Expanding the reach of genome editing

Alia THERAPEUTICS

Letizia Goretti, CEO

BIO USA 2024

At Alia Therapeutics,
we see a future where diseases are cured at their roots,
a future where genetic medicine is a safe and viable option
to restore hope and health for every person.

CRISPR *is* ready for prime time

Panel Says That Innovative Sickle Cell Cure Is Safe *Enough* for Patients
The decision by an advisory committee may lead to Food and Drug Administration approval of the first treatment for humans that uses the CRISPR gene-editing system. **New York Times, Oct. 31, 2023**

Intellia Therapeutics Announces FDA Clearance of IND Application to Initiate a Pivotal Phase 3 Trial of NTLA-2001 for the Treatment of Transthyretin (ATTR) Amyloidosis with Cardiomyopathy. **Globe NewsWire, Oct 18th 2023**

however

- 3BN nucleotide pairs
- Off-target effects
- Efficiency limitations
- Delivery limitations
- Immunogenicity
- Commercial viability

"Currently available tools are not sufficient to address the complexity of gene and cell therapy applications" - Prof. A. Cereseto

KEY HIGHLIGHTS

GENOME EDITING COMPANY HEADQUARTERED IN ITALY

World class science from the discoveries of Prof. Anna Cereseto at the University of Trento

Top Tier Platform and Capabilities to expand the application of the genome editing toolbox for the treatment of a broad spectrum of disorders

Pioneering *in vivo* and *ex vivo* proof of concept for therapeutic approaches that are **precise, safe, and effective**

Solid and expanding **IP**

Seed **funding from leading EU and Italian VCs**

TEAM ALIA

INTERNATIONAL INDUSTRY LEADERS WORLD CLASS SCIENTIFIC ADVISORS LEADING EU INVESTORS

Management team

Letizia Goretti
CEO

Antonio Casini, PhD
Founder and CTO

Francesca Zagari, PhD
Senior Project Manager

Scientific advisor board

Prof. Anna Cereseto, PhD
Founder and SAB chairman

Prof. Alberto Auricchio, MD, PhD
University of Naples/TIGEM

Prof. Chiara Bonini, MD
Vita Salute University

Prof. Angelo Lombardo, PhD
Vita Salute University/SR-TIGET

Prof. Nicola Segata, PhD
University of Trento

Board of Directors

Silvano Spinelli
Chairman

Letizia Goretti
CEO

Paola Pozzi
Sofinnova partners

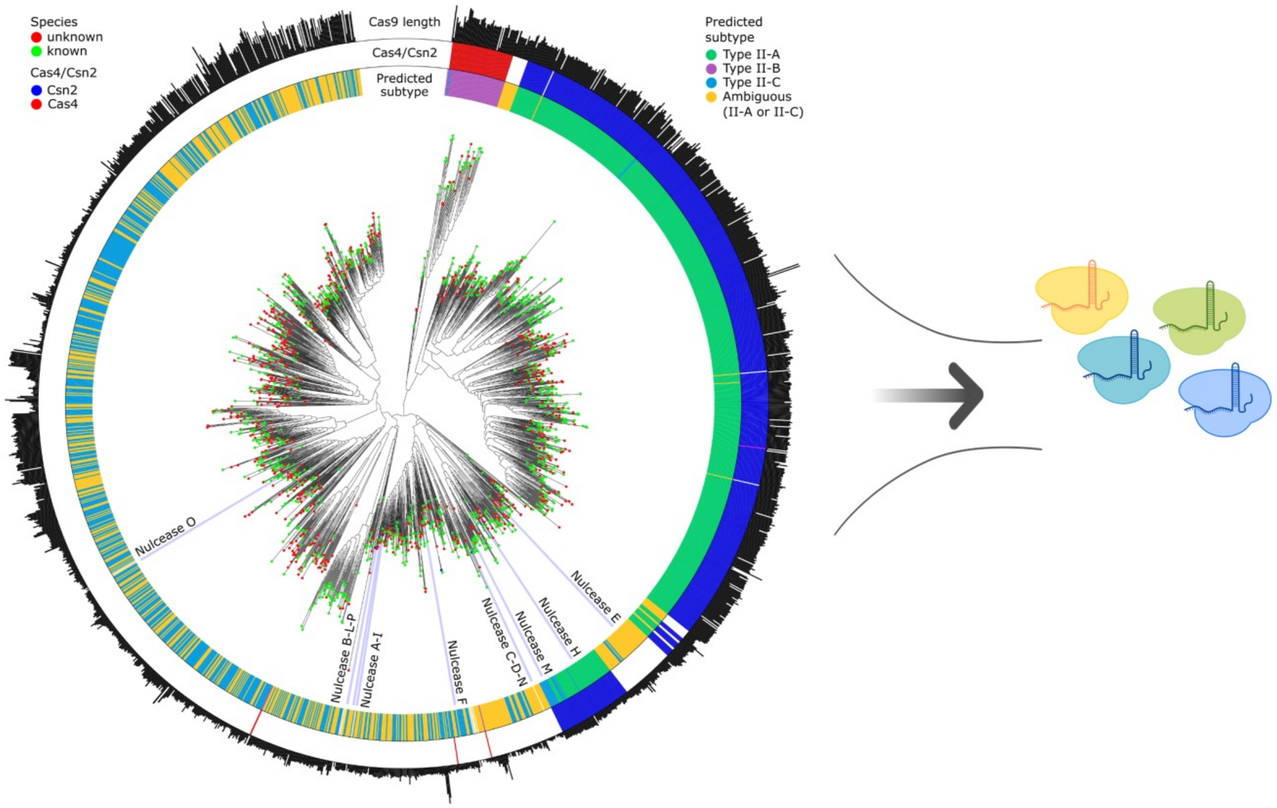
Adel Nada
Independent Director

Pioneering groundbreaking solutions to expand the reach of genome editing and develop therapeutic approaches that are precise, safe and effective.

Program	Editing approach	Discovery	Proof of Concept	Preclinical to IND	Clinical Stage
IN VIVO Strategy : make gene editing a precise, safe and effective therapeutic option					
Ad RP (RHO)	**All in 1-AAV Allele-specific and mutation-independent deletion**				
EX VIVO Strategy : exploit vast and novel CRISPR portfolio in ex-vivo cell programming for I/O cell therapies and immunological diseases					
T-Cell programming	**Simultaneuos Muliplex Editing**				
PLATFORM Strategy : Future Proofing through novel editing approaches and novel target hypothesis					
Type I, Type II (Cas9) Type V CRISPR systems	**KO, KI Large deletions and insertions Base, prime, epigenome editing Nickase**				

Expanding the range of targetable genomic regions through the discovery of novel therapeutic nucleases from the human microbiome

Top tier CRISPR discovery platform



Key Differentiating Capabilities

- Next Generation Type I, Type II (Cas9), Type V CRISPR
- Commensal human microbiome (37°)
- Active and Specific in human cells
- Increased PAM diversity
- gRNA specificity
- Directed evolution and rational protein engineering capabilities
- 10 + patent families, novel and proprietary
- All editing strategies
- All delivery modalities

First-in class mutation-independent and allele-specific targeting strategy to treat RHO dependent autosomal dominant mutations causing Retinitis Pigmentosa (adRP)

Unmet Need

- 30% of all dominant Retinitis Pigmentosa cases (adRP)
- 200+ mutations in the RHO gene
- No treatment options
- Leading to blindness

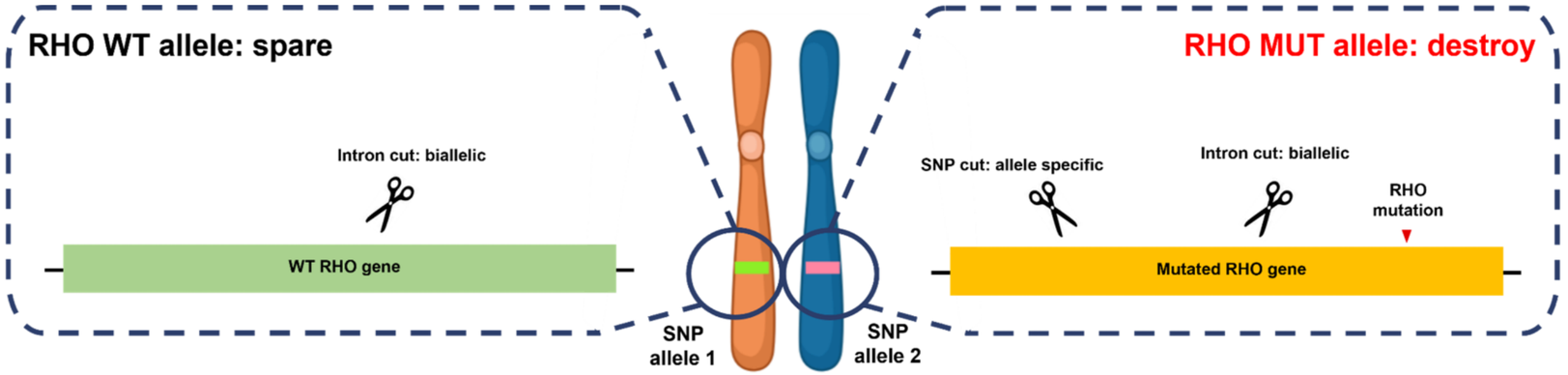
Mutation-independent and allele-specific RHO targeting strategy

<u>Requires highly specific and precise gene editing tools</u>

- Selectively abolishes the expression of mutant alleles
- Spares the wild-type counterpart, preserving photoreceptor function

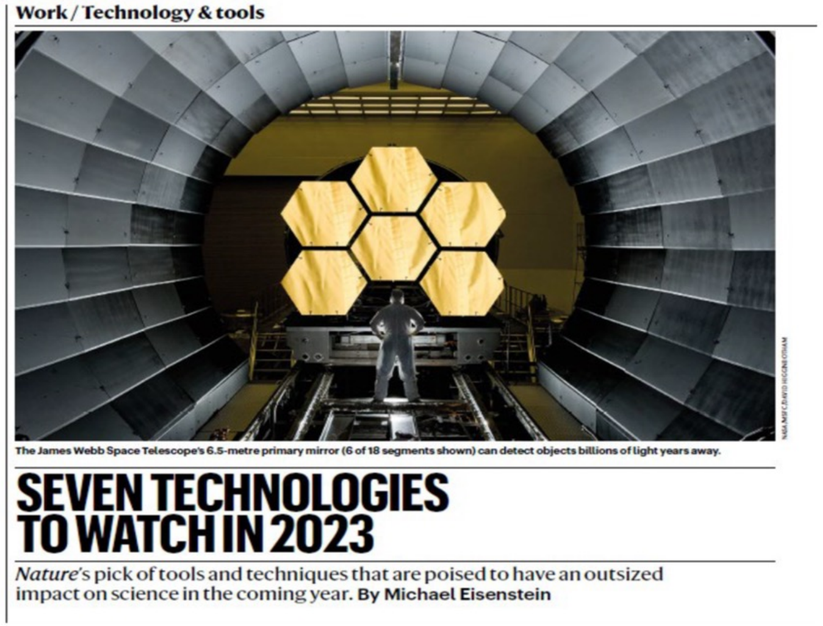
Strategic advantages

- One product to target multiple mutations
- All in 1 AAV delivery
- Expansion to other autosomal dominant conditions



KEY TAKE AWAY

SCIENCE PEOPLE CAPABILIITIES COLLABORATIONS



Work / Technology & tools

The James Webb Space Telescope's 6.5-metre primary mirror (6 of 18 segments shown) can detect objects billions of light years away.

SEVEN TECHNOLOGIES TO WATCH IN 2023

Nature's pick of tools and techniques that are poised to have an outsized impact on science in the coming year. **By Michael Eisenstein**

796 | Nature | Vol 613 | 26 January 2023

Top Tier Science, Leadership, Platform and Capabilities to expand the application of genome editing for the treatment of a broad spectrum of disorders

On track to establishing *in vivo* and *ex vivo* proof of concept for therapeutic approaches that are **safe, effective, and precise**

Fostering **collaborations to accelerate access to life-changing treatments**

APPENDIX: REFERENCES AND PUBLICATIONS

Publications

1. An optimized SpCas9 high-fidelity variant for direct protein delivery ***Molecular therapy,* 2023**
2. Automated identification of sequence-tailored Cas9 proteins using massive metagenomic data, ***Nature Communications,* 2022**
3. A highly specific SpCas9 variant is identified by in vivo screening in yeast**, *Nature Biotechnology,* 2018**
4. VSV-G enveloped vesicles for traceless delivery of CRISPR-Cas9, ***Molecular therapy,* 2018**

Congress presentations

1. Novel and compact CRISPR nucleases for the allele-specific and mutation-independent treatment of autosomal dominant retinitis pigmentosa – **ESGCT 2023, Poster presentation**
2. CoCas9, a compact nuclease from the human microbiome for efficient and precise genome editing **- ESGCT 2023, Poster presentation**
3. Novel Cas9 Orthologs Expand The Genome Editing Toolbox For CRISPR- based therapeutics – **ASGCT 2023 , Oral presentation**
4. A novel CRISPR nuclease targeting an Usher syndrome deep-intronic mutation restores USH2A splicing - **ESGCT 2022, Poster presentation**
5. Mutation-Independent and Allele-Specific Targeting of Autosomal Dominant Retinitis Pigmentosa Using High-Fidelity CRISPR Nucleases – **ASGCT 2022 Poster presentation**

Member of Marie Curie (MSCA) consortia:

- IMMERGE “storming immune monogenic conditions through multiomic and gene editing approaches”
- GET-IN “game changing innovations in viral vector production, design of experiments, quality by design, digital twin simulation, CRISPR genome editing and organoid-on-chip engineering”