RARE Thinking for RARE Solutions

Leader in Ribosome Targeted Genetic Therapies

November 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

Uniquely positioned to transform Eloxx and create significant value for shareholders

Right **new leadership** with a track record of success

Powerful technology **platforms to target the human ribosome**

Focused on **high unmet need** mutationally driven **rare diseases and cancers**

Programs with **existing clinical validation** that **derisk drug development**

Eloxx PHARMACEUTICALS

New Eloxx leadership team with track record of turnarounds

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. Ali Hariri
SVP & Chief Medical Officer

- Significant experience in rare disease product development
- Expertise across a range of therapeutic areas

SANOFI GENZYME
IONIS
Takeda

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

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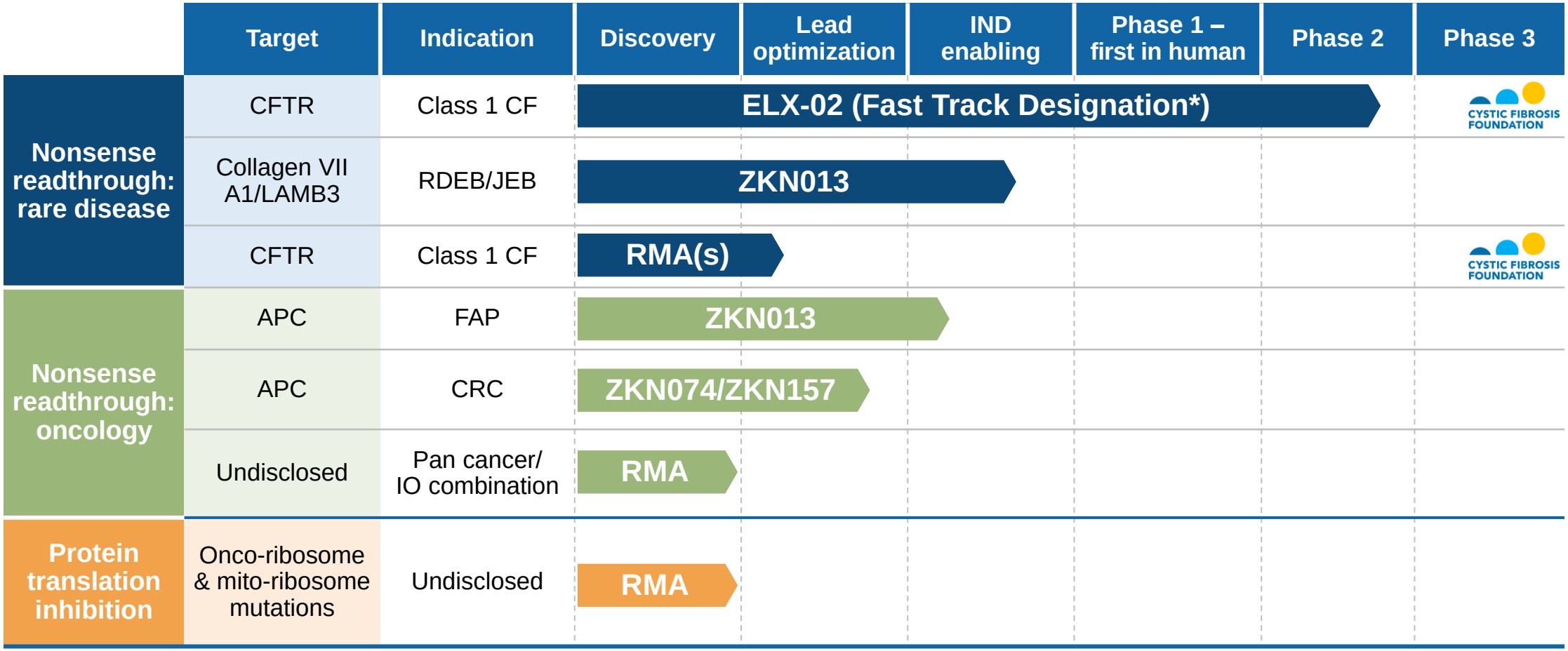
Deep pipeline of synergistic potential first-in-class therapies



***ELX-02 has received Fast Track Designation from the FDA for the treatment of CF patients with nonsense mutations**
Class 1 CF: Cystic fibrosis patients with class1 mutations; **RDEB/JEB:** Recessive Dystrophic/Junctional Epidermolysis Bullosa; **FAP**: Familial adenomatous polyposis; **CRC:** Colorectal cancer

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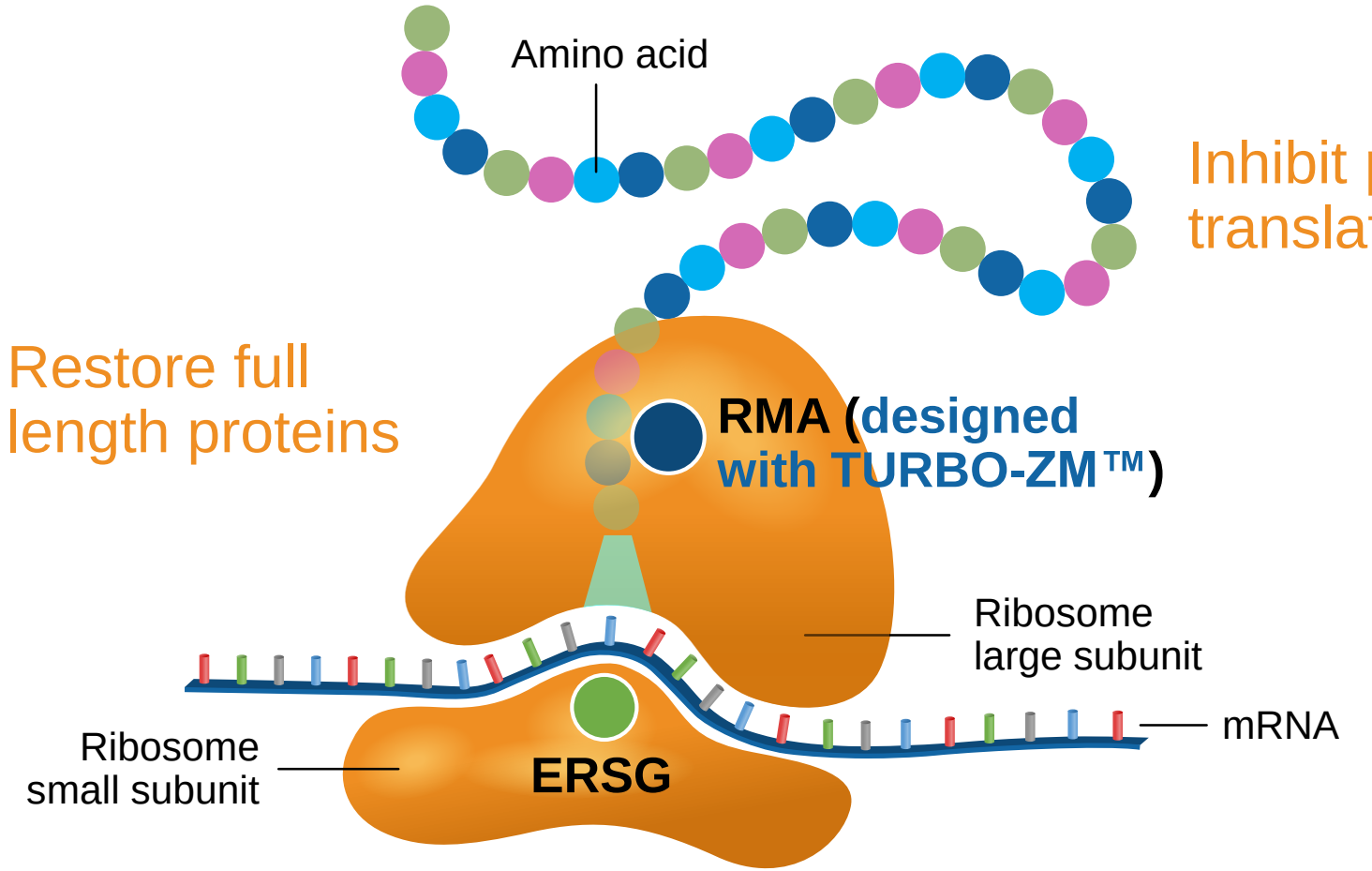
Two platform technologies uniquely positioned to correct protein translation defects

Ribosome = “protein factory”: Potential to correct mRNA and ribosomal mutations



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

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Strong evidence of readthrough activity with ribosome binding 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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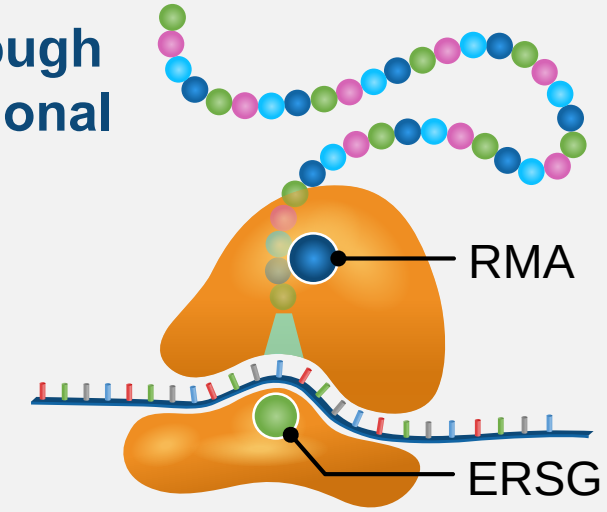
Large and broad potential applications for ribosome targeted genetic therapies

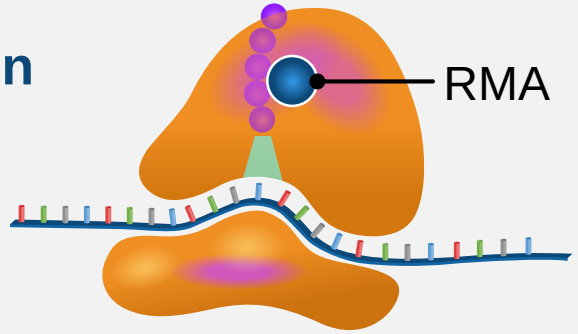
Readthrough = "Functional Gene Therapy"



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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Class 1 Cystic Fibrosis

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ELX-02 is a First in Class drug in Phase 2 development for Class I CF patients with nonsense mutations

- ELX-02 designed as **superior readthrough** agent to Gentamicin
- **Compelling preclinical activity** observed in highly translatable models
- Ongoing **Phase 2 monotherapy** to **evaluate** safety and **biological activity** expected to **readout in Q4 2021**

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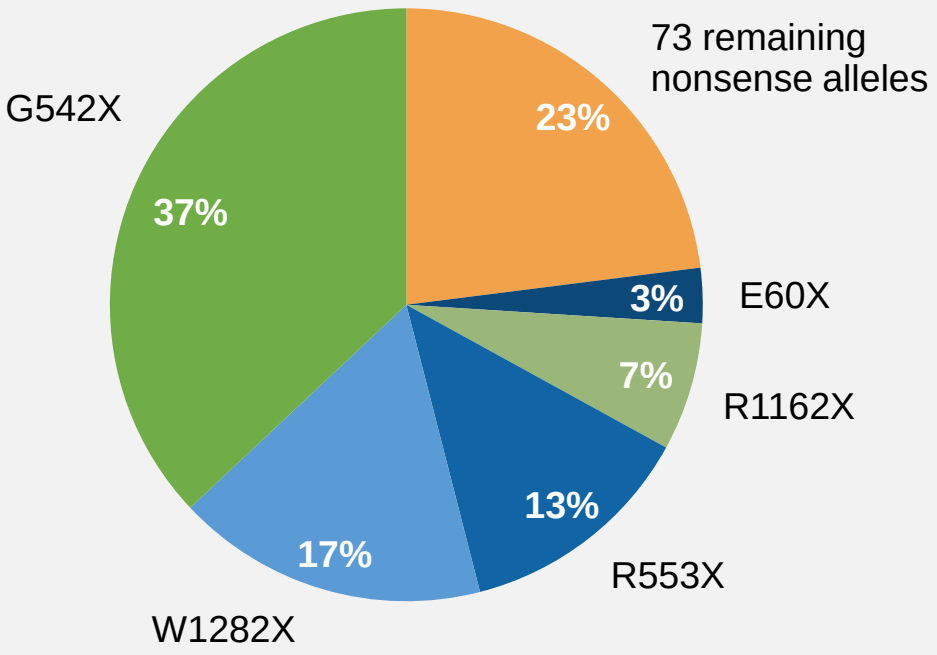
Development of ELX-02 in high unmet need Class 1 Cystic Fibrosis supported by gentamicin clinical results

Class 1 CF (patients with nonsense mutations) opportunity and clinical rationale

N=12% of all CF patients[1], $1.5-3B TAM

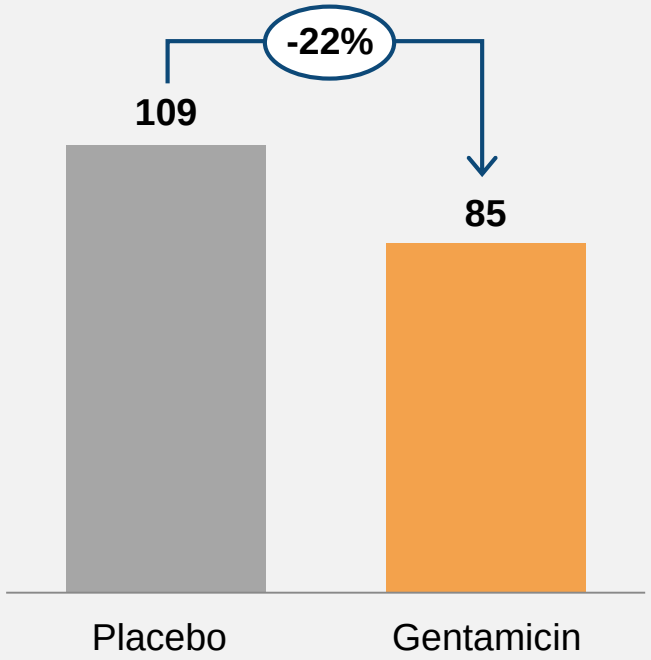
Nonsense allele frequency of global CF patient population



Class 1 CF

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

Change in sweat chloride (mM/L)



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

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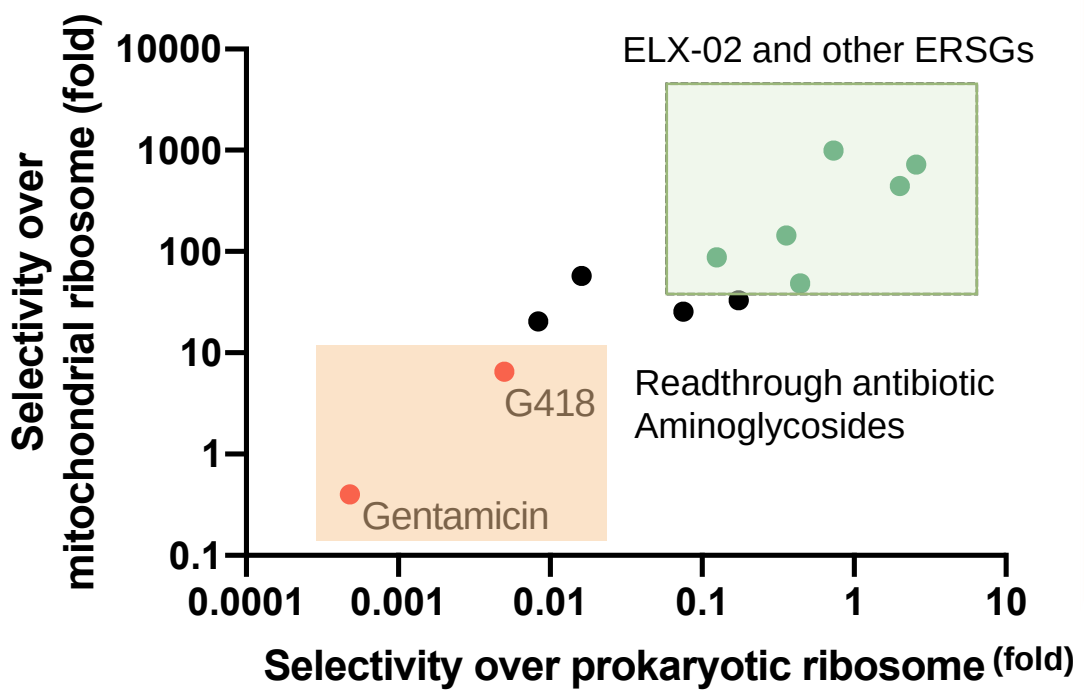
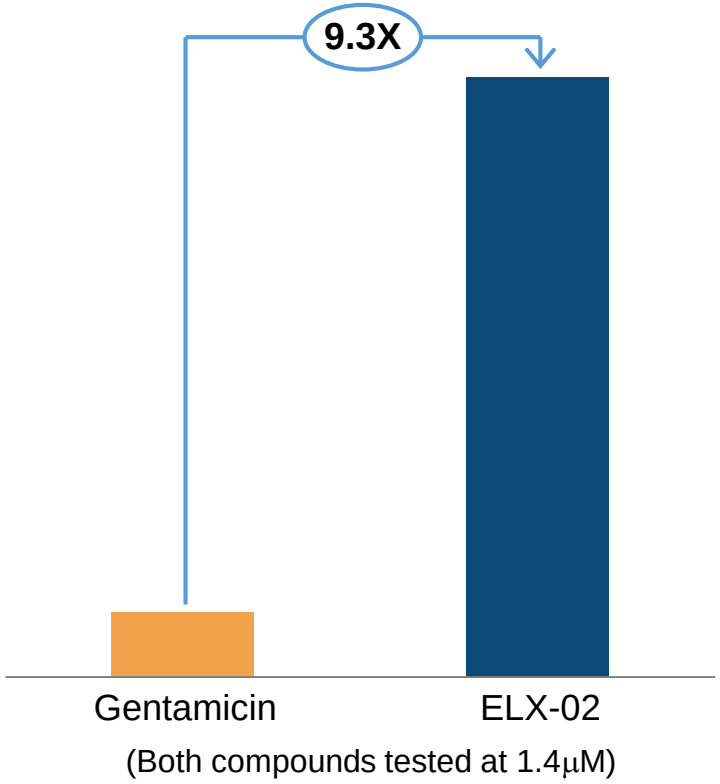
ELX-02 –Improved efficacy and decreased mitochondrial toxicity versus gentamicin

Eukaryotic ribosome selectivity comparison[1]



CFTR G542X Readthrough activity (dual luciferase reporter assay)[1]



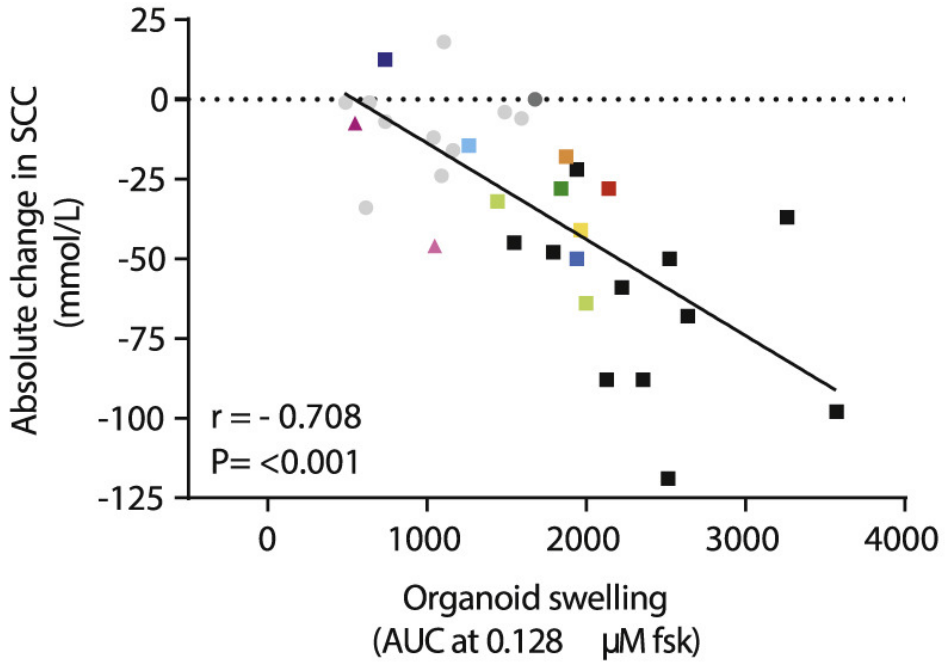
[1]Data adapted from: *J Med Chem*. 2012 Dec 13;55(23):10630-43.1;

ELX-02 activity tested in clinically validated CF patient organoid swelling assays

CF patient organoid swelling observed in response to Kalydeco and Orkambi

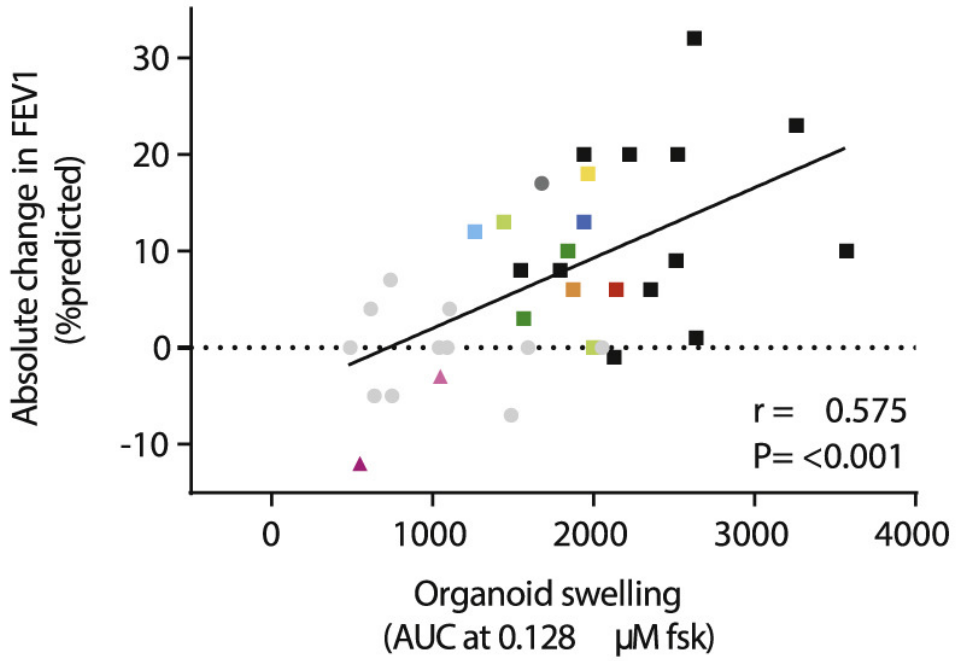
Organoid swelling vs. sweat chloride change

Organoids vs. SCC (n=33)



Organoid swelling vs. FEV_1 change

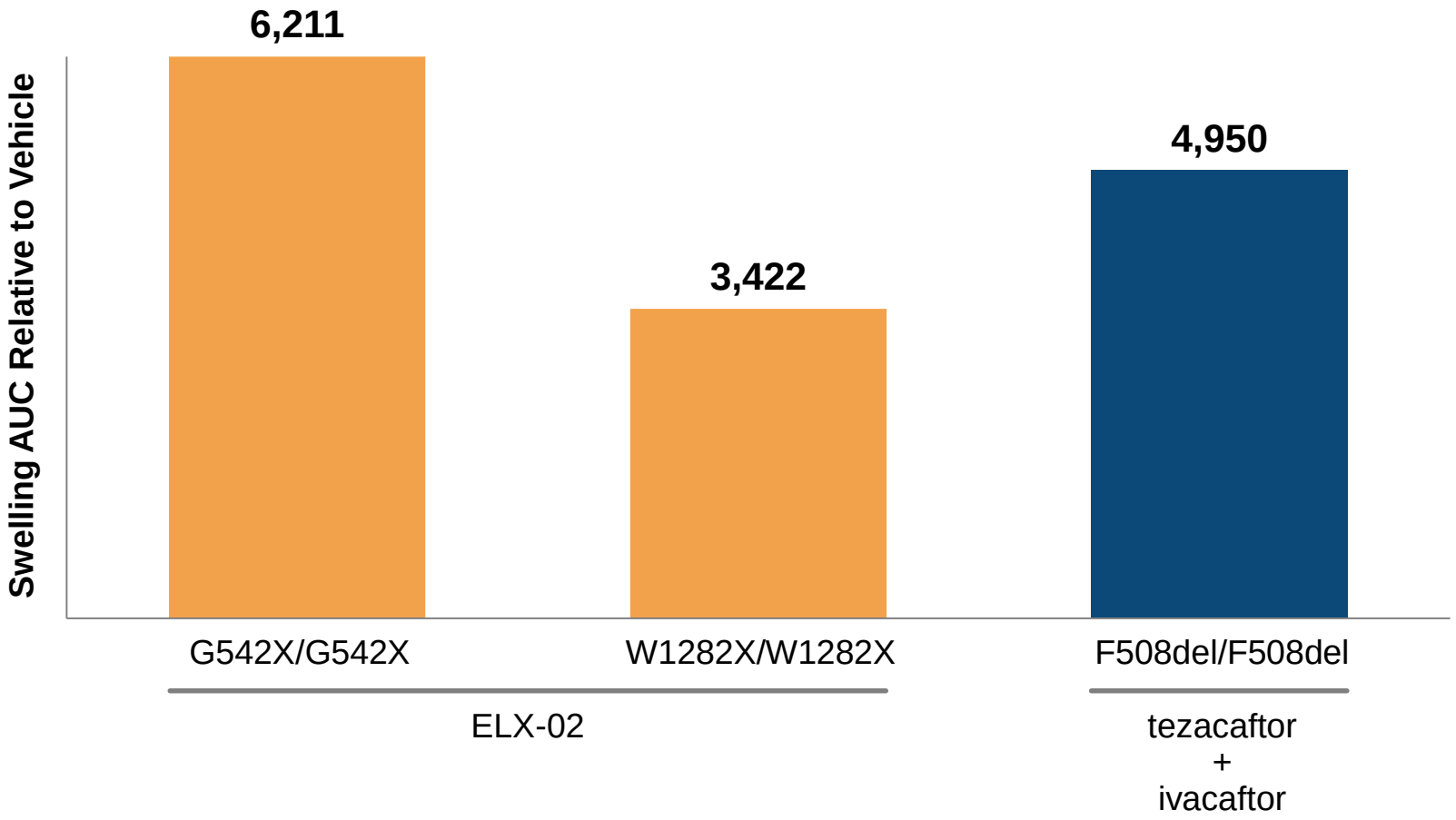
Organoids vs. FEV_1 (n=35)



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

ELX-02 swelling response in Class 1 CF organoids comparable to Symdeko in Class 2 organoids

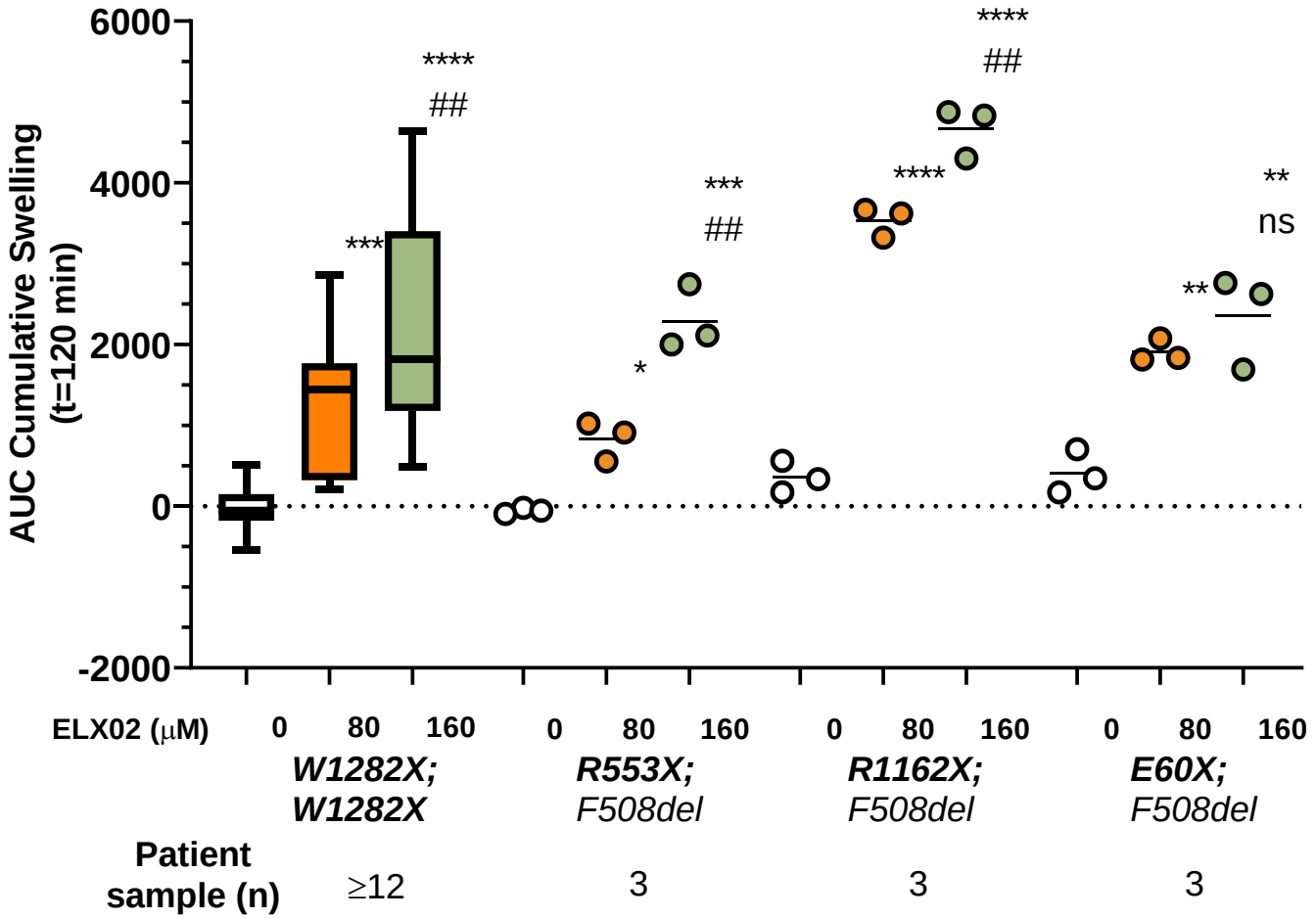
Cumulative organoid swelling in Class I and Class II CF Patient organoids after 48 hours of treatment (t=120 mins)*



*Forskolin concentration: 0.8uM; ELX-02 concentration: 172uM. Data generated at HUB

ELX-02 active across multiple Class 1 genotypes in a dose dependent manner

Swelling response to ELX-02 across various CF patient organoids*



* All exposures for 48 hours. Data generated by HUB

ELX-02 Phase 2 CF trial designed to evaluate safety and sweat chloride reduction with a 5mmol/L target

ELX-02 Phase 2 design

Dose 1	Dose 2	Dose 3	Dose 4
0.3 mg/kg SC QD for 7 days	0.75 mg/kg SC QD for 7 days	1.5 mg/kg SC QD for 7 days	Up to 3 mg/kg SC QD for 14 days

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

Encouraging Safety Results:

- **Well tolerated** in >100 subjects across Phase 1 SAD/MAD and Phase 2 Cystinosis studies
- Safety Review Committee has allowed dose **escalation up to top dose**

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

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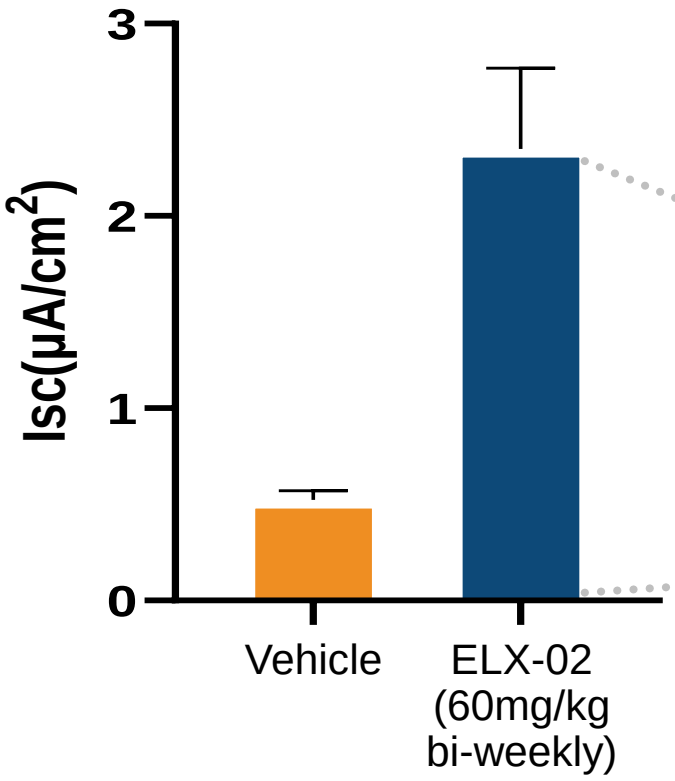
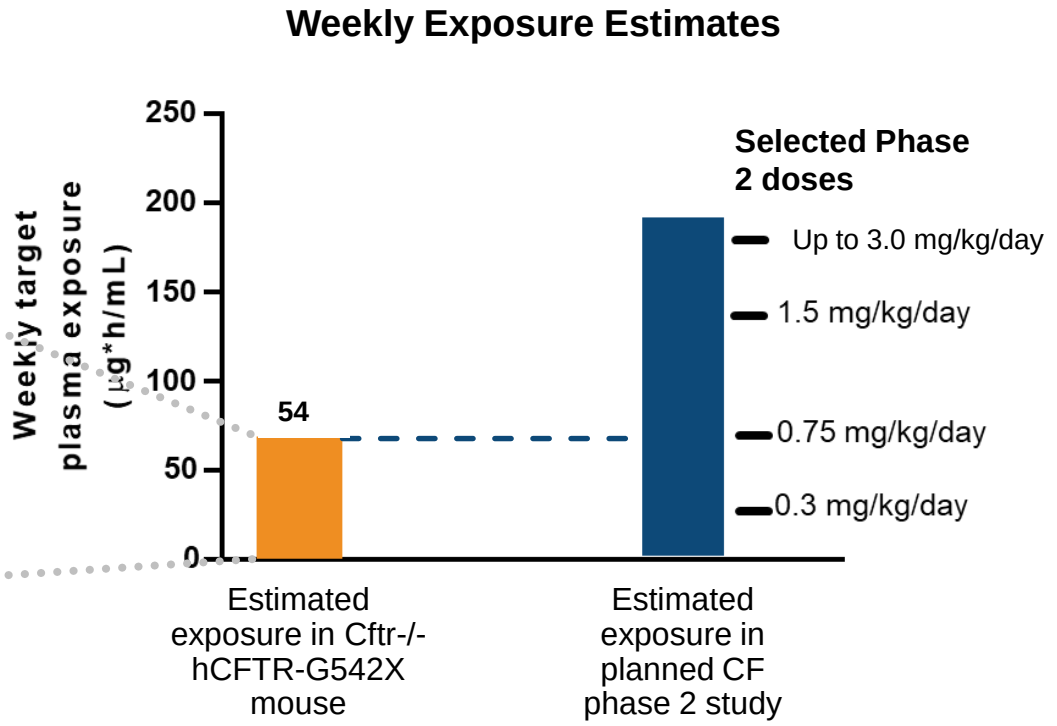
Phase 2 ELX-02 doses selected from efficacious exposure and doses in *in vivo* models

Cftr-/- hCFTR-G542X mouse intestinal current with ELX-02 treatment



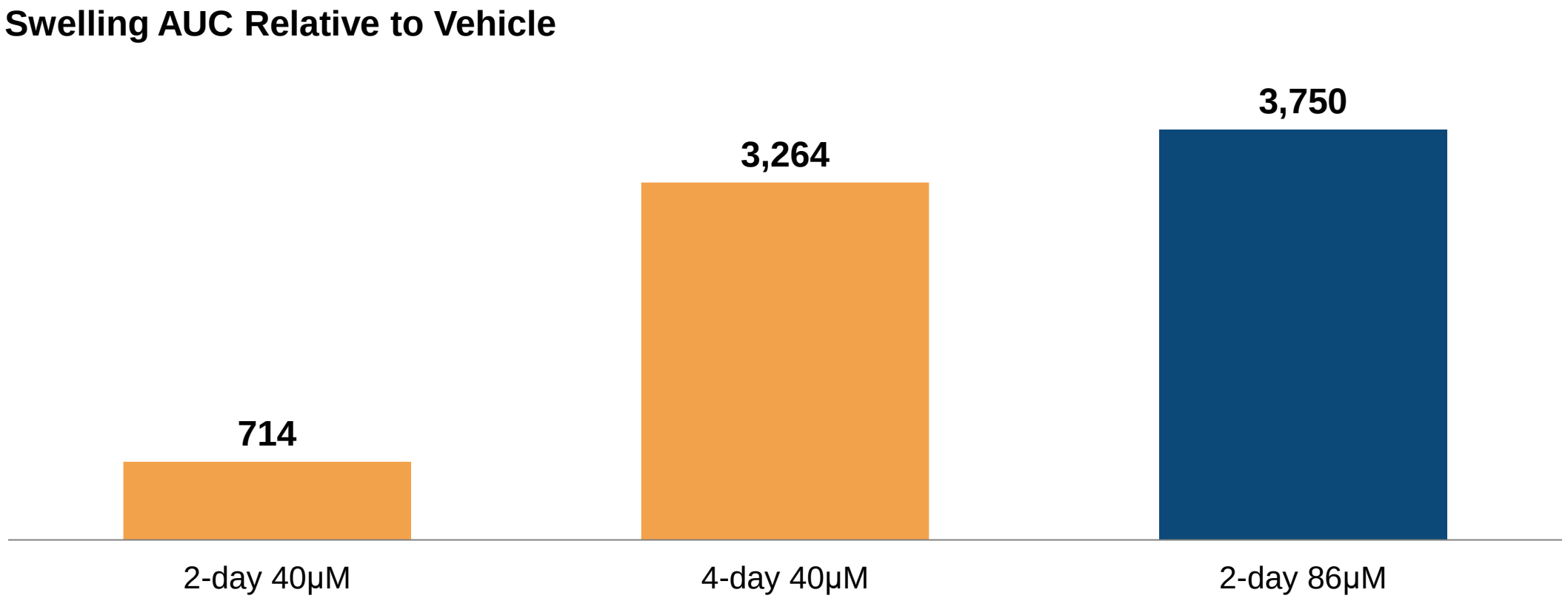
Estimated ELX-02 weekly plasma exposure across Phase 2 doses*



* Based on PBPK (Physiologically based pharmacokinetic) model built with with data from in vivo studies

Longer ELX-02 treatment enhances response

Experiment performed in G542X/G542X patient derived organoids

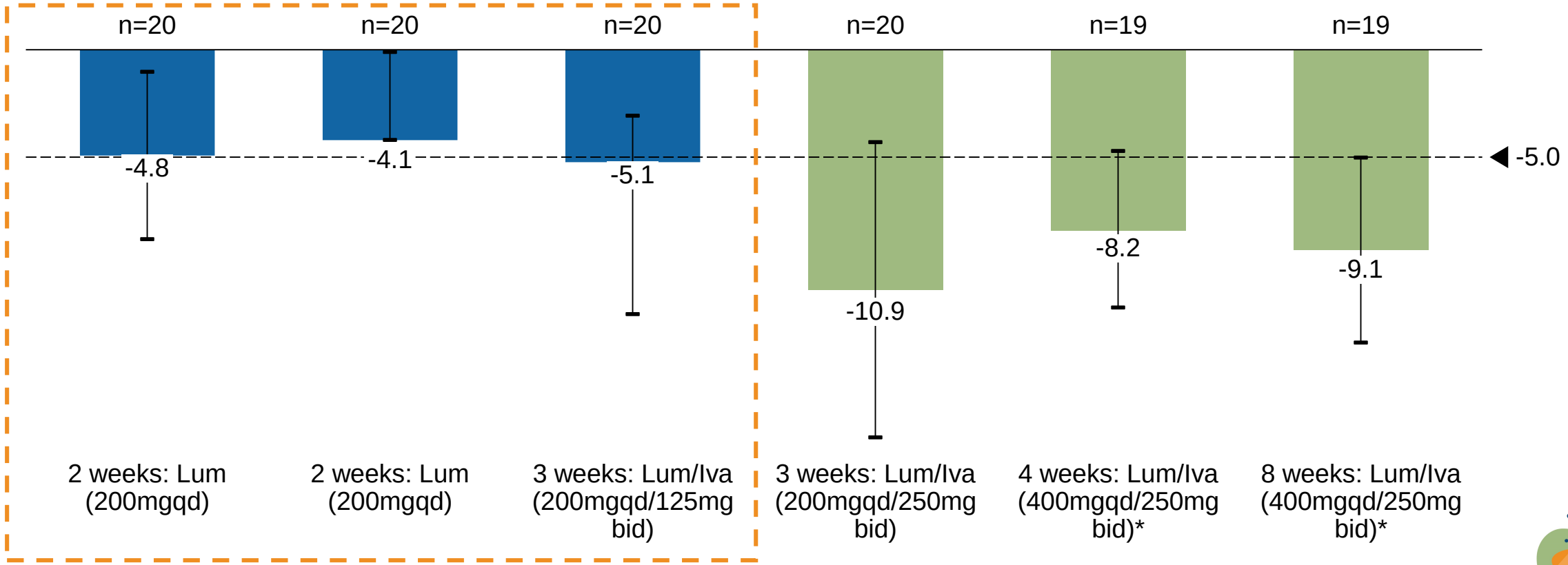


All experiments conducted at HUB

Targeting a 5 mmol sweat chloride reduction similar to clinical trial experience with Orkambi

Sweat chloride change in Hom delF508 patients in Phase 2 trials

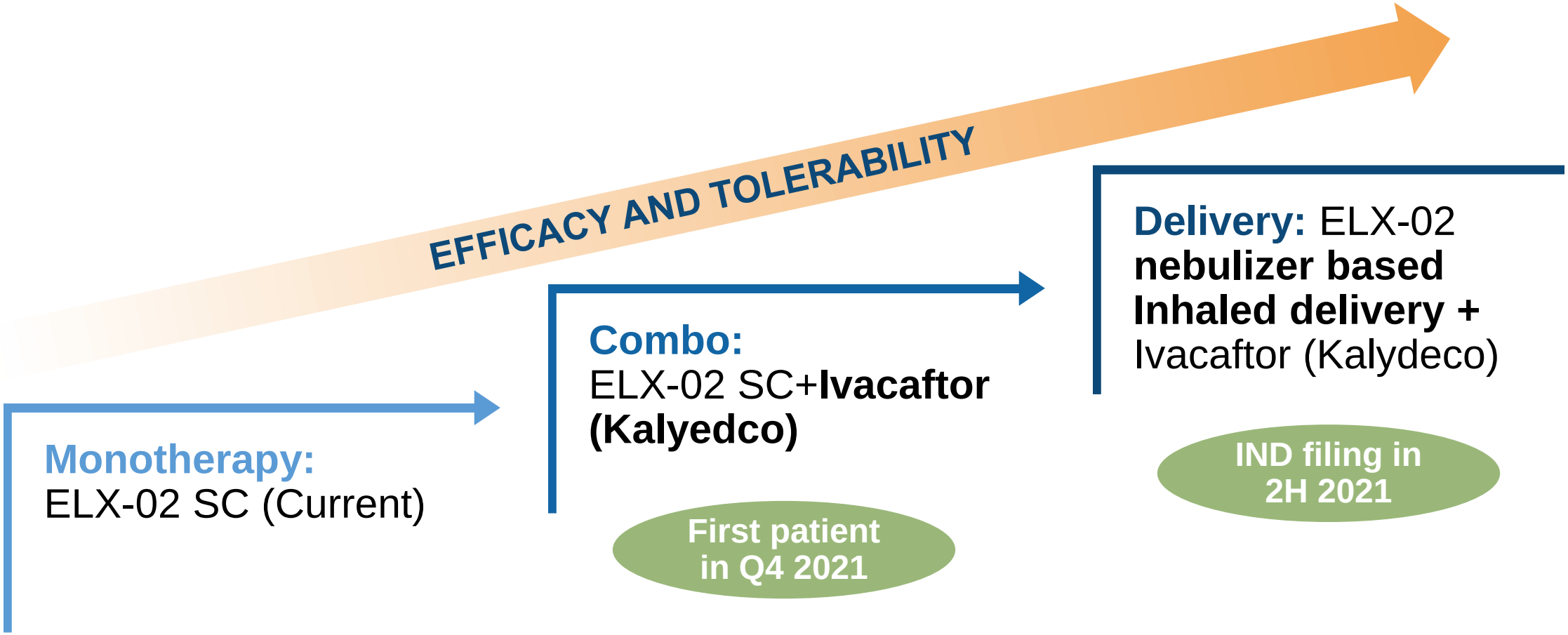
Sweat chloride changes in Hom F508del CF Patients treated with Lumcaftor/Ivacaftor (Orkambi)



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

* Approved Orkambi dose

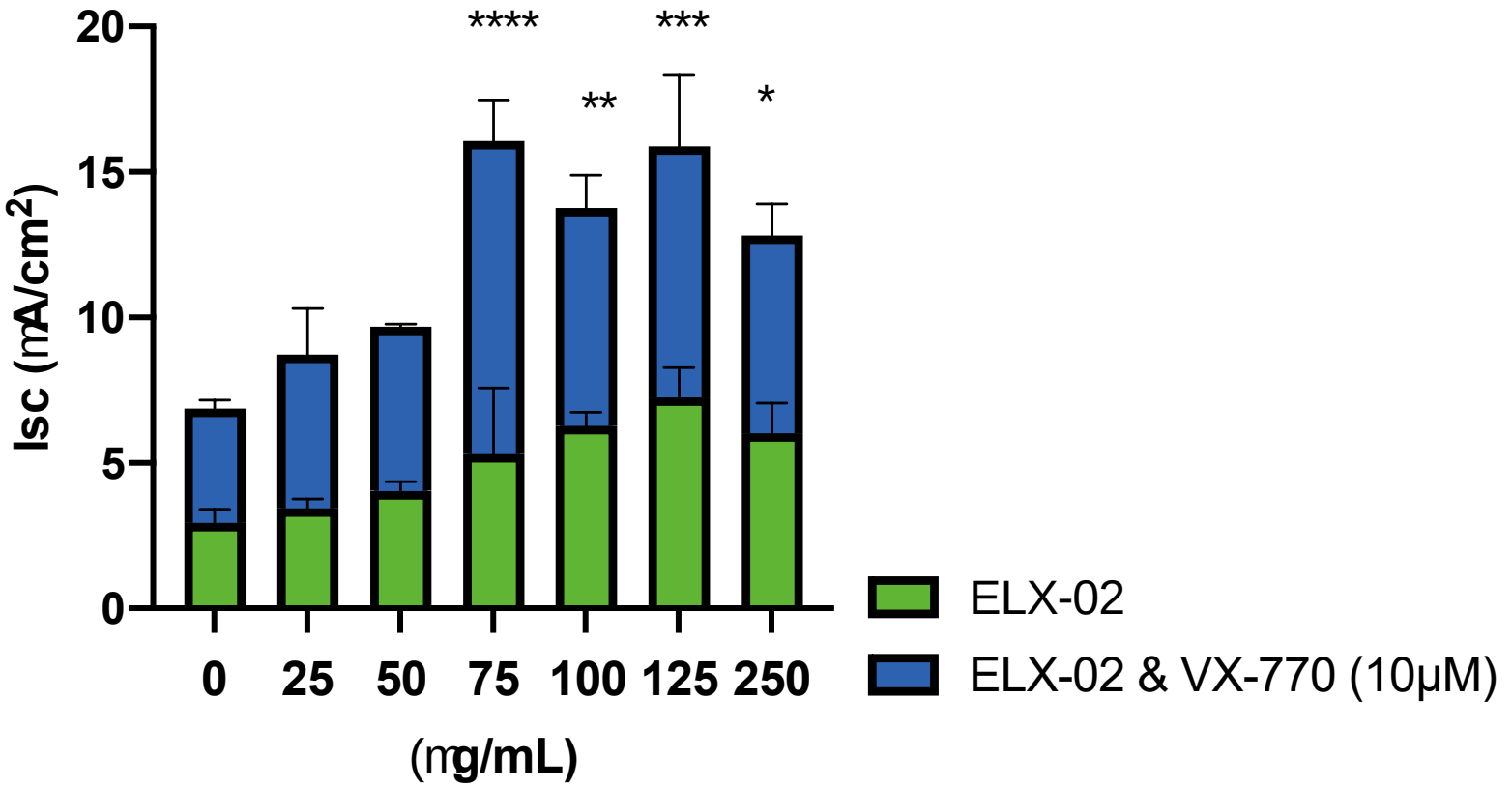
ELX-02 monotherapy program foundation for achieving transformative outcomes for CF Class 1 patients



2-3 fold dose dependent increase observed in CFTR activity with ELX-02 in combination with Kalydeco (VX-770)

Functional CFTR activity with combination of ELX-02 and VX-770 *in vitro*

Using chamber results heterozygous G542X/Fdel508 HBE cells*

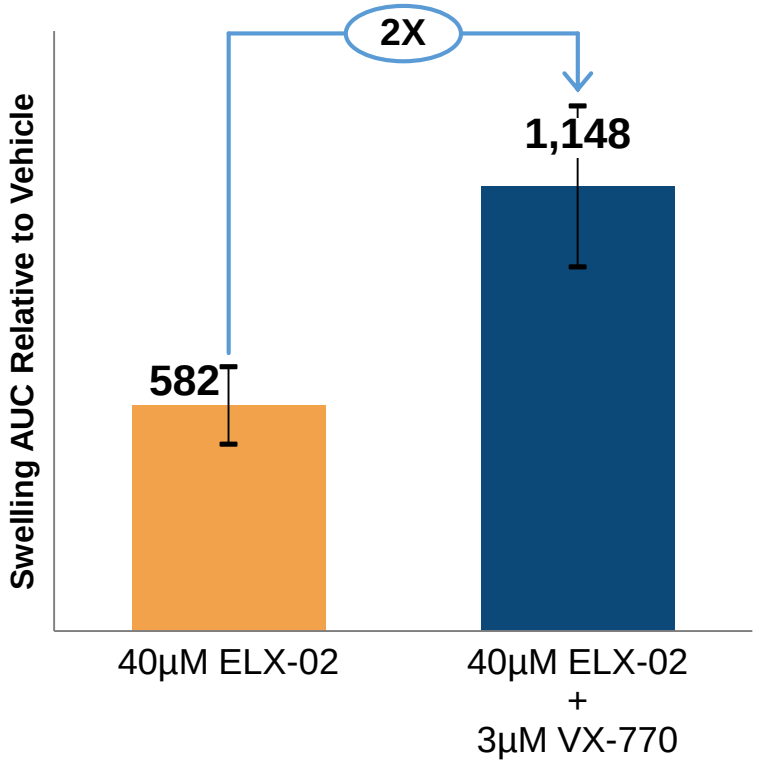


*Human Broncho Epithelial cells

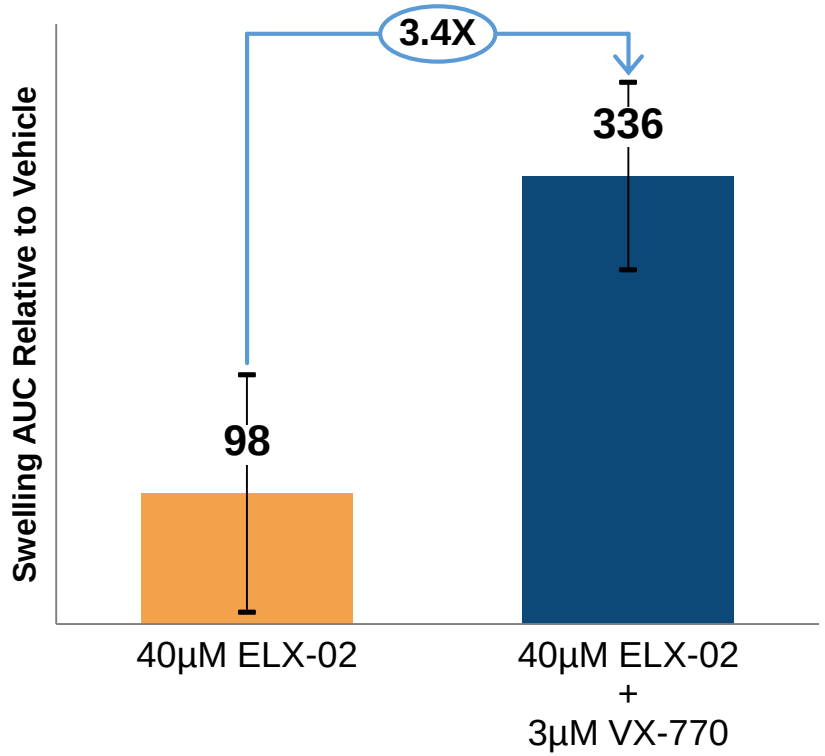
Kalydeco enhances ELX-02 activity across different nonsense mutations

Swelling response to 48 hours of treatment of CF patient organoids*

CFTR G542X/G542X Organoids (AUC at t=120min)



CFTR W1282X/W1282X Organoids (AUC at t=120min)



Forskolin concentration: 0.8uM; Swelling adjusted for control. Data generated at HUB

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Expanding current combination study across all sites and all Class 1 nonsense mutation CF patients

Expanded combination trial study design includes longer dosing

All Class 1 CF patients with nonsense mutations

Primary Endpoint: **Safety**, tolerability and pharmacokinetics

Secondary endpoints: **Sweat chloride** and FEV1

N = up to 30

Dose: 1.5mg/kg/day ELX02 + ivacaftor (150mg bid)

Duration: **5 weeks**: 1 week ELX-02 Monotherapy. 4 weeks of combination therapy with Ivacaftor following Physician review

Q4 2021: First patient expected to be dosed. 1H 2022: Report topline data

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Standard of care inhaled therapies paves path for ELX-02

Convenient

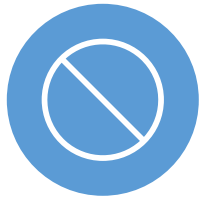
Inhaled antibiotic therapy is standard of care in Cystic fibrosis patients (e.g., Tobramycin, aztreonam, dornase alfa)

Well Tolerated

Tobramycin an aminoglycoside similar to ELX-02, is well tolerated in inhaled form

High Potency

Higher local drug exposure with lower systemic safety risk proven with Tobramycin



No Formulation Change

ELX-02 subcutaneous formulation suitable for inhalation administration

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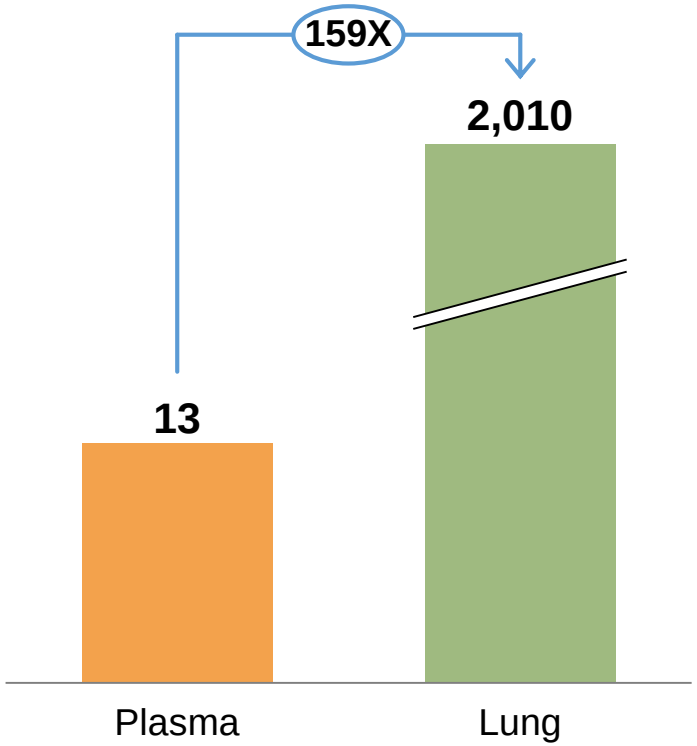
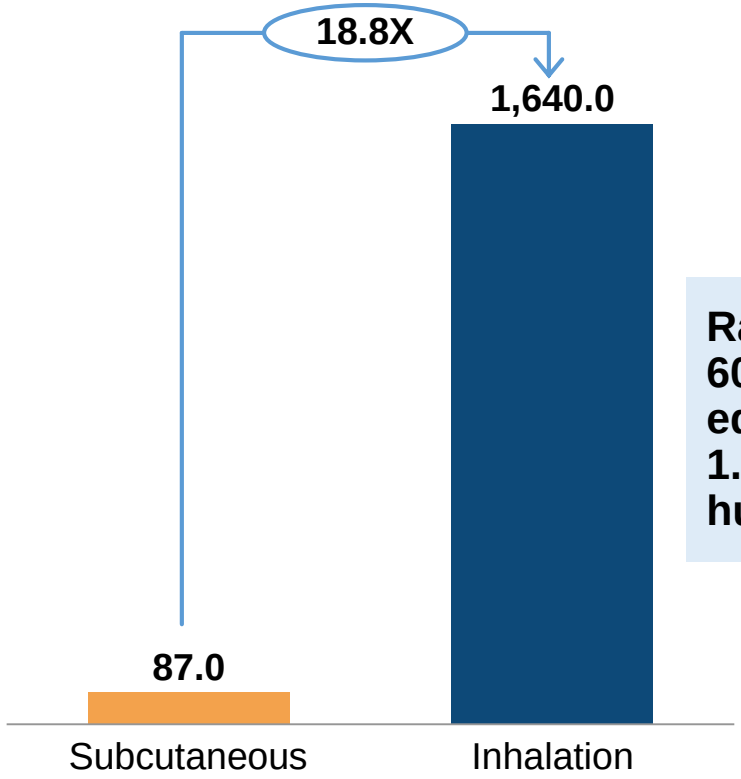
Meaningfully higher lung exposure with inhaled ELX-02 opens path to significantly higher activity

Lung vs Plasma exposures with inhaled vs. subcutaneous dosing

ELX-02 Rat drug exposure 69mg/kg inhaled ($AUC_{0\text{-}24hr}$ µg*hr/mL)



Estimated rat lung exposure 60 mg/kg sc vs. 69 mg/kg inhaled ($AUC_{0\text{-}24hr}$ µg*hr/ml)



Rat dose of 60-69 mg/kg equivalent to 1.5 mg/kg human sc dose

TURBO-ZM™ platform and RMA programs: RDEB/JEB, FAP and CF

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TURBO-ZM™ (TUning the RiBOsome with Zikani Molecules) platform has potential to fully unlock macrolide activity

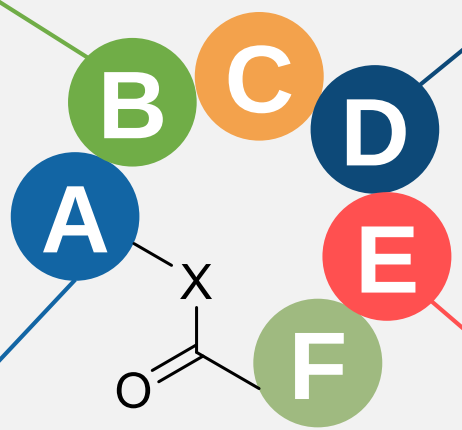
TURBO-ZM™: Applying macrolide SAR to RMA design

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

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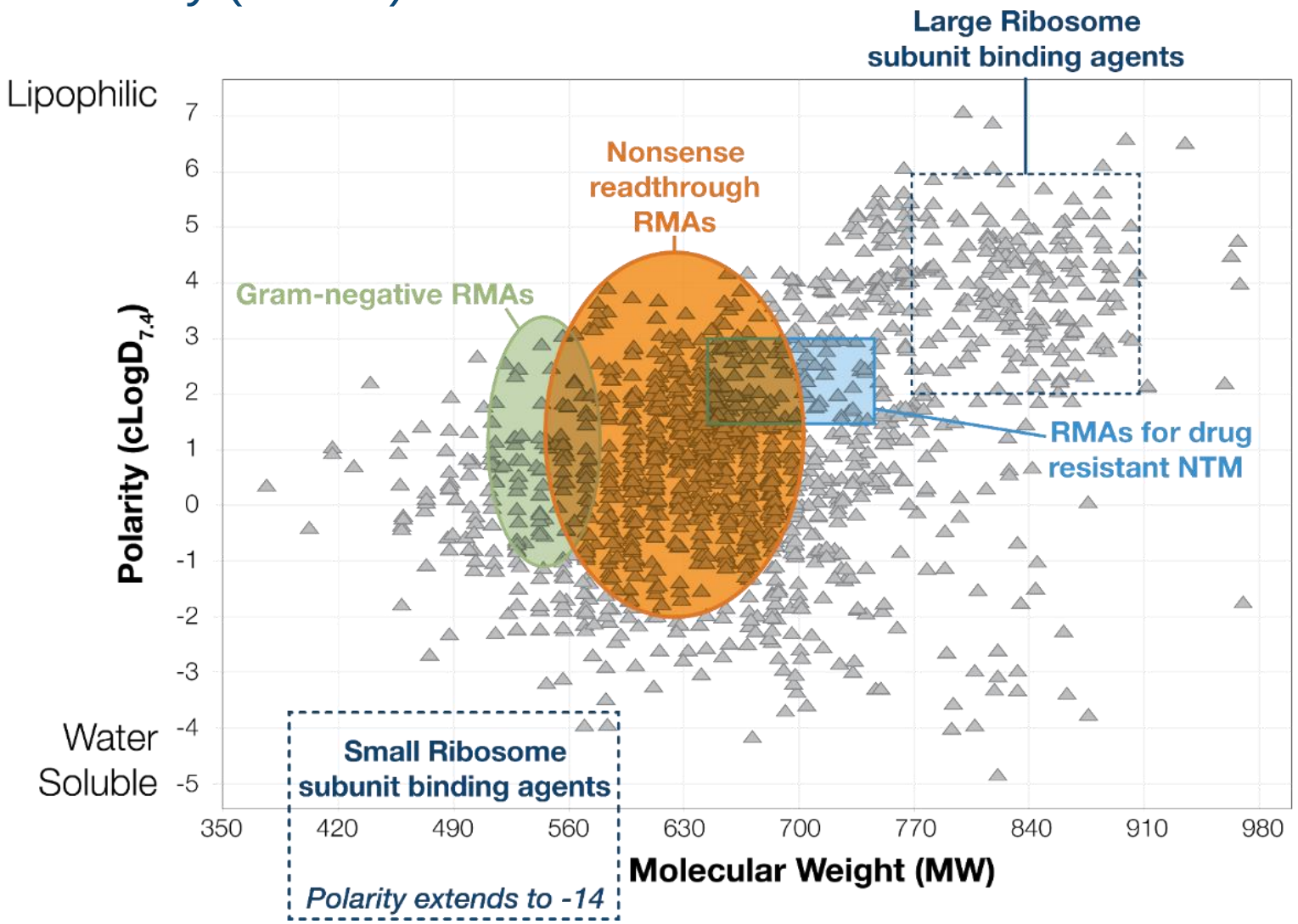
Growing library of RMAs with drug-like properties

Zikani RMA Library (2000+)



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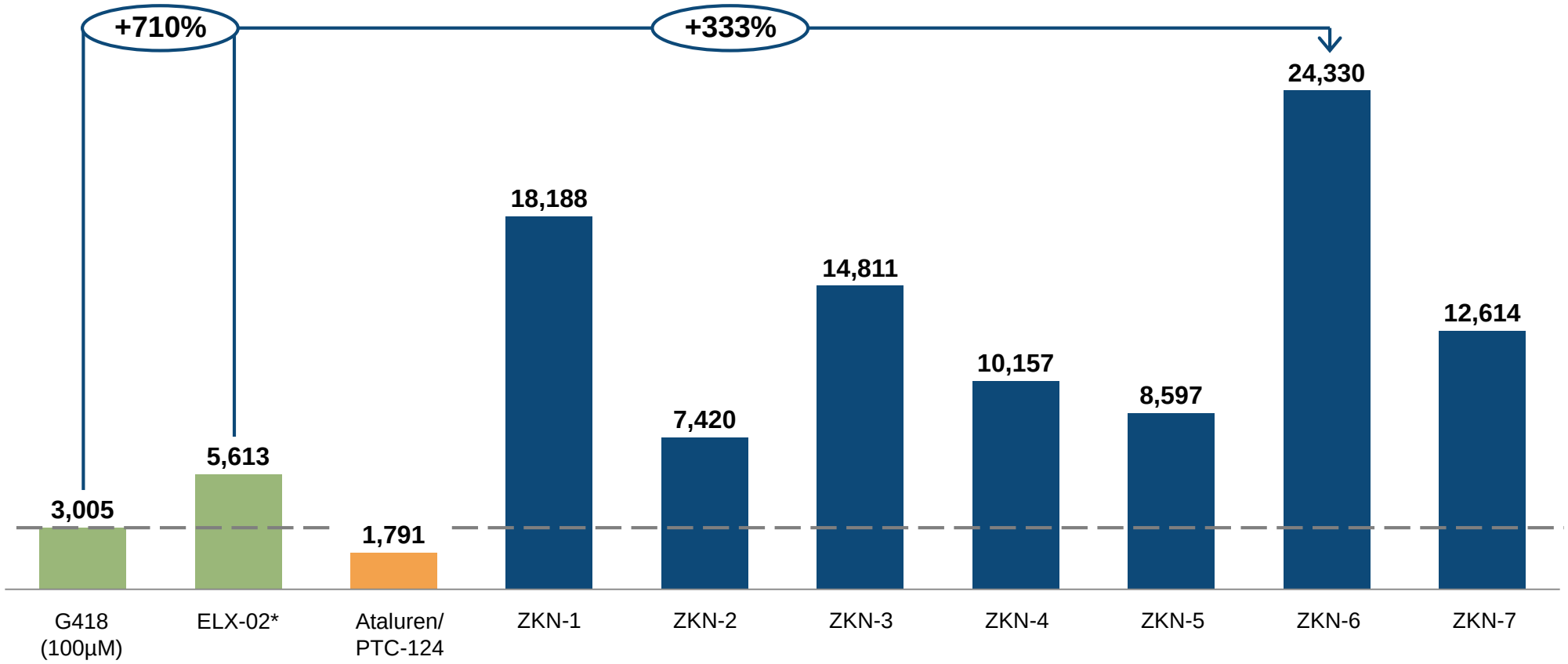
RMAs and ELX-02 showed superior readthrough to alternatives

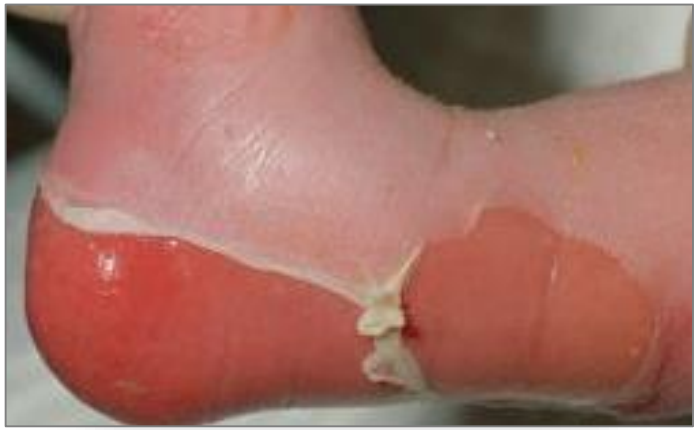
Readthrough Emax of selected RMA hits relative luciferase units compared to DMSO in W134X Nanoluc reporter assay



*Synthesized by Zikani prior to acquisition by Eloxx

RDEB/JEB: Clinical results for gentamicin validate opportunity for ribosome targeted readthrough agents

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

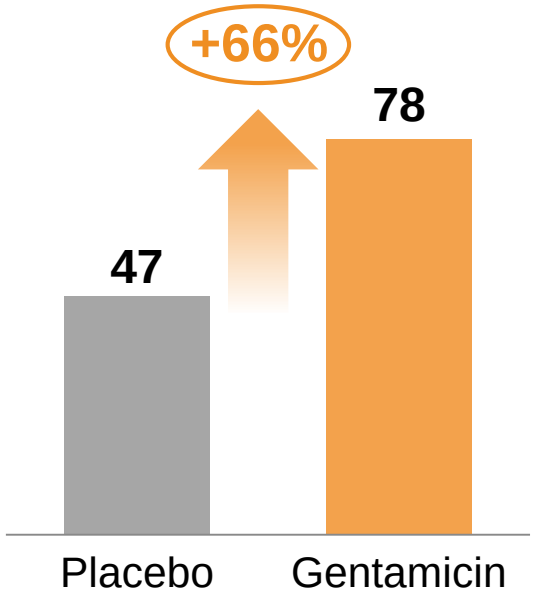
~4,000 patients, $1.5B TAM

RDEB

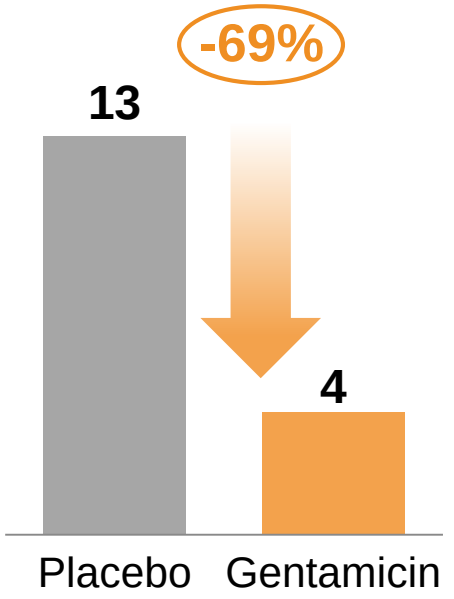
Gentamicin treatment of RDEB patients

(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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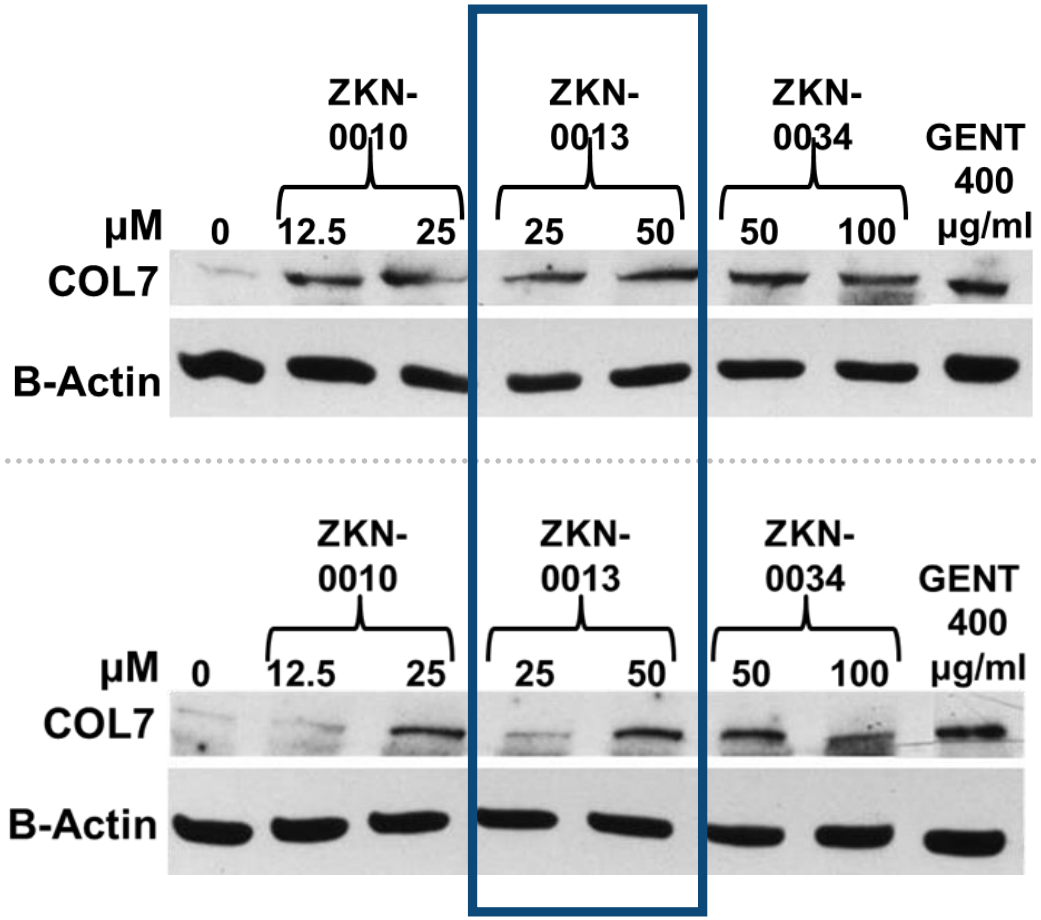
RDEB: RMAs restored functional collagen protein in primary patient cells at levels comparable to high dose gentamicin

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 observed 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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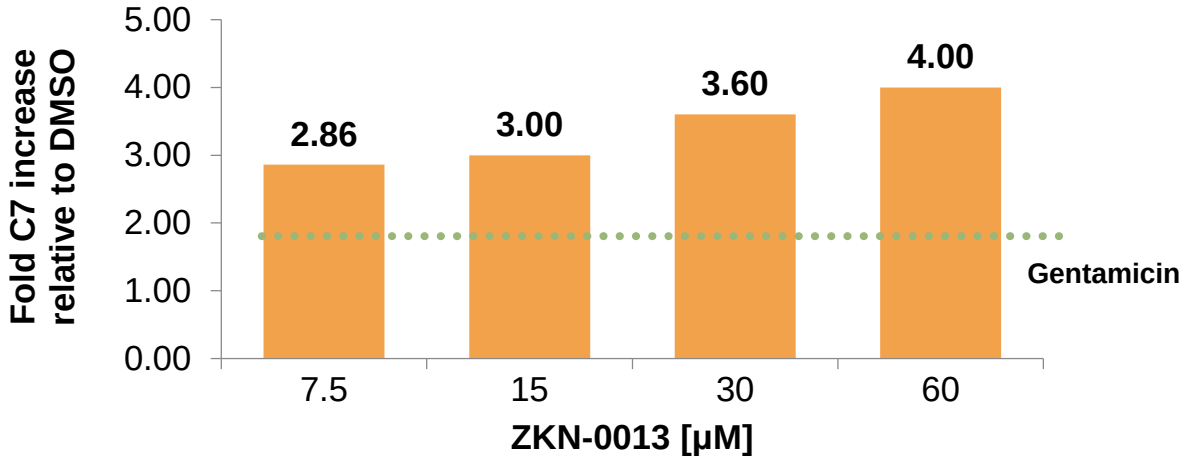
Achievable once daily oral dosing sufficient to safely restore therapeutic levels of full length COL7

COL7 in treated RDEB patient keratinocytes*



- Primary RDEB patient keratinocytes with COL7 mutations (R2610X/R2610X)
- Similar results demonstrated against other mutations

Data generated in collaboration with academic partner

14-day rat safety study (oral dose) tissue exposure

	30 mg/kg	100 mg/kg	300 mg/kg
Average skin Exposure (µM)	24.12	92.38	222.5
	NOAEL		**MTD**

- Human equivalent of 300-400 mg QD
- GLP safety studies expected to begin by end of 2021
- On track to file IND submission in 2022

Data generated at CRO

* 48 hours treatment with media and compounds replaced and refreshed at 24 hours. Results from Western Blot experiments

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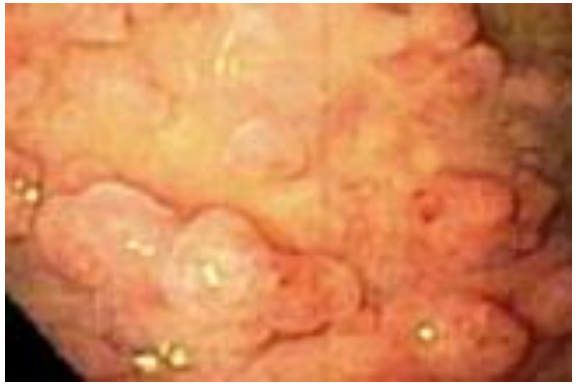
APC readthrough: Supported by positive prior clinical success of Erythromycin in FAP

APC mutant Familial Adenomatous Polyposis (FAP) and CRC



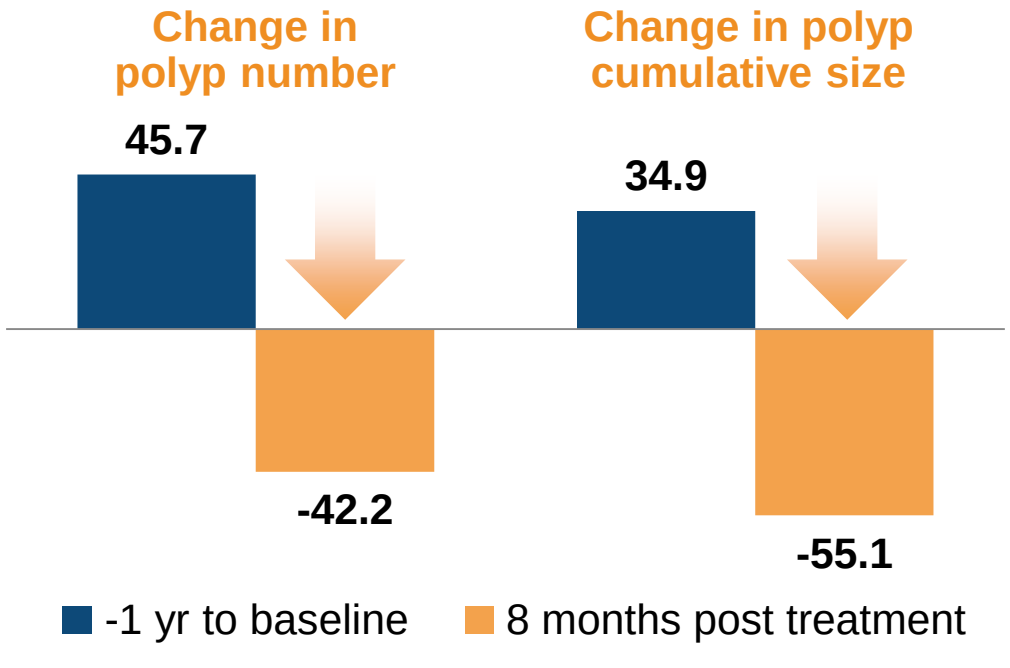
- Mutations in the Adenomatous Polyposis Coli (APC) gene (tumor suppressor gene)
- FAP patients develop CRC by age 40
- 80% of CRC patients have an APC mutation

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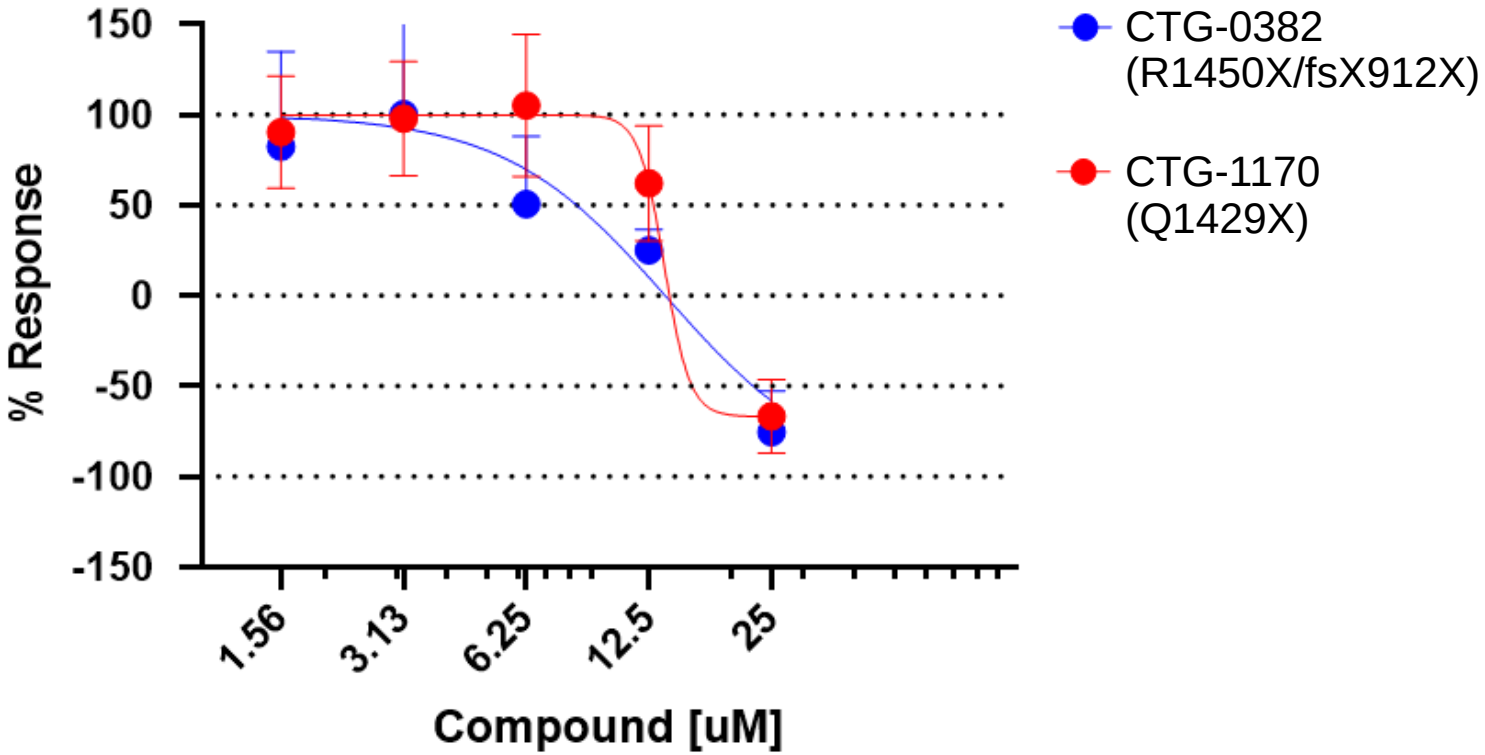
Clear path treating FAP supported by activity observed in APC mutant cancer patient tumor grafts

Responses to ZKN-013 observed in colorectal cancer patient derived tumor grafts ex-vivo

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

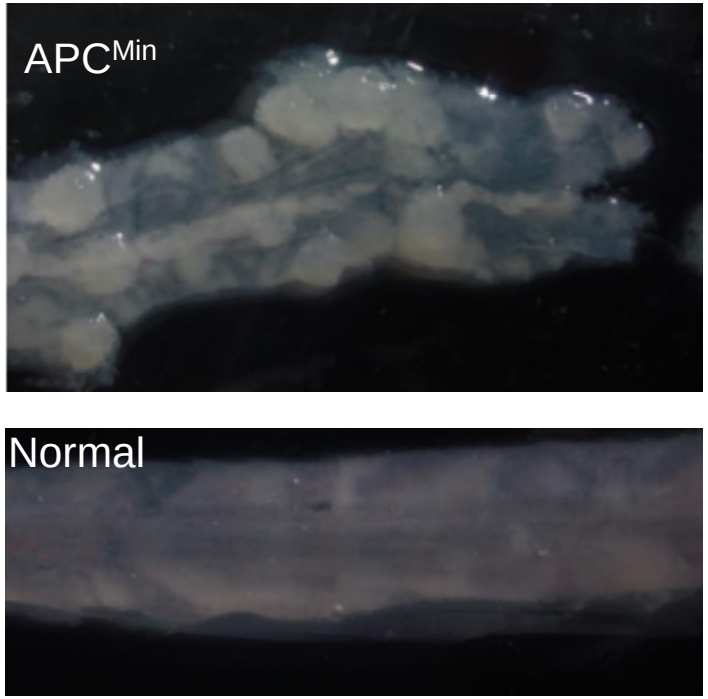
ZKN-013



APC^{Min} mice in vivo study to support the potential of ZKN-013 in FAP

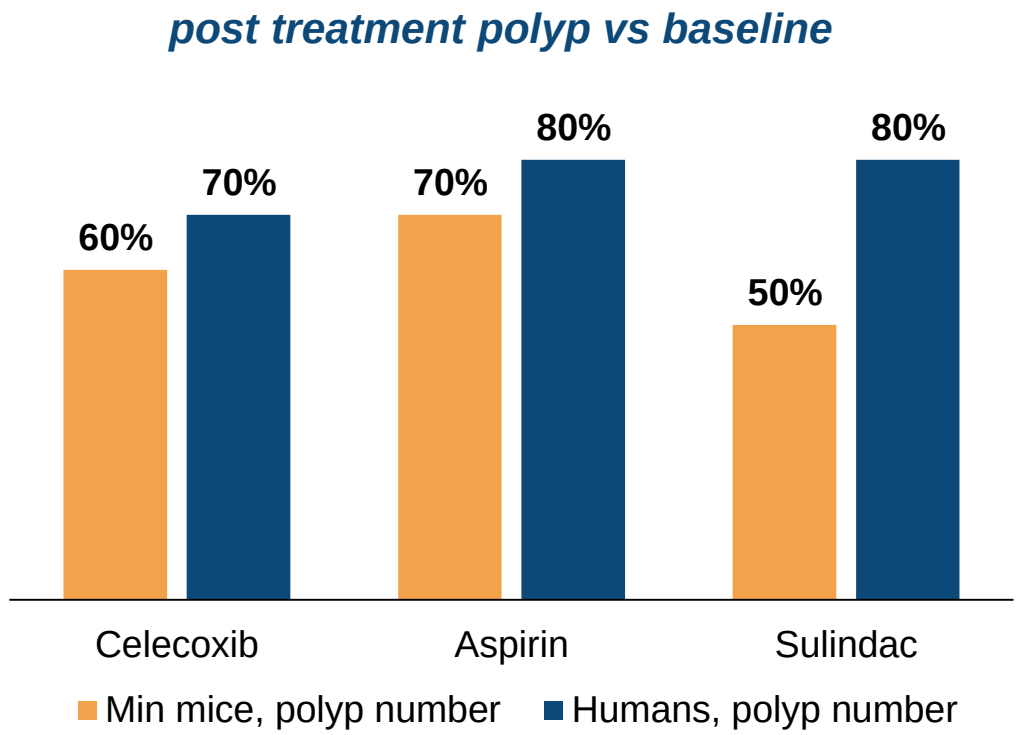
Clinical translational of APC^{Min} mouse for FAP drug development

Polyps in APC^{Min} mouse intestinal segment[1]



Erythromycin in APC^{Min} mice showed 33% reduction in polyps

Drug activity in APC^{Min} mice vs FAP patients[2]



8-week study in APC^{Min} mice planned to evaluate potential of RMAs to treat FAP; Data in Q4 2021

1.Sci. Rep. 2020 Feb 20;10(1):3064

2. Figure adapted from Corpet, DE and Pierre, F. *Cancer Epidemiology, Biomarkers and Prevention* 2003,12, 391-400

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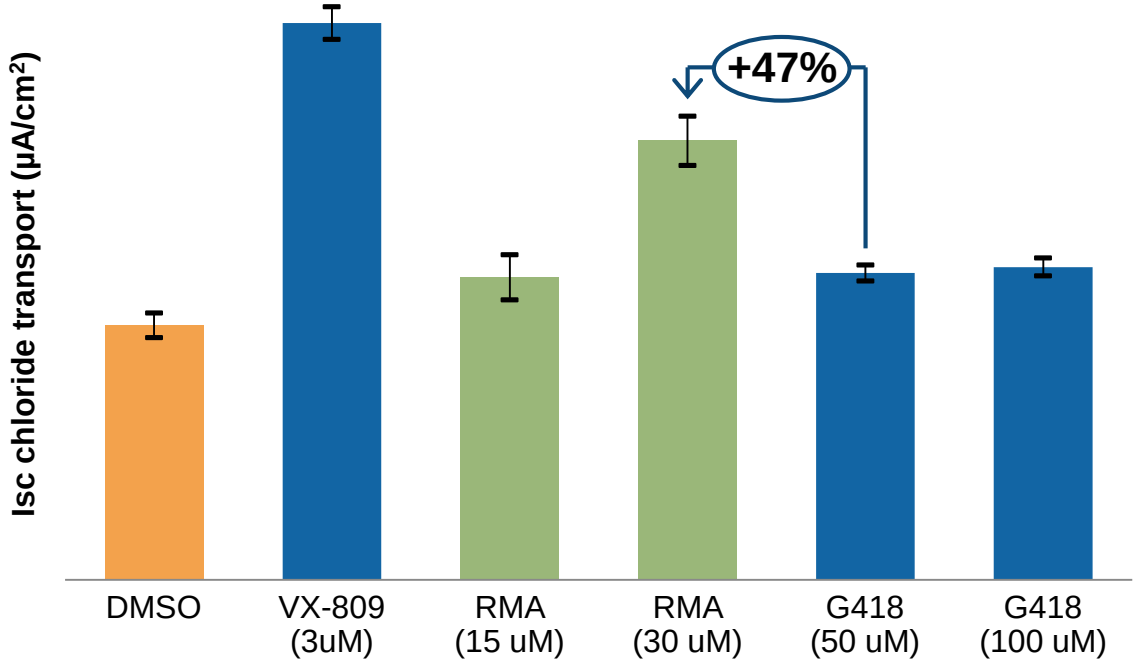
Developing next generation oral readthrough therapies supported by a $2.6M CF Foundation grant

Summary of Class 1 CF preclinical data

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



Data generated at Chantest

*Forskolin 10 μM/1μM VX-770 - both chambers

**VX 809 and RMA data averaged from 2 separate Ussing chamber results

Milestones and selected financials

Corporate and clinical milestones

1H 21

- ✓ Awarded $2.6M grant from Cystic Fibrosis Foundation
- ✓ Completed enrollment of ELX-02 monotherapy arms in ongoing Phase 2 trials

4Q 21

- Expect data from ongoing Phase 2 trial of ELX-02 monotherapy arms in CF
- First patient dosed in combination arm of Phase 2 trial of ELX-02
- GLP safety studies for ZKN-013 to begin
- Results for ZKN-13 in APC^{Min} mouse model results expected
- Colon cancer xenograft (cell line *in vivo*) study results

2022

- 1H: Topline results from combination Phase 2 trial of ELX-02
- 2H 2022: File IND for inhaled ELX-02
- 2H 2022 End of Phase 2 meeting for monotherapy ELX02
- 2022: IND submission for RDEB/JEB expected

Q2 2021 selected financials

$56.7M Cash and cash equivalents

$9.3M Long term debt

Cash expected to be sufficient to fund operations into 1Q23

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We are positioned to transform Eloxx and create significant value for shareholders

Platform company focused **on novel small molecule Gene Therapies** targeting **rare diseases and cancers**

Three rare disease programs with over $5B market potential

Expect to readout clinical data in our lead CF program in the 4th Quarter

Right **new leadership** with a track record of success

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