Company Presentation

2021 LD Micro Invitational XI – June 9, 2021

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Auris Medical at a glance

- **A biomedical company in full transformation**
- **Headquartered in Bermuda / operations in Switzerland**

altamira therapeutics	**RNA therapeutics** Extrahepatic targets Preclinical		**New focus**
altamira medica	**Allergy and viral infection** OTC nasal spray (Bentrio™) Pre-launch		**Spin-off or divestiture 12-18 mos**
Auris Medical Cochlear therapies	**Vertigo** Rx nasal spray Phase 2	**Tinnitus and hearing loss** Rx intratympanic Phase 3 → partnering	

Nasdaq EARS → CYTO

RNA Therapeutics

Acquisition of Trasir Therapeutics, Inc.

- Privately held, based in Tampa FL
- Pioneer in extrahepatic nucleic acid delivery
- OligoPhore™ platform
- World-wide exclusive license from Washington University
- Share-based transaction
- Transaction closed on June 1, 2021

Become leading company in RNA therapeutics for extrahepatic targets

- Review of strategic options initiated in fall 2020
  - Underappreciated development pipeline
  - Need for fundamental changes
- Trasir Therapeutics most attractive option
  - Strong science / truly innovative / differentiated
  - Disruptive potential / high growth potential
  - Global market for RNA therapeutics > $1 billion in 2020
  - Investor familiarity with RNA delivery technology
  - Fit with own experience in cell-penetrating peptides
- Trasir Therapeutics looking for partner to translate cutting-edge science into therapeutics

Oligonucleotide therapeutics landscape*

*list not exhaustive; does not include ASO companies

Current challenges in oligonucleotide delivery

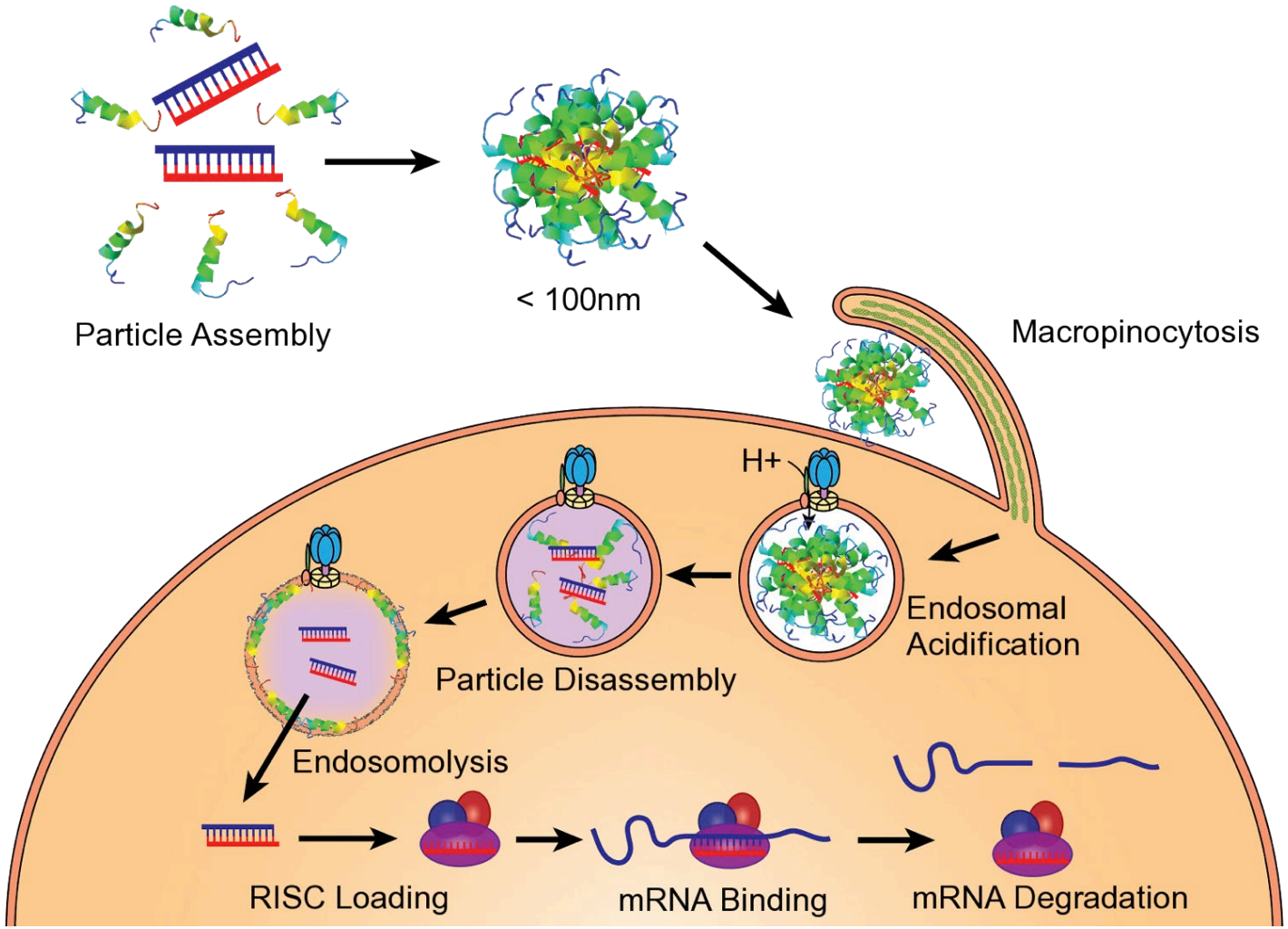
- Current state-of-the-art for delivery of oligonucleotide therapeutics
  - Viral-based vectors
  - Lipid nanoparticles (LNPs)
  - Ligand conjugates
- Delivery technologies remain a key rate-limiting step for unlocking the potential of RNA therapeutics:
  - Viral based delivery vectors suffer from lack of transduction efficiency and target specificity
  - LNPs and currently available ligand conjugates using GalNac technology preferentially target the liver, and many have suboptimal therapeutic index

How OligoPhore™ works

Trasir's **peptide-based OligoPhore™** technology allows for safe and effective delivery of RNA payloads:

- *Stability*: siRNA complexed in nanoparticle format for, and only released inside of cells after uptake
- *Extrahepatic delivery*: not sequestered in liver, but permeates inflamed pathological tissues
- *Endosomal escape*: pH-dependent nanoparticle disassembly, followed by full release of siRNA into cytoplasm
- *Selectivity*: silences molecular targets in diseased tissues only
- *Safety*: no cellular or adaptive immune responsivity to nanoparticle components or siRNA after multiple serial doses, and no organ toxicities in mice

Summary of OligoPhore™ mechanism of action



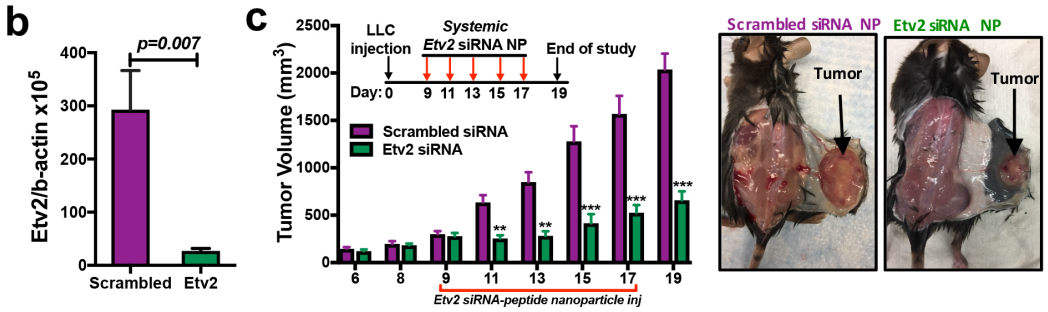
Biotechnology Advances. 2015. 10.1016/j.biotechadv.2015.05.005
ACS Nano. 2013. 10.1021/nn403311c

Preclinical data from murine disease models (siRNA payloads)

- Pancreatic and colorectal cancer (KRAS)
- Ovarian cancer (TAM: AXL)
- Lung cancer (ETV-2)
- Metastatic Melanoma (NFkB)
- Adult T Cell Leukemia/Lymphoma (NFkB)
- Sarcoma (MYCT-1)
- Necrotizing enterocolitis (NFkB)
- Rheumatoid and osteoarthritis (NFkB)
- Atherosclerosis (JNK2)
- Metabolic syndrome/Obesity (ASXL2)
- Aortic Aneurysm (NFkB)

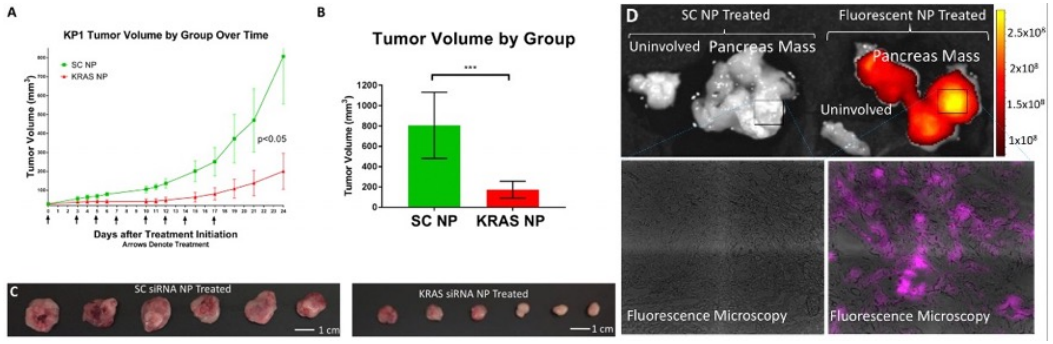
Key in vivo data from oncology models (siRNA delivery)

Effective knockdown of ETV-2 siRNA in Lewis Lung cancer model



JCI Insight. 2018. 10.1172/jci.insight.97349

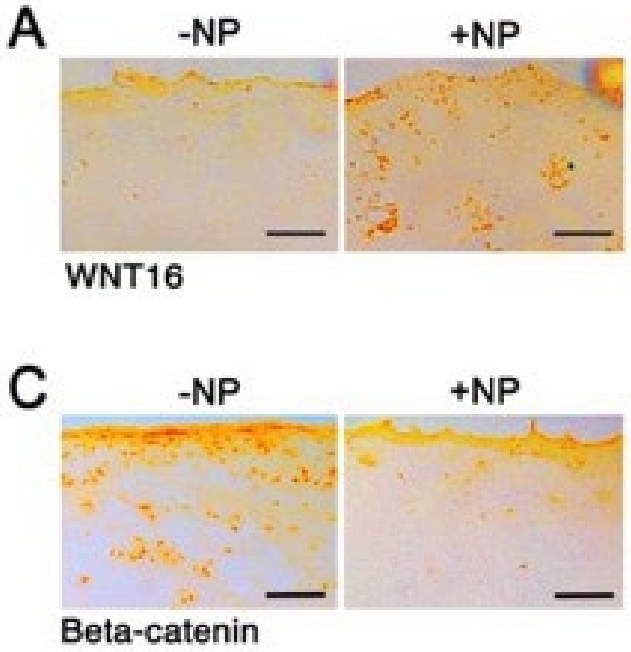
KRAS siRNA for pancreatic tumor



Oncotarget. 2019. 10.18632/oncotarget.27109

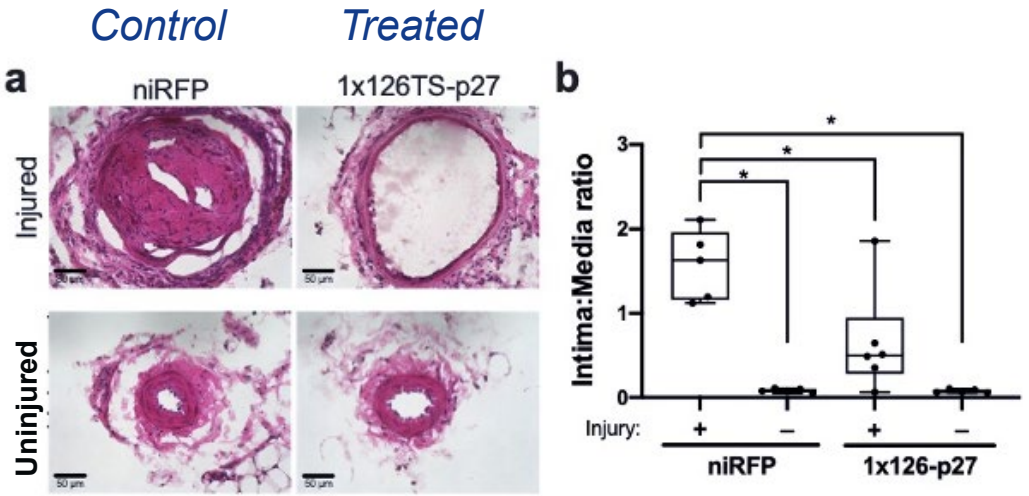
OligoPhore™ delivering mRNA payloads

Osteoarthritis (ex vivo): WNT 16 mRNA transfection in human cartilage explants



Pharmaceutics. 2020. PMC7022671

Atherosclerosis (in vivo): p27^{Kip1} mRNA transfection in vascular smooth muscle cells (femoral artery wire injury)



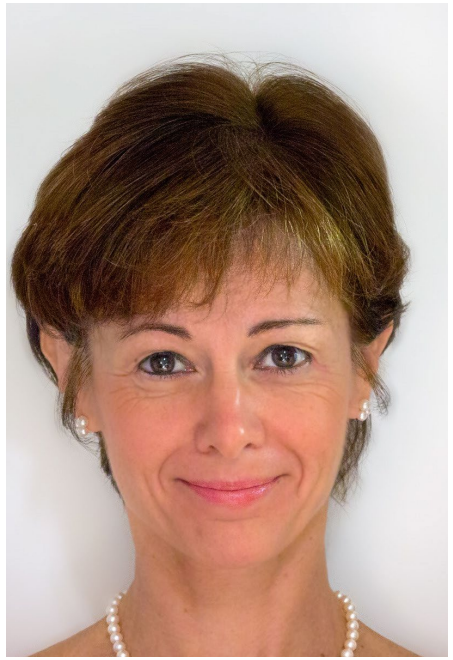
Molecular Therapeutics. 2021. 10.1016/j.ymthe.2021.01.032

Development plan

- Initial development focus on siRNA applications
- Select first therapeutic indication (AM-401)
- Favoring oncology and/or orphan drug indications
- Advance research on mRNA and other potential payloads
- Non-human primate pivotal toxicology study
- Team of in-house experts, complemented by network of consultants and CROs in EU and US

Our new CSO: Samuel Wickline, MD

- Founder and majority shareholder of Trasir Therapeutics
- Director of Health Heart Institute, Chair in Cardiovascular Medicine, Professor of Cardiovascular Sciences, Molecular Physiology and Pharmacology, and Medical Engineering at University of South Florida (USF)
- Professor of Medicine, Physics, Biomedical Engineering, and Cell Biology and Physiology at Washington University
- Funded continuously for 30+ years by NIH (~ $50 million)
- Author of > 300 research papers
- Holds > 50 issued or filed U.S. patent applications



Proposed new BoD member: Margrit Schwarz, PhD MBA

- 25 years of experience in biopharmaceutical R&D across multiple indications and modalities, incl. RNA delivery
- Multiple IND filings and one approved drug (Repatha)
- Leadership roles at Amgen, Boehringer Ingelheim, Roche, Genevant
- Universities of Muenster and Cologne (DE)
- UT Southwestern Medical Center, Dallas TX
- Columbia Business School, New York

Viral Infection and Allergy

“Exposure to small airborne particles is equally, or even more, likely to lead to infection with SARS-CoV-2 as the more widely recognized transmission via larger respiratory droplets and/or direct contact with infected people or contaminated surfaces.”

Tang et al., 2021

Bentrio™ was conceived…

… during the first Covid-19 lockdown and developed with the aim of bringing a safe, effective and affordable means for mitigating risks related to SARS-CoV-2 rapidly to the market

Bentrio™ is designed to help to:

- reduce the viral load and risk of infection from airborne viruses
- prevent the onset and alleviate allergic symptoms caused by airborne allergens

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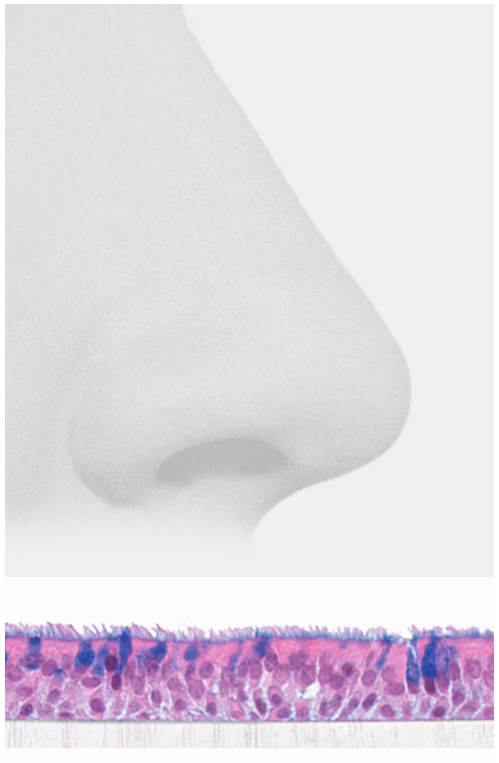
Danger in the Air

Every day you breathe in just over 2000 gallons of air…



Nasal mucosa

- Up to 90% of air inhaled via the nose
- Exposure to airborne virus, bacteria, allergen or dirt particles
- Nasal mucosa acts as a protective barrier against these particles
  - Secretes mucus which traps particles
  - Clearance via the throat
- Occasionally overwhelmed or breaks down
  - Nasal dryness or irritation
  - Mucosal damage
- Allergic reactions (hay fever, dust mite allergies…)
- Viral infections (influenza, common cold, SARS, MERS…)

How AM-301 Acts

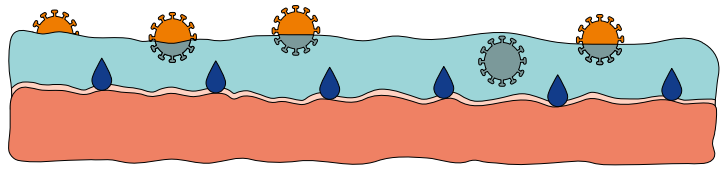
Complements the natural defense of the nasal mucosa

Triple protective effect aids in the defense against airborne particles

Protects
as a physical barrier
the nasal mucosa

Traps
airborne particles through
electrostatic effects

Humidifies
the nasal mucosa and
thus aids its functionality



- Protective barrier
- Nasal mucosa
- Binding of virus & allergen particles
- Humidification of nasal mucosa

Key Features of AM-301

A nasal spray for convenient self-protection

Trap to remove
Capturing particles
for discharge with mucus

→ It's more than a barrier
- Trapping various airborne virus, allergen or dirt particles
- Electrostatic effects work a priori with any charged particle

Drug free
Contains no active
pharmaceutical ingredient

→ It's a medical device
- No pharmacological, metabolic or immunologic activity
- Only physical effects

Preservative free
Safety by design including
special spray pump

→ It's well tolerated
- Commonly used preservatives tend to harm mucus membranes
- Commonly used preservatives may give unpleasant sensation

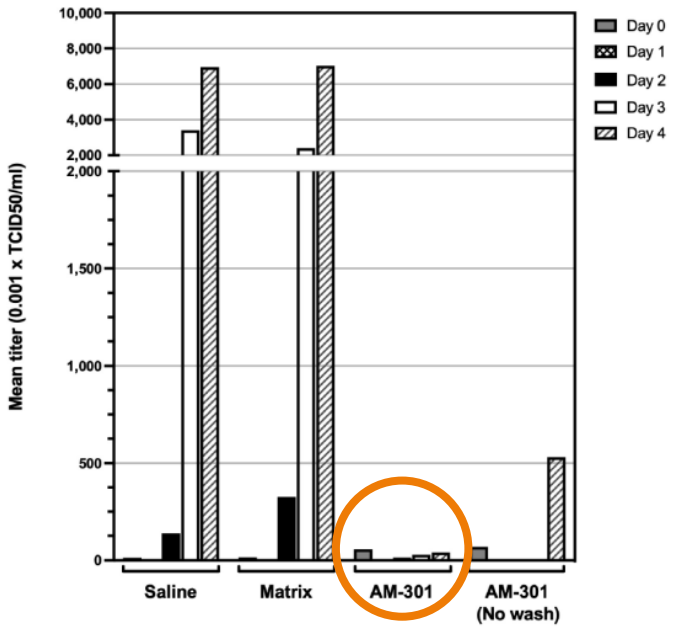
Protects for ≥ 3 hours
Gel designed for extended
nasal residence time

→ It's convenient
- Gel becomes liquid upon shaking, allowing to spray it
- Liquid turns into gel again when applied into nose

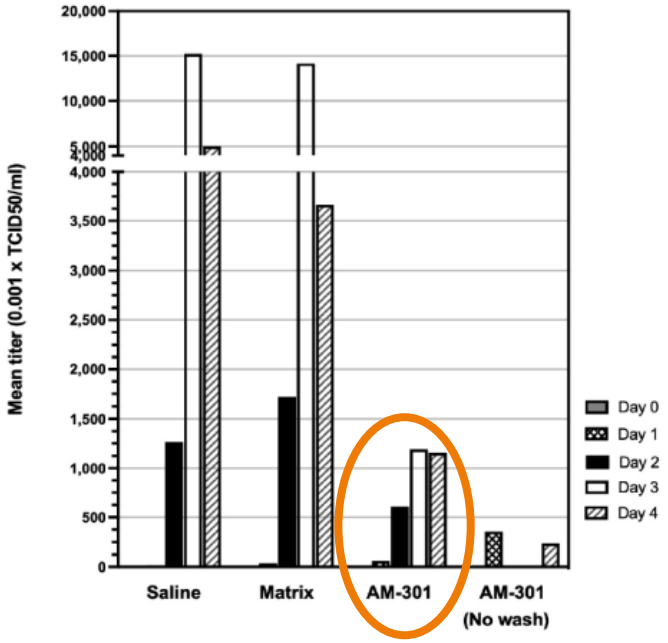
Efficacy in SARS-CoV-2

- Reconstituted human nasal epithelium model
  - Functional nasal mucosa
  - Without help from immune system or mucociliary clearance
  - Read-out through median Tissue Culture Infectious Dose, $TCID_{50}$, in Vero cells
- Daily treatment with Bentrio (AM-301)

Prevention – start 10' before



Mitigation – start 30 hrs after



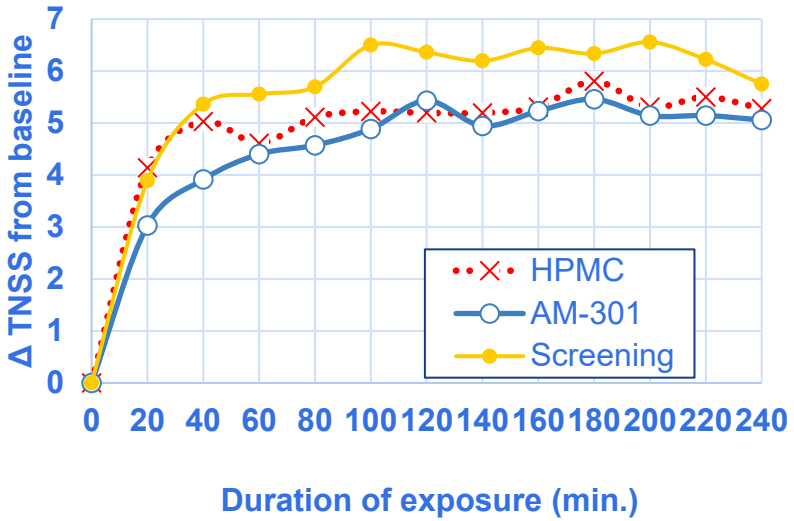
- Highly effective protection
  - >99% reduction in viral titer
- Activity also post infection
  - Significant deceleration of viral titer growth

Efficacy in Allergy

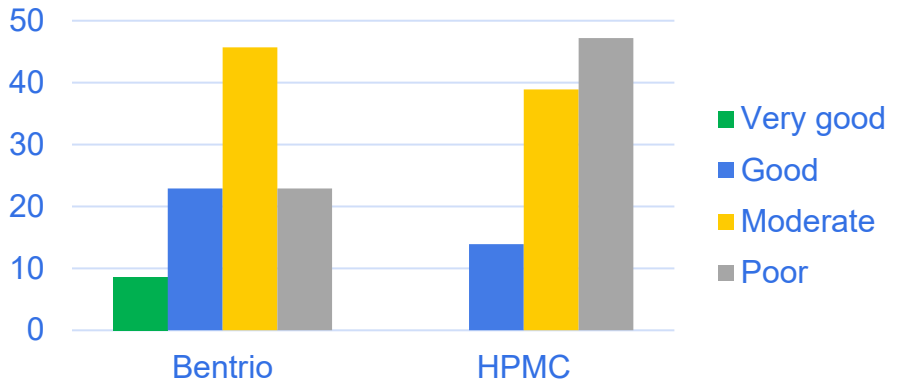
- Clinical pollen chamber study
- Open-label randomized cross-over study
- 36 patients with allergic rhinitis to grass pollen
- Single dose of Bentrio™ or HPMC powder spray prior to 4 hours of controlled pollen exposure

- Study met primary efficacy endpoint = substantial equivalence to predicate device for 510(k)
- Fast onset – significantly better at 20’ and 40’ timepoints
- Protective effect for 4 hours

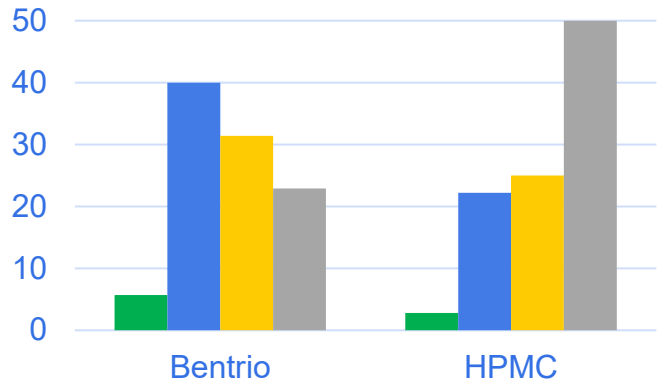
Mean change from baseline



Efficacy rated by subjects (%)



Efficacy rated by clinicians (%)



Next steps with Bentrio™

Expanding body of evidence

- Covid-19 study
  - Prevention and treatment
  - Rapid study start in India
- Seasonal allergic rhinitis study
  - 14 days of treatment
  - Allergy season in southern hemisphere
- House dust mite challenge study
- Various in vitro and in vivo studies

Commercial

- Europe
  - CE mark / conformity in May 2021
  - Preparing market launch in selected countries
- USA
  - 510(k) pre-submission meeting in May 2021
  - Submission for allergy in early Q3 2021
  - Discussions about viral infection ongoing
- Discussions with potential distribution partners
- Significant, scalable contract manufacturing capacity

Market Potential for Bentrio™

Addressing frequent conditions

Viral infections

- Human rhinovirus (HRV) is most common cause of upper respiratory tract infection
- US revenues for could and cough remedies: > $12 billion in 2021 www.statista.com
- Influenza resulted in 9-45 million illnesses, 140,000-810,000 hospitalizations and 12,000-61,000 deaths annually since 2010 Centers for Disease Control and Prevention
- Covid-19: 174 million cases and 3.74 million deaths to date

Allergies

- About 7.8% of people 18 and over in the US have hay fever Schiller et al., 2010
- 11.1 million visits to physician offices with primary diagnosis allergic rhinitis National Ambulatory Medical Care Survey
- $4 billion market size for OTC allergy medicines in US in 2020 www.ibisworld.com

Air pollution

- > 90% of the world's population exposed to unhealthy air, 5th highest mortality risk factor globally WHO
- E.g. causing 1.8 m premature deaths p.a. in China Global Alliance on Health and Pollution

Viral Infection and Allergy

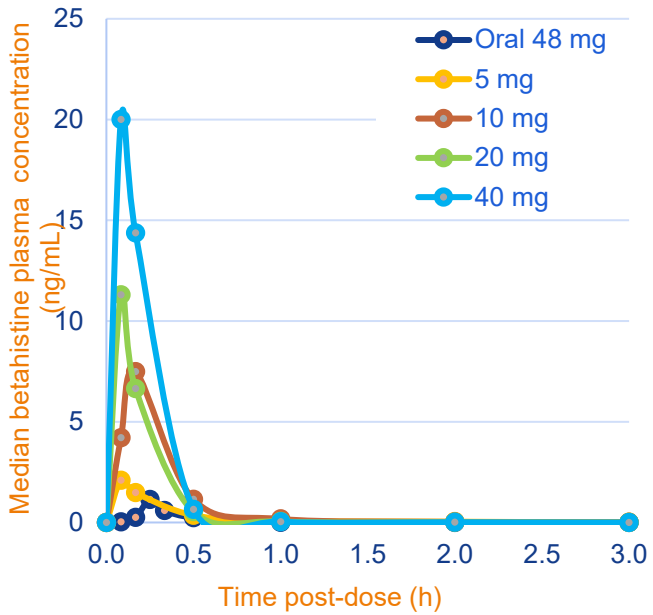
Intranasal Betahistine for Treating Vertigo

AM-125 Acts as a Vestibular Stimulant

- 35.4% of the US population ≥ 40 years experience vestibular dysfunction[1]
- Lifetime prevalence of vertigo interfering with daily activities is 3-8%[2]
- Betahistine – unique vestibular stimulant
  - World-wide SOC, but no longer marketed in US
  - Current worldwide annual sales ~$450 million[3]
- Rx options in US essentially limited to vestibular suppressants
- AM-125 addresses betahistine's weak point = poor oral bioavailability (~1%)
  - Capture part of existing oral betahistine market
  - Bring betahistine back to US

[1] *Agrawal et al., 2009*
[2] *Murdin et al., 2015*
[3] *Oral betahistine, manufacturer prices (IMS).*

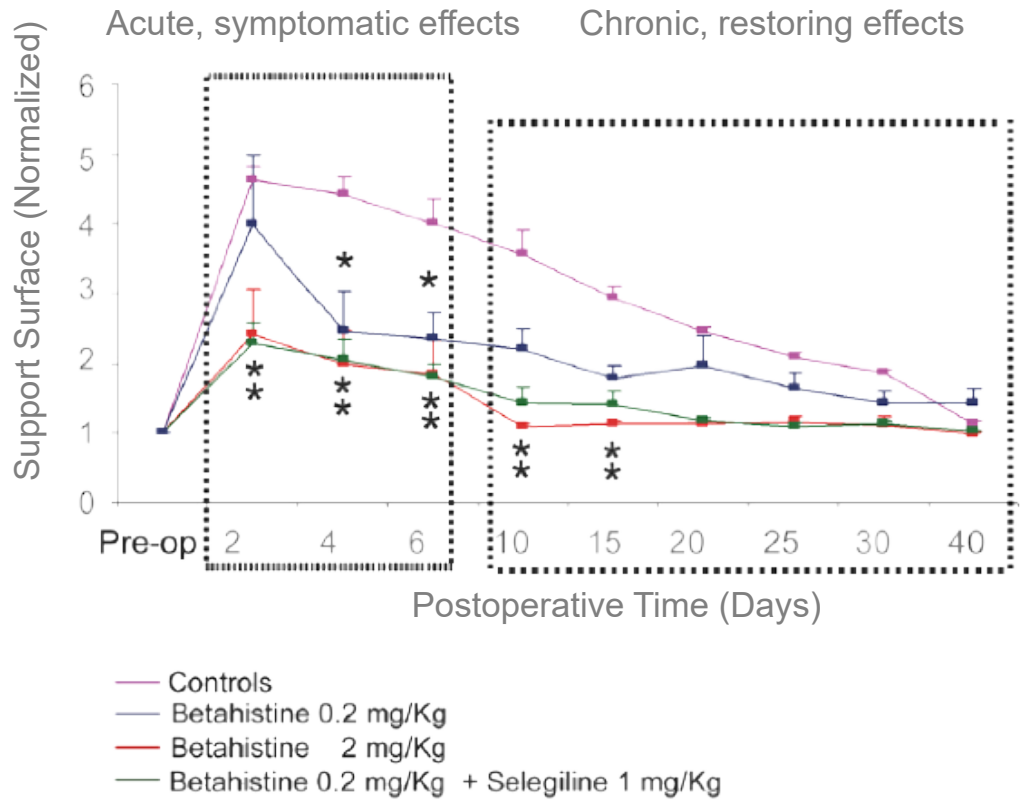
Superior bioavailability of intranasal betahistine



- *Betahistine targets the histaminergic system*
  - *Increases inner ear and cerebral blood flow*
  - *Increases histamine turnover and enhances histamine release in CNS*
  - *Enhances release of acetylcholine, dopamine and norepinephrine in CNS*
- *Relative bioavailability of AM-125 vs. oral betahistine (daily dose) = 5 to 29 x*

Higher Bioavailability Translates Into Better Efficacy

Cats undergoing unilateral section of vestibular nerve



When treated with high dose betahistine, cats experienced:

- Faster improvement of acute symptoms than lower dosages
- Accelerated vestibular compensation
- Significant increase of histaminergic activity in hypothalamus
- Substantially higher bioavailability
- Similar effect with low dose betahistine + MAO inhibitor selegiline

Tighilet et al. (2018). Betahistine treatment in a cat model of vestibular pathology: pharmacokinetic and pharmacodynamic approaches. Front Neurol. 11(9):431.

AM-125 Development & Milestones

Development Plan

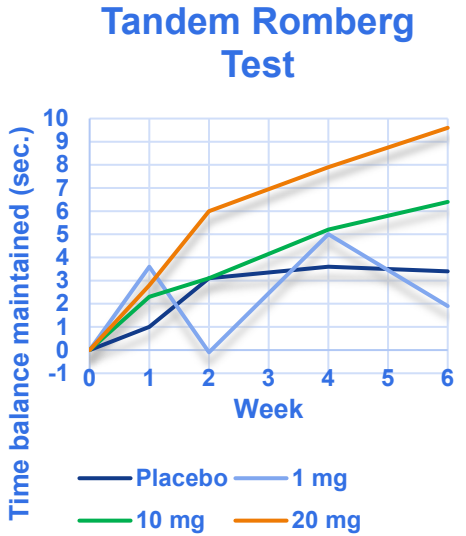
Target Indication and Patient Benefit

- Treatment of acute peripheral vertigo
- Enhance vestibular function
- Improve and accelerate vestibular compensation
- Get patients back on their feet asap!

Clinical Milestones

- **First Ph1 trial** in 40 healthy volunteers (2015)
- **Second Ph1 trial** in 72 healthy volunteers (2018)
  - Both showing significantly higher bioavailability vs. oral delivery
  - Treatment safe and well tolerated (maximum 40 mg t.i.d.)
- **Ph2 trial** in 118 acute vertigo patients (ongoing)
  - Acute vertigo following neurosurgery
  - Treatment for 4 weeks, 2-week treatment-free follow-up
  - Battery of balance tests + HRQOL questionnaires

Recent and Upcoming Milestones



Interim results from TRAVERS Phase 2 trial Part A in 31 patients suffering from acute vertigo following neurosurgery, treated t.i.d. for four weeks

- Part A: dose dependent improvement in balance + other outcomes
- Continuing with 10 and 20 mg t.i.d. in Part B
- Data read-out in fall 2021 (subject to Covid-19 developments)
- IND and start Phase 3 in late 2021 / early 2022

Upcoming Milestones

Q2 2021	Launch AM-301 in selected markets
Q2 2021	Target indication for AM-401
Q3 2021	Submission 510(k) for AM-301
Q3 2021	Start Covid-19 trial with AM-301 in India
Q3 2021	Completion recruitment Part B AM-125 Ph2 trial
Q4 2021	Read-out Covid-19 trial
Q4 2021	Read-out from Part B AM-125 Ph2 trial
Q1 2022	IND AM-125 / AM-201
Q1 2022	Start AM-125 Ph3 trial