



Acquisition of Trasir Therapeutics Strategic Repositioning

Business Update – June 3, 2021

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- **Trasir Therapeutics acquisition**
 - **RNA therapeutics landscape**
 - **Oligonucleotide delivery**
 - **OligoPhore™ platform**
 - **Company repositioning**
 - **Outlook**

Agenda

Acquisition of Trasir Therapeutics, Inc.

Privately held, based in Tampa FL

Pioneer in extrahepatic oligonucleotide delivery

OligoPhore™ platform

World-wide exclusive license from Washington University

Triangular merger with Auris Medical Inc.

Share-based transaction

Transaction closed on June 1, 2021

Why Trasir Therapeutics?

- Review of strategic options initiated in fall 2020
 - Underappreciated development pipeline
 - AM-301 / BentrionTM as catalyst
 - 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

Our vision for Trasir Therapeutics

Become leading company developing
oligonucleotides for extrahepatic therapeutic targets

- Initiate the preclinical development of the first pipeline program (project code AM-401)
- Oncology and/or rare disease indication
- IND submission targeted for late 2022
- Explore further potential applications of OligoPhore™ platform for delivery of siRNA, mRNA and gene editing constructs
- Leverage platform's potential through strategic partnering

Oligonucleotide therapeutics landscape*

RNAi



mRNA



Gene Editing



*list not exhaustive; does not include ASO companies



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
- Founder of 2 other biotech startups

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

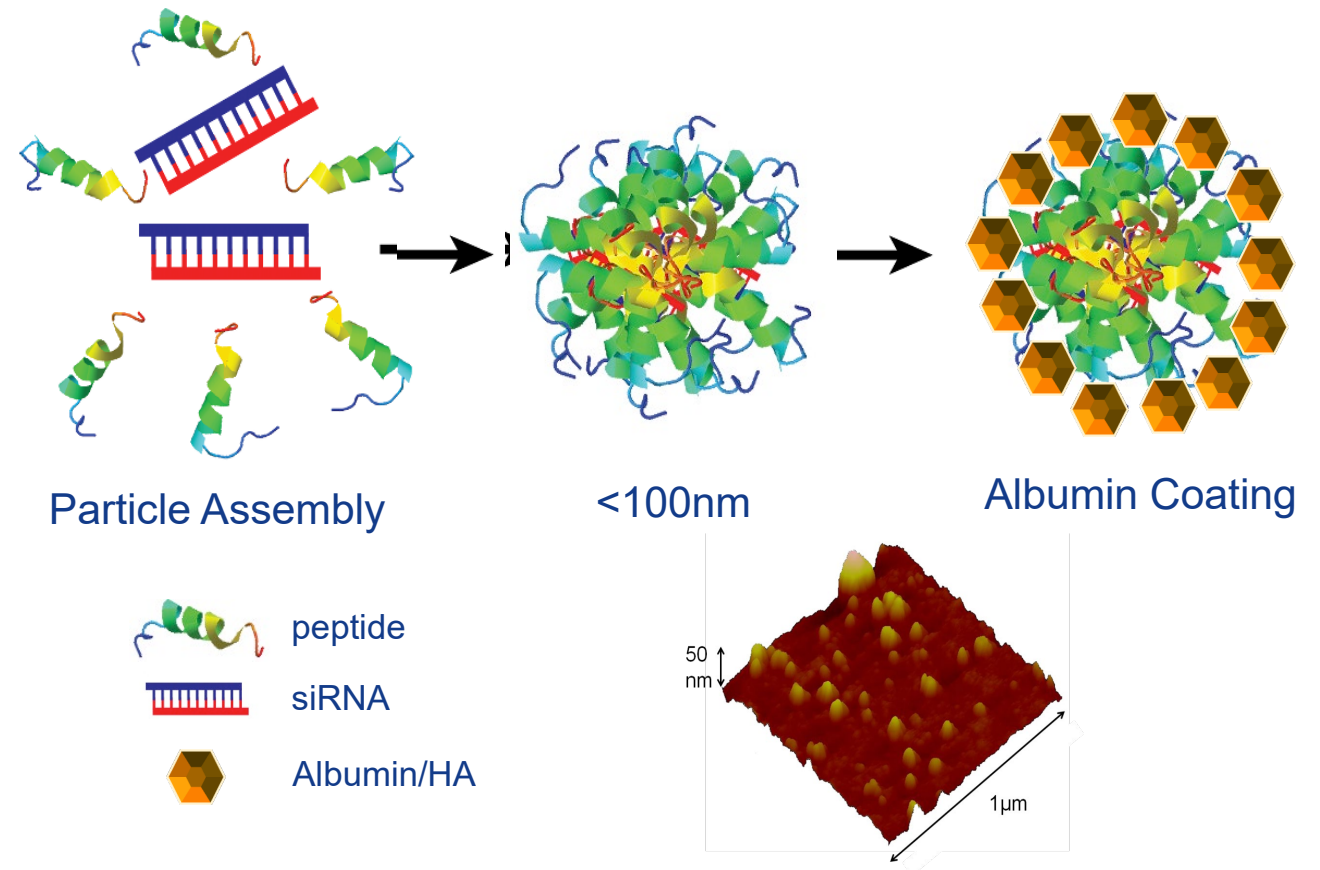


How OligoPhore™ works

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

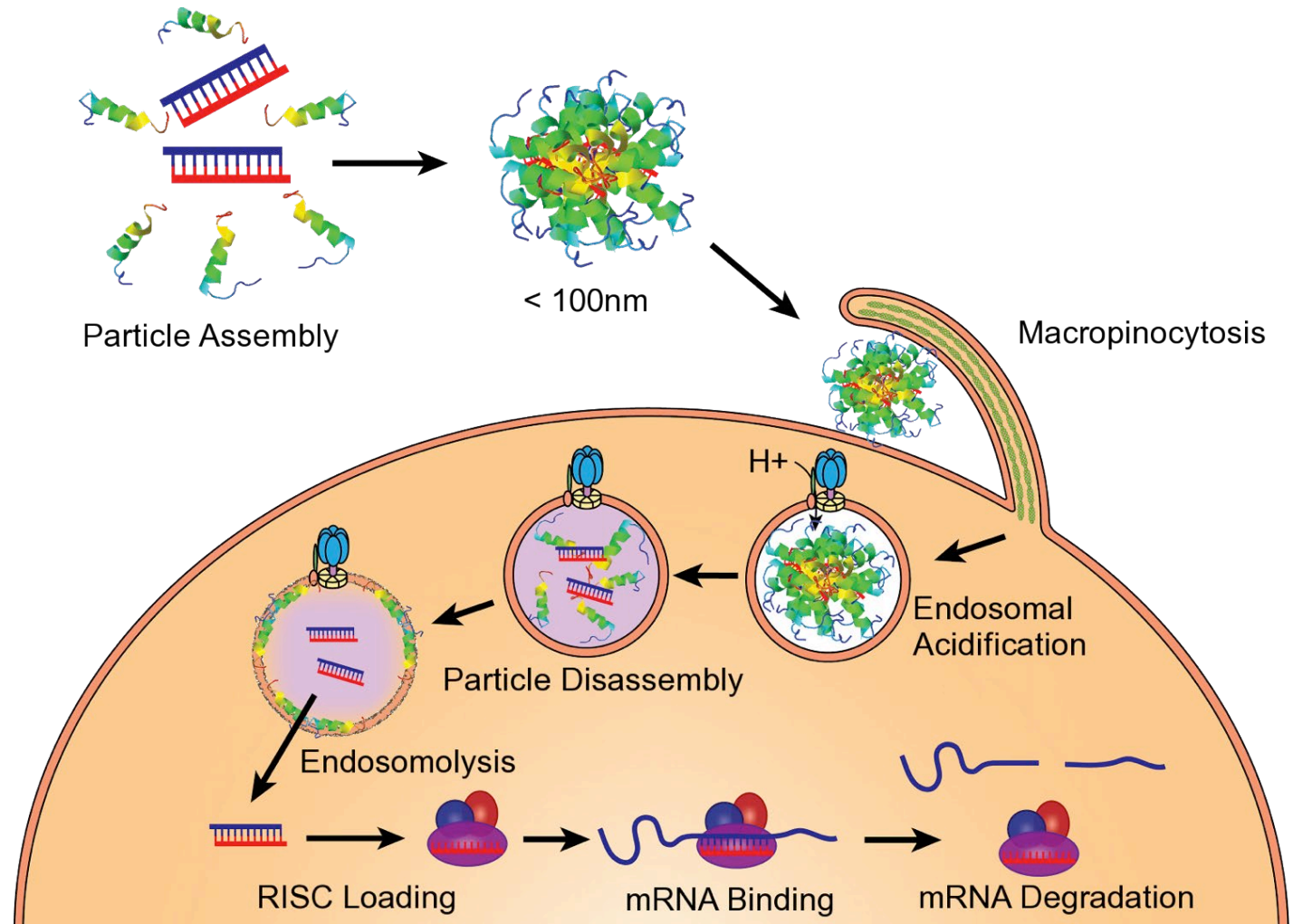
- **Stability:** siRNA complexed in nanoparticle format for, and only released inside of cells after uptake
- **Extrahepatic delivery:** not sequestered in liver, but permeates inflamed pathological tissues
- **Endosomal escape:** pH-dependent nanoparticle disassembly, followed by full release of siRNA 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

Stable peptide-siRNA polyplex formulation



ACS Nano. 2013. 10.1021/nn403311c

Summary of OligoPhore™ mechanism of action

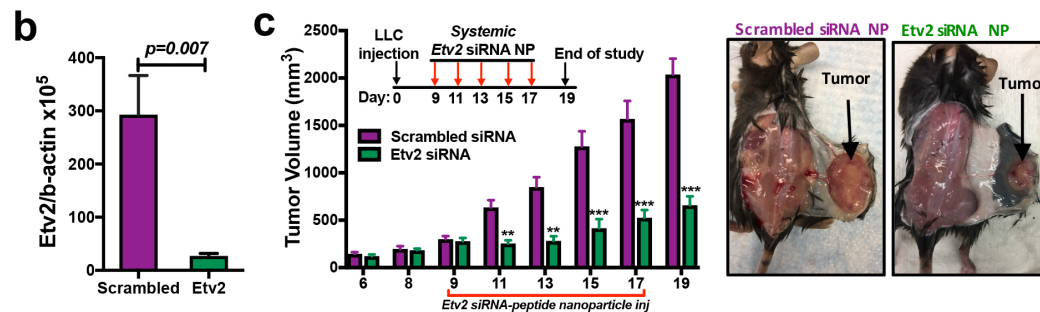


Preclinical data from murine disease models (siRNA payloads)

- 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)

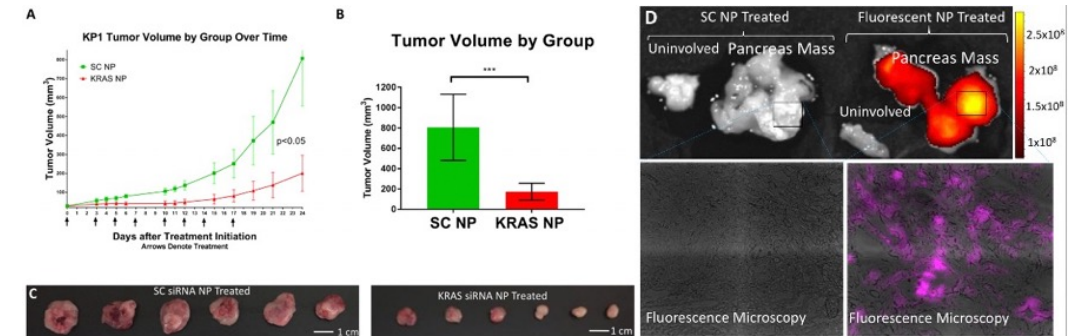
Key in vivo data from oncology models (siRNA delivery)

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



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

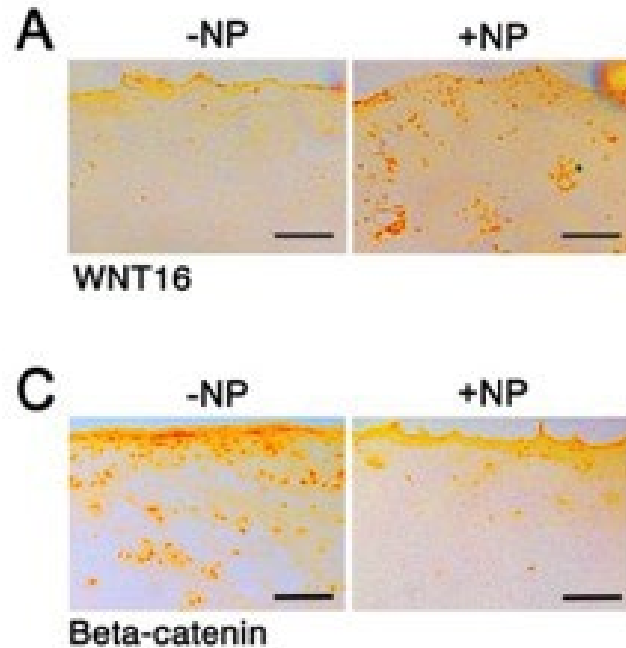
KRAS siRNA for pancreatic tumor



Oncotarget. 2019. 10.18632/oncotarget.27109

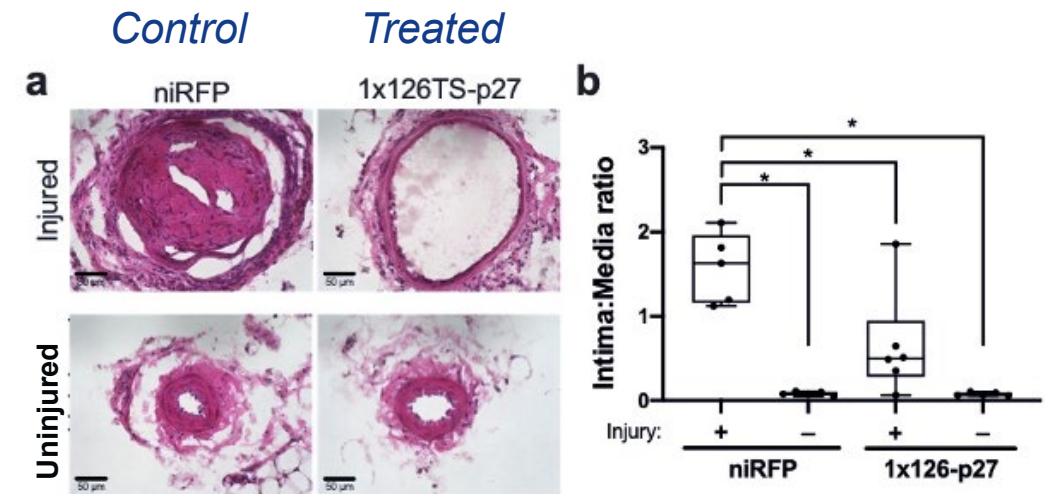
OligoPhore™ delivering mRNA payloads

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



AM-401 development plan

Initial development focus on siRNA applications

Select therapeutic indication

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

Reposition the Company



RNA therapeutics
Systemic, local, Rx



**Nasal spray – allergy
and viral infection, OTC**



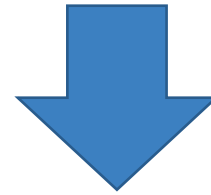
Tinnitus, hearing loss
Local, Rx

- Focus on development of RNA therapeutics
- Spin off or divest existing assets in neurotology, rhinology and allergology
- Investors prefer “pure plays”
- Prepare for separation within 12-18 months
- Important milestones
- Aim to unlock and create significant shareholder value

**Proposed
change of
company
name**



EARS



CYTO

Subject to approval by July 2021 Extraordinary General Meeting



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

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



altamira
therapeutics