RARE Thinking for RARE Solutions

Creating a World Leader in Ribosome Targeted Genetic Therapies

April 2021

Forward-looking statements

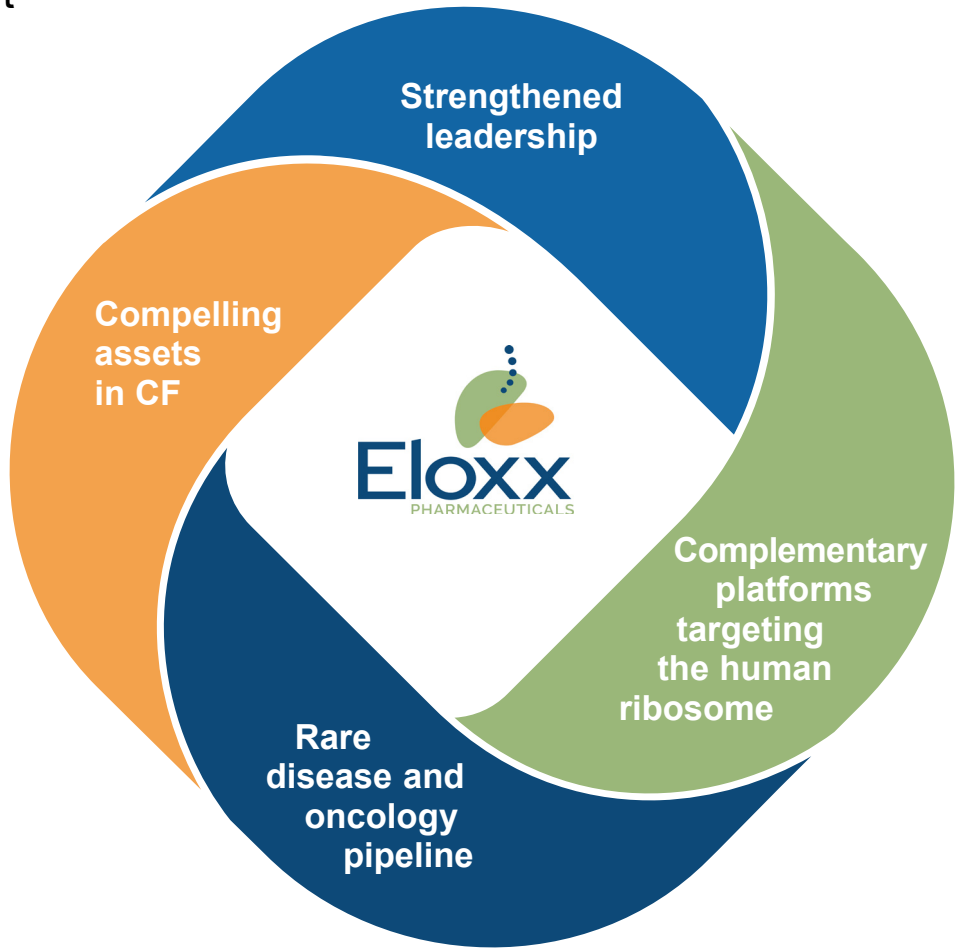
This presentation contains forward-looking statements, which are generally statements that are not historical facts. Forward-looking statements can be identified by the words *"expects," "anticipates," "believes," "intends," "estimates," "plans," "will," "outlook"* and similar expressions. Forward-looking 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 PHARMACEUTICALS

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

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

- 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**

- **Eukaryotic Ribosome Selective Glycosides (ERSGs):** Safer Aminoglycosides designed with human ribosome selectivity
- **TURBO-ZM™:** Proprietary synthetic chemistry platform to design novel macrolide- based **oral Ribosome Modulating Agents (RMAs)**

*__RDEB__ and __JEB__: Recessive Dystrophic and Junctional Epidermolysis Bullosa; __APC__: Adenomatous Polyposis Coli

Eloxx PHARMACEUTICALS

Meet the new Eloxx Leadership Team

Sumit Aggarwal
President and CEO

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

progenity
McKinsey&Company
Adage Capital Management

Vijay Modur
Head of Research & Development

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

MERCK
NOVARTIS
SANOFI GENZYME

Neil Belloff
COO and General Counsel

- 30+ years business and legal experience
- GC and executive leadership roles

Celgene
Deutsche Telekom

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

Eloxx PHARMACEUTICALS

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 fill vacancies and serve out remaining terms

Eloxx PHARMACEUTICALS

Strong advisors and collaborators supporting programs

Key collaborators

CYSTIC FIBROSIS FOUNDATION

ecfs

Hubrecht Institute

Rina Arbesfeld

KOL **FAP/APC**

TEL AVIV UNIVERSITY

Mei Chen

KOL **DEB**

Keck School of Medicine of USC

Key advisors

Prof. Eitan Kerem

Cystic Fibrosis

Former Head of Pediatrics Hadassah Hospital

Former SAB member Vertex

Keith Flaherty

Oncology, Chairman SAB

Loxo Oncology co-founder

HARVARD MEDICAL SCHOOL

Pedro Huertas

Clinical Translation

ex-CMO Eloxx, Shire

Eloxx PHARMACEUTICALS Shire

Dr. David Sidransky

Oncology

Advaxis, Champions Oncology

JOHNS HOPKINS MEDICINE

Dr. Andrew South

Epidermolysis Bullosa

Jefferson
Philadelphia University + Thomas Jefferson University
HOME OF SIDNEY KIMMEL MEDICAL COLLEGE

David Bedwell

Readthrough, Rare diseases

UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

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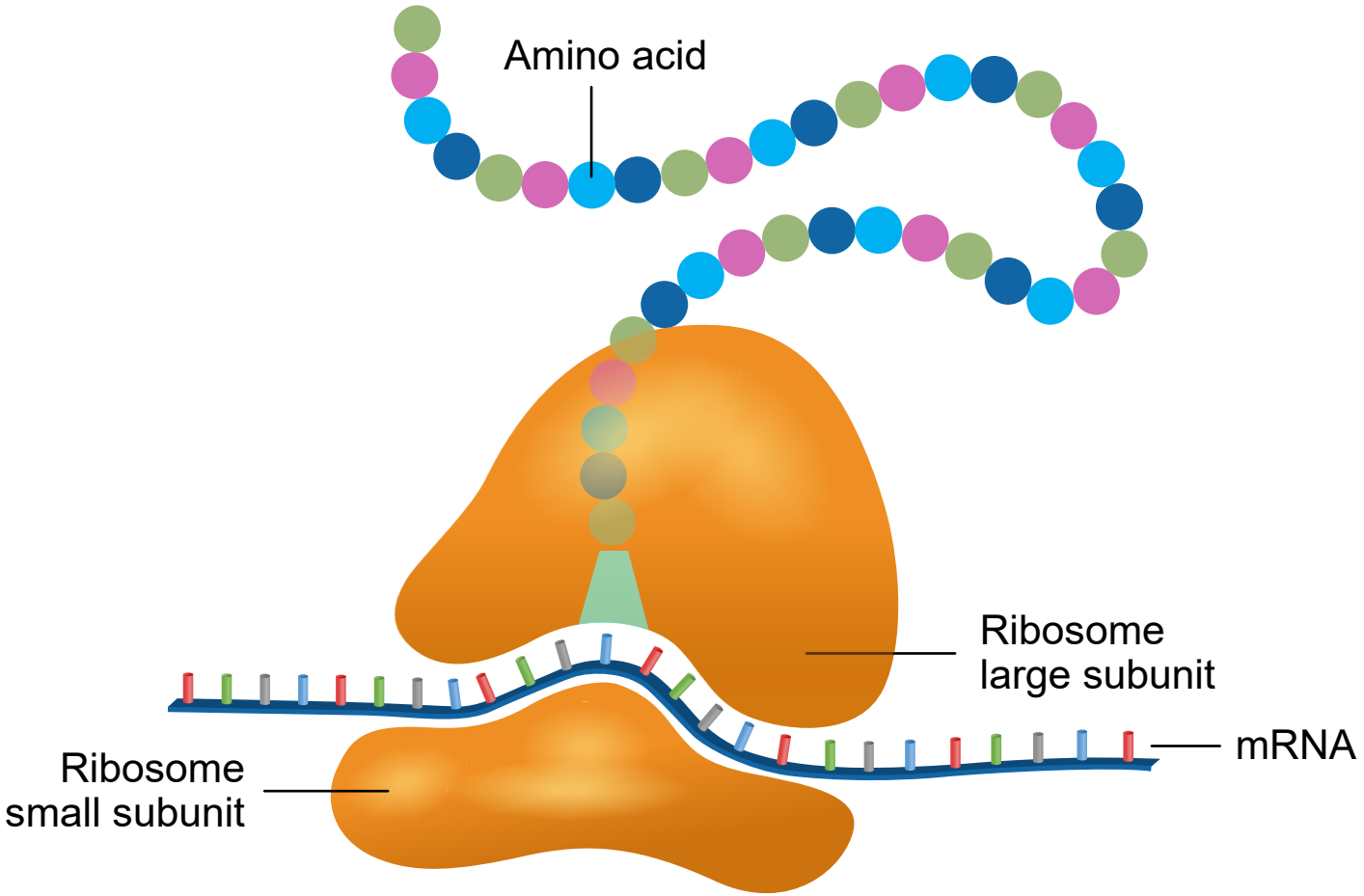
Complementary human ribosome targeting technologies that address defects in protein translation

Ribosome = “protein factory”: Correcting mRNA and ribosomal mutations

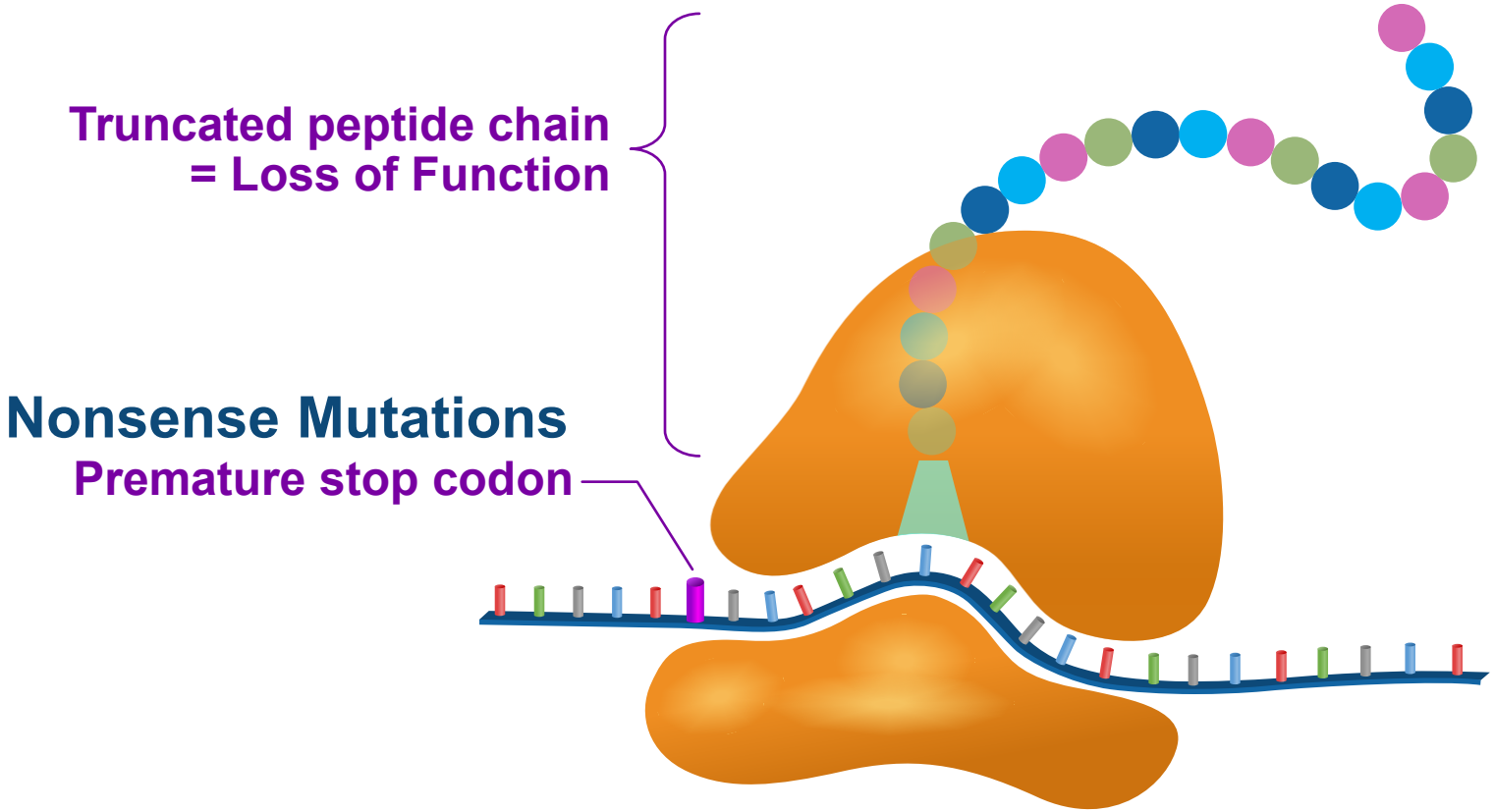


RMA: Ribosome Modulating Agent; **ERSG:** Eukaryotic Ribosome Selective Glycoside

Eloxx PHARMACEUTICALS

Complementary human ribosome targeting technologies that address defects in protein translation

Ribosome = “protein factory”: Correcting mRNA and ribosomal mutations



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Eloxx PHARMACEUTICALS

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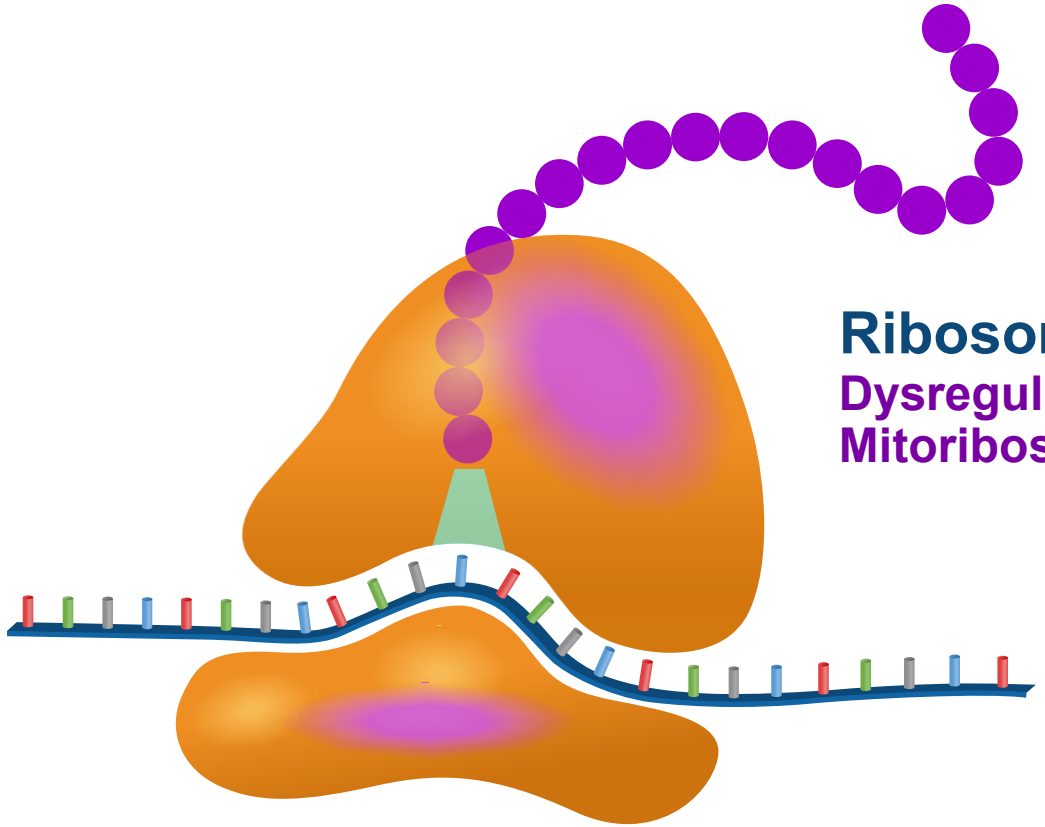

Ribosomal mutations
Dysregulated Onco- and Mitoribosomes

RMA: Ribosome Modulating Agent; **ERSG:** Eukaryotic Ribosome Selective Glycoside

Eloxx PHARMACEUTICALS

Complementary human ribosome targeting technologies that address defects in protein translation

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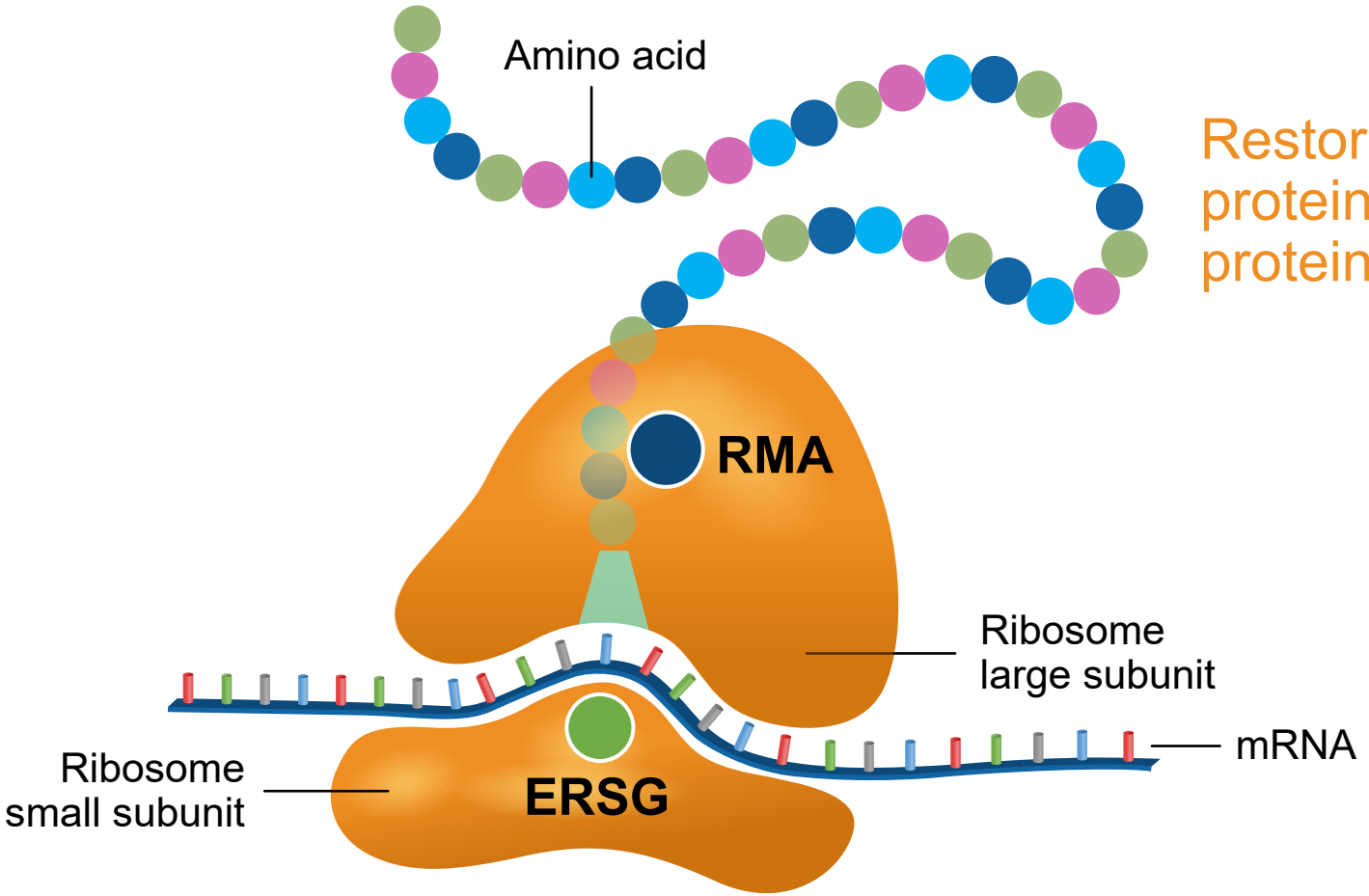

Restore full length proteins **and** inhibit protein translation

RMA: Ribosome Modulating Agent; **ERSG:** Eukaryotic Ribosome Selective Glycoside

Eloxx PHARMACEUTICALS

Strong evidence of readthrough activity with macrolides and aminoglycosides

Clinically relevant readthrough reported in over 36 different rare diseases

Diseases	Evidence	Readthrough Agent(s) Tested	
		Macrolides	Aminoglycosides
Familial Adenomatous Polyposis (FAP)	Clinical[1]	Ery, Tyl	Gen
Cystic Fibrosis Class 1	Clinical[2]	Tyl	Gen, G418
Duchenne Muscular Dystrophy	Clinical[3]		Gen
Dystrophic Epidermolysis Bullosa (RDEB)	Clinical[4]		Gen, G418
Lysosomal Storage Disorders, e.g., MPSI (Hurler), cystinosis	*ex vivo*[5]		Gen, G418
Rett Syndrome	*ex vivo*[5]	Ery	Gen
Spinal Muscular Atrophy (SMA)	*ex vivo*[5]	Azm, Ery	Gen
Ataxia-Telangiectasia (ATM)	*ex vivo*[5]	Ery	Gen
Usher syndrome/retinitis pigmentosa (RP)	*in vivo* Preclinical[6]		Gen, G418

Macrolides: Erythromycin (Ery); Tylosin (Tyl); Azithromycin (Azm)
Aminoglycosides: Gentamicin (Gen); Geneticin (G418)

[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; [6]Goldmann, T, Hum Gene Ther. 2011 May;22(5):537-47.

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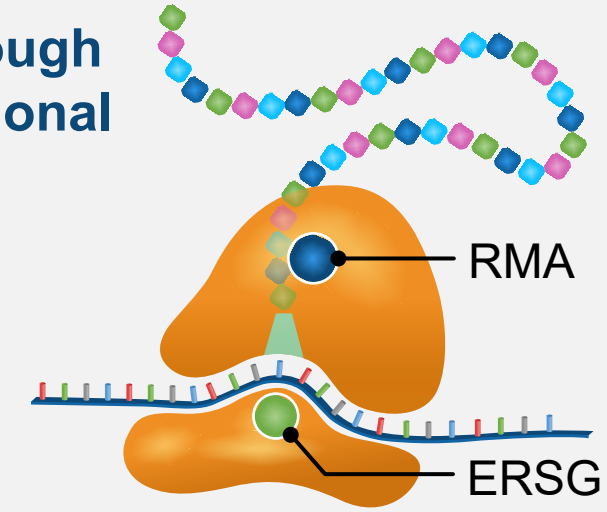
Large and broad applications for human ribosome targeted genetic therapies

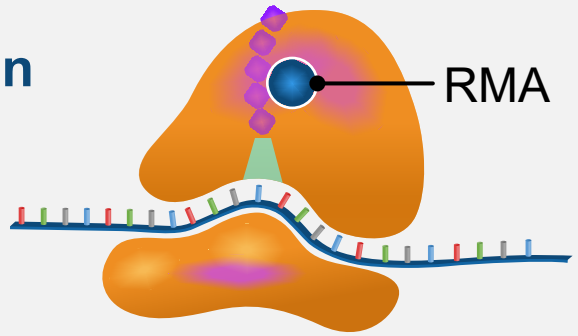
Readthrough = "Functional Gene Therapy"



Stop codon readthrough in rare diseases and cancer

- 10–12% of patients across **>1800 rare diseases**
- **6–10% of cancer patients** have nonsense mutations in **tumor suppressor genes**
- **20–30% of neoantigens in cancer patients** have nonsense mutations

Protein Translation Inhibition



Onco- and mitoribosomal cancers:

- Myc amplified lymphomas – (e.g., MALT, Burkitt, DLBCL)
- Hereditary Ribosomopathies
- HPV associated cancers (Head & Neck, Cervical)
- Triple Negative Breast, KRAS mutated Pancreatic Cancer, etc.

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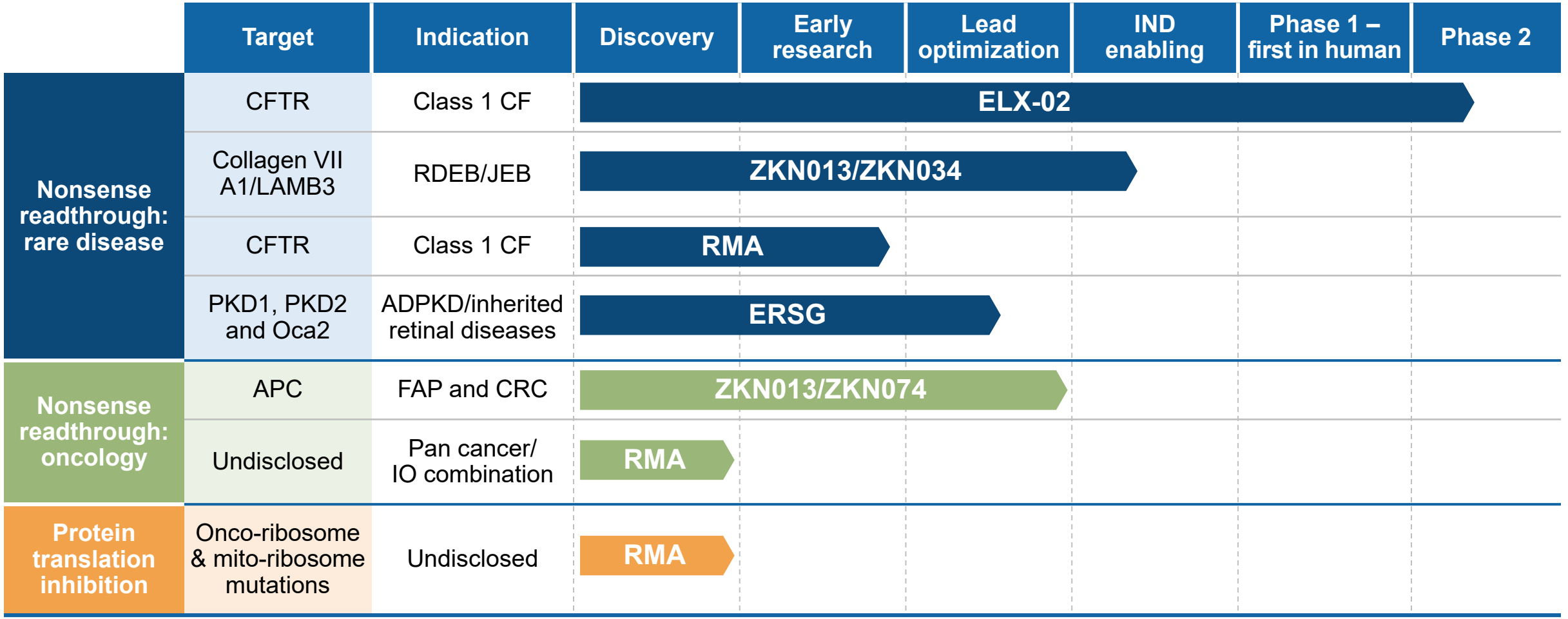
Deep pipeline of synergistic potential first-in-class therapies



***Class 1 CF:** Cystic fibrosis patients with class1 mutations; **ADPKD:** Autosomal dominant polycystic kidney disease; **FAP:** Familial adenomatous polyposis; **CRC:** Colorectal cancer

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ELX-02 (Clinical) and ERSG Preclinical programs

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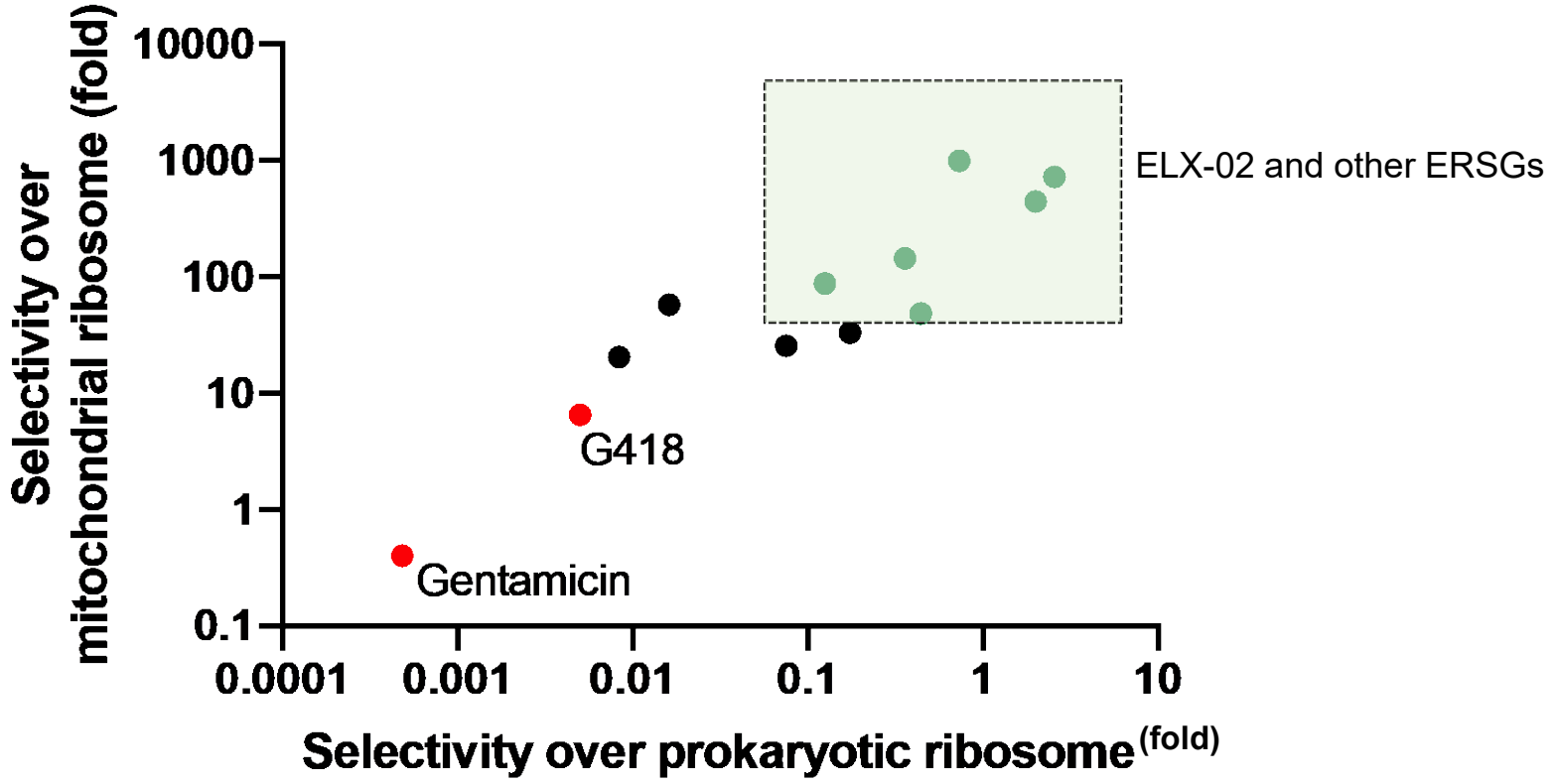
ERSGs like ELX-02 designed to expand human ribosome selectivity and therapeutic index over aminoglycosides

Eukaryotic ribosome selectivity comparison



Data adapted from: J Med Chem. 2012 Dec 13;55(23):10630-43.

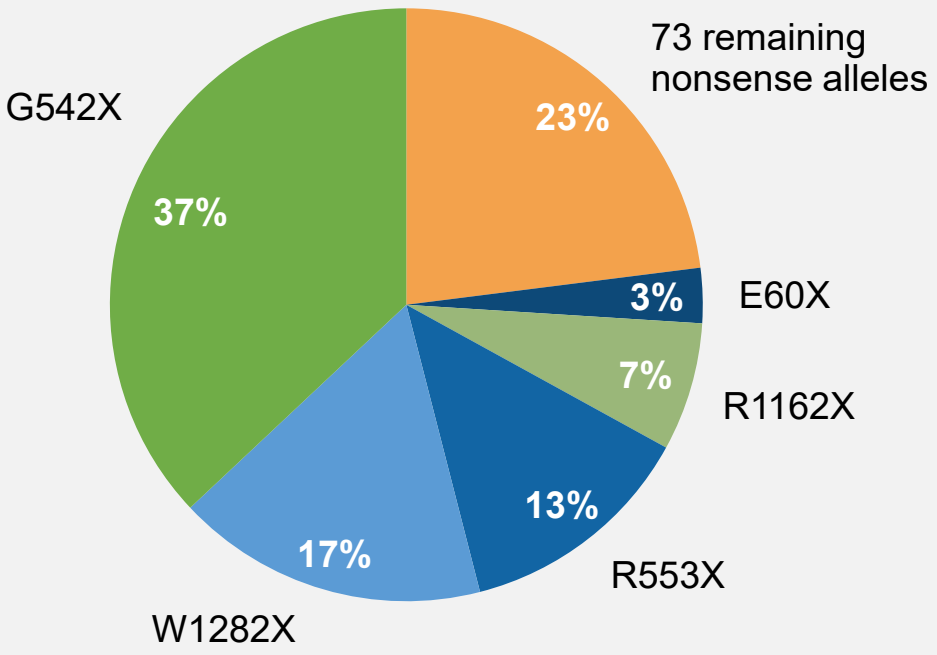
Eloxx PHARMACEUTICALS

Clinical validation for gentamicin supports ELX-02 use in treating Class 1 Cystic Fibrosis nonsense mutation patients

Class 1 CF opportunity and clinical rationale

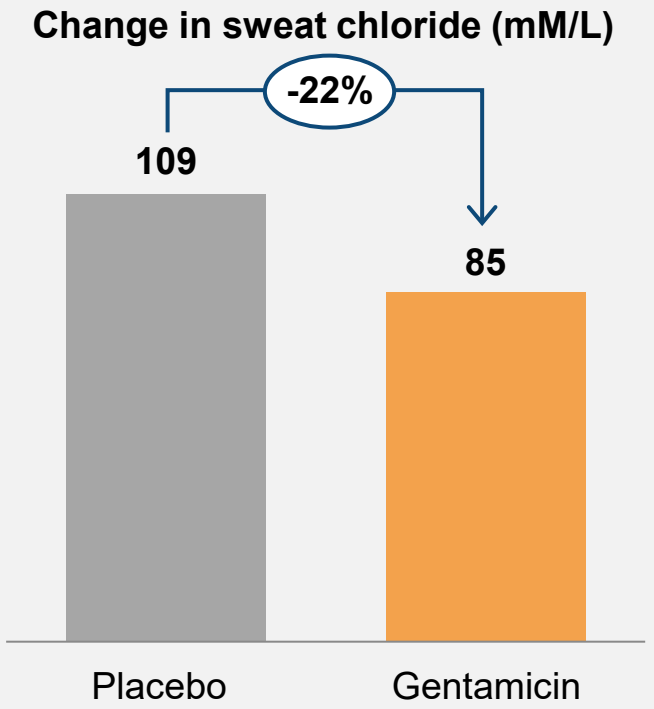
N=12% of all CF patients[1]

Nonsense allele frequency of global CF patient population



Class 1 CF

Gentamicin treatment 9 patients
(10 mg/kg iv, qd for 15 days)[2]



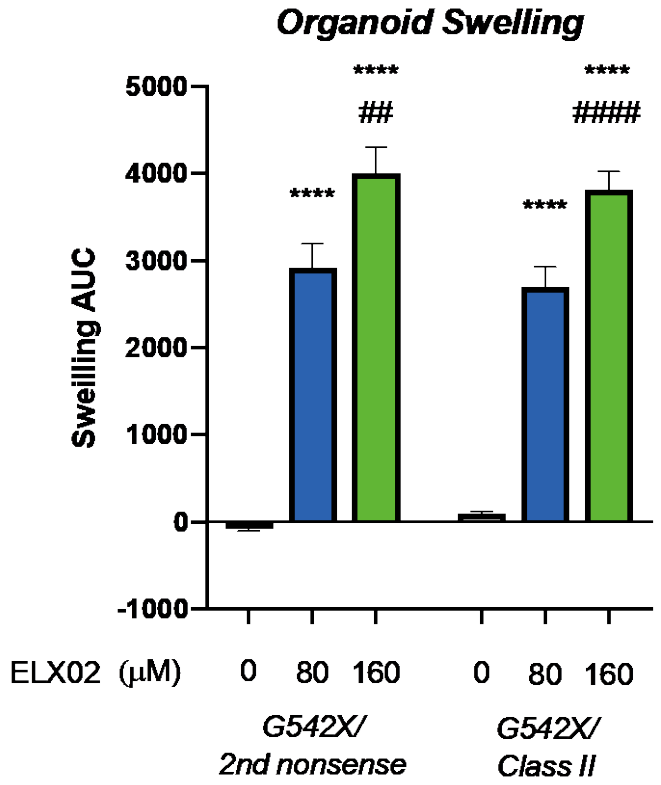
No currently approved drugs to treat CFTR nonsense mutations

[1] Allelic frequency based on CFTR2 database (July 2020); CF population data based on 2019 Patient Registry Report.
[2] Sermet-Gaudelus, I. BMC Med. 2007 Mar 29;5:5

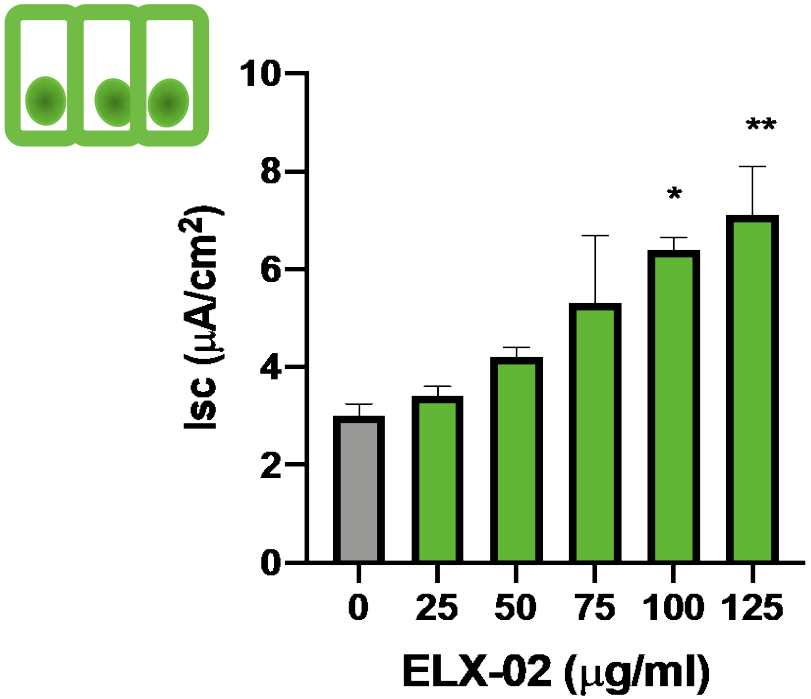
Eloxx PHARMACEUTICALS

High ELX-02 efficacy in organoid swelling and Ussing chamber experiments

Swelling response in G542X CF patient organoids[1]



Ussing chamber results heterozygous G542X/Fdel508 HBE cells



*p<0.05, **p<0.01
HBE cells were incubated for 2 days with ELX-02

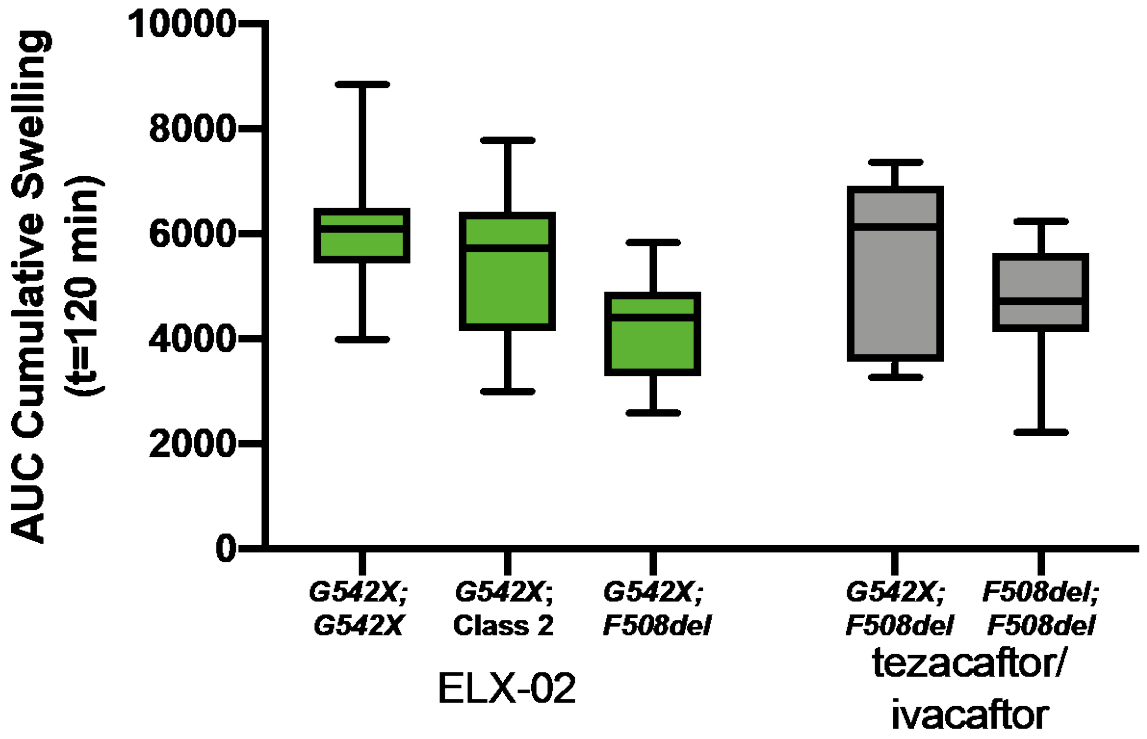
[1]Ordinary one-way ANOVA with Tukey's multiple comparison testing was used; **** p<0.0001 versus vehicle control, ## p<0.01 versus next lower concentration, #### p<0.0001 versus next lower concentration. Data represent >40 biological replicates per group from 2 or 4 independent patient organoids, respectively.

Eloxx PHARMACEUTICALS

Swelling response in Class 1 CF organoids with ELX-02 compares favorably with Symdeko in Class 2 organoids

Swelling response in Class 1 and Class 2 CF patient organoids when treated with ELX-02 vs. Symdeko

Organoid swelling (0.8 µM forskolin)



ClinicalTrials.gov Identifier: US Trial NCT04135495, EU/IL Trial NCT04126473

* From baseline to Day 7 of treatment periods 1-3, and Days 7 and 14 of treatment period 4

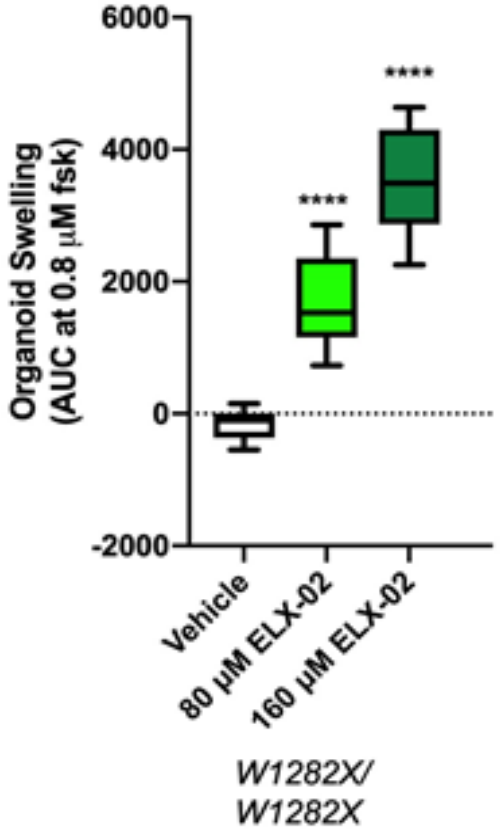
** Lancet Respir Med. 2014 Jul;2(7):527-38., *N Engl J Med*. 2010 Nov 18; 363(21): 1991–2003.

Eloxx PHARMACEUTICALS

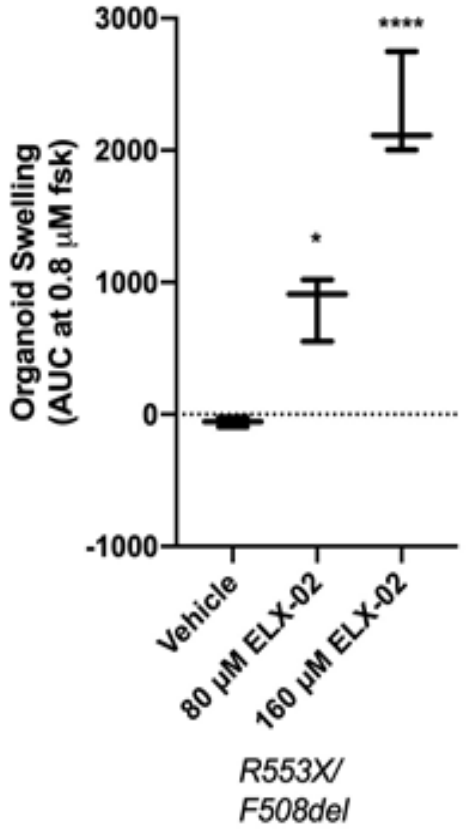
ELX-02 efficacy seen across CFTR nonsense mutations

Swelling response in CF patient organoids

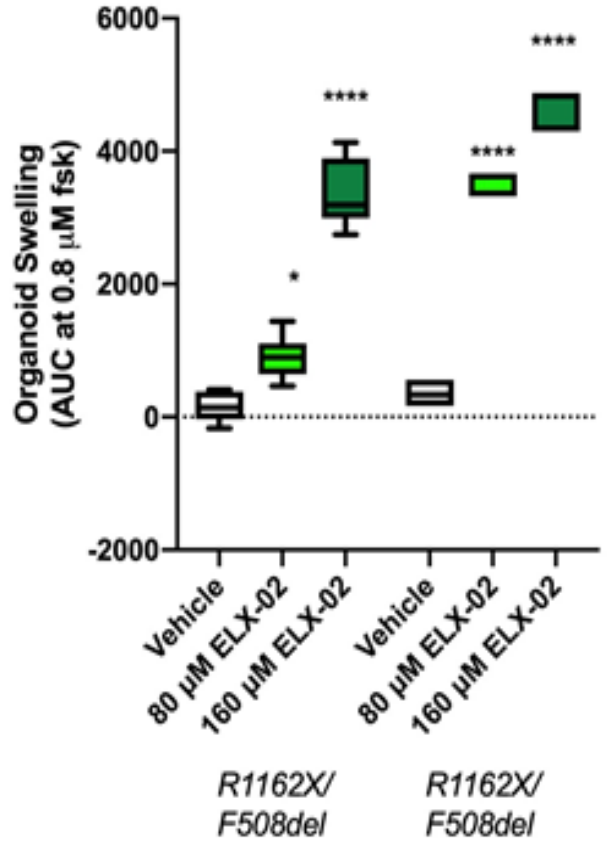
W1282X response example



R553X response example



R1162X response example



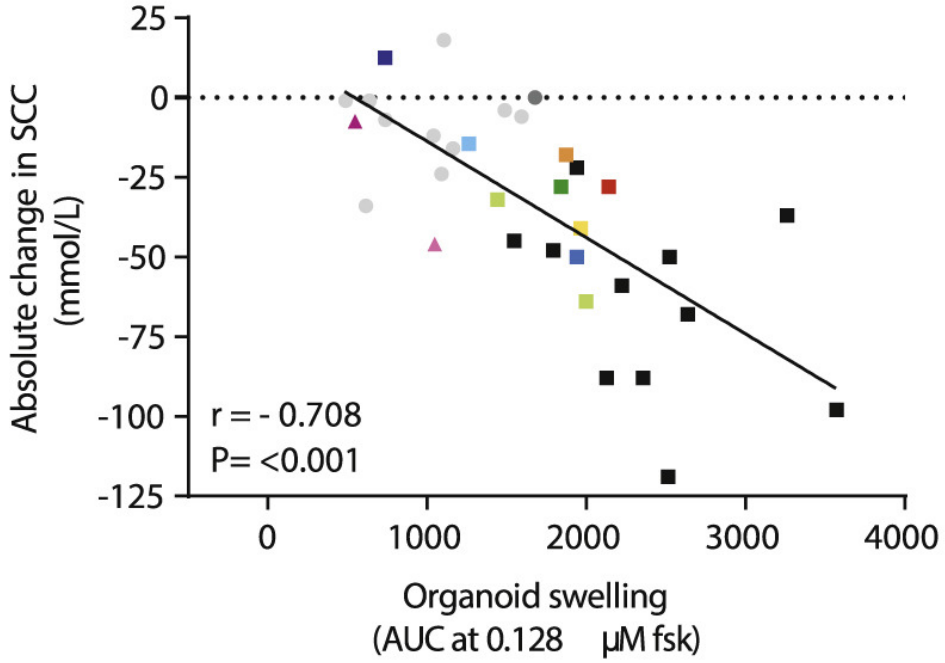
Eloxx PHARMACEUTICALS

Swelling in CF patient organoids treated with Kalydeco / Orkambi correlates with sweat chloride and FEV_1 changes

CF patient organoid swelling response to Kalydeco and Orkambi

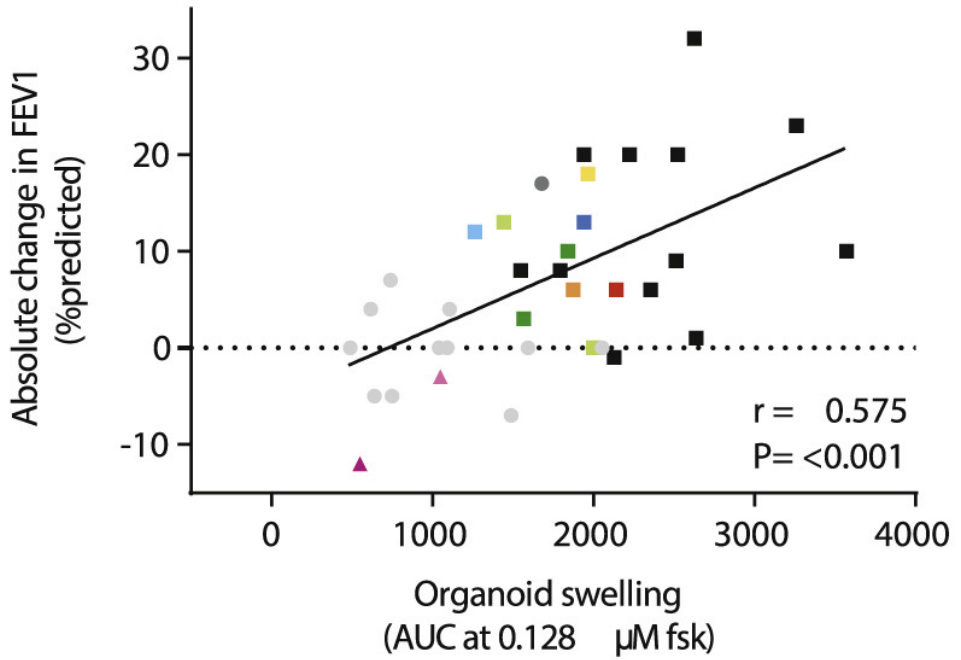
Organoid swelling vs. sweat chloride change

Organoids vs. SCC (n=33)



Organoid swelling vs. FEV_1 change

Organoids vs. FEV_1 (n=35)



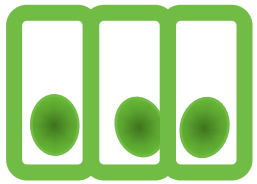
Cell Rep. 2019 Feb 12;26(7):1701-1708.e3.

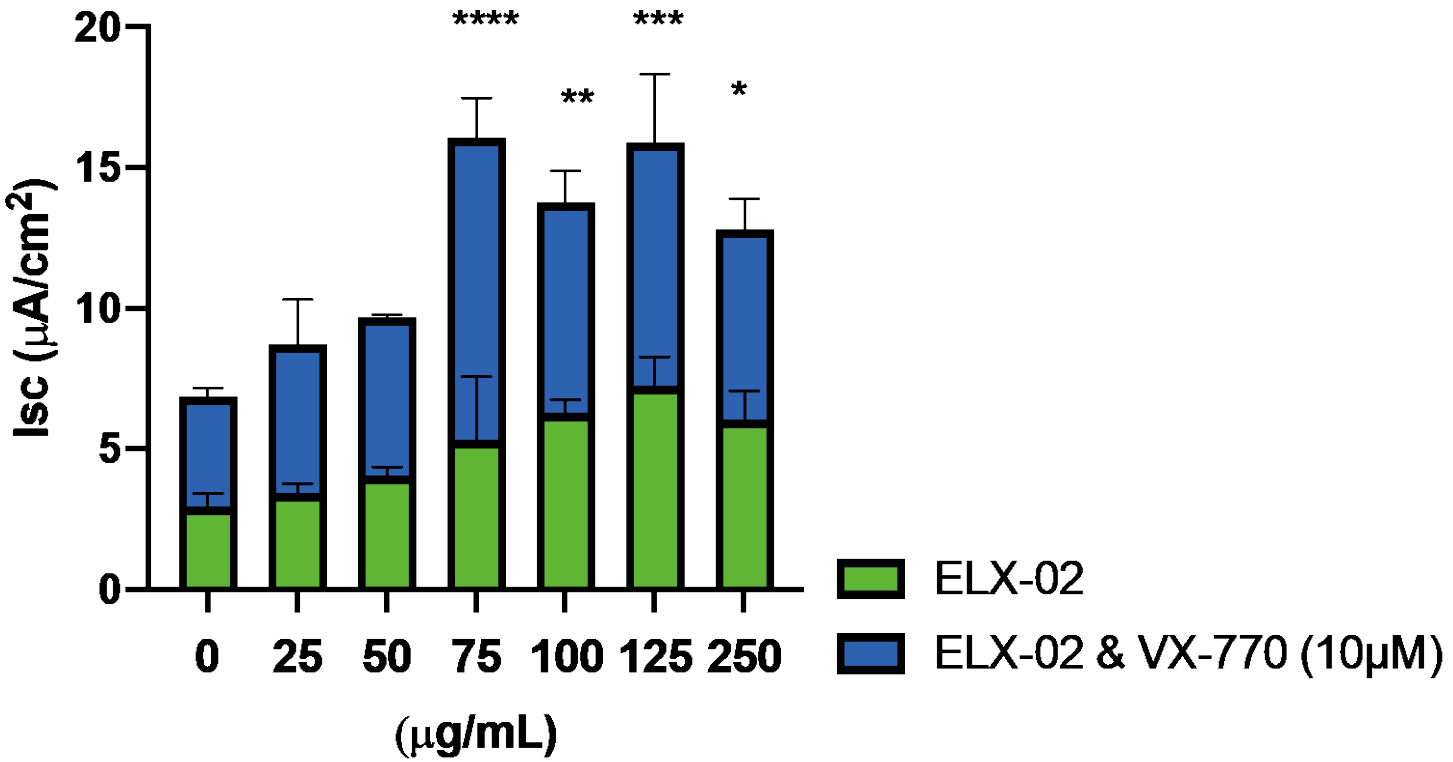
Eloxx PHARMACEUTICALS

ELX-02 shows synergy with Kalydeco (VX770- a potentiator)

Ussing Chamber experiment: Treatment of Het G542X HBE cells

G542X/F508del





Eloxx PHARMACEUTICALS

ELX-02 well tolerated in Phase 1 and 2 clinical studies

>100 subjects exposed to ELX-02 to date and generally WELL TOLERATED

PHASE 1: Healthy volunteers and subjects with various severities of renal dysfunction

- Single and Multiple ascending doses studied from 0.3 to 7.5 mg/kg. **Generally well tolerated**
- No dose limiting toxicities, SAEs or off target effects
  - No nephrotoxicity or vestibular toxicity
- Most common AE was mild injection site reaction
- 5 transient and reversible cases of high frequency audiometry shift
- Highly reproducible PK over the dose range studied

PHASE 2: Nephropathic cystinosis with homozygous CTNS W138X who previously received kidney transplant

- **Generally well tolerated:** No treatment-related serious adverse events, nephrotoxicity, or ototoxicity
- Mild injection site reactions reported
- No meaningful changes in eGFR or serum creatinine
  - Consistent with preservation of kidney function
- Pharmacokinetics consistent with previous studies in healthy volunteers
- **Safety Review Committee approval to enroll patients ages 12 years and older**

Data presented at scientific meetings in 2019 and published in peer reviewed journals in 2021

Phase I trial records: NCT03776539, NCT03309605, NCT03292302,
Phase II trial record: NCT04069260

Eloxx PHARMACEUTICALS

ELX-02 Phase 2 cystic fibrosis trial designed to evaluate safety and short term sweat chloride reduction

ELX-02 Phase 2 program principally designed for safety and dose finding in CF patients, with sweat chloride as PD biomarker

Population
- Up to 24 CF patients with a *G542X* mutation on one or both alleles

Primary outcome measures
- Safety, tolerability, and pharmacokinetics

Secondary outcome measures
- Change from baseline in sweat chloride concentration*
- Change from baseline in percent predicted forced expiratory volume (ppFEV1)*

Locations
- Europe, Israel & USA, opening additional sites in Canada and Australia

Safety Review Committee has allowed dose escalation up to top dose with no drug-related serious adverse events reported to date

DESIGN: Intra-patient dose escalation through 4 increasing doses of ELX-02

Dose 1
0.3 mg/kg
SC QD for 7 days

Dose 2
0.75 mg/kg
SC QD for 7 days

Dose 3
1.5 mg/kg
SC QD for 7 days

Dose 4 (individualized)
Up to 3 mg/kg
SC QD for 14 days

ClinicalTrials.gov Identifier: US Trial NCT04135495, EU/IL Trial NCT04126473

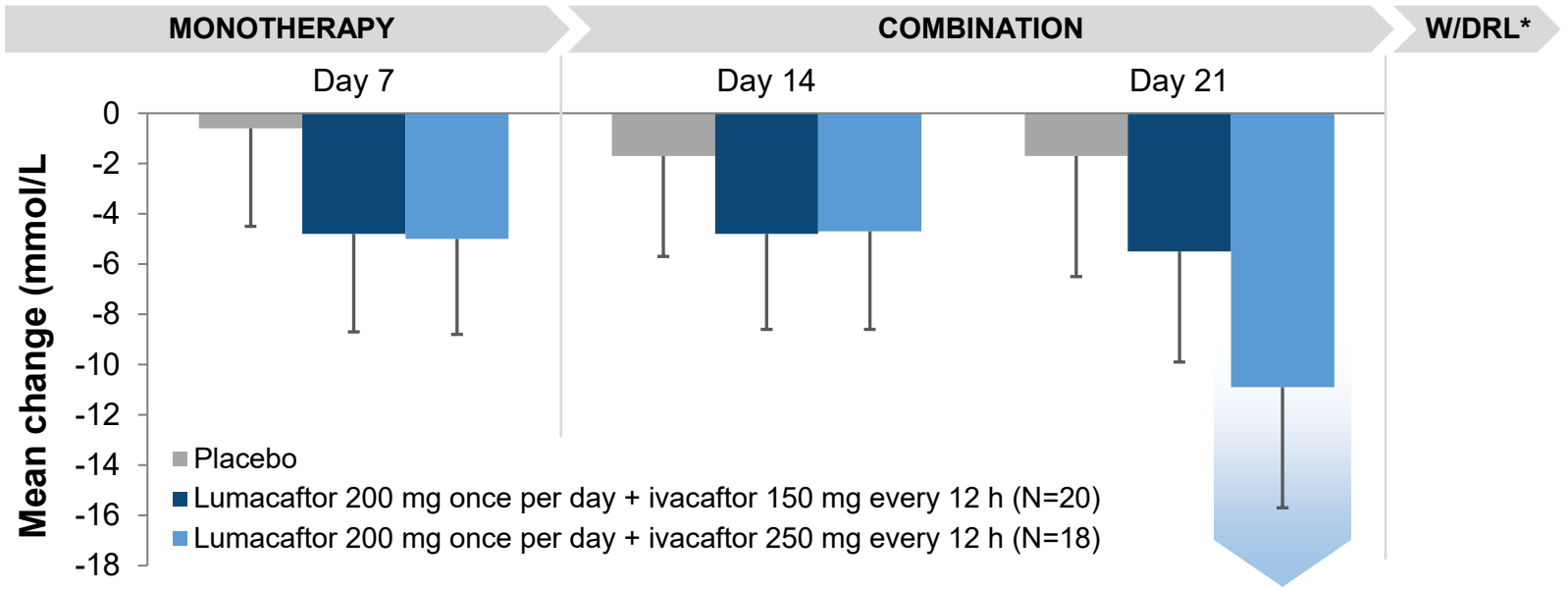
* From baseline to Day 7 of treatment periods 1-3, and Days 7 and 14 of treatment period 4

Eloxx PHARMACEUTICALS

ORKAMBI confirmed sweat chloride reduction, but no FEV_1 change in similar small P2 safety trial

Orkambi Ph 2 (Cohort 1) trial – Changes in sweat chloride

Treatment in homozygous delta F508 CF patients



Sweat chloride change at day 21 is decreased (–10·9 mmol/L) for high dose group

FEV_1 – Ph2

FEV_1 improvement is not significant for any dose group in small short trial

FEV_1 – Ph3

Larger and longer ORKAMBI Ph3 trial showed +2.6% FEV_1 change leading to its approval

P2 trials for Kalydeco and Orkambi found changes in sweat chloride to be less variable in small studies than FEV_1/ppFEV_1, which were not significant in many cohorts

* **W/DRL** = Withdrawal period

Lancet Respir Med. 2014 Jul;2(7):527-38.

Eloxx PHARMACEUTICALS

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, with no serious adverse events in over 100 subjects exposed to ELX-02 to date
- Consistent pharmacokinetics across both single and multiple-dose accumulations

Phase 2 CF trials designed for rapid clinical signal

- Study designed to confirm safety and biological activity via changes in sweat chloride
- Funding provided by Cystic Fibrosis Foundation (CFF), sanctioned by CFF-TDN & ECFS-CTN (high priority ranking)

CYSTIC FIBROSIS FOUNDATION
ADDING TOMORROWS

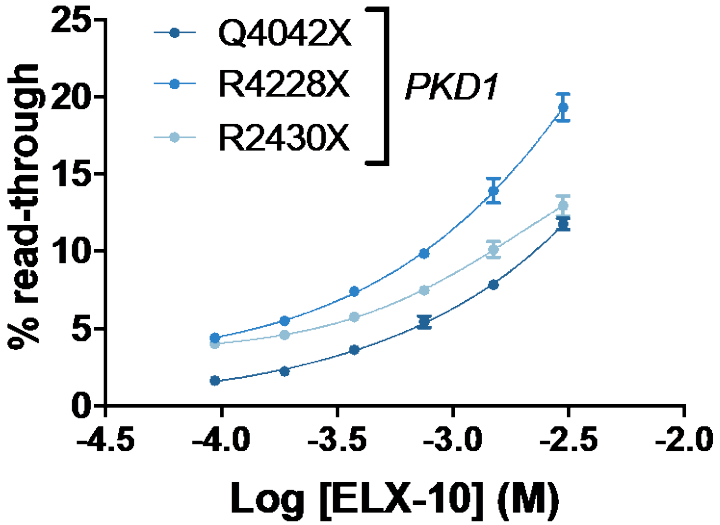
- **Expect to complete enrollment in Phase 2 clinical trials by midyear and report data in 2H 2021**
- **Orphan drug designation for the treatment of CF**

Eloxx PHARMACEUTICALS

Readthrough shown in preclinical models with other ERSG's in rare kidney and ocular diseases

Polycystic Kidney Disease (ADPKD)

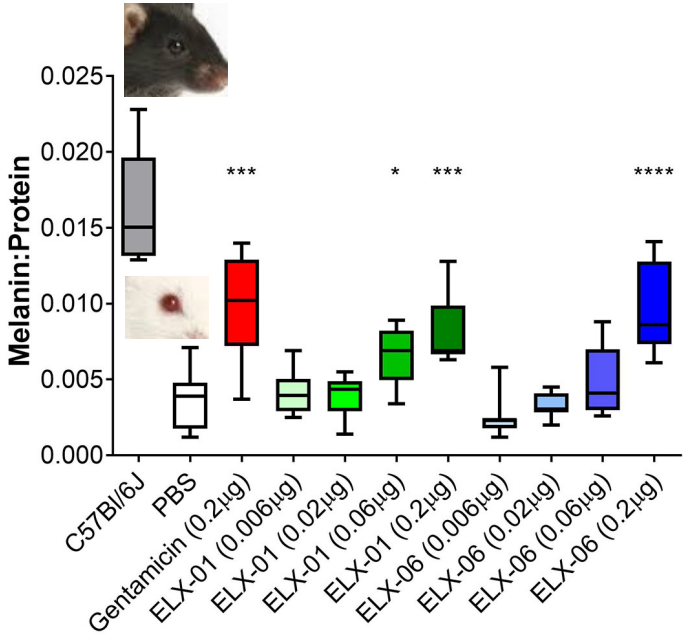
Readthrough in nonsense mutations in PKD1 gene with ELX-10 in dual luciferase assay



- Mutations in PKD1 or PKD2 lead to cyst growth
- **Affects 6–10% of patients on dialysis** and renal transplant in the US

Inherited Retinal Diseases (IRDs)

Single dose study in SJL/J mouse with R262X mutation in OCA2 gene 1



- Usher syndrome and Retinitis Pigmentosa are most common diseases
- **Approx. 2000 patients in the US**

TURBO-ZM™

Eloxx PHARMACEUTICALS

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

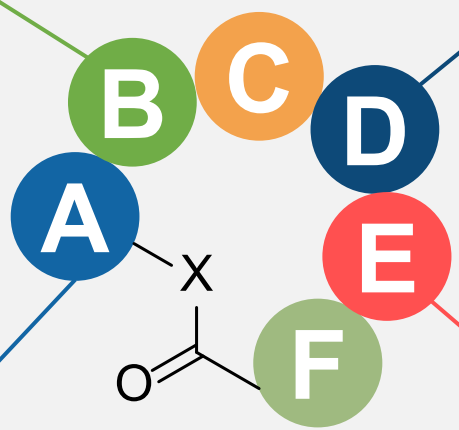
TURBO-ZM™: Applying macrolide SAR to RMA design

TURBO-ZM

Optimize for:
- Readthrough
- Protein translation inhibition

Interact with the peptide sequence

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



Essential for ribosomal binding

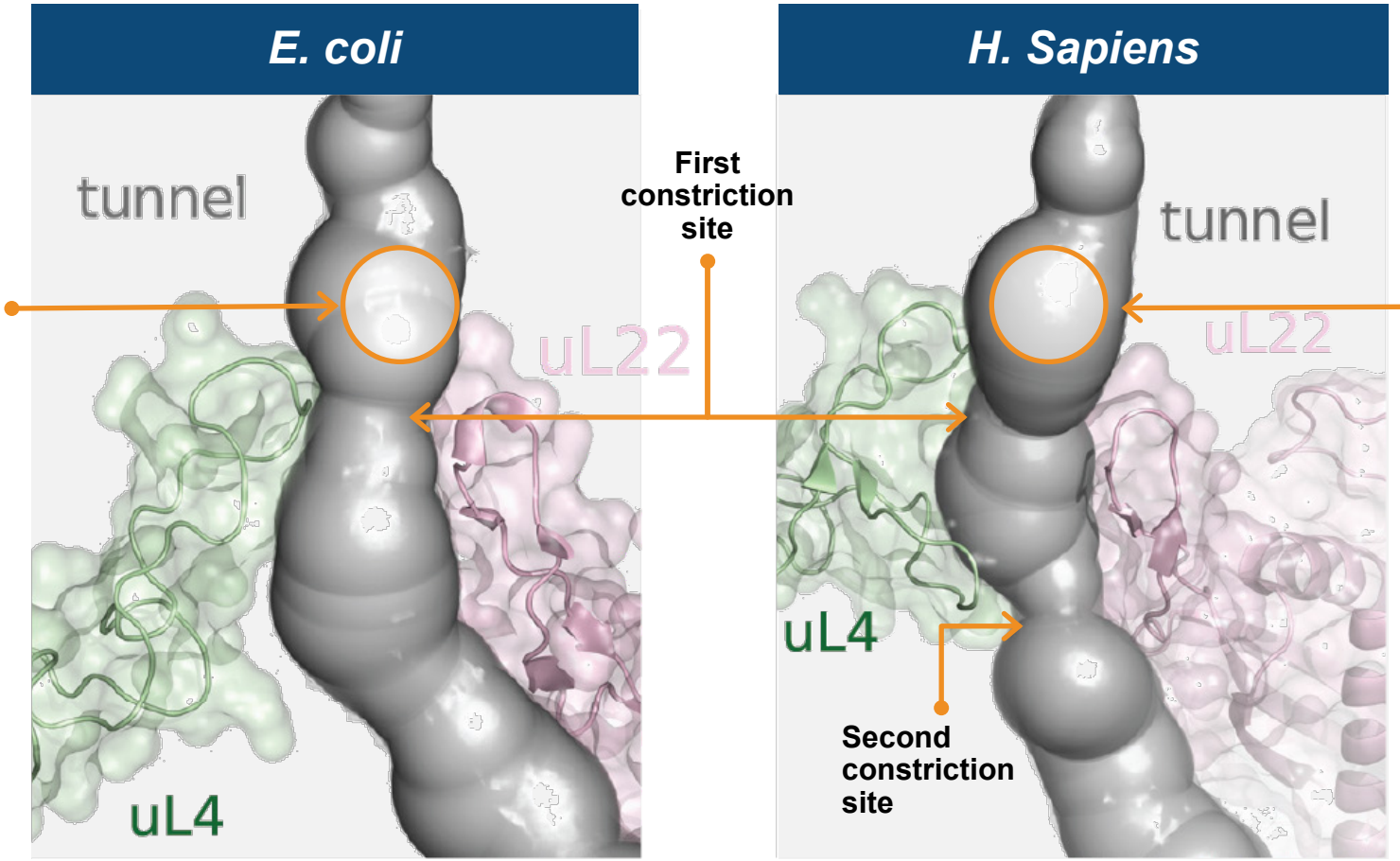
RMA core required for ribosomal binding

Modulate cytoplasm and mitochondrial ribosome binding activity

Eloxx PHARMACEUTICALS

Strong rationale for macrolides to bind to 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

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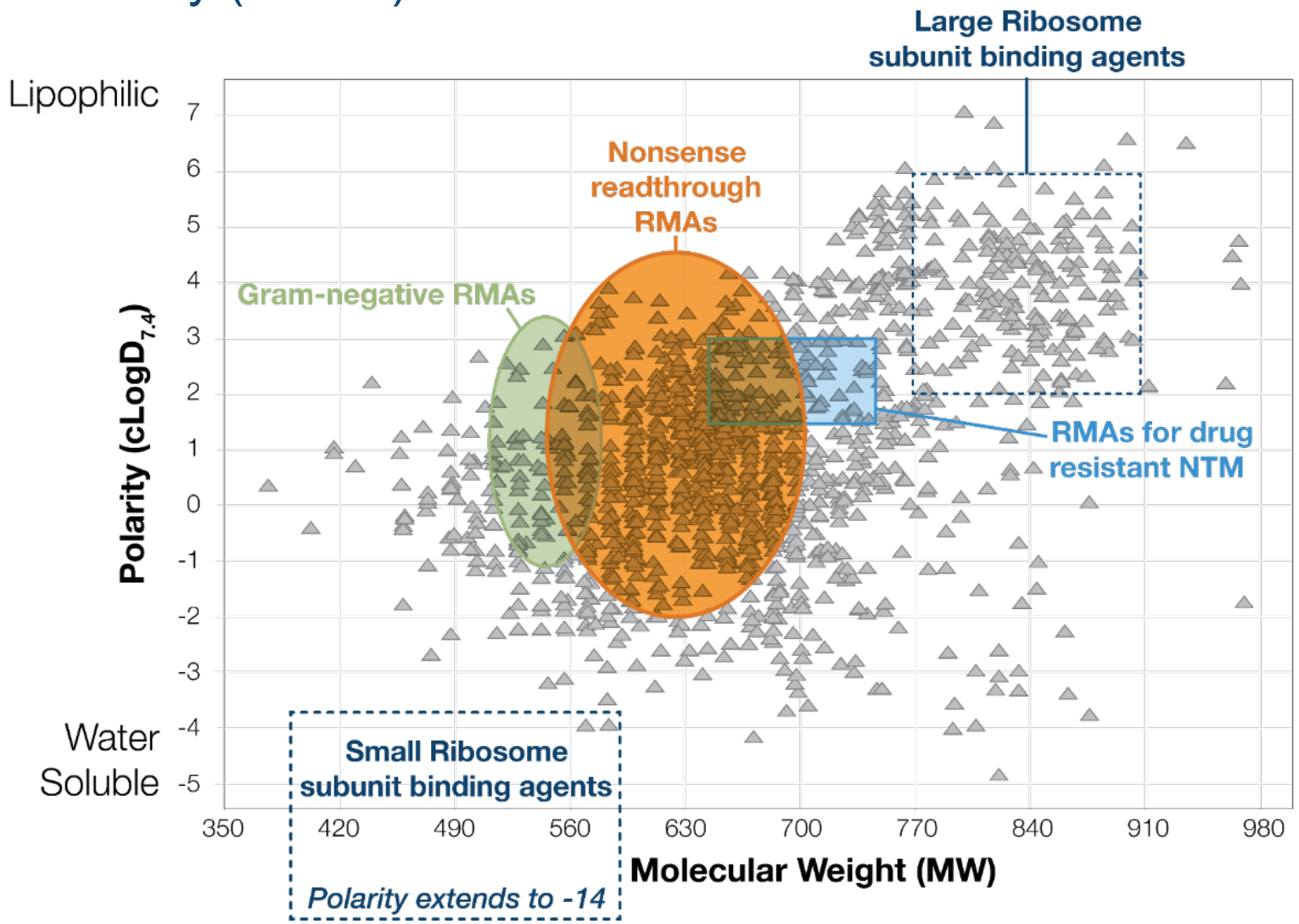
Growing library of RMAs with drug-like properties

Zikani RMA Library (2000+)



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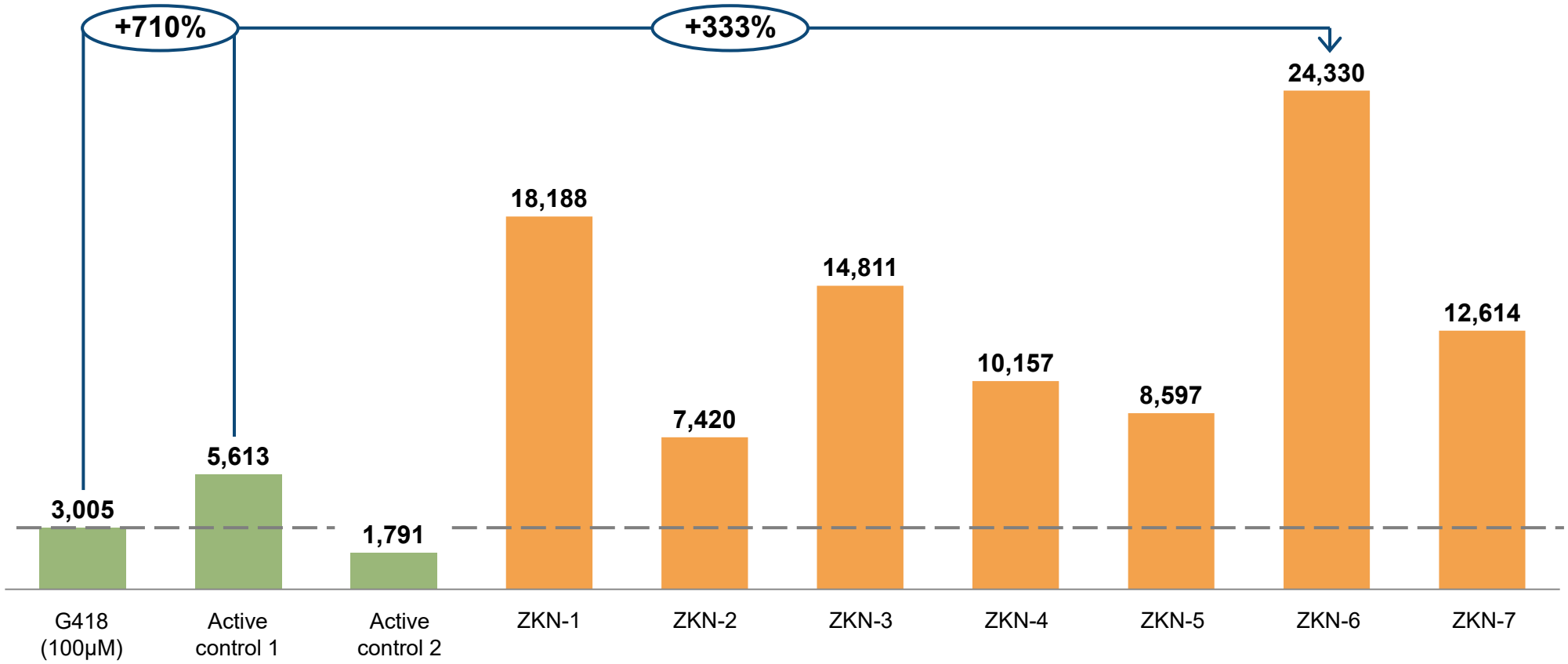
RMAs show superior readthrough to alternatives

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



RMA Preclinical programs: RDEB/JEB, CF and FAP

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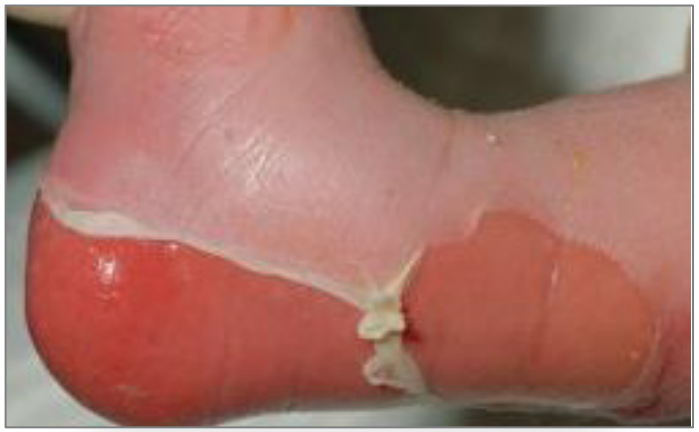
RDEB/JEB: Clinically validated path for RMAs in rare skin disease targeting patients with nonsense mutations

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

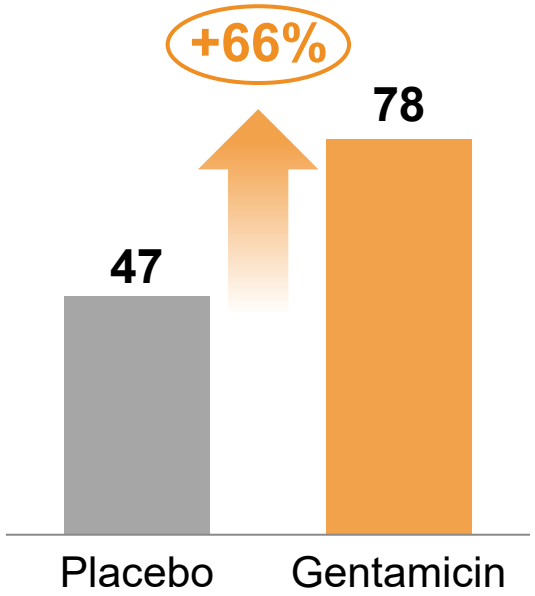
~4,000 patients, $1.5B TAM

RDEB

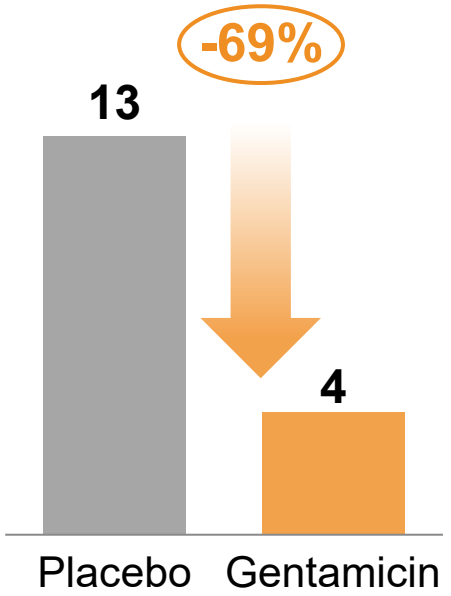
Gentamicin treatment of RDEB patients

(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; [2] Hammersen, Johanna et al. *Dermatology* May 2019

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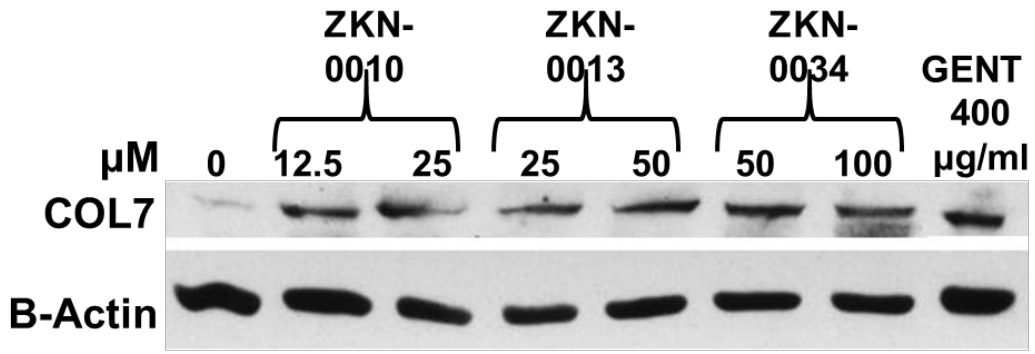
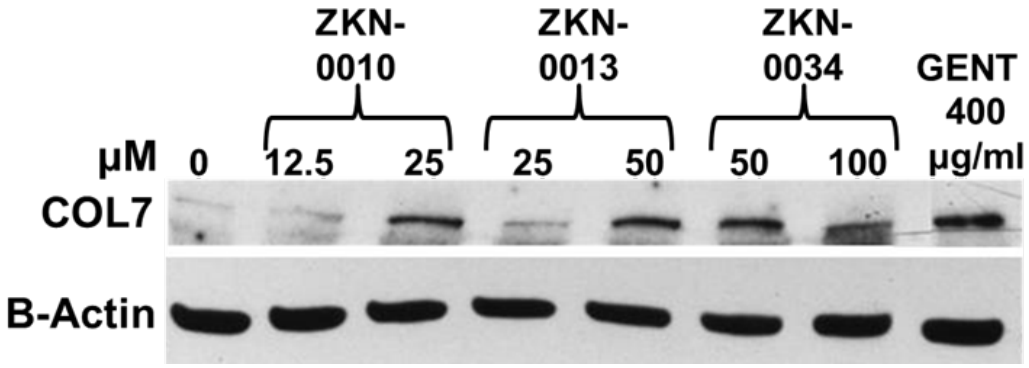
RDEB: RMAs restore functional collagen protein in primary patient cells comparable to high dose gentamicin

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

- ✔ **COL7 RESTORED in responders to Gentamicin**
- ✔ **30 to 60-day protein half-life**
- ✔ **RMAs 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.

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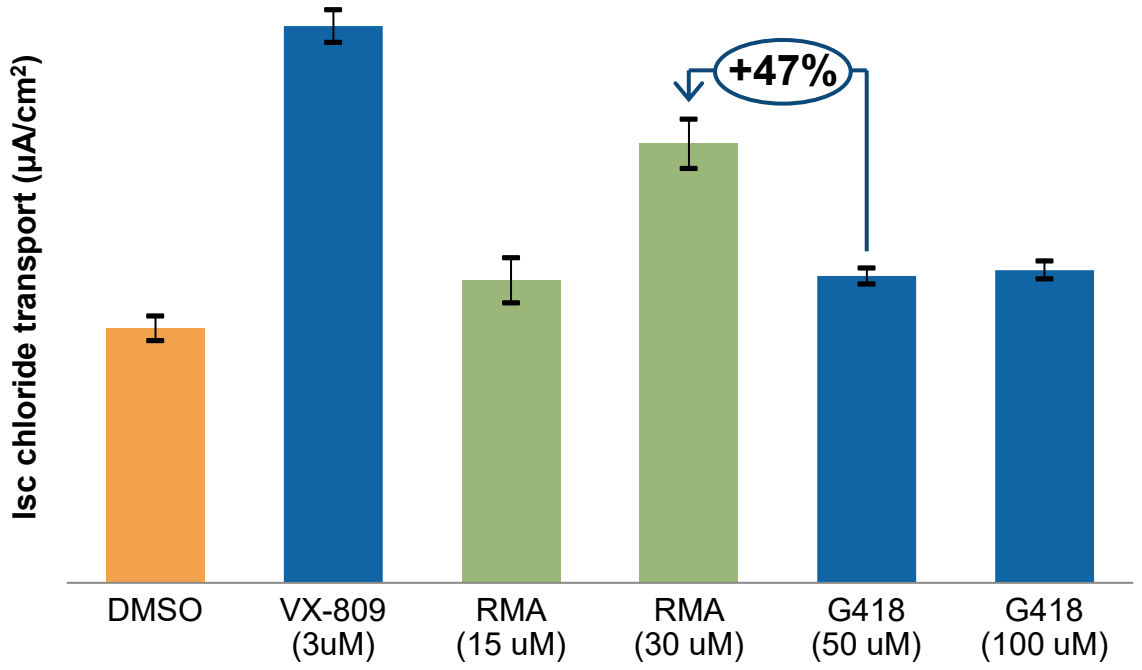
Class 1 CF: RMA lead showed highest ever readthrough preclinical Ussing chamber assay

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"*

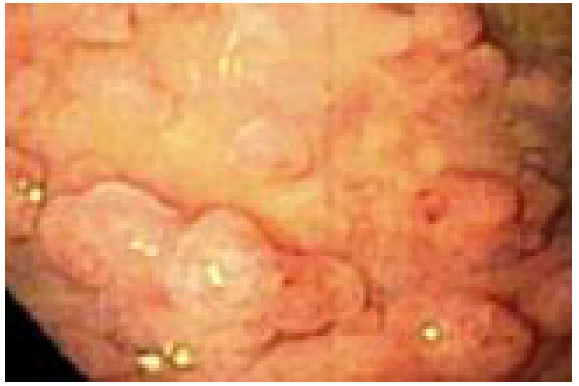
Submitted $2.5M grant to CF Foundation to support through development candidate

*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



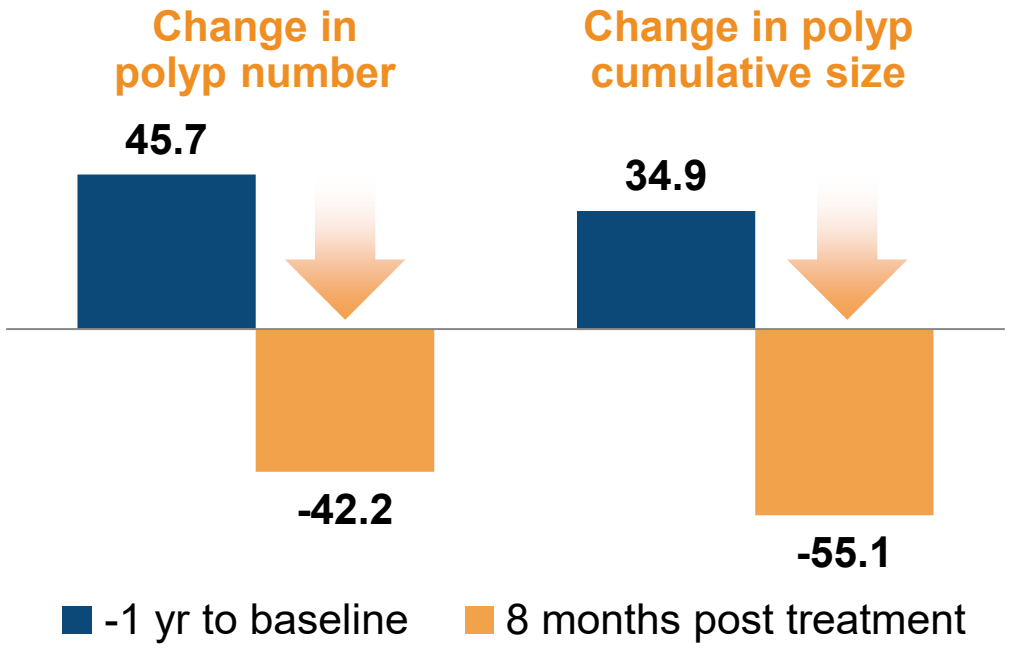
- Mutations in the Adenomatous Polyposis Coli (APC) gene (tumor suppressor gene)
- FAP patients develop CRC by age 40
- 80% of CRC patients have an APC mutation

8,000–12,500 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

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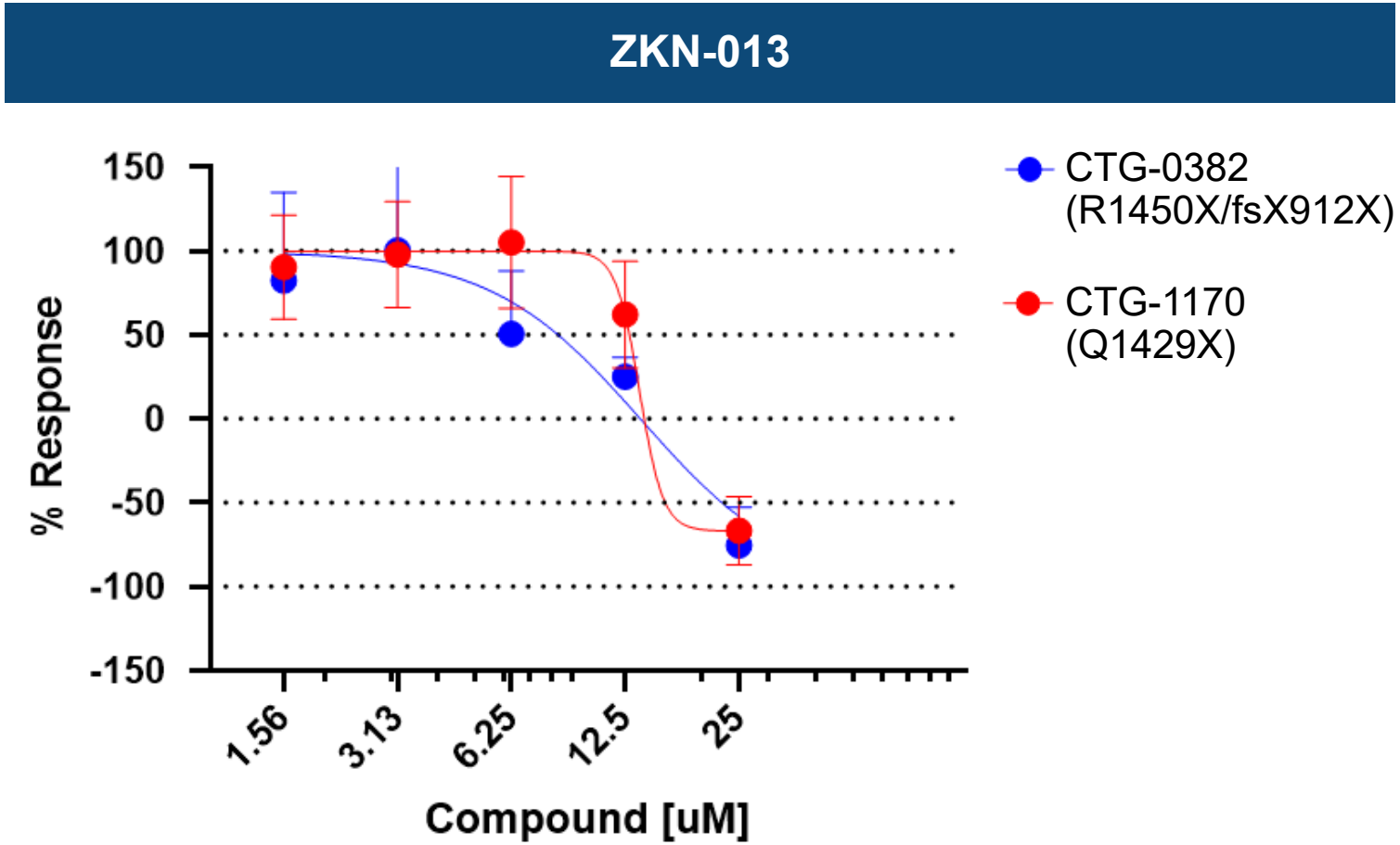
Clear path treating FAP supported by efficacy in APC mutant cancer patient tumor grafts

Efficacy of ZKN-013 in colorectal cancer patient derived tumor grafts ex-vivo

- Ex-vivo sensitivity assessment in tumor grafts
- Potent tumor growth inhibition
  - GI50<15uM
- Cancer xenograft studies planned in 2021



Positioned to be the world leader in ribosome targeted genetic therapies

Proprietary ribosome targeted small molecule platforms targeting rare diseases and oncology

Deep pipeline led by clinical stage program to treat class 1 nonsense mutations in Cystic Fibrosis

Expect to file first IND for first-in-class oral RDEB/JEB program expected in 2022; expect to file 1 IND per year after 2022

Right leadership, team, and advisors

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