Zikani THERAPEUTICS

Corporate Fact Sheet
December 2019

New Oral Therapeutics for Treating Rare Diseases

TUning the RiBOsome with Zikani Molecules- TURBO-ZM

We are committed to fully exploiting our platform to develop novel Ribosome Modulating Agents (RMAs)

Leadership Team

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Key Collaborators

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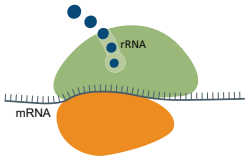
Christopher Viehbacher
Gurnet Point Capital

Anja Harmeier
Roche Venture Fund

Ribosomal RNAs: therapeutic targets with high unmet medical need

Ribosomal RNAs (rRNAs) form the translation machinery that generates functional proteins from genetic sequences



Modulation of the interactions between ribosomes and mRNAs is a proven therapeutic approach to address a range of diseases such as:

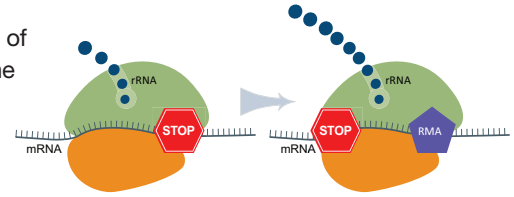
Rare Genetic Diseases:	Inflammatory Disorders:	Cancers:
CF, FAP	Crohn's disease	Colon and pancreatic

Our Focus: nonsense mutation readthrough to treat rare diseases

Traditional ribosome binding nonsense read through agents are limited by their lack of specificity for human ribosomes and safety profiles

Compounds	Specificity	Clinical Application	Safety Limitations
Aminoglycosides	Bacterial rRNA	DMD, Class 1 CF, EB	Nephrotoxicity, ototoxicity
Macrolides	Bacterial rRNA	FAP, Rhett Syndrome, SMA	QT prolongation, cardiac arrhythmia

Zikani's TURBO-ZM platform allows rapid synthesis of novel compounds that can be optimized to target the human ribosome in a disease-specific manner.



Approach de-risked given historical clinical and ex vivo evidence

Indications with Supporting Translational Evidence

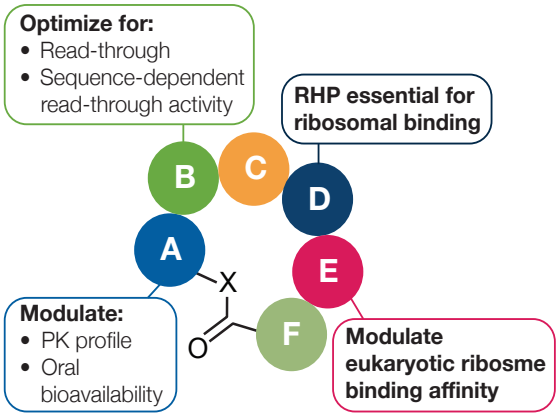
Indication	Translational Evidence	Readthrough agent tested
FAP and APC driven Colorectal cancer	Clinical[1]	Erythromycin, Tylosin, Gentamicin
Cystic Fibrosis Class 1	Clinical[2]	Gentamicin, Tylosin, Geneticin
Duchenne Muscular Dystrophy	Clinical[3]	Gentamicin
Dystrophic Epidermolysis Bullosa	Clinical[4]	Gentamicin, Geneticin
Lysosomal Storage Disorders, e.g., MPSI (Hurler), cystinosis	Ex vivo patient-derived cells[5]	Gentamicin, Geneticin
Rett Syndrome	Ex vivo patient-derived cells[5]	Azithromycin, Gentamicin
Spinal Muscular Atrophy (SMA)	Ex vivo patient-derived cells[5]	Azithromycin, Gentamicin
Ataxia-Telangiectasia (ATM)	Ex vivo patient-derived cells[5]	Azithromycin, Gentamicin, Erythromycin
Ocular indications, e.g., Usher syndrome/ retinitis pigmentosa (RP)	In vivo/Preclinical[6]	Gentamicin, Geneticin

[1]Kariv, R. Ann. Oncol. 2018, 29, suppl3; [2]Sermet-Gaudelus, I. BMC Med. 2007, 5, 5; [3]Malik, V. Ther. Adv. Neurol. Disord. 2010, 3, 379; [4]Woodley, D. J Clin Invest. 2017;127(8):3028; [5]Caspi, M., J Mol Med (Berl). 2016 Apr;94(4):469-82; 6Goldmann, T, Hum Gene Ther. 2011 May;22(5):537-47.

Platform

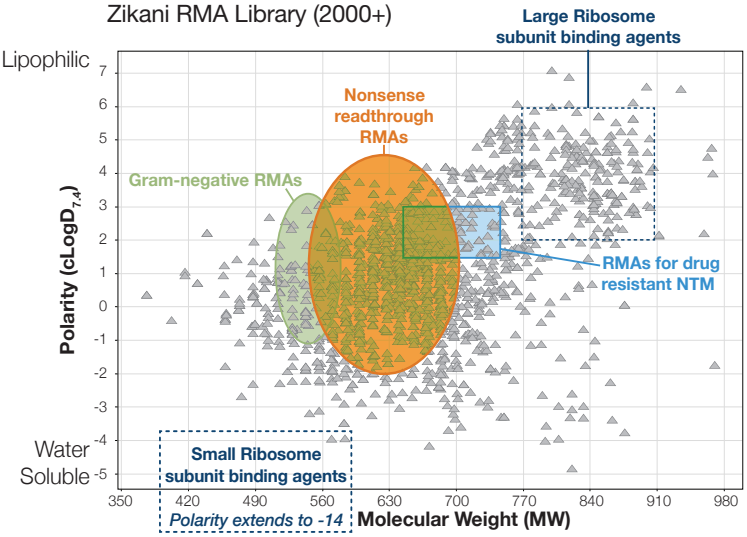
Zikani's TURBO-ZM platform yields a novel class of highly specific oral ribosomal modulators

Ribosome Modulating Agents (RMA) – Areas of optimization



RMAs designed as traditional small molecules

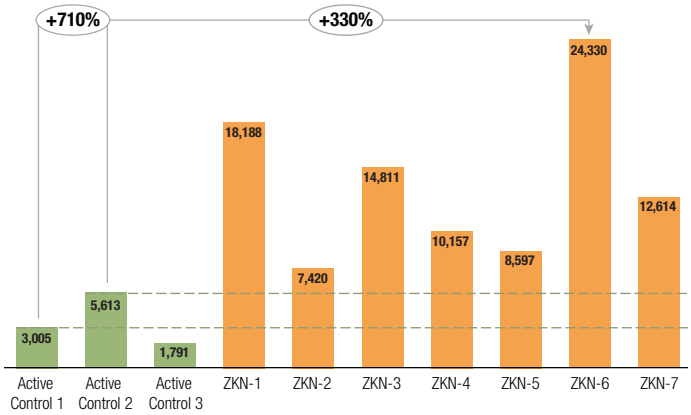
Zikani RMA Library (2000+)



Efficacy

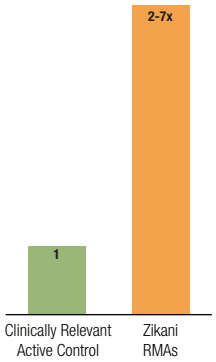
Strong activity of Zikani RMAs vs relevant positive controls in multiple diseases

Readthrough Emax of selected RMA hits
Relative Luciferase Units compared to DMSO in W134X Nanoluc Reporter Assay



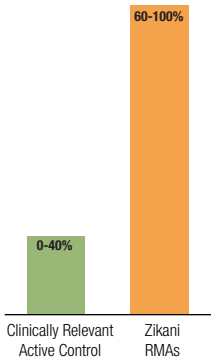
Meaningfully higher in vitro and ex vivo efficacy in rare Class 1 CF, FAP, and APC mutant CRC

Efficacy of RMAs in Class 1 CF patients in various in vitro and ex vivo functional assays[1]



FAP Dual reporter with APC nonsense mutations[2]

Cell Apoptosis in CRC patient derived Organoids with APC nonsense mutations[3]



Programs

Promising early data in additional rare nonsense mutation driven genetic diseases

Summary of data – fold increase over clinically relevant active controls

Class 1 Cystic Fibrosis

- 2-fold to 7-fold higher protein production in HBE cells with R1162X Class 1 CF mutations in ELISA assay
- 2-fold to 4-fold higher membrane potential/current in CFTR minigene with G542X Class 1 mutations
- Up to 2-fold higher current in Ussing Chamber assay in heterozygous G542X mutated HBE cells

Familial Adenomatous Polyposis (FAP)

- 60% to 100% cell apoptosis in CRC patient derived organoids with R1450X and Q1338X mutations
- 3-fold to 39-fold higher Wild type (WT) protein in R1450X mutation dual reporter assay
- 7-fold to 12-fold higher WT protein in E1309X mutation dual reporter assay

Contact
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[1]Includes Western blot, Membrane polarization and ussing chamber assays performed by academic and industry collaborators.
[2]Dual reporter assay in an APC gene construct with a nonsense mutation. Tested R1450X and E1309X mutations. Data generated by academic collaborator.
[3]Cell viability assay evaluating response to drug in fully differentiated CRC patient organoids. Performed at HUB.