RARE Thinking for RARE Solutions

Leader in Ribosome Targeted Genetic Therapies

October 12, 2021

Forward-looking statements

This presentation (and the accompanying oral discussion) contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements other than statements of present and historical facts contained in this press release, including without limitation, statements regarding our expected cash burn and future financial results, the expected timing of trials and results from clinical studies of our product candidates and the potential of our product candidate to treat nonsense mutations are forward-looking statements. Forward-looking statements can be identified by the words “aim,” “may,” “will,” “would,” “should,” “expect,” “explore,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential,” “seeks,” or “continue” or the negative of these terms similar expressions, although not all forward-looking statements contain these words.

Forward-looking statements are based on management's current plans, estimates, assumptions and projections based on information currently available to us. Forward-looking statements are subject to known and unknown risks, uncertainties and assumptions, and actual results or outcomes may differ materially from those expressed or implied in the forward-looking statements due to various important factors, including, but not limited to: our ability to progress any product candidates in preclinical or clinical trials; the uncertainty of clinical trial results and the fact that positive results from preclinical studies are not always indicative of positive clinical results; the scope, rate and progress of our preclinical studies and clinical trials and other research and development activities; the competition for patient enrollment from drug candidates in development; the impact of the global COVID-19 pandemic on our clinical trials, operations, vendors, suppliers, and employees; our ability to obtain the capital necessary to fund our operations; the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights; our ability to obtain financial in the future through product licensing, public or private equity or debt financing or otherwise; general business conditions, regulatory environment, competition and market for our products; and business ability and judgment of personnel, and the availability of qualified personnel and other important factors discussed under the caption “Risk Factors” in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2021, as any such factors may be updated from time to time in our other filings with the SEC, accessible on the SEC’s website at *www.sec.gov* and the “Financials & Filings” page of our website at *https://investors.eloxxpharma.com/financial-information/sec-filings.*

All forward-looking statements speak only as of the date of this presentation and, except as required by applicable law, we have no obligation to update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

This presentation also contains estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events, or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical, and general publications, government data and similar sources.

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Opening Remarks

Sumit Aggarwal
President and CEO

Today's Agenda

Topic	Speaker
Opening Remarks	Sumit Aggarwal, President & CEO
Remaining Unmet Need in Cystic Fibrosis	Dr. Eitan Kerem
ELX-02: First-in-class Therapy for Class I Cystic Fibrosis Patients	Dr. Vijay Modur, Head of R&D
ELX-02: Program Expansion	Dr. Vijay Modur, Head of R&D
Key Takeaways & Closing Remarks	Sumit Aggarwal, President & CEO

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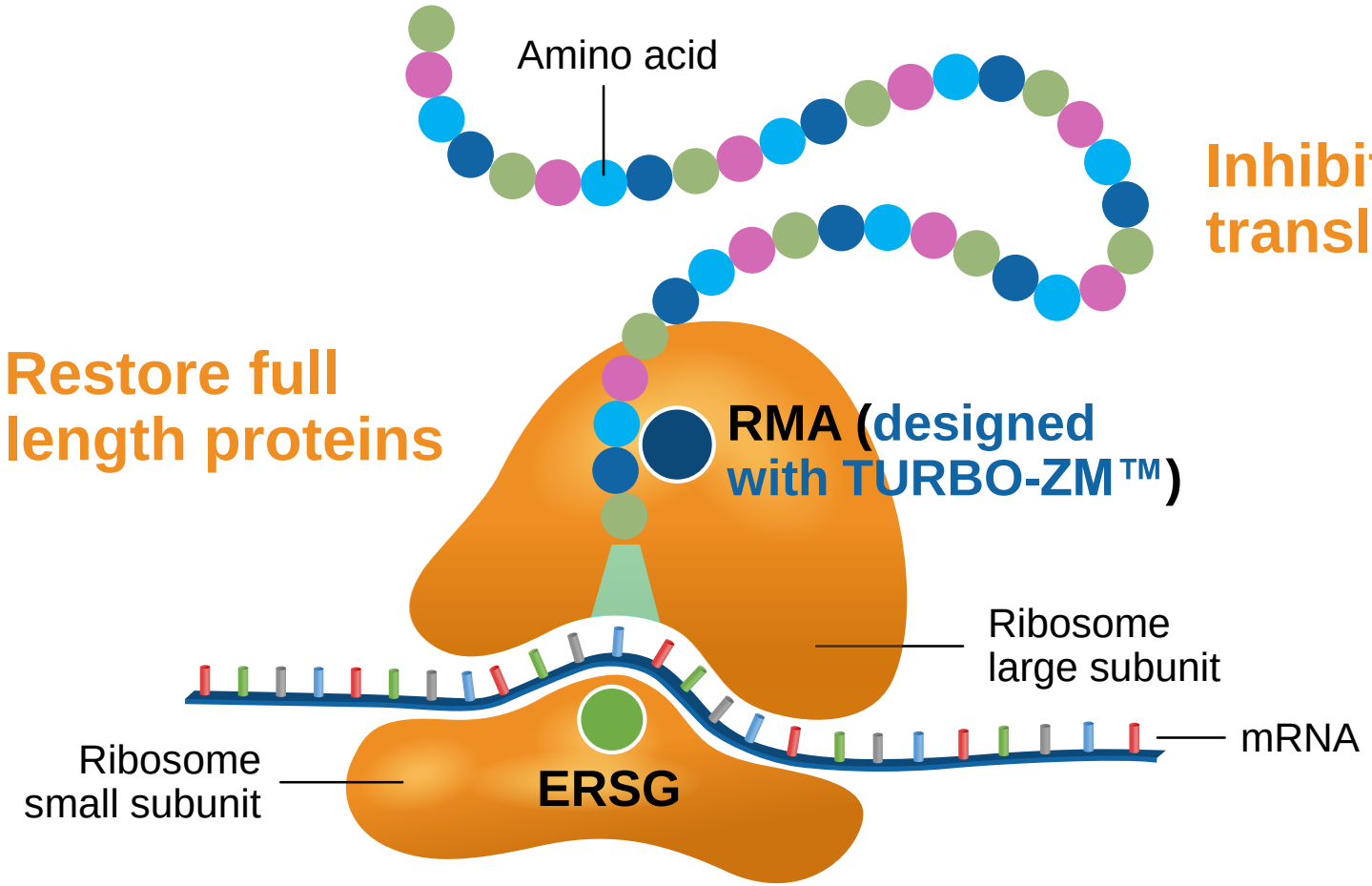
Two platform technologies uniquely positioned with potential to correct protein translation defects

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



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

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

	Target	Indication	Discovery	Lead optimization	IND enabling	Phase 1 – first in human	Phase 2	Phase 3
Nonsense readthrough: rare disease	CFTR	Class 1 CF	ELX-02 (Fast Track Designation*)					CYSTIC FIBROSIS FOUNDATION
	Collagen VII A1/LAMB3	RDEB/JEB	ZKN013					
	CFTR	Class 1 CF	RMA(s)					CYSTIC FIBROSIS FOUNDATION
Nonsense readthrough: oncology	APC	FAP	ZKN013					
	APC	CRC	ZKN074/ZKN157					
	Undisclosed	Pan cancer/ IO combination	RMA					
Protein translation inhibition	Onco-ribosome & mito-ribosome mutations	Undisclosed	RMA					

***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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Professor Eitan Kerem: Globally renowned key opinion leader in Cystic Fibrosis

- Former Chairman, Department of Pediatrics at Hadassah University Hospitals, Jerusalem
- Principal investigator in many national and international multi-center Cystic Fibrosis clinical trials. Author of key publications in the field.
- Involved in formulating the guidelines that paved the road to the standardization of CF care in Europe and other parts of the world.
- **Selected awards:**
  - 2014: ECFS Award acknowledging his substantial and remarkable contribution to cystic fibrosis research
  - 2016: Honorary Fellowship of the Royal College of Pediatrics and Child Health, UK.
- **Education**
  - Hebrew University – Hadassah Medical School
  - Pediatric residency at the ”Bikur Holim” Hospital in Jerusalem
  - Fellowship in pediatric respiratory diseases at the Hospital for Sick Children in Toronto, Canada

Remaining Unmet Need in Cystic Fibrosis

Dr. Eitan Kerem

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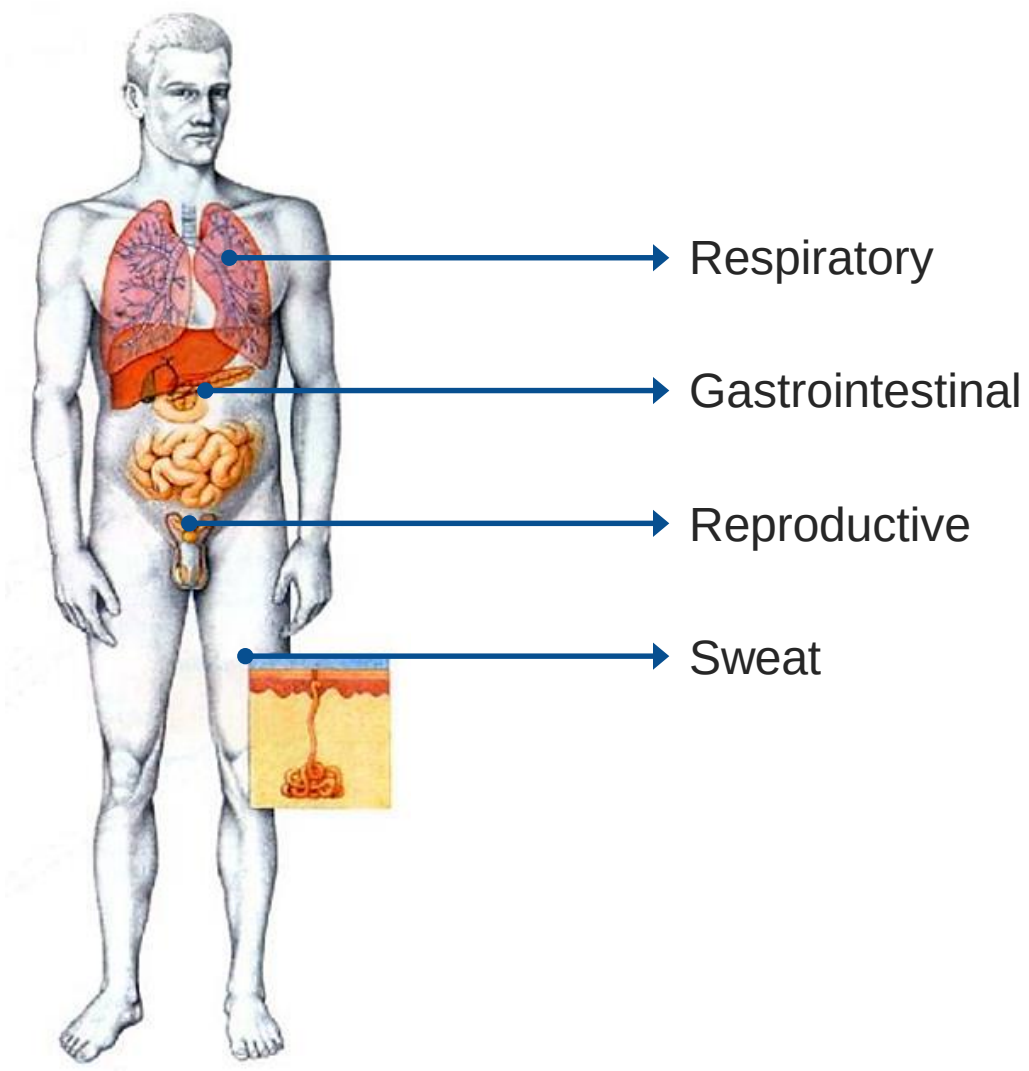
Rebecca – 27 year old female

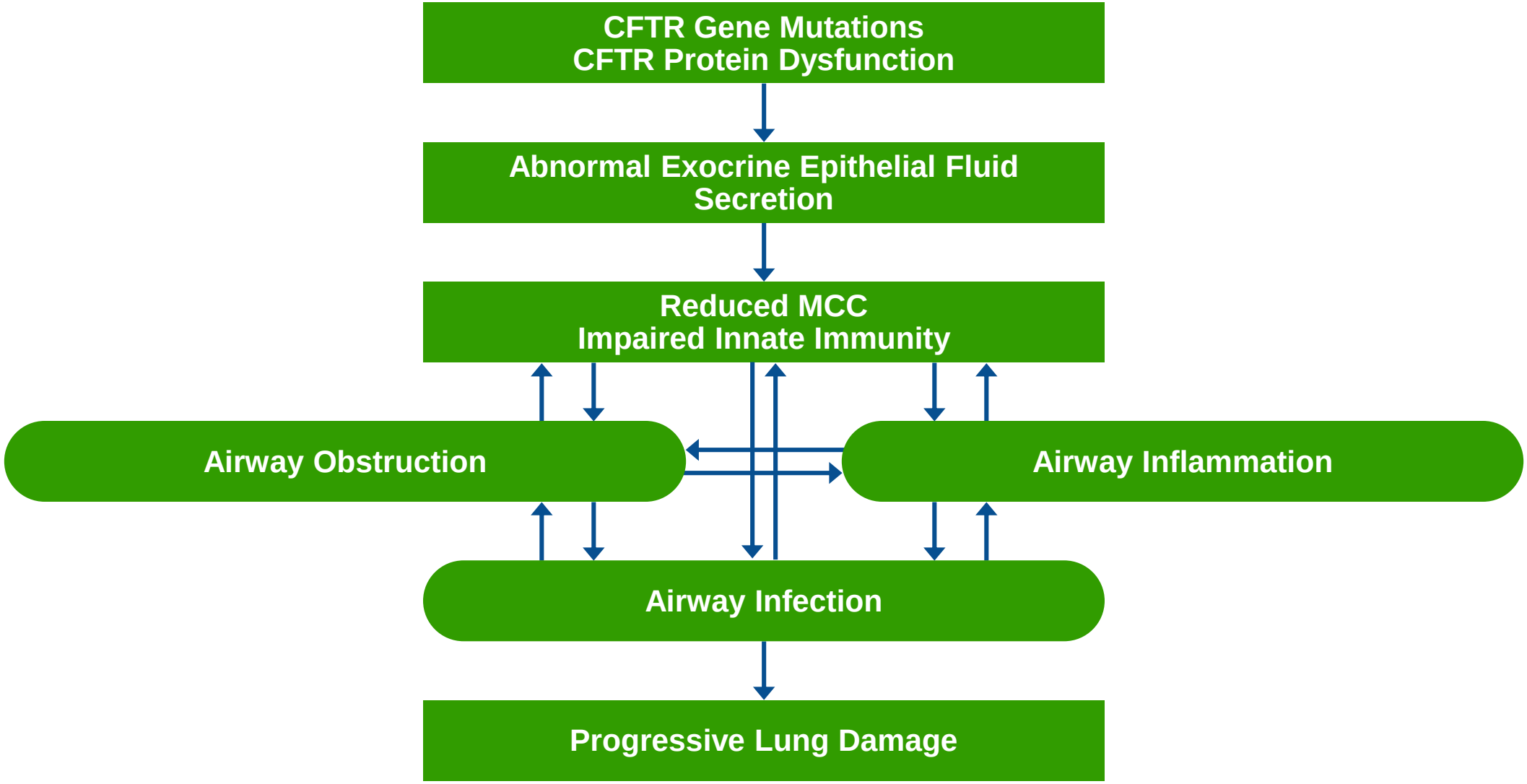
- Born with intestinal bowel obstruction (meconium ileus)
- Sweat chloride 107 mmol/L (normal up to 60)
- Genotype W1282X/W1282X
- Had many hospitalizations during childhood for respiratory exacerbations and was treated with intra venous antibiotics
- Sputum cultures grow aggressive bacteria like pseudomonas
- Her daily treatment included:
  - 2 inhalations every day with hypertonic saline
  - 1 inhalation of pulmozyme
  - 2 inhalations of antibiotics
  - Physiotherapy to drain lung secretions 45 minutes every day
  - 8 capsules of pancreatic enzymes with every meal (30–40 per day)
  - 2 tablets of multivitamins
  - 1 tablet of azithromycin

- 2017 – Married
- 2019 – Gave birth to a sweet daughter
- 2020 – Pulmonary function deteriorated and she needs O2
- 2021 – Bed ridden and on the list for lung transplantation

Organs affected in Cystic Fibrosis patients

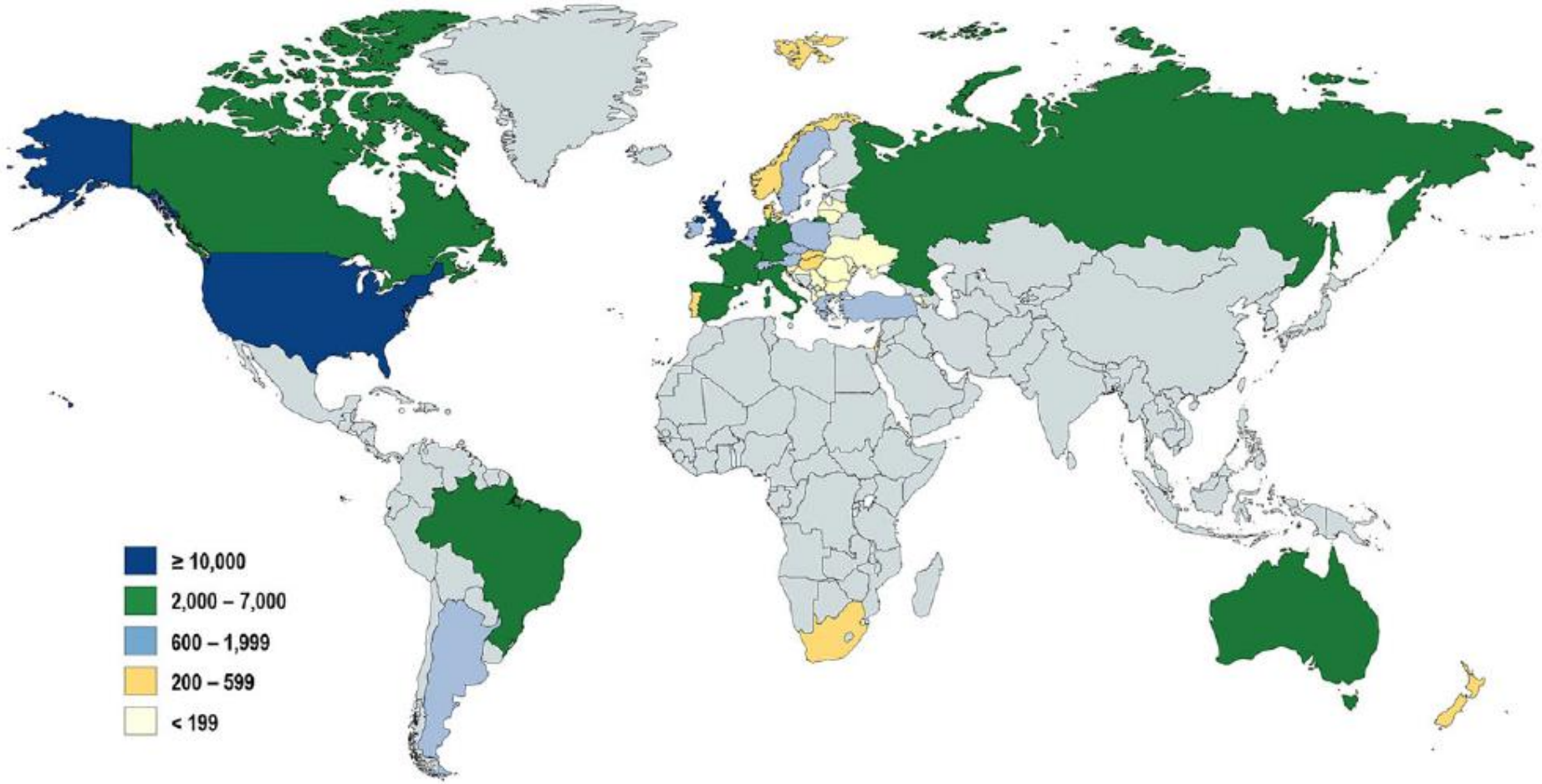


Hadassah Medical Center
Hadassah Children

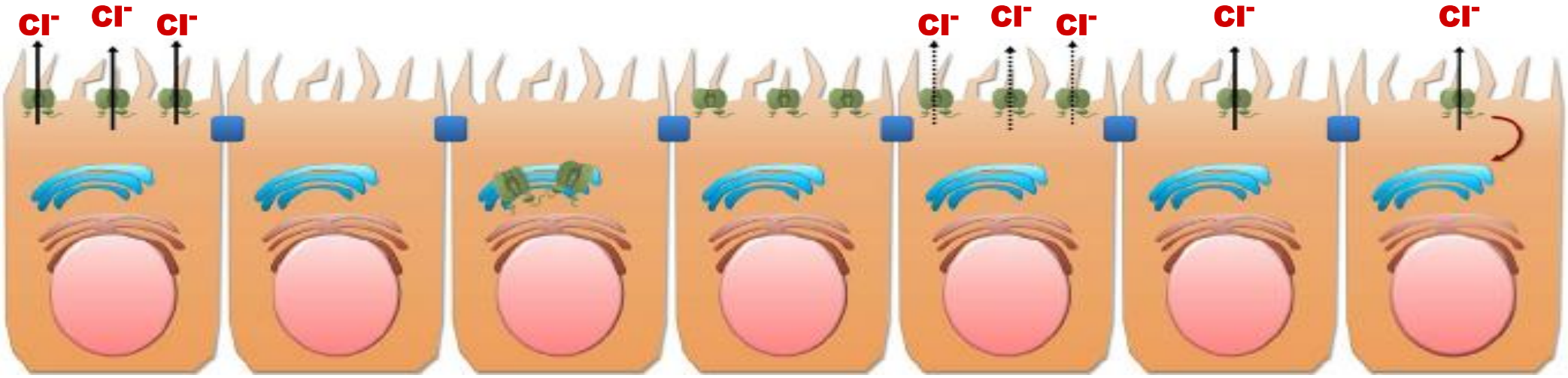


CF distribution according to the total number of patients registered (~100,000 patients worldwide)

1st United States
2nd Untied Kingdom
3rd France
4th Germany
5th Italy
6th Brazil
7th Canada
8th Australia
9th Russia
10th Spain



Hadassah Medical Center
Hadassah Children



	No CFTR on the Cell Membrane		Non Functional CFTR on the Cell Membrane	Reduced Functional CFTR on the Cell Membrane		
wt-CFTR	I	II	III	IV	V	VI
	No Protein	No Traffic	No Function	Less Function	Less Protein	Less Stable
	G542X (a) 394delTT (a) 1717-1G>A (b)	R1066C A561E F508del	G551D S549R G1349D	R117H R334W	A455E 3272-26A>G 3849 + 10 kb C >T	c.120del23 rF508del
	10–15% of the Patients with No Therapy	Correctors – Enable Mutant CFTR to Reach the Cell Surface	Potentiators – Augment cAMP-dependent Cl- Channel Activity of Mutant CFTR at the Cell Surface			

Endpoints for clinical trials in CF

Clinical endpoints

- Pulmonary function (FEV_1, LCI)
- BMI
- Number of Exacerbations
- Quality of life questionnaire
- Patient reported symptoms

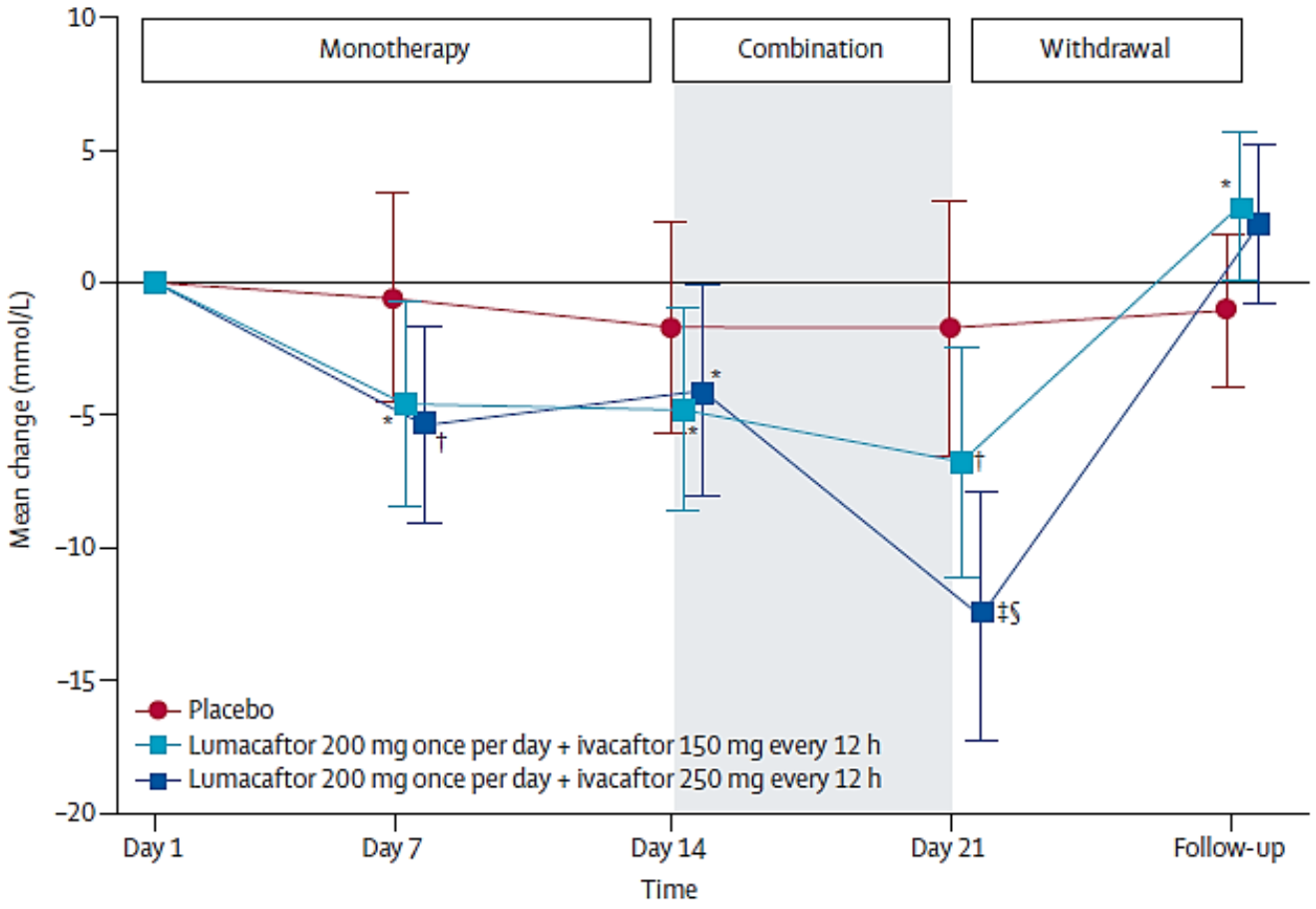
Surrogates for CFTR function

- Sweat chloride levels
- Nasal potential difference

A CFTR corrector (lumacaftor) and a CFTR potentiator (ivacaftor) for treatment of patients with cystic fibrosis who have a phe508del *CFTR* mutation: a phase 2 randomized controlled trial

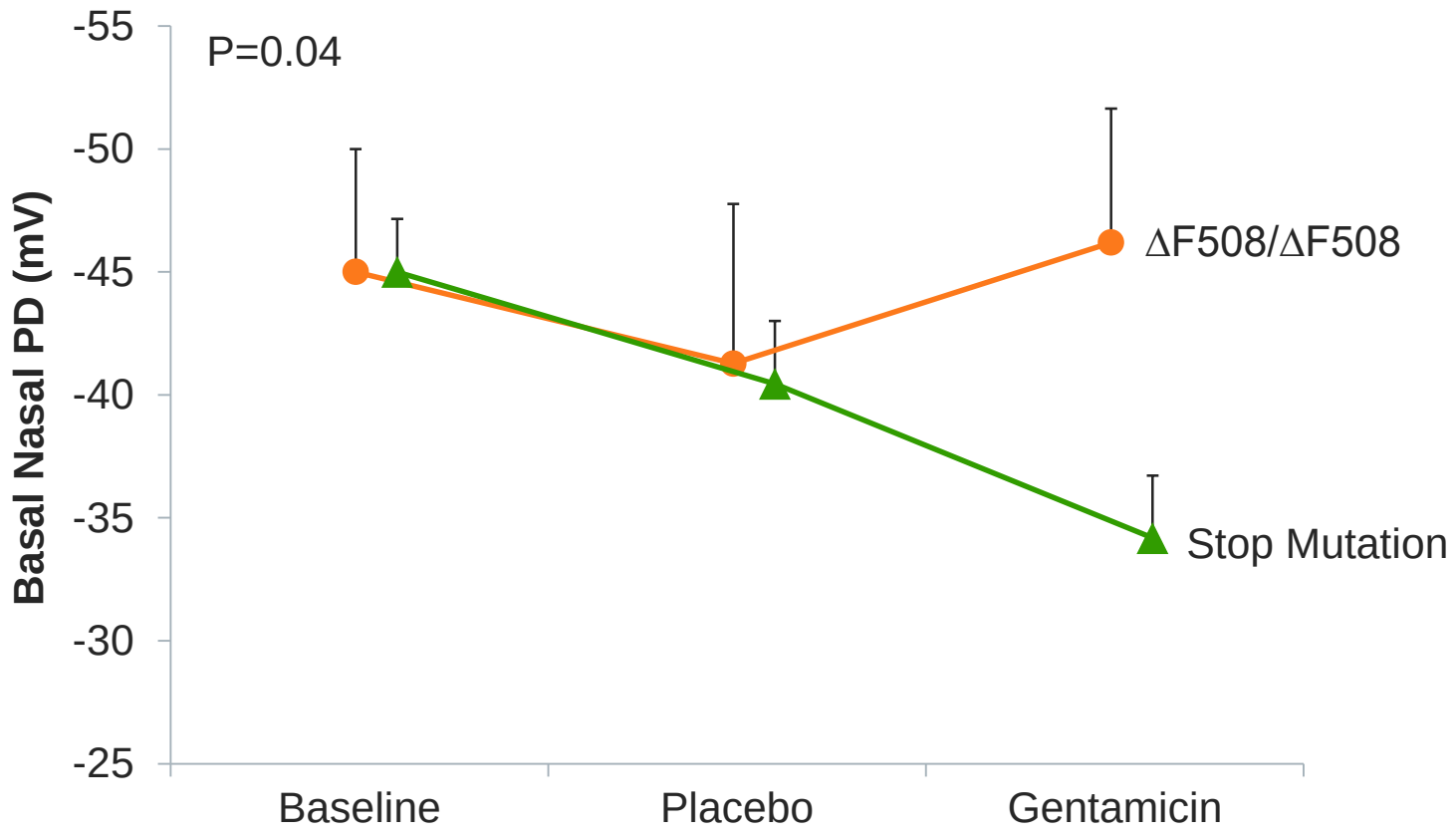
Michael P Boyle, Scott C Bell, Michael W Konstan, Susanna A McColley, Steven M Rowe, Ernst Rietschel, Xiaohong Huang, David Waltz, Naimish R Patel, David Rodman, on behalf of the VX09-809-102 study group*

Change in Mean Sweat Chloride Concentration for Cohort 1



Means are least-square means based on an ANCOVA model adjusted for treatment, baseline, and baseline age. Bars are 955 CI. *p<0.05 for within-treatment group change from baseline. †p<0.01 for within-treatment group change from baseline. ‡p0.001 for within-treatment group change from baseline. §p<0.01 vs. placebo.

Gentamicin effect in Class I nonsense mutation sets a new paradigm



 Wilschanski et al. *NEJM* 2003.

Hadassah Medical Center
Hadassah Children

Summary

- CF is a devastating disease leading to respiratory failure
- Despite new therapies for CF, Class I patients harboring nonsense mutations have no disease modifying options
- Sweat chloride and FEV1 are the key endpoints in CF trials
- **Even small changes in sweat chloride can predict efficacy to induce FEV1 improvement**
- Gentamicin has shown promise in CF patients with Class I nonsense mutation

ELX-02: First-in-class Therapy for Class I Cystic Fibrosis Patients

Dr. Vijay Modur
Head of R&D

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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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Gentamicin shows readthrough activity but has failed to translate to clinical practice

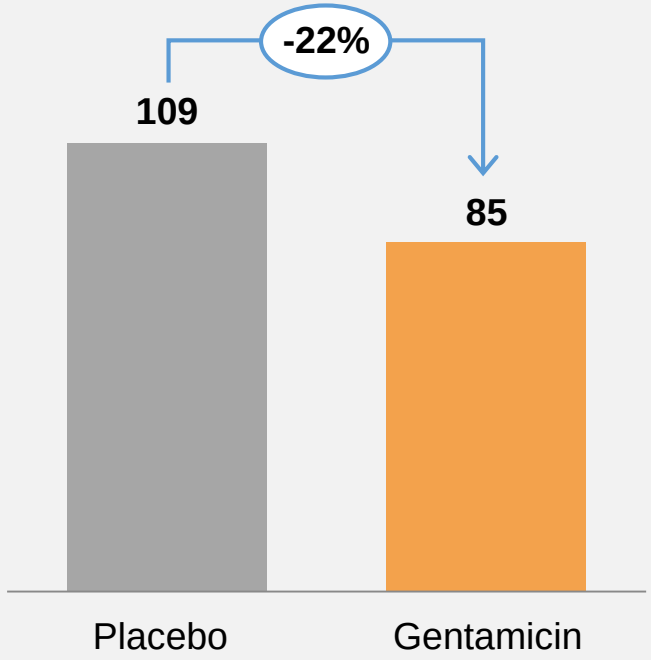
Readthrough activity of Gentamicin across rare diseases and CF

Selected rare diseases	Evidence
Cystic Fibrosis Class 1	Clinical[1]
Duchenne Muscular Dystrophy	Clinical[2]
Dystrophic Epidermolysis Bullosa (RDEB)	Clinical[3]
Lysosomal Storage, e.g., MPSI (Hurler), cystinosis	*ex vivo*[4]
Rett Syndrome	*ex vivo*[4]
Spinal Muscular Atrophy (SMA)	*ex vivo*[4]
Ataxia-Telangiectasia (ATM)	*ex vivo*[4]
Usher syndrome/retinitis pigmentosa (RP)	*in vivo* Preclinical[5]

Gentamicin treatment 9 patients

(10 mg/kg iv, qd for 15 days)[1]

Change in sweat chloride (mM/L)



Not used in clinical practice

- × **Toxic to kidney and internal ear**
- × **Low potency**
- × **Limited by IV delivery**

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

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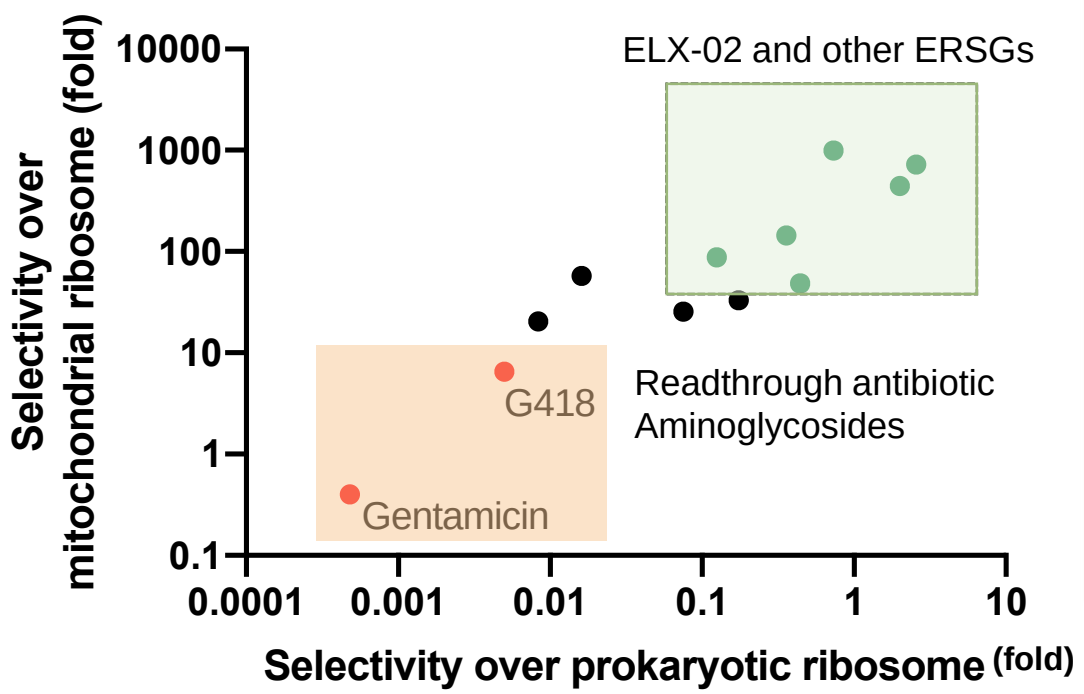
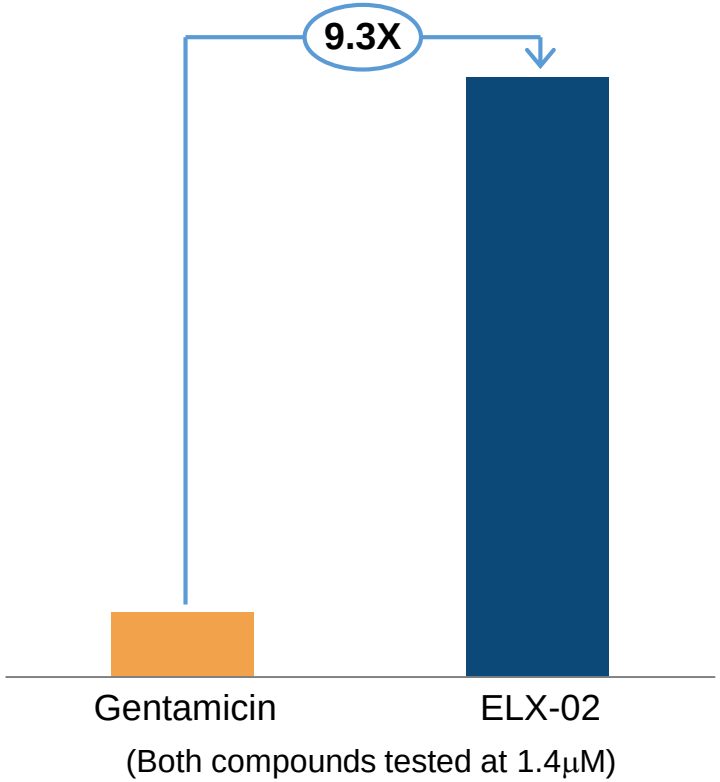
ELX-02: Greater activity and decreased mitochondrial toxicity versus gentamicin

Eukaryotic ribosome selectivity comparison[1]



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



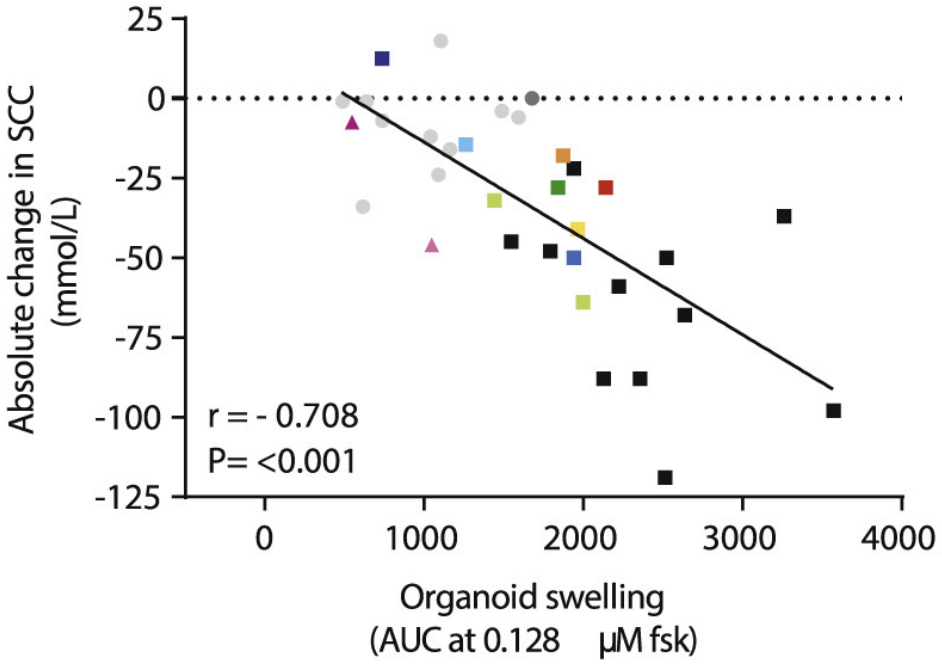
[1]Data adapted from: *J Med Chem*. 2012 Dec 13;55(23):10630-43.1;

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

CF patient organoid swelling observed in response to Kalydeco and Orkambi

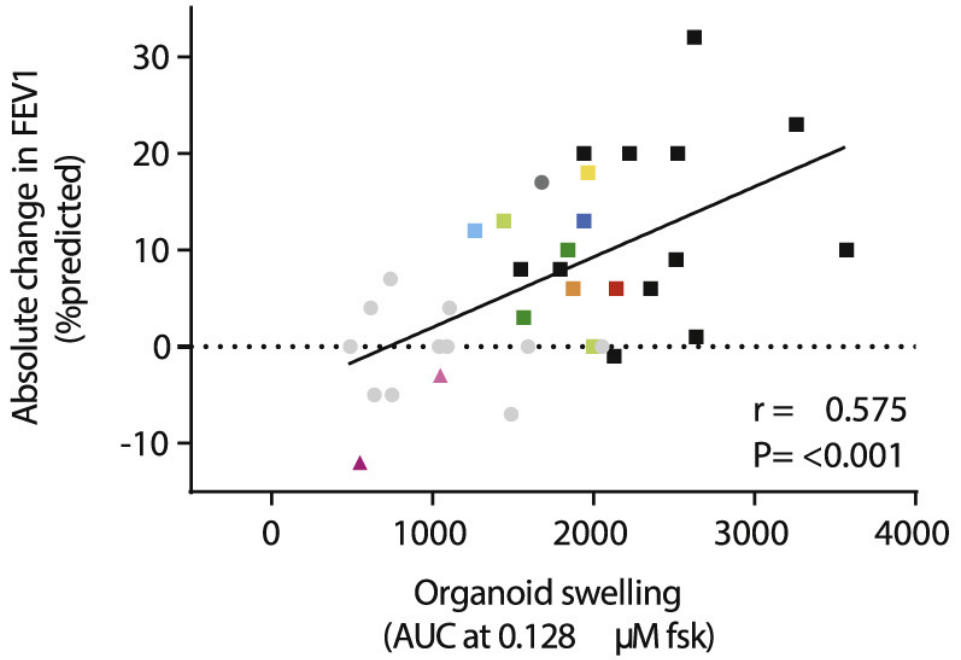
Organoid swelling vs. sweat chloride change

Organoids vs. SCC (n=33)



Organoid swelling vs. FEV_1 change

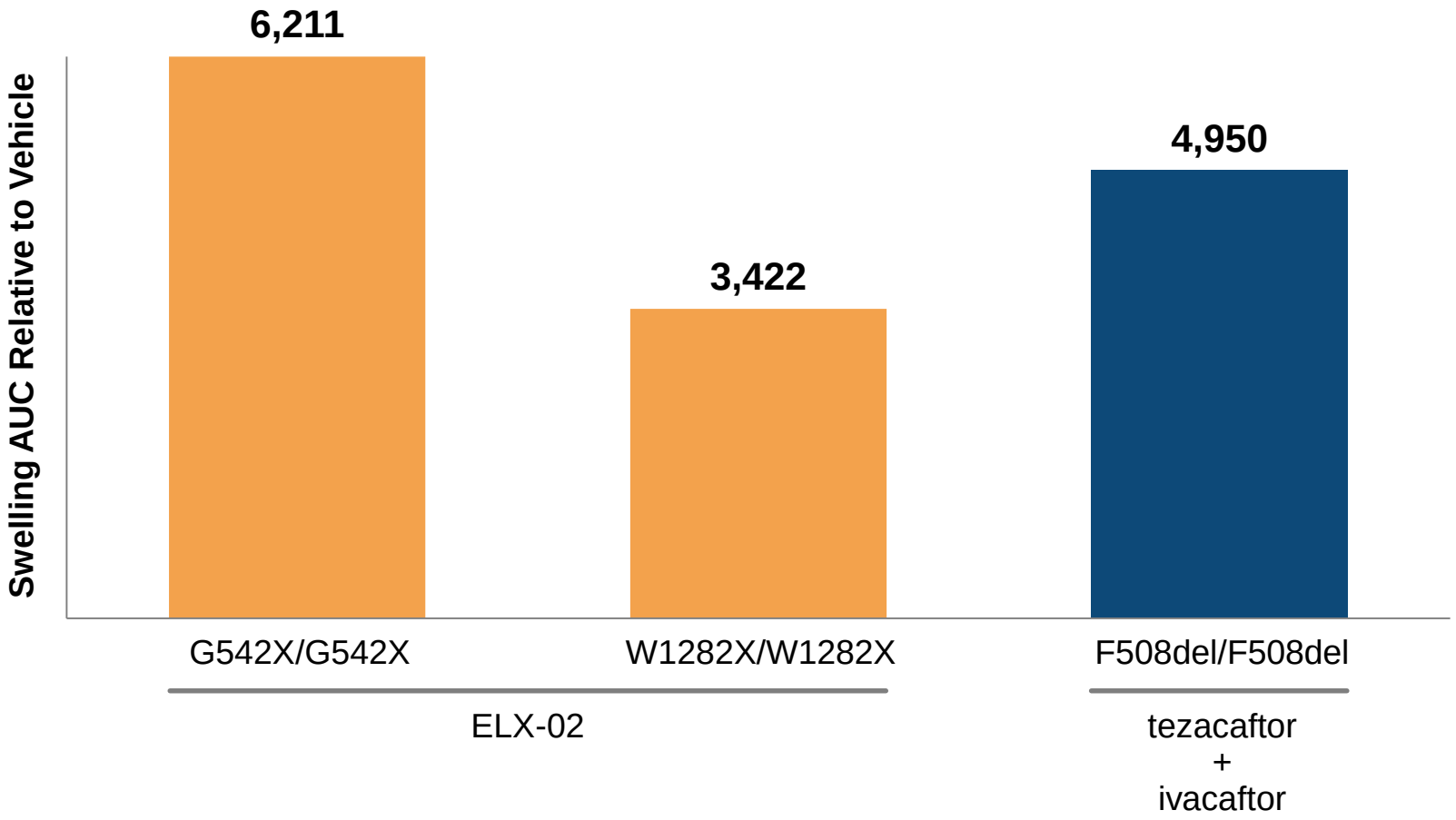
Organoids vs. FEV_1 (n=35)



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

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

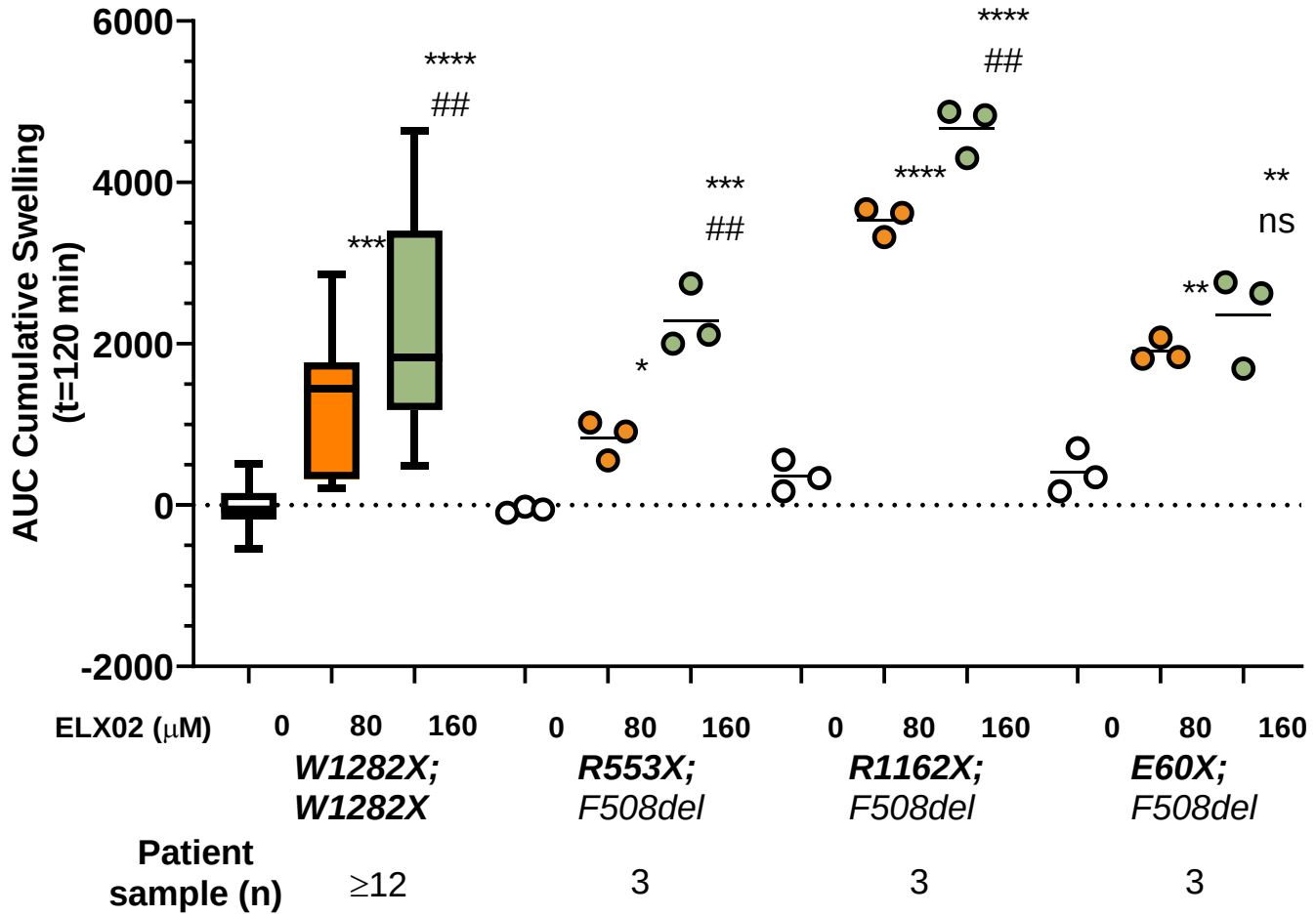
Cumulative organoid swelling in Class I and Class II CF Patient organoids after 48 hours of treatment (t=120 mins)*



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

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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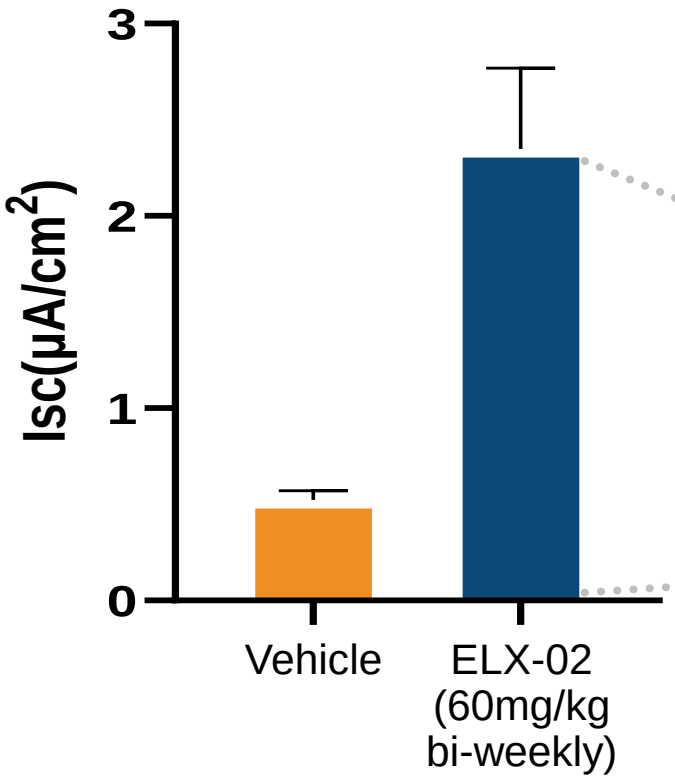
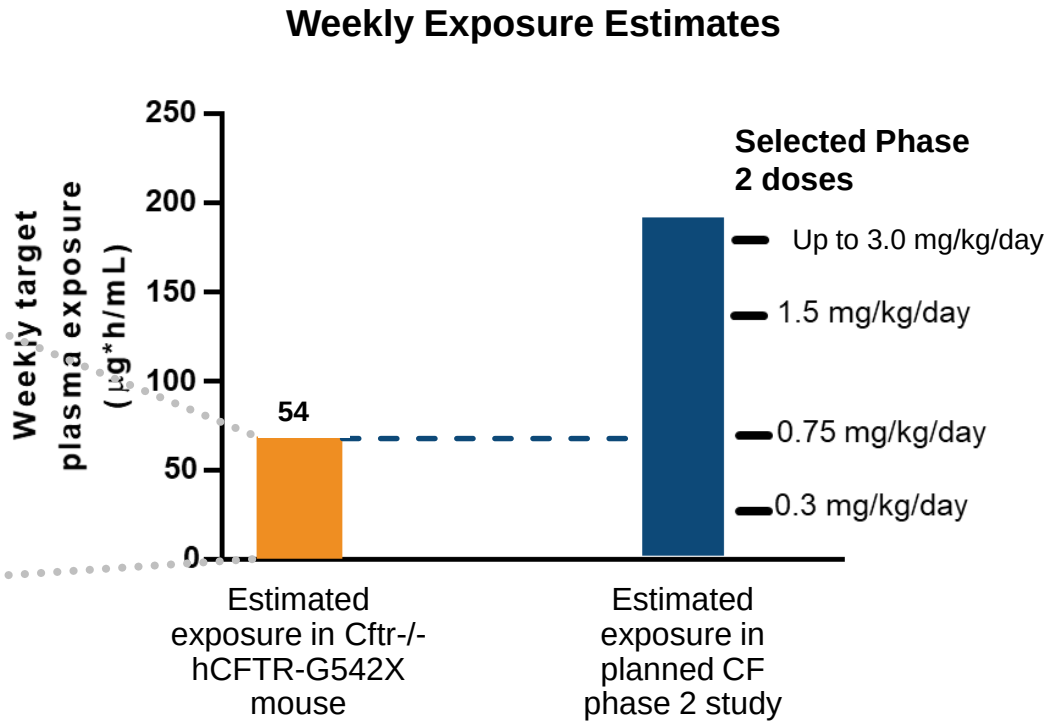
Phase 2 ELX-02 doses based on activity and doses in *in vivo* models

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 data from in vivo studies

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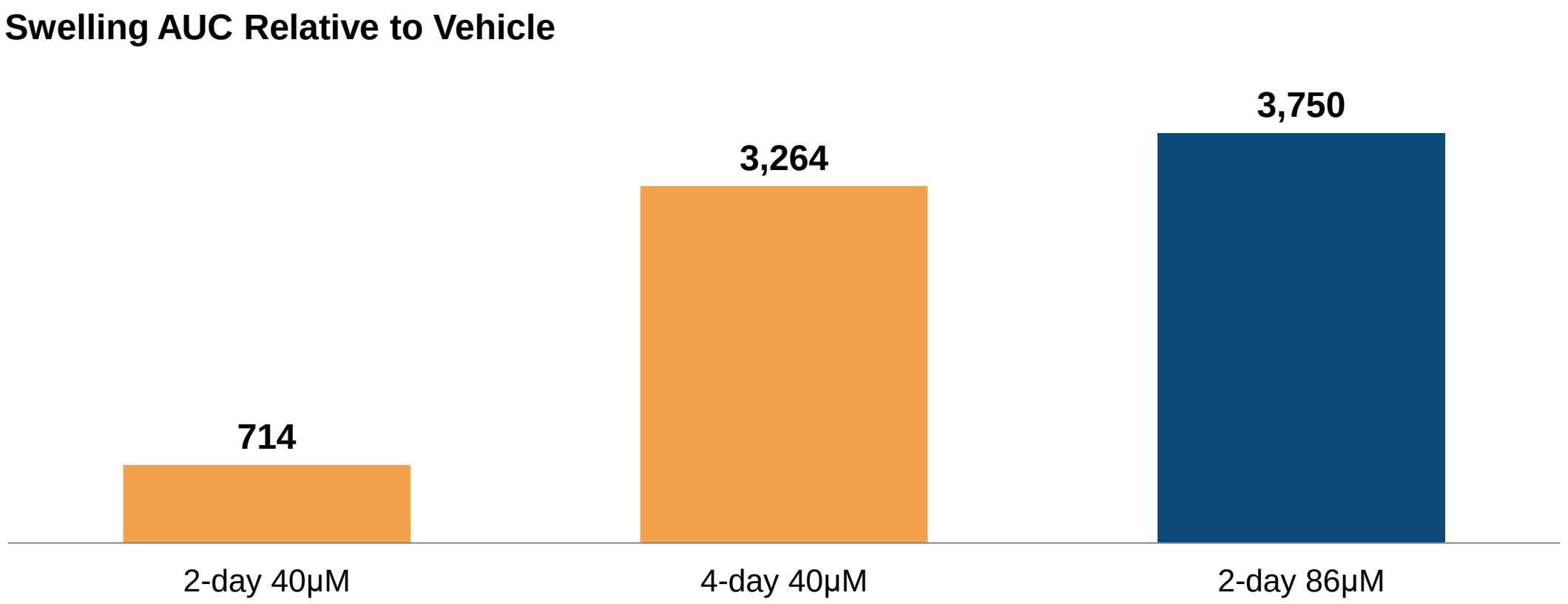
Similar activity observed at lower doses with longer ELX-02 exposure

Experiment performed in G542X/G542X patient derived organoids

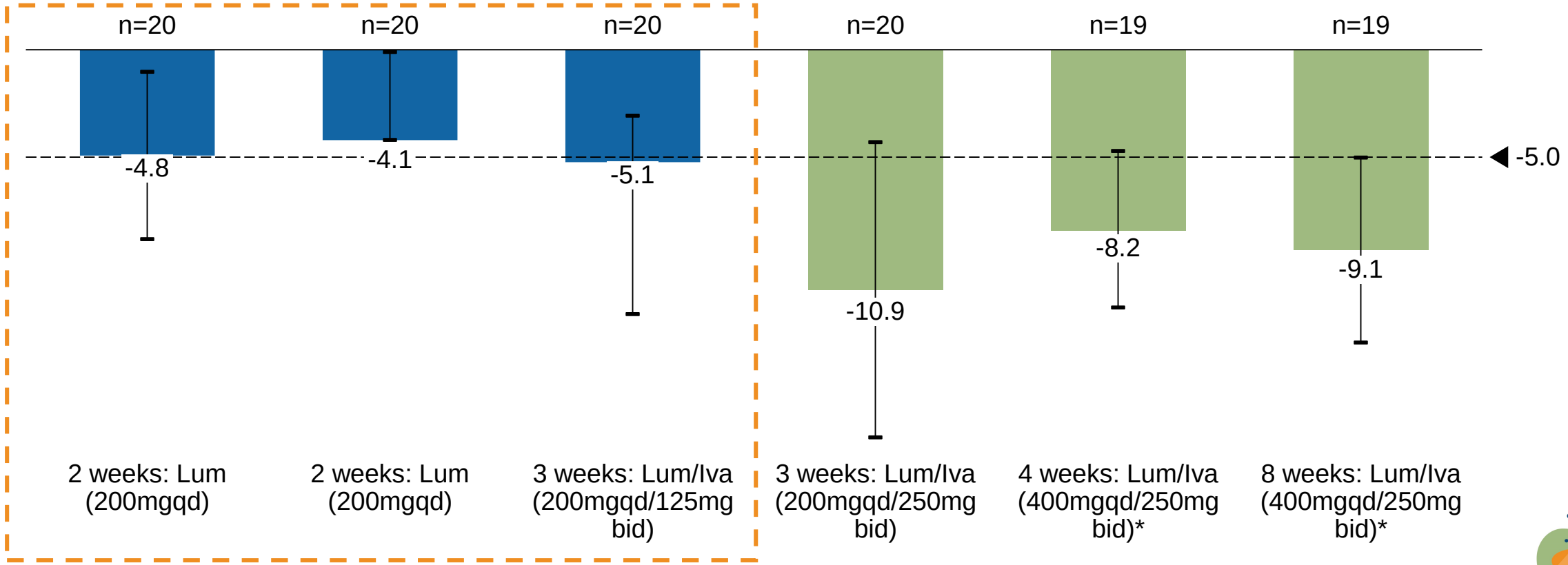


All experiments conducted at HUB

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 Program Expansion

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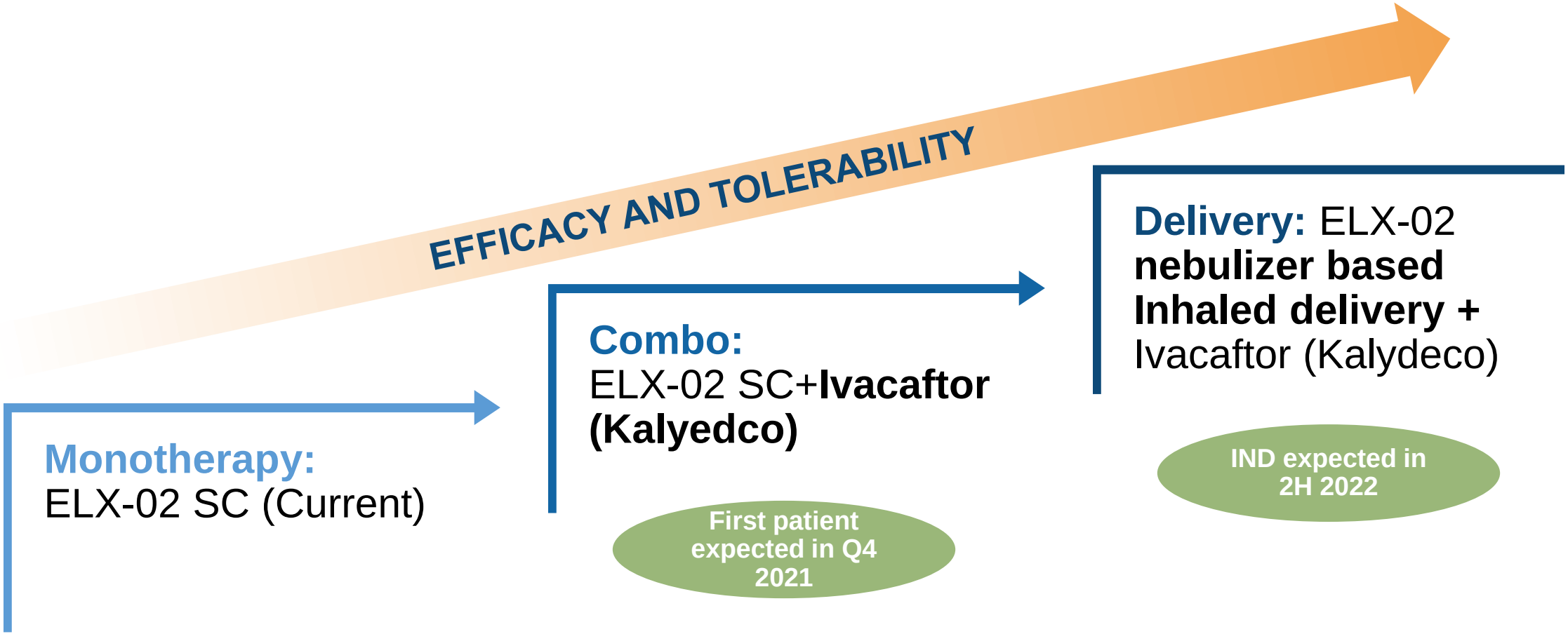
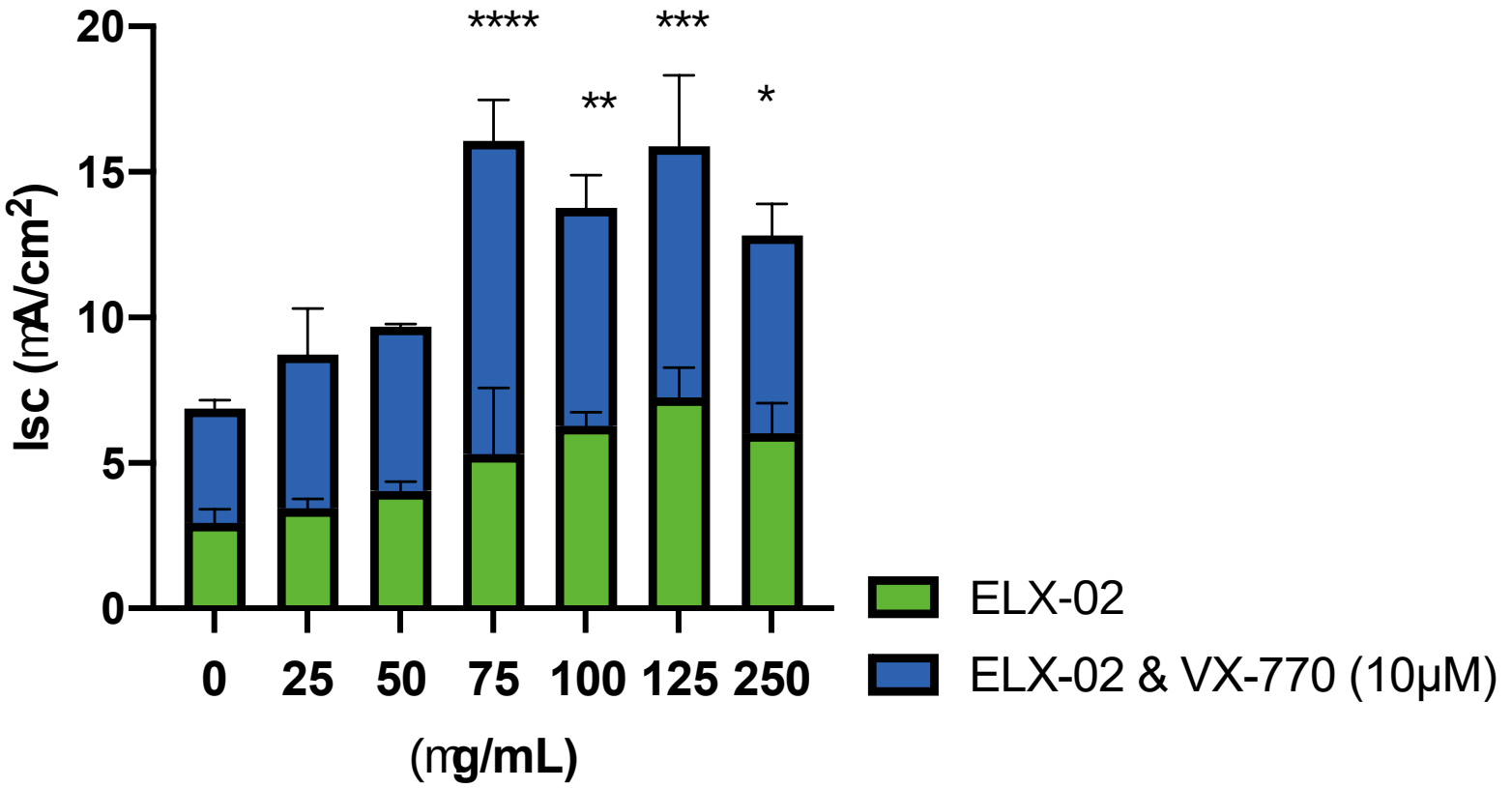
ELX-02 monotherapy program foundation for achieving transformative outcomes for CF Class 1 patients



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*

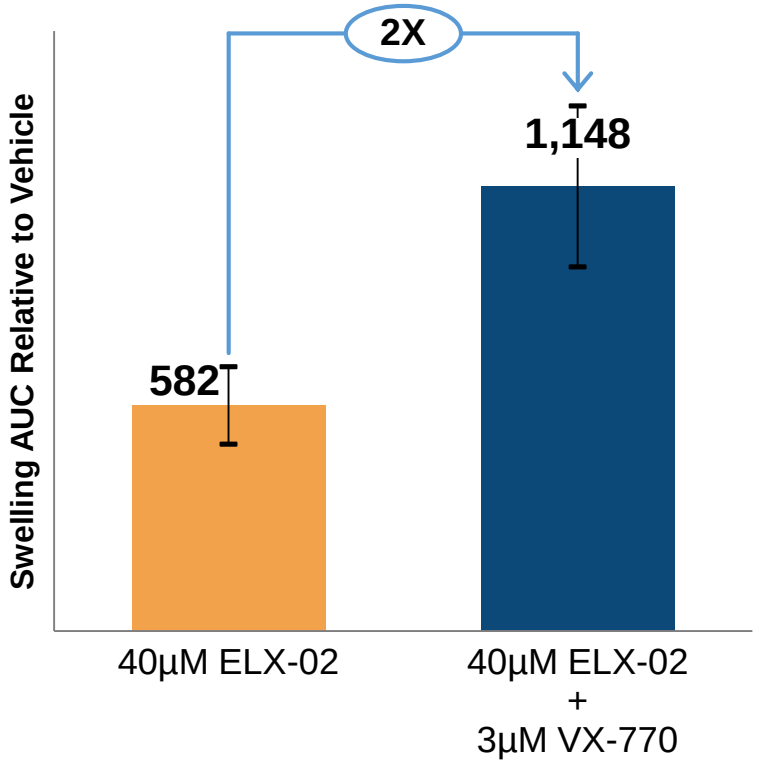


*Human Broncho Epithelial cells

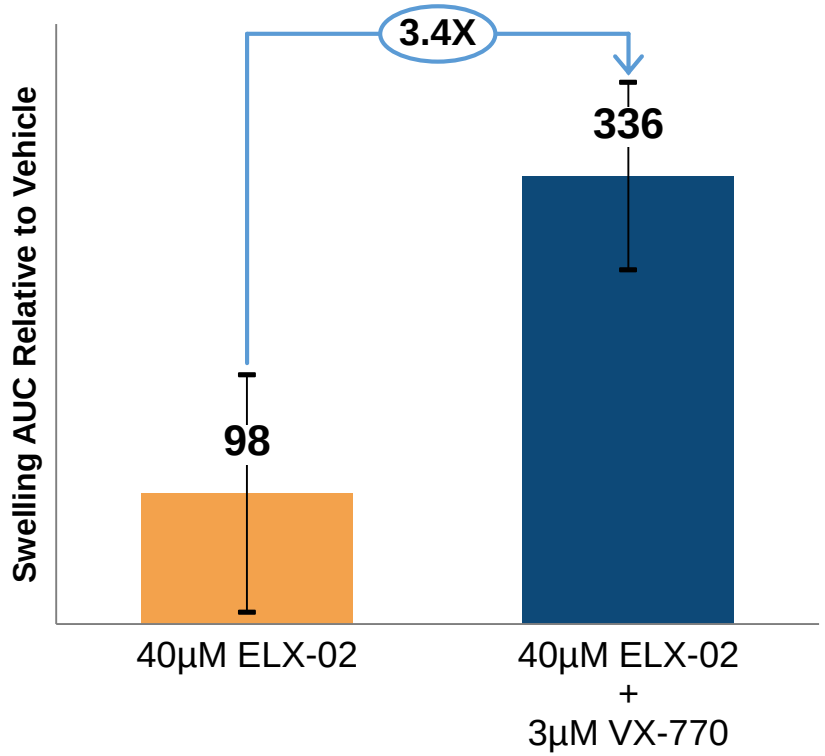
Kalydeco enhances ELX-02 activity across different nonsense mutations

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/g/day ELX02 + ivacaftor (150mg bid)

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

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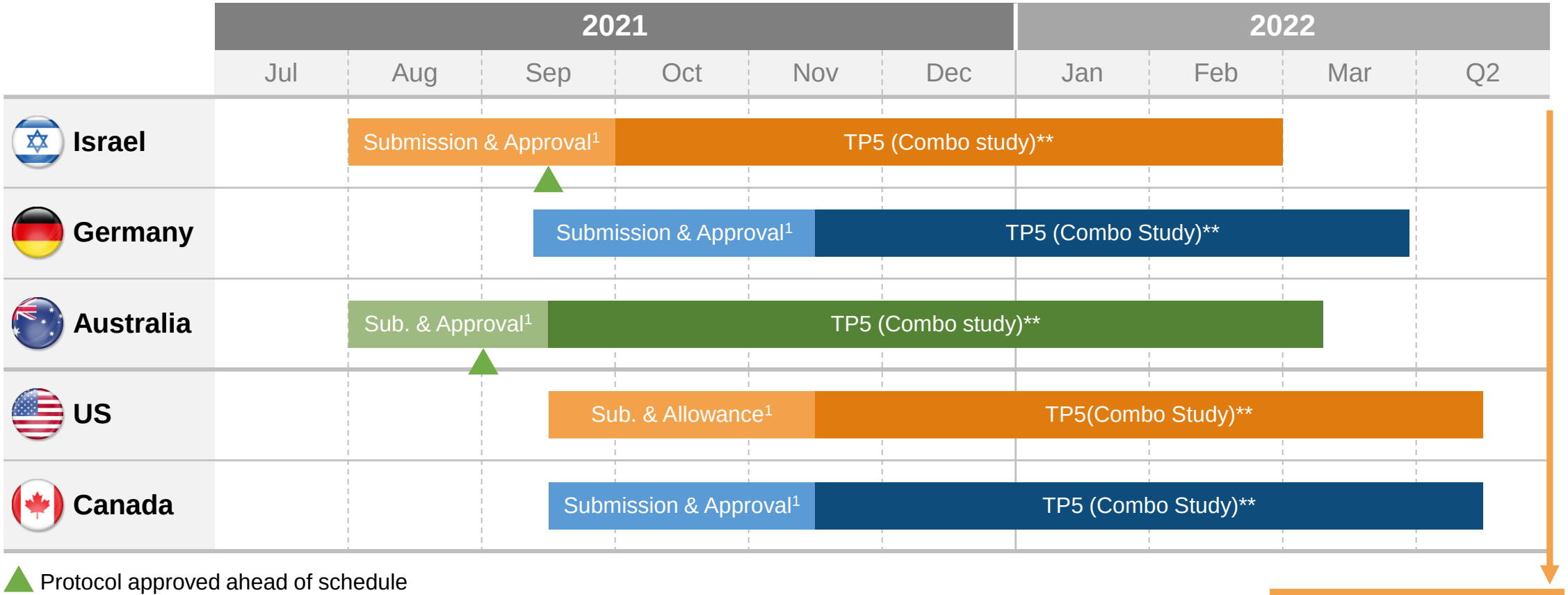
First Patient in combination study expected to be dosed in Israel in Q4 2021 with topline data by 1H 2022



[1] CTA in Israel, Germany, Canada. CTN in Australia. IND in US. ** COVID dependency

Standard of care inhaled therapies paves path for ELX-02

Convenient

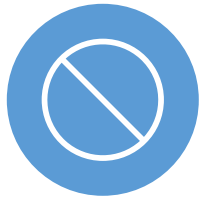
Inhaled antibiotic therapy is standard of care in Cystic fibrosis patients (e.g., Tobramycin, aztreonam, dornase alfa)

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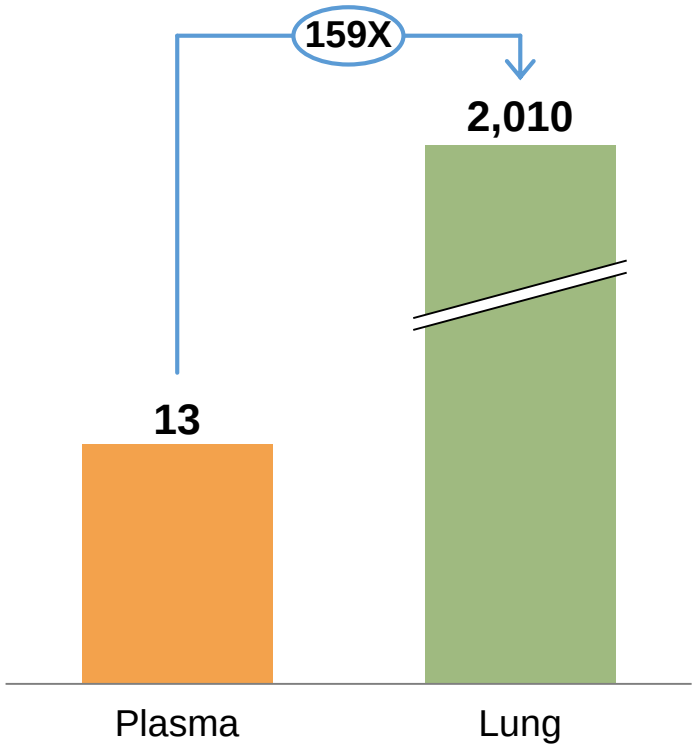
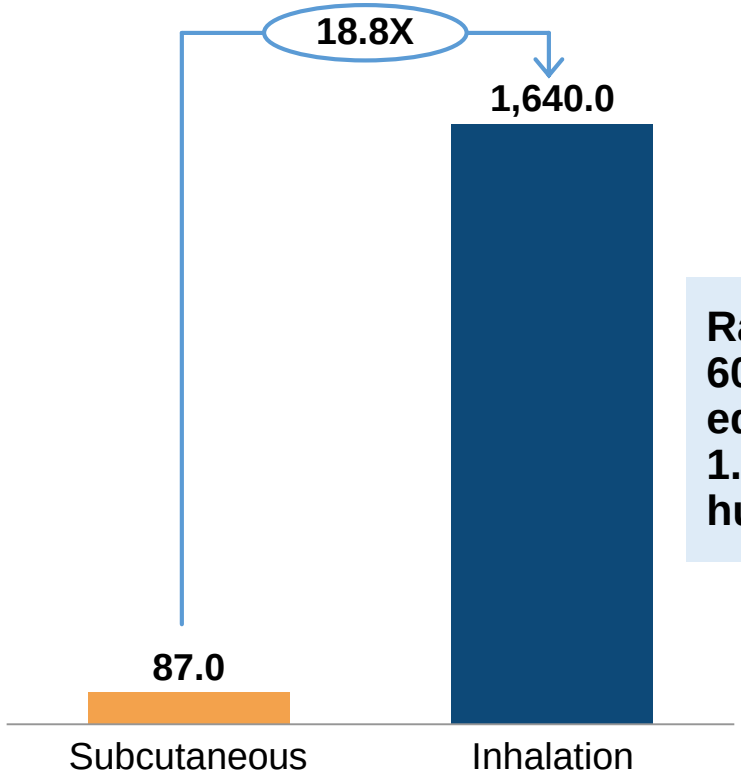
Meaningfully higher lung exposure observed with inhaled ELX-02 opens path to significantly higher activity

Lung vs Plasma exposures with inhaled vs. subcutaneous dosing

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



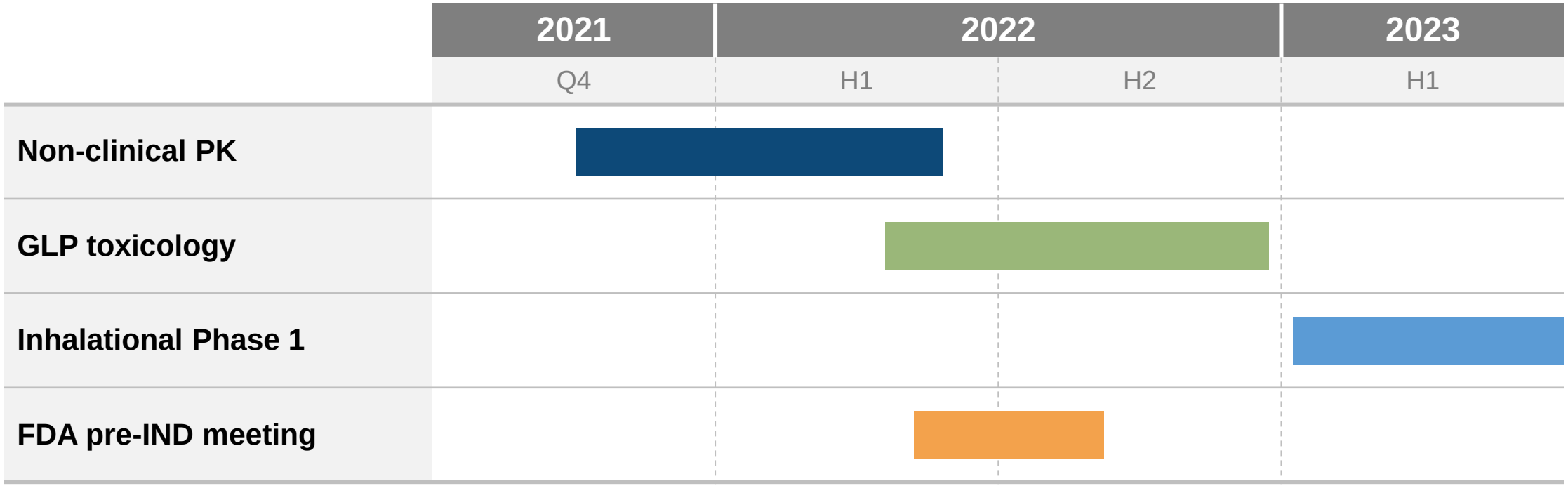
Estimated rat lung exposure 60 mg/kg sc vs. 69 mg/kg inhaled ($AUC_{0\text{-}24hr}$ µg*hr/ml)



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

ELX-02 inhalation IND targeted for 2H 2022

Parallel development of subcutaneous and inhaled ELX-02



ELX-02 CF Program Milestones

ELX-02 milestones

4Q 21

- ✓ Completed enrollment of ELX-02 monotherapy arms in ongoing Phase 2 trials
- Report 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
- Initiate IND enabling studies for inhalation

1H 22

- Report data from combination therapy Phase 2 trial of ELX-02
- Initiate GLP toxicology studies with inhaled ELX-02

2H 22

- Submit IND for inhaled ELX-02
- End of Phase 2 meeting for subcutaneous version

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Key Takeaways & Closing Remarks

Sumit Aggarwal
President and CEO

Key Takeaways

- New leadership team with track record of execution
- Significant unmet need remains for Class 1 CF patients
- ELX-02 designed as superior readthrough agent to Gentamicin with compelling preclinical activity
- Ongoing Phase 2 monotherapy to evaluate safety and biological activity expected to readout in Q4 2021
- Combination and inhaled delivery have potential for transformative outcomes

Positioned to create significant value for patients and shareholders

Eloxx PHARMACEUTICALS

Deep pipeline of synergistic potential first-in-class therapies

	Target	Indication	Discovery	Lead optimization	IND enabling	Phase 1 – first in human	Phase 2	Phase 3
Nonsense readthrough: rare disease	CFTR	Class 1 CF	ELX-02 (Fast Track Designation*)					CYSTIC FIBROSIS FOUNDATION
	Collagen VII A1/LAMB3	RDEB/JEB	ZKN013					
	CFTR	Class 1 CF	RMA(s)					CYSTIC FIBROSIS FOUNDATION
Nonsense readthrough: oncology	APC	FAP	ZKN013					
	APC	CRC	ZKN074/ZKN157					
	Undisclosed	Pan cancer/ IO combination	RMA					
Protein translation inhibition	Onco-ribosome & mito-ribosome mutations	Undisclosed	RMA					

***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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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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Questions?

Answers.

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