Eloxx Pharmaceuticals

Creating a Leader in Ribosomal RNA-Targeted Genetic Therapy
Eloxx Acquires Zikani Therapeutics

April 1, 2021

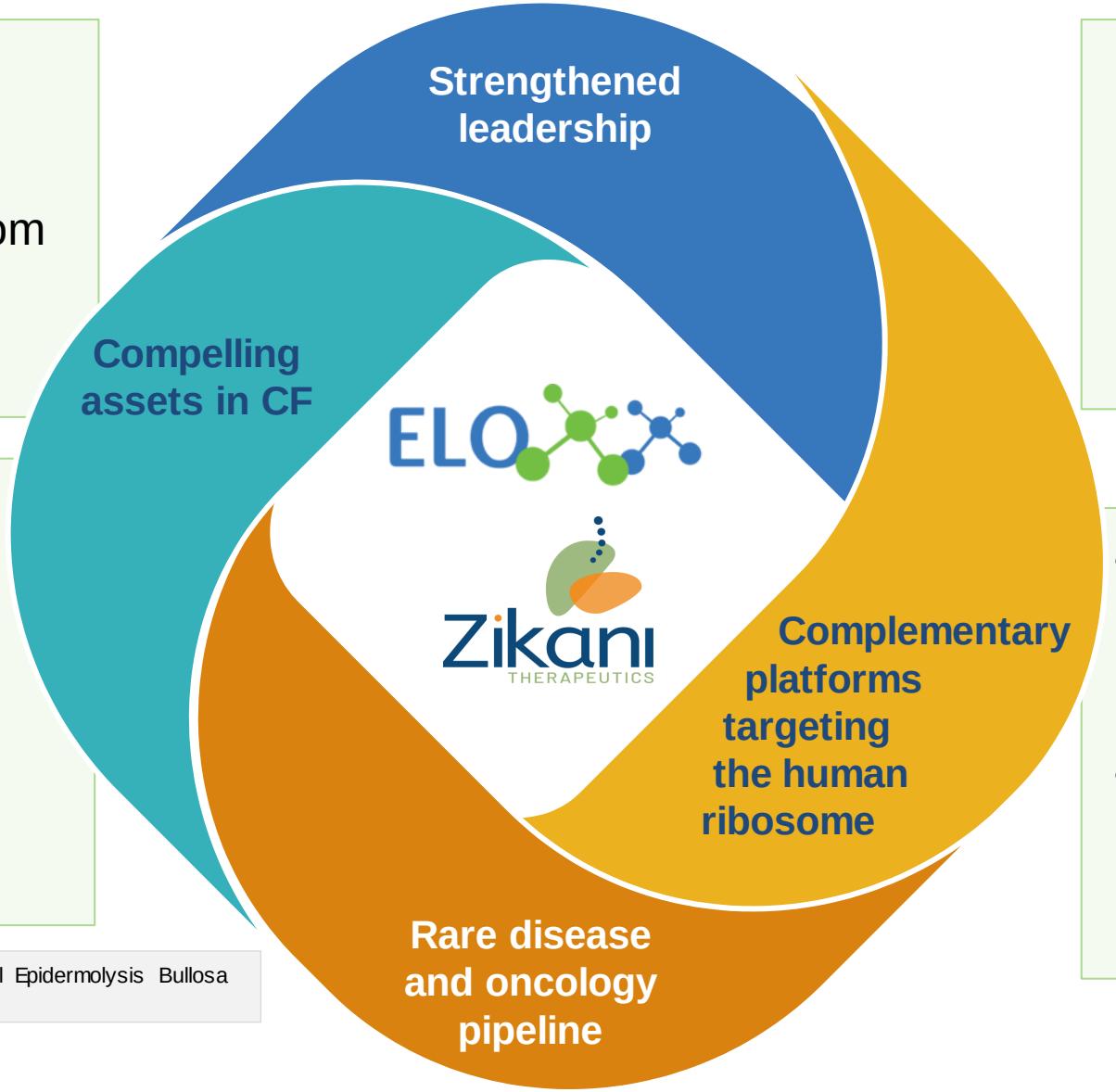
Forward-looking statements

This presentation contains forward-looking statements, which are generally statements that are not historical facts. Forward-looking statements can be identified by the words *"expects," "anticipates," "believes," "intends," "estimates," "plans," "will," "outlook"* and similar expressions. Forward-looking statements are based on management's current plans, estimates, assumptions and projections, and speak only as of the date they are made. We undertake no obligation to update any forward-looking statement in light of new information or future events, except as otherwise required by law. Forward-looking statements involve inherent risks and uncertainties, most of which are difficult to predict and are generally beyond our control. Actual results or outcomes may differ materially from those implied by the forward-looking statements as a result of the impact of a number of factors, including: the development of the Company's readthrough technology; the approval of the Company's patent applications; the Company's ability to successfully defend its intellectual property or obtain necessary licenses at a cost acceptable to the Company, if at all; the successful implementation of the Company's research and development programs and collaborations; the Company's ability to obtain applicable regulatory approvals for its current and future product candidates; the acceptance by the market of the Company's products should they receive regulatory approval; the timing and success of the Company's preliminary studies, preclinical research, clinical trials, and related regulatory filings; the ability of the Company to consummate additional financings as needed; the impact of global health concerns, such as the COVID-19 global pandemic, on our ability to continue our clinical and preclinical programs and otherwise operate our business effectively; including successfully integrating the combined companies; as well as those discussed in more detail in our Annual Report on Form 10-K and our other reports filed with the Securities and Exchange Commission.

Eloxx + Zikani: Positioned to be the world leader in ribosome RNA-targeted genetic therapies

- **ELX-02**: in Phase 2 development for Cystic Fibrosis (CF)
- Preclinical CF program from Zikani pipeline
- **ELX-02 data readout in 2H 2021**

- Expect to file IND for **RDEB* and JEB*** program in 2022
- Advance programs in **inherited and advanced colon cancer** targeted at restoring APC* tumor suppressor protein



- President and CEO: **Sumit Aggarwal**
- Head of R&D: **Dr. Vijay Modur**

- **TURBO-ZM™**: Proprietary synthetic chemistry platform to design **novel macrolide-based oral** small molecules
- **Ribosome Modulating Agents (RMAs):** Potent oral ribosome modulators with favorable therapeutic index

***RDEB and JEB:** Recessive Dystrophic and Junctional Epidermolysis Bullosa
***APC:** Adenomatous Polyposis Coli

Significantly expands and strengthens leadership team

Zikani leadership team to join Eloxx

Sumit Aggarwal
President and CEO

- 20+ years investing and transforming healthcare companies
- Raised >$150M
- Biotech Investor

progenity®

McKinsey&Company

Adage | Capital Management

Dr. Vijay Modur
Head of Research & Development

- 20+ years in translation and drug development
- Led Venglustat rare disease program at Sanofi

MERCK

NOVARTIS

SANOFI GENZYME

Dr. Roger Clark
Head of Discovery Sciences

- 20+ years medicinal chemistry
- Architect of Zikani RMAs

TETRAPHASE PHARMACEUTICALS

BAYER

Daniel Geffken
Interim Chief Financial Officer

- 30+ years building companies
- Closed $2B in equity and debt financings for public and private companies

Danforth Advisors
Knowledge. Discipline. Perspective.

Apellis

HOMOLOGY Medicines, Inc.

TKT

ELO

Transaction overview

Consideration

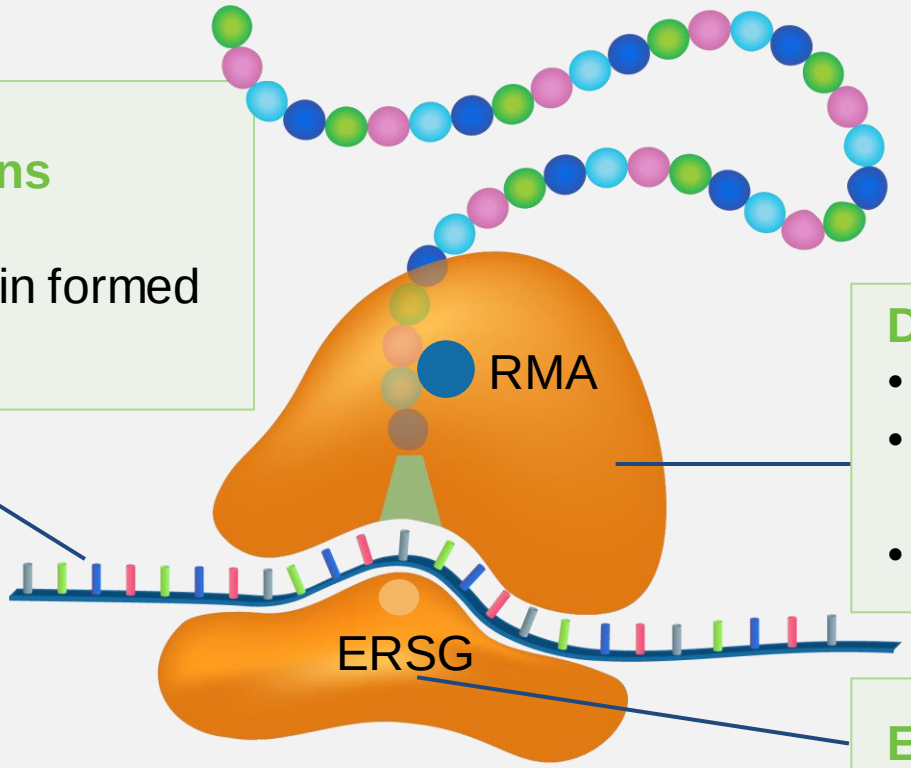
- Eloxx issued ~ 7.6 million shares
- Zikani stockholders have pro forma ownership ~ 16% of Eloxx

Board changes

- Silvia Noiman, Ph.D., and Martijn Kleijwegt stepped down from Eloxx Board
- Alan Walts, Ph.D., and Raj Parekh, Ph.D., current Zikani directors, appointed to fulfill vacancies and serve out remaining terms

Acquisition combines complementary platforms in targeting the human ribosome

Ribosome = "Protein Factory"



Genetic nonsense mutations

- **Premature stop codon**
- Less than full length protein formed = loss of function

Dysregulated Ribosomes

- **Onco- and mitoribosomes**
- Selective translation of oncogenic proteins
- Aids hyperproliferative phenotype

ELX-02

- **ELX-02 has shown clinically relevant readthrough of CFTR in pre-clinical models**

RMA: Ribosome Modulating Agent
ERSG: Eukaryotic Ribosome Selective Glycoside

ELX-02: Potential for transformative efficacy in Class 1 CF patients

Demonstrated efficacy in clinically relevant pre-clinical models	• Swelling response in Class 1 CF patient organoids • Induces CFTR activity of up to 30% of normal; confirmed in Ussing Chamber • Active across broad range of mutations
Safety demonstrated in clinical studies	• Generally well-tolerated for chronic dosing • Consistent pharmacokinetics across both single and multiple-dose accumulations
Phase 2 CF trials designed for rapid clinical signal	• Study designed to confirm safety and changes in sweat chloride confirming biological activity

Expect to complete enrollment in Phase 2 clinical trials by midyear and report data in 2H 2021

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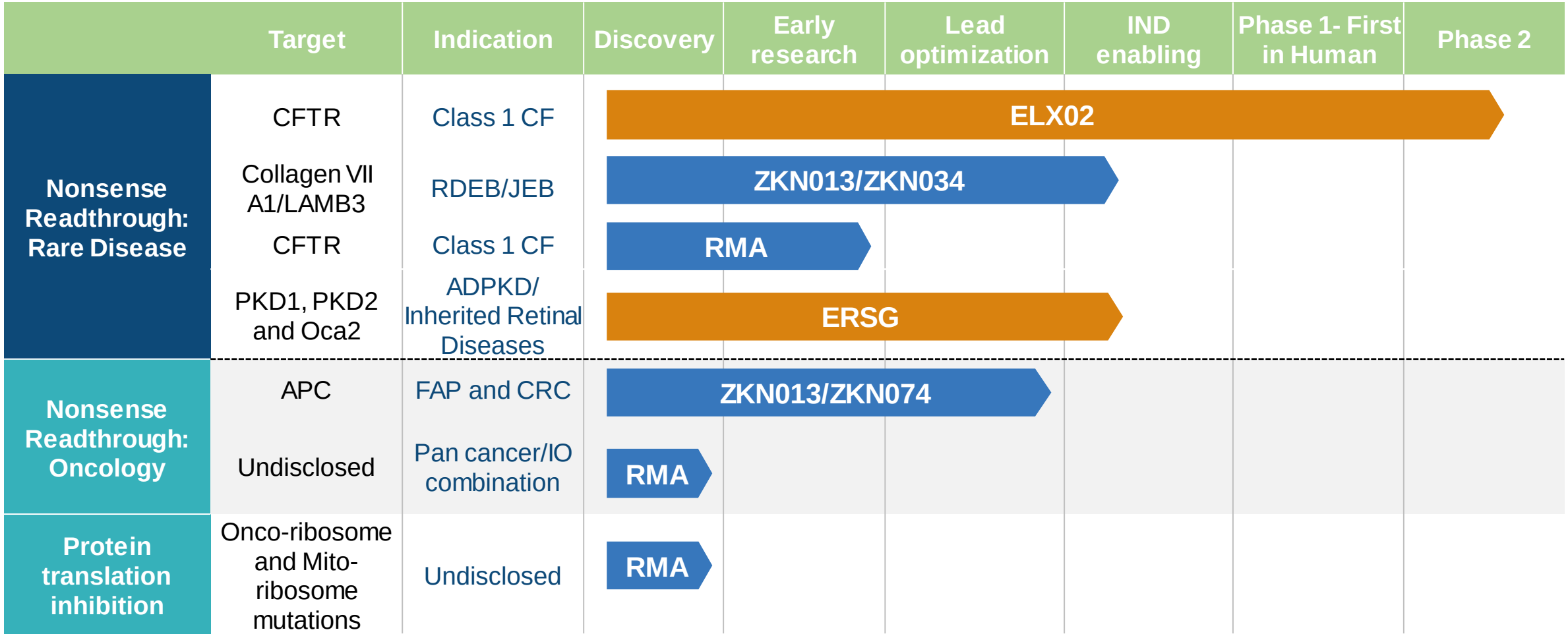
CYSTIC FIBROSIS FOUNDATION
ADDING TOMORROWS

Deep pipeline of synergistic potential first-in-class therapies



***Class 1 CF:** Cystic fibrosis patients with Class1 mutations **ADPKD**: Autosomal Dominant Polycystic Kidney Disease **FAP:** Familial Adenomatous Polyposis **CRC:** Colorectal Cancer

Zikani Therapeutics Introduction

TURBO-ZM™ (Tuning the Ribosome with Zikani Molecules) platform fully unlocks the potential of macrolides

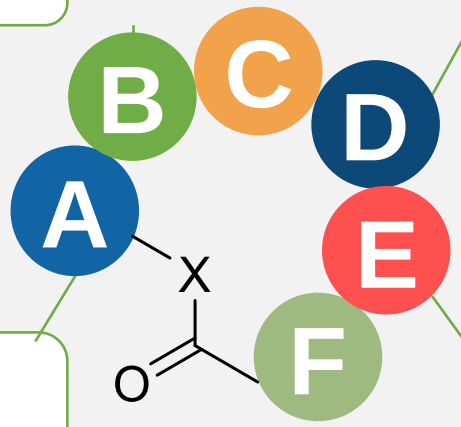
TURBO-ZM™: Applying Macrolide SAR to RMA Design

TURBO-ZM

Optimize for:
- Readthrough
- Protein translation inhibition

Interact with the peptide sequence

Modulate:
- PK
- Safety: cardiac, liver
- Oral bioavailability



Essential for ribosomal binding

RMA core required for ribosomal binding

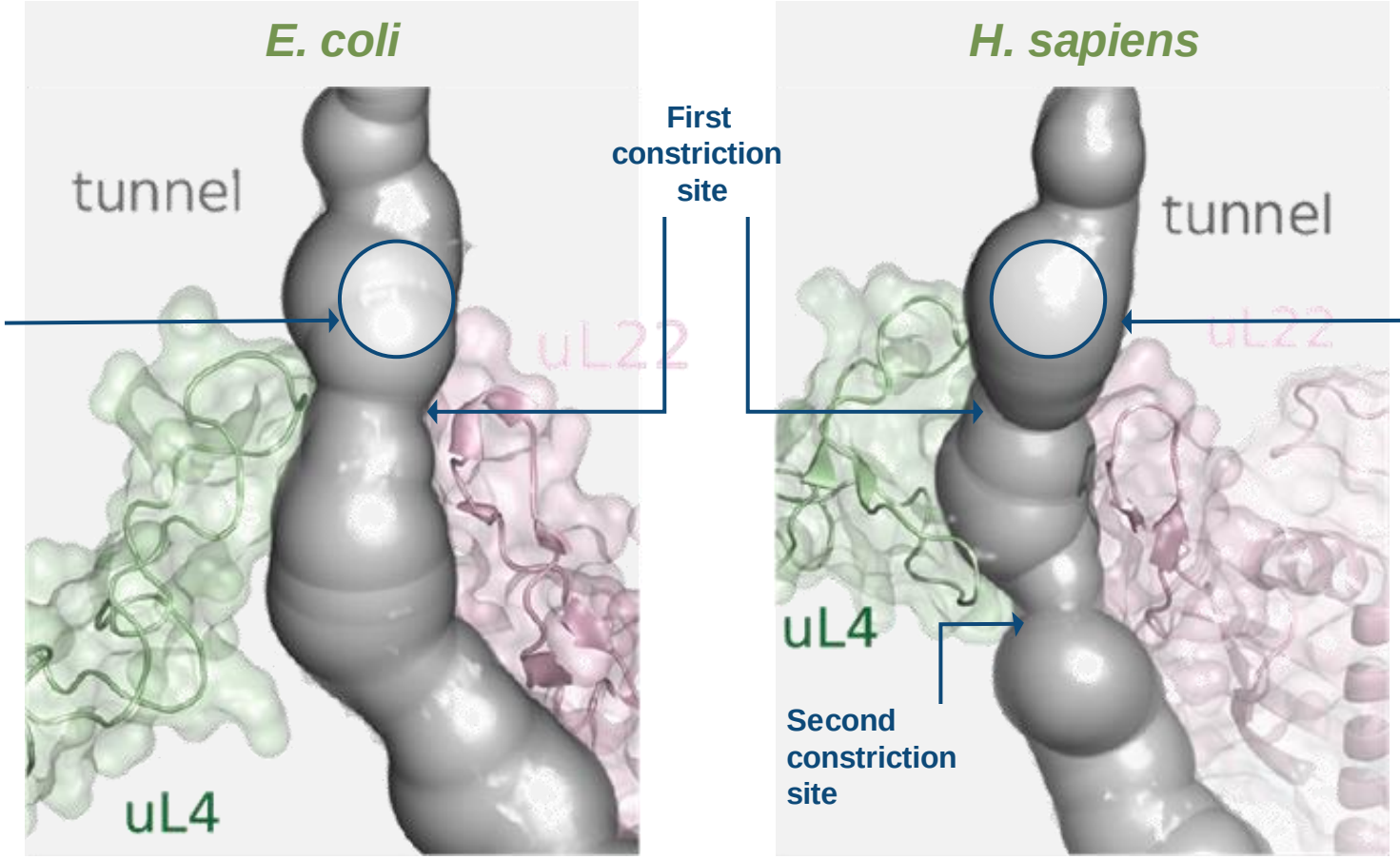
Modulate cytoplasm and mitochondrial ribosome binding activity

Zikani THERAPEUTICS

Strong rationale for macrolides to bind the human ribosome

Nascent peptide exit tunnel in E. coli vs. Human ribosomes[1]

Macrolide binding site in prokaryotic (bacterial) ribosome

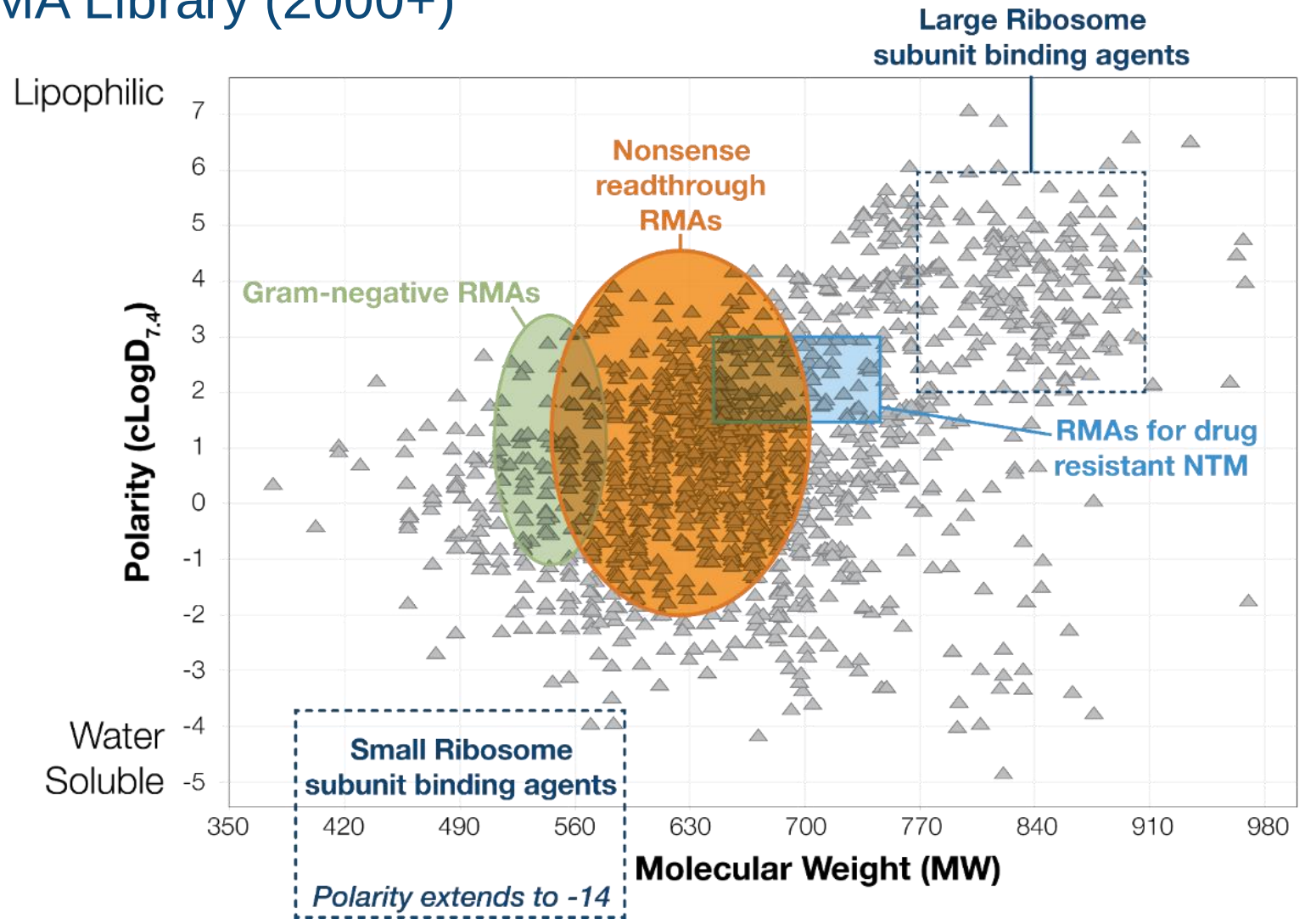


75% of binding site conserved in the human (eukaryotic) ribosome[1]

[1]Nucleic Acids Res. 2019;47(8):4198-4210

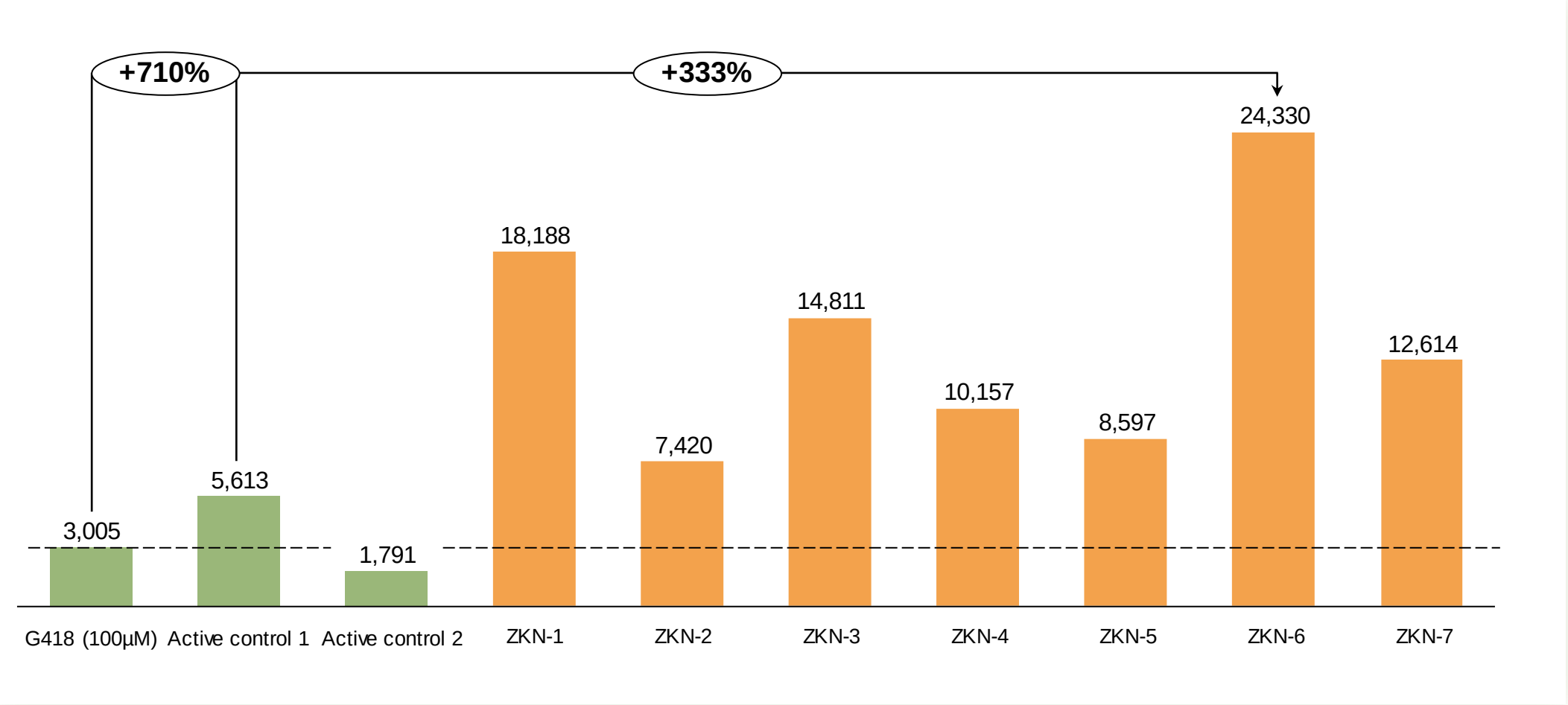
Growing library of RMAs with drug-like properties

Zikani RMA Library (2000+)



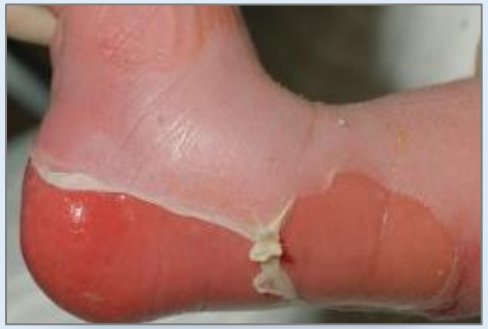
RMAs show superior readthrough to alternatives

Readthrough Emax of selected RMA hits relative luciferase units compared to DMSO in W134X Nanoluc reporter assay



RDEB/JEB: Clinically validated path for RMAs in rare skin disease targeting patients with nonsense mutations

RDEB and JEB



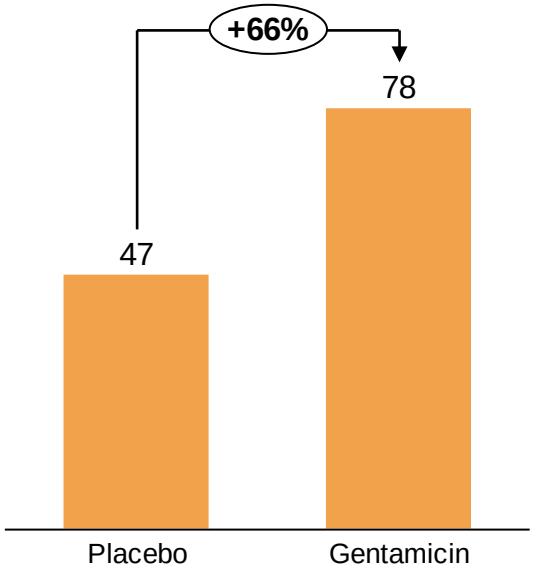
- Mutations in COL7A1 gene (Collagen) and LAMB3(Laminin)
- Most RDEB patient develop skin cancer by age 35
- Average mortality of JEB patients is 18 months

~4,000 patients, $1.5B TAM

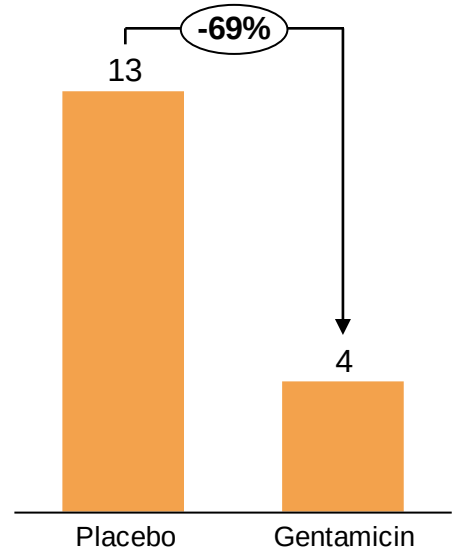
RDEB

Gentamicin treatment of RDEB patients
(0.1% gentamicin ointment tid for 2 weeks; n=5)[1]

Wound closure at 3 months, %



Total blistering events at 3 months



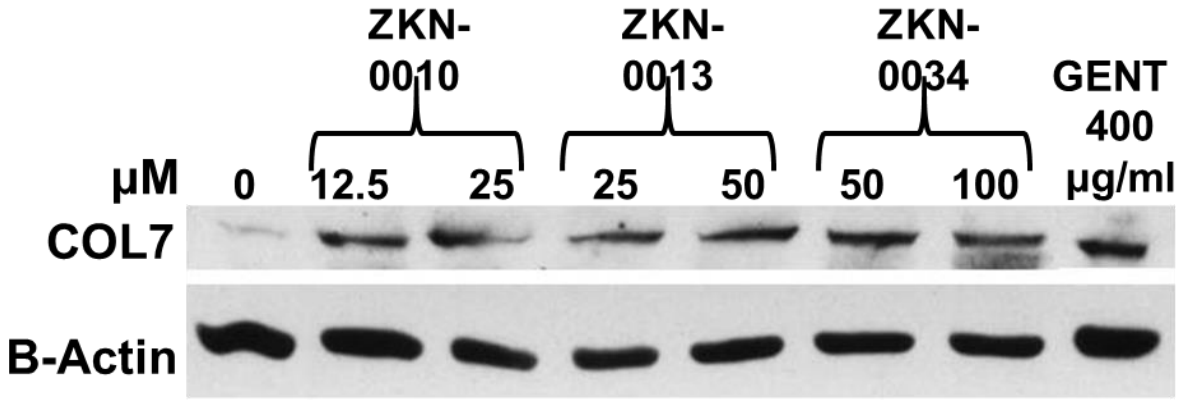
RDEB and JEB: Recessive Dystrophic and Junctional Epidermolysis Bullosa

[1]Woodley, DT. J Clin Investig 2017, 127, 3028-3038; 2Hammersen, Johanna et al. Dermatology May 2019

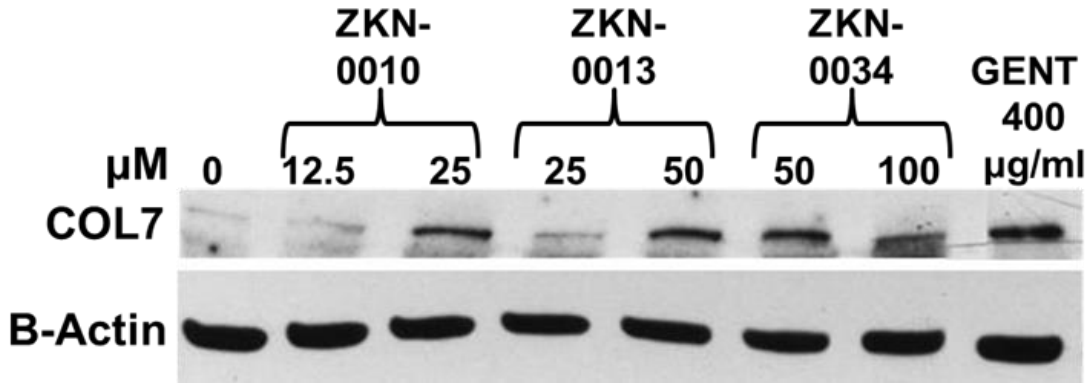
RDEB: RMAs restore functional collagen protein in primary patient cells comparable to high dose gentamicin

COL7 with 48 hr. exposure in RDEB patient derived **primary** fibroblasts*

Full length protein in Hom R578X COL7A Fibroblasts**



Full length protein in R613X/R1683X COL7A Fibroblasts**



Data generated in collaboration with academic partner

- Assay with proven translation to clinic
- 30 to 60-day Col7 protein half-life
- RMAs compounds exceed clinical efficacy threshold of 10% Gentamicin 845uM

* Fibroblasts isolated from patients two and five in gentamicin clinical trial. J Clin Invest 2017, 127, 3028-3038

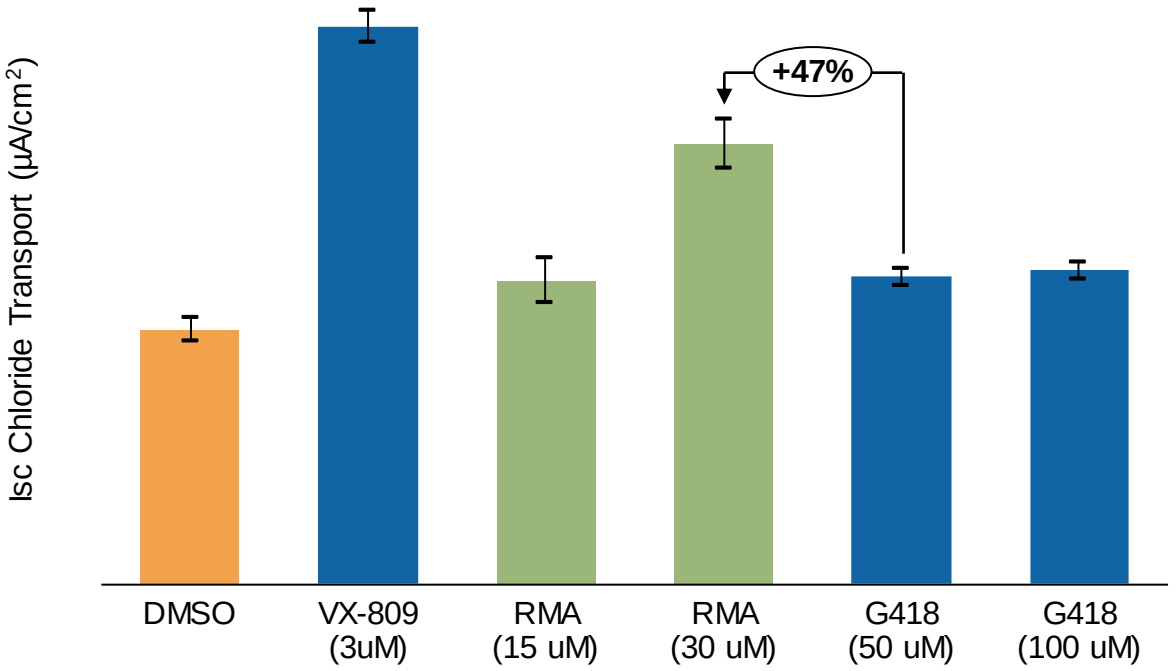
** 48 hours treatment with media and compounds replaced and refreshed at 24 hours. Study repeated twice with equivalent results.

Zikani THERAPEUTICS

Class 1 CF: RMA lead showed highest ever readthrough preclinical Ussing chamber assay

Summary of Class 1 CF data

Het G542X Human Broncho Epithelial (HBE) cells Ussing Chamber
Steady state modulator response measurement**



Data generated at Chantest

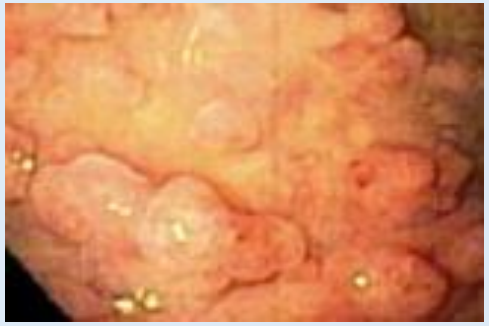
> Never seen before impressive single agent activity from non aminoglycoside class – need to advance this program
>
> *– CF Foundation*
>
> *Encouraged to apply for "Path to Cures"*

- **Submitted $2.5M grant to CF Foundation to support through development candidate**

* Forskolin 10 µM/1µM VX-770 - both chambers
** VX 809 and RMA data averaged from 2 separate Ussing chamber results

APC readthrough: Supported by positive prior clinical success of Erythromycin in FAP

APC mutant Familial Adenomatous Polyposis (FAP) and CRC



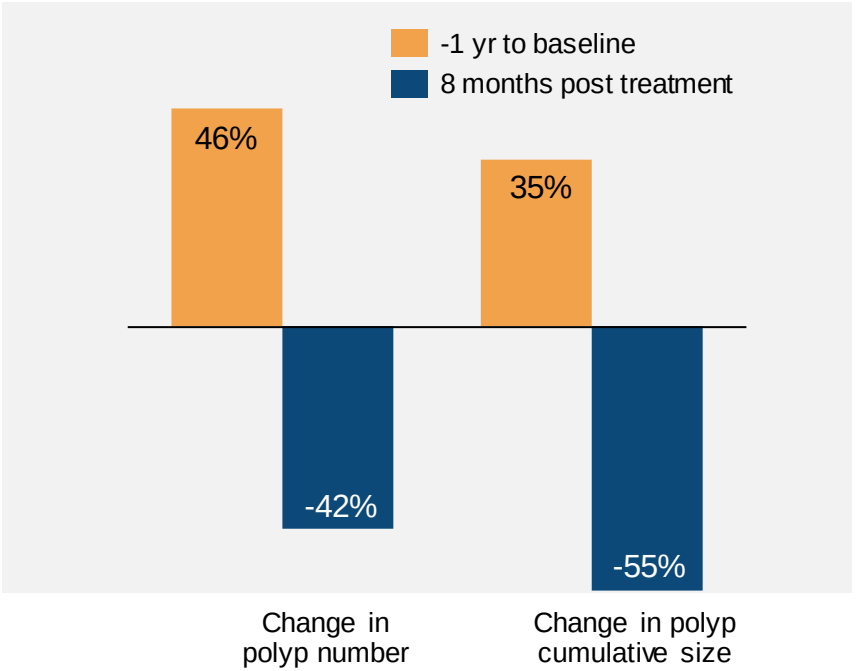
- Mutations in the Adenomatous Polyposis Coli (APC) gene (tumor suppressor gene)
- FAP patients develop CRC by age 40
- 80% of CRC patients have an APC mutation

8,000-12,5000 FAP patients in the US/EU; 210,000 CRC patients WW

Clinical trial success in FAP with Erythromycin

Erythromycin treatment
(250 mg/day po for 4 months)

Change in polyp burden at 12 months[1]



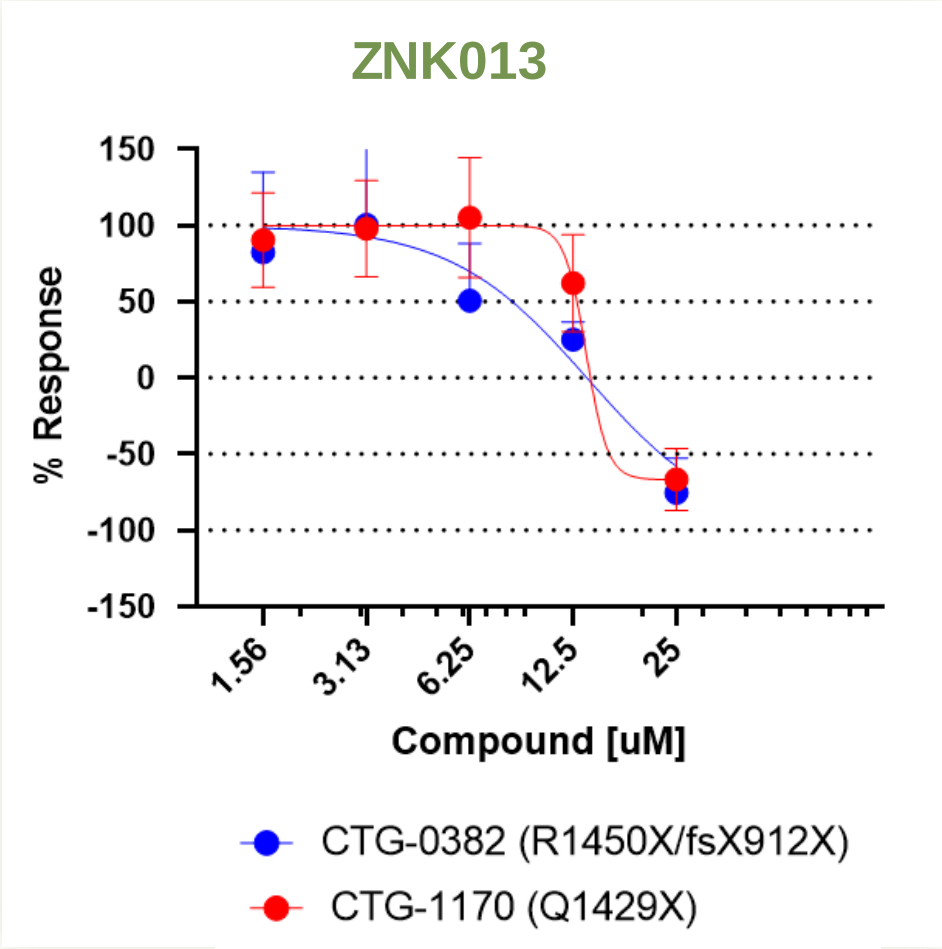
[1]Kariv, R. Int J Cancer. 2019 doi: 10.1002/ijc.32557

Zikani THERAPEUTICS

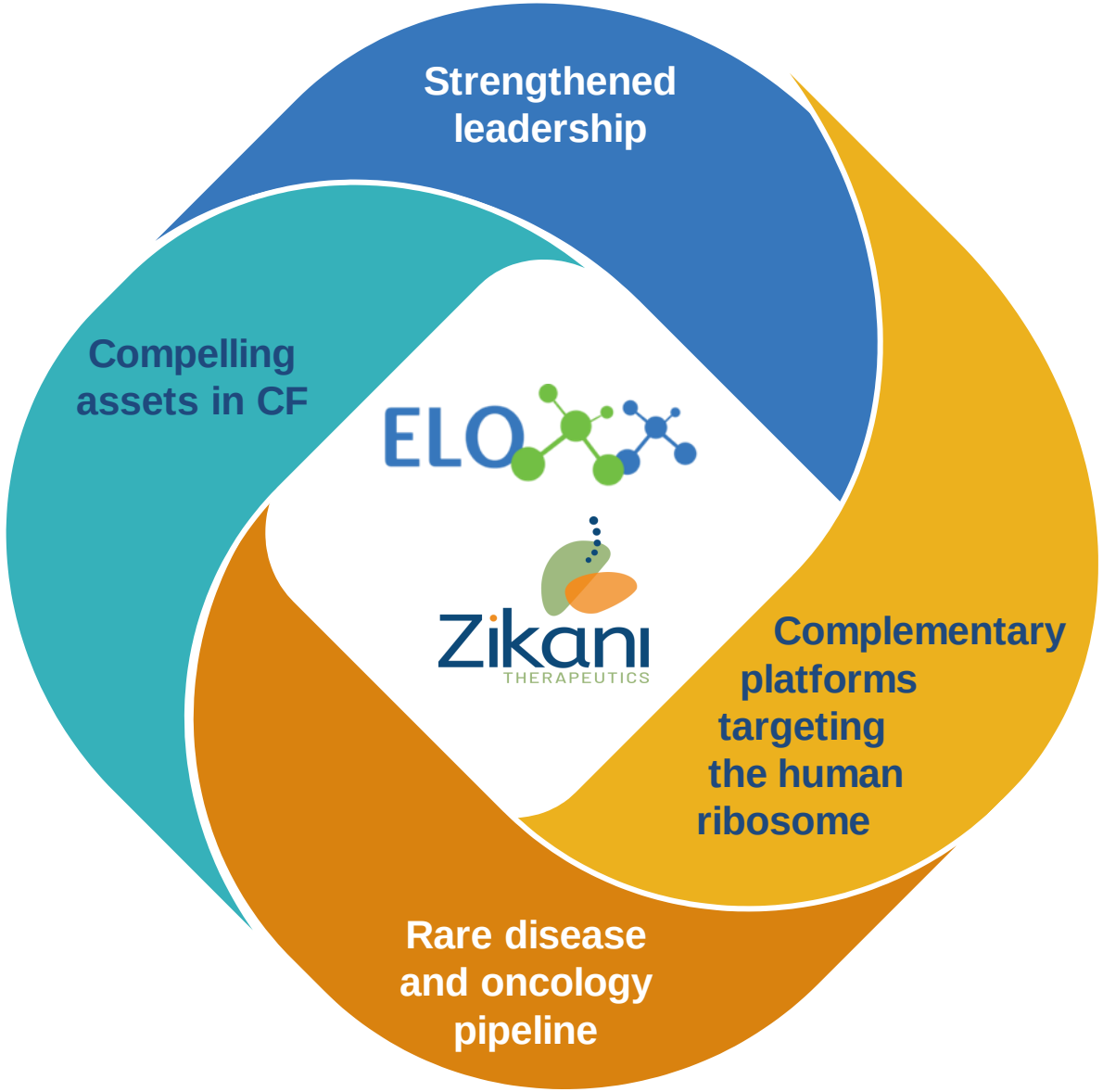
Clear path in treating FAP supported by efficacy in APC mutant cancer patient tumor grafts

Efficacy of ZN013 in colorectal cancer patient derived tumor grafts ex-vivo

- Ex-vivo sensitivity assessment in tumor grafts
- Potent tumor growth inhibition
  - GI_{50}<15uM
- Cancer xenograft studies planned in 2021



Eloxx + Zikani: Positioned to be the world leader in ribosome RNA-targeted genetic therapies

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