease-modifying anti-rheumatic drugs (DMARDs)
 - Non-steroidal anti-inflammatory drugs (NSAIDs)
 - Corticosteroids
- 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**
 8,501,930 B2 8/2013 Brooma et al.
 8,617,516 B2 12/2013 Wickline et al.
 2005/0191746 A1* 9/2005 Van CB01 59/300 435-455

(71) Applicant: **Washington University**, St. Louis, MO (US)
 2007/0275923 A1 11/2007 Chen et al.
 2011/0123438 A1 5/2011 Wickline et al.

(72) Inventors: **Samuel A. Wickline**, St. Louis, MO (US); **Kirk Hou**, St. Louis, MO (US)
 FOREIGN PATENT DOCUMENTS
 WO 2005/084548 A2 9/2005
 WO 2007/069090 A2 6/2007
 WO 2011/030188 A1 3/2011
 WO 2014/07758 A1 7/2014
 WO 2017/004512 A1 1/2017

(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
 Examination Report for related CA application 2,306,834 dated Aug. 23, 2016, 5 pages.
 Partial Supplementary European Search Report dated Aug. 9, 2016 from related EP Application No. 1475277.7, 10 pages.
 International Search Report and Written Opinion dated Oct. 4, 2016 from International Patent Application No. PCT/US2016/040678, 10 pp.

Related U.S. Application Data
 Continuation-in-part of application No. PCT/US2014/010212, filed on Jan. 3, 2014.
 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 15/13 (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 15/11** (2013.01); **C12N 15/13** (2013.01); **C12N 15/87** (2013.01); **A61K 33/00** (2013.01); **C12N 23/10/14** (2013.01); **C12N 23/10/35/3** (2013.01); **C12N 23/20/32** (2013.01); **H10T 42/8/2992** (2015.01)

(53) **Field of Classification Search**
 CPC — C07K 14/00; A61K 47/48315; A61K 38/16
 USPC 530/326
 See application file for complete search history.

(54) **References Cited**
 U.S. PATENT DOCUMENTS
 7,098,032 B2 8/2006 Tishbetzky et al. CB01 59/300 7,446,099 B2* 11/2008 Van 424,912
 7,795,380 B2 9/2010 Rice et al.

(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

Management Overview



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 in late 2023
 - 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%
- Remaining stake to be divested



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™, SemaPhore™, CycloPhore™



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, and "therapeutics" is written below it in a smaller, lowercase, sans-serif font.

altamira
therapeutics

DELIVERING RNA – BEYOND THE LIVER
