RARE Thinking for RARE Solutions

Topline ELX-02 Combination Phase 2 Cystic Fibrosis (CF) Results

September 14, 2022

Forward-looking statements

This press release 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, the expected timing of trials 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, 2022, 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/financials-filings.

All forward-looking statements speak only as of the date of this press release 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.

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Summary of Phase 2 results

Combination treatment did not achieve statistical significance for efficacy endpoints

Assessment of responders shows drug activity for ELX-02

Higher drug exposure in lung needed to generate therapeutic benefit

Path forward in CF to be determined together with the CF Foundation

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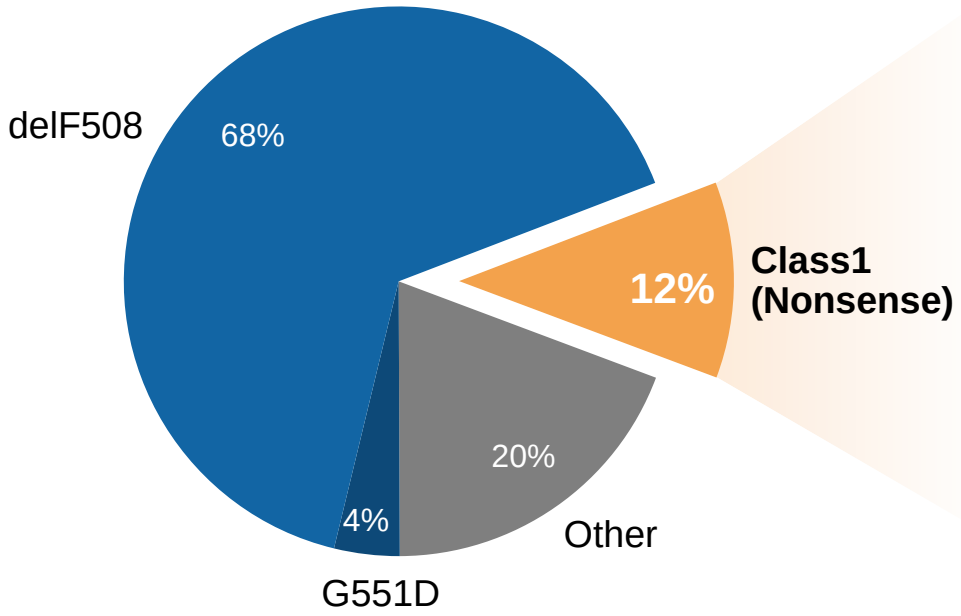
Class 1 CF patients carrying nonsense mutations have the most severe phenotype

CF patients by mutation type[1]

Total CF Patients =70,000 – 100,000



- **No functional CFTR** created
- **More severe disease presentation**
- **Higher rate of FEV1 decline**
- **No approved therapies**
- ELX-02 granted **Orphan Drug and Fast Track Designation** by FDA

CYSTIC FIBROSIS FOUNDATION

CF Foundation committed to additional funding of up to $15.9 million for ELX-02 clinical program in March 2022

[1] Allelic frequency based on CFTR2 database (July 2020); CF population data based on 2019 Patient Registry Report

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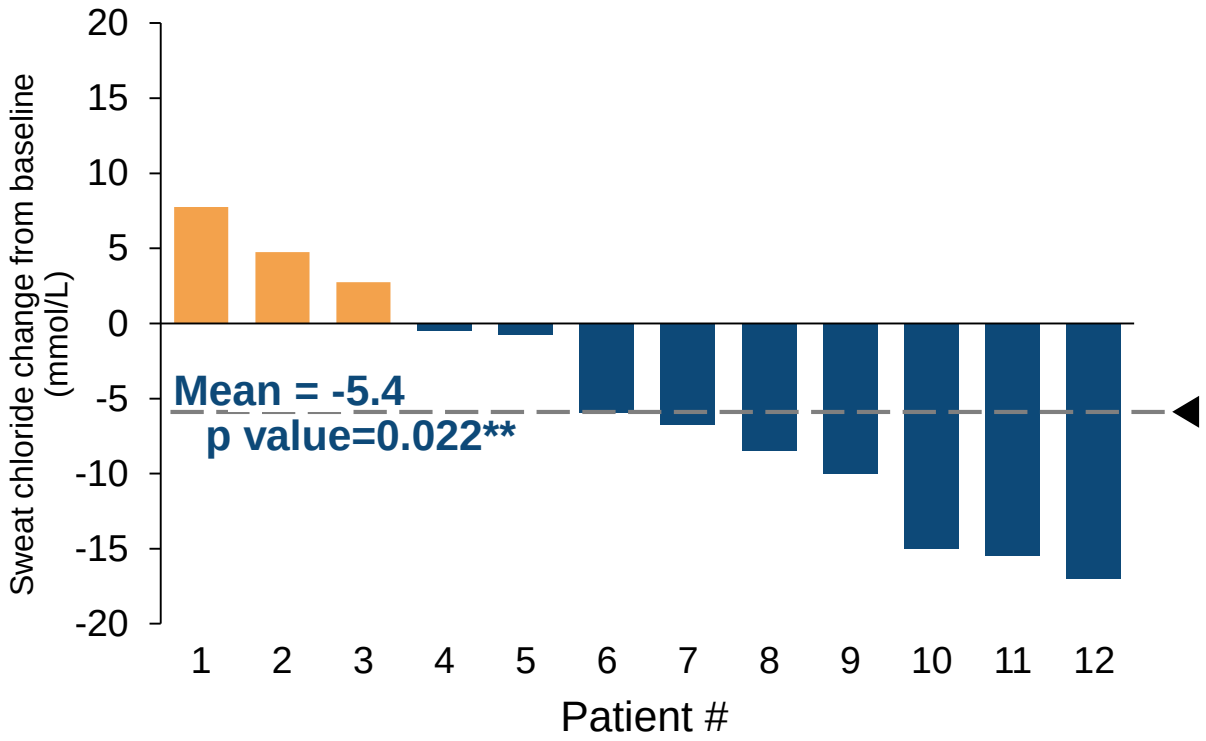
Recap: Significant reduction in sweat chloride observed with 1-week ELX-02 monotherapy treatment (Nov 2021)

ELX-02 intra-patient dose escalation monotherapy Phase 2 trial results

Change in sweat chloride from baseline in G542X CF patients after 1 week treatment with ELX-02 (mmol/L)*



	Sweat chloride change (SCC) in mmol/L
Responders (mean)	-8.9
Response rate	9/12 (75%)

*Drug response evaluated based on difference between end of the treatment period to the average baseline for each patient excluding patients that had a greater than 15mmol/L variability in sweat chloride between right and left arms or between screening and day 1

** Results at the variable doses of 1.5mg/kg up to 3.0 mg/kg were not significant with only N=7 completers. Current data assessed to be sufficient to select 1.5 mg/kg/day for future studies

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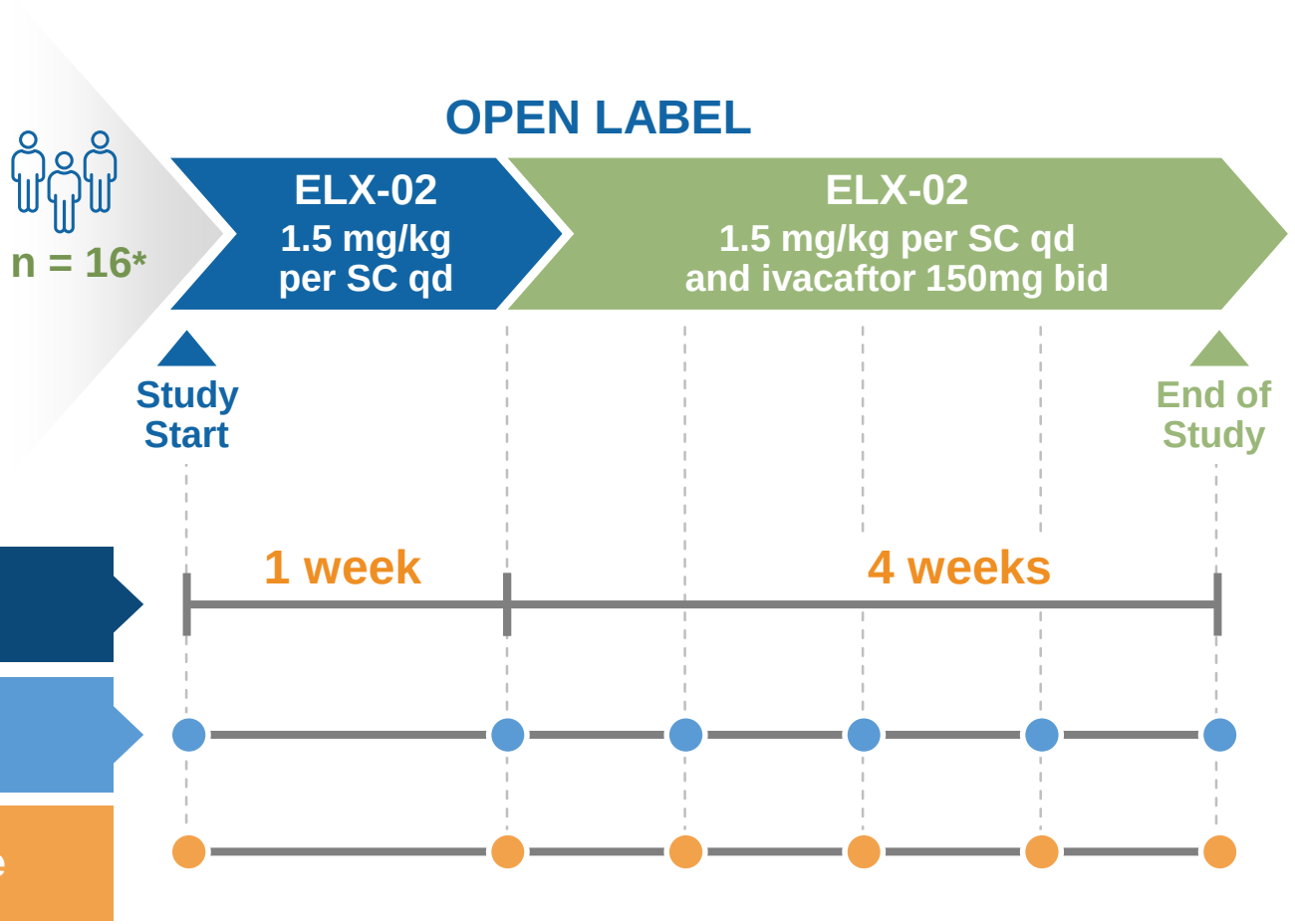
Expanded 5-week Phase 2 trial to evaluate FEV1 and safety in combination with ivacaftor

ELX-02 and ivacaftor combination in Class 1 CF Phase 2: Study Design

Inclusion Parameters	Criteria
Genotype	All Patients with nonsense mutations
Age	All patients >12 years
FEV1	>40%



* Trial designed to enroll up to 24 patients

No systemic safety signals observed for ELX-02

Cumulative safety experience across all Phase 2 patients

No ELX-02 related serious adverse events (SAEs)

ELX-02 was well tolerated at 1.5 mg/kg dose across Phase 2 patients (n=31)

- Combination therapy at 1.5 mg/kg showed drug related discontinuations
  - 2 patients discontinued due to injection site reactions (mild to moderate)
  - 1 patient withdrew from trial due to injection burden prior to dosing
  - 1 patient with tinnitus*

* Patient had an undisclosed history of tinnitus

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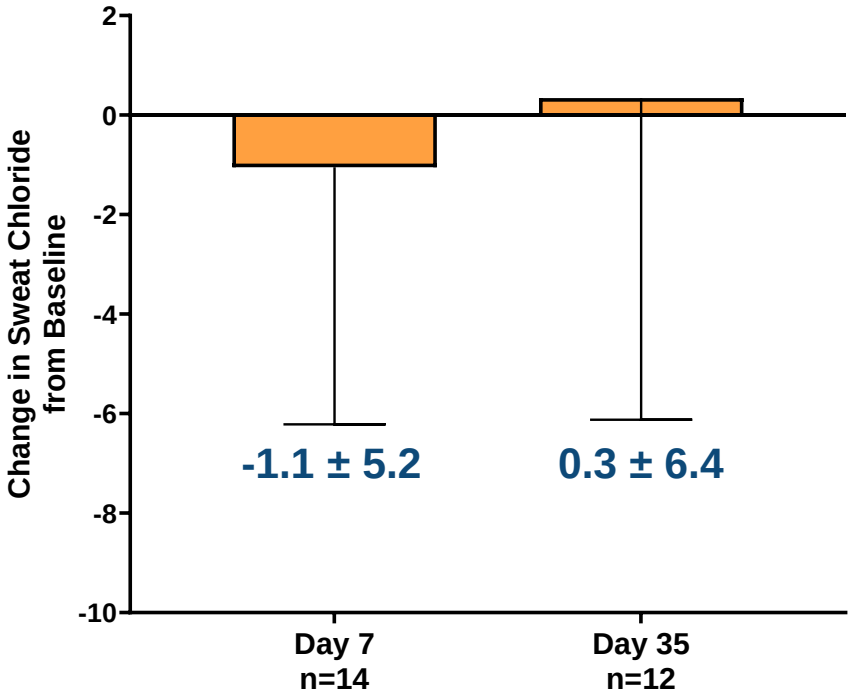
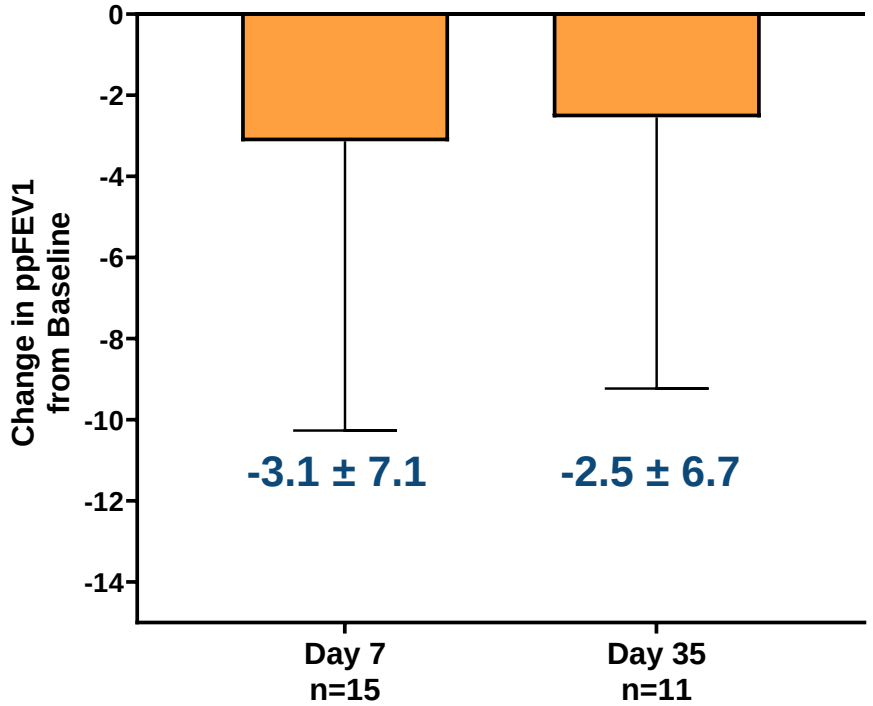
Combination of ELX-02 with ivacaftor did not achieve statistical significance for efficacy endpoints

SCC and FEV1 change from baseline at Day 7 and Day 35

Mean SCC from baseline



Mean FEV1 change from baseline



No incremental benefit observed with ivacaftor combination

Error bars: Standard deviation

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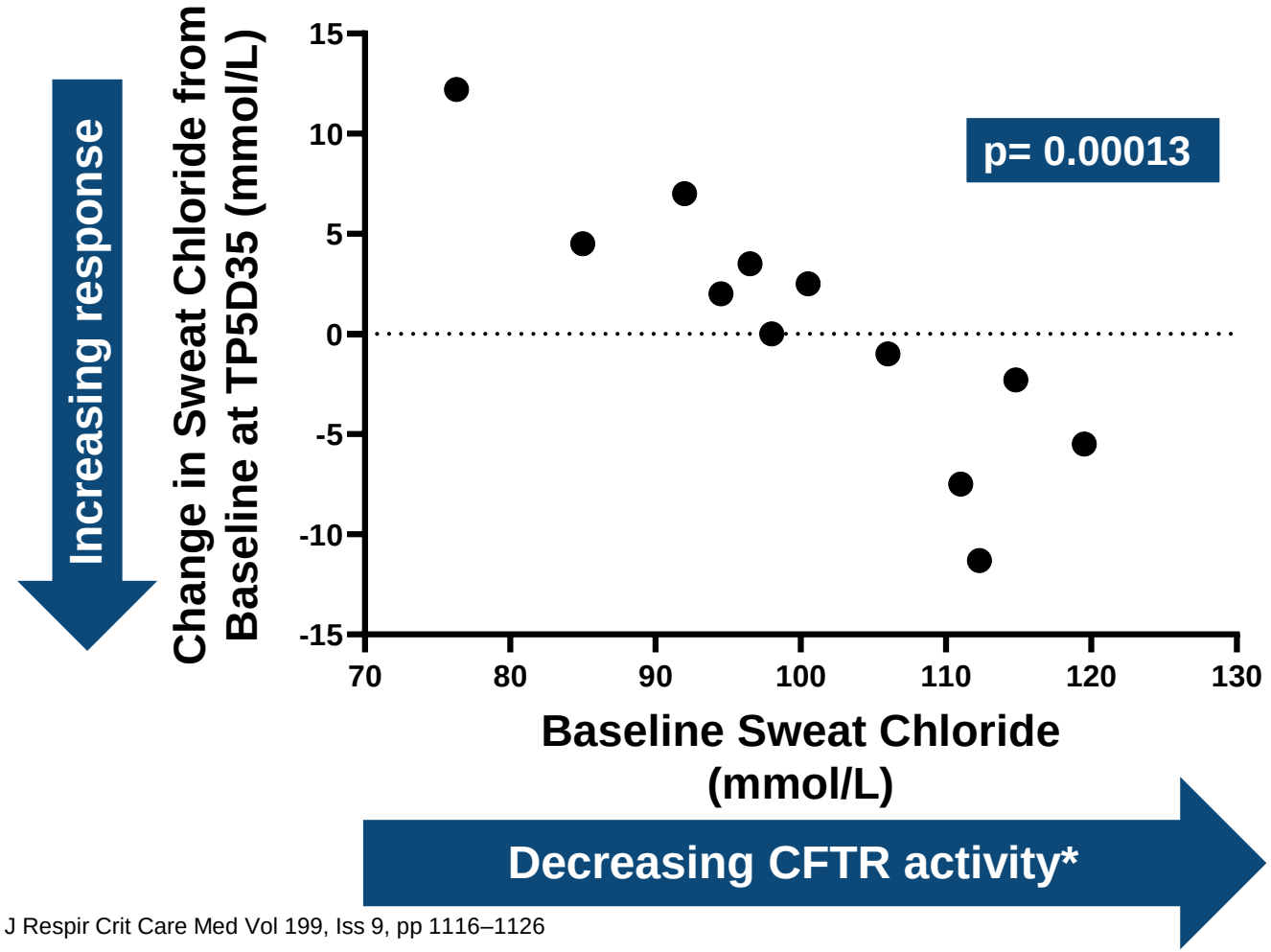
Responder assessment showed drug activity

Baseline sweat chloride vs. SCC at Day 35

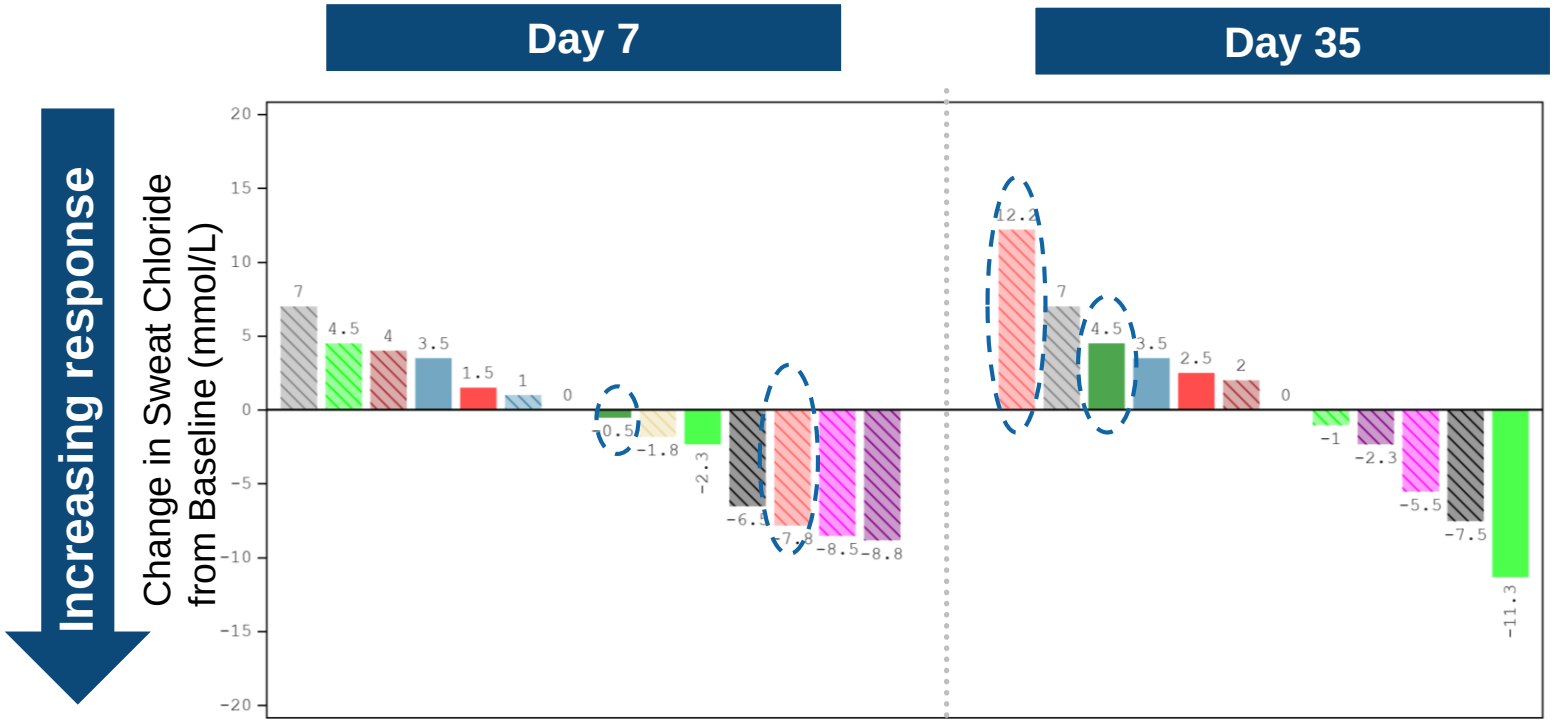


Prior Phase 2 monotherapy showed a similar relationship with treatment response

*Am J Respir Crit Care Med Vol 199, Iss 9, pp 1116–1126

High sweat chloride variability confounded activity signal in responders

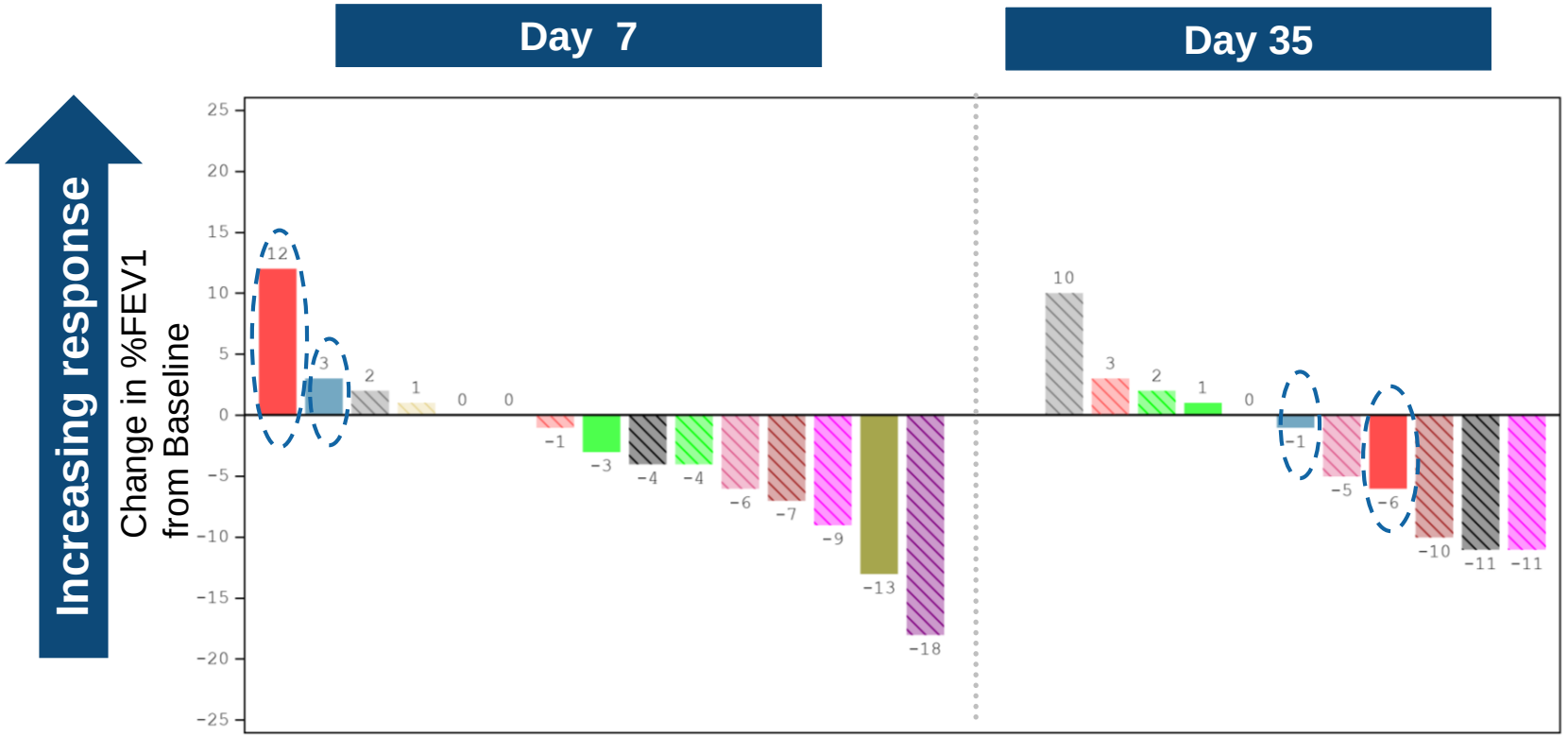
SCC at Day 7 and Day 35 by patient



	SCC at Day 7 Mean (SD)	SCC at Day 35 Mean (SD)
Responder	-5.2 (3.5)	-5.5 (4.1)
Responder rate	7/14 (50%)	5/12 (42%)

Similar variability in lung function measurement confounded activity signal in responders

Change in FEV1 from baseline at Day 7 and Day 35 by patient



	FEV1 change at Day 7 Mean (SD)	FEV1 change at Day 35 Mean (SD)
Responder	+4.5 (5.1)	+4.0 (4.1)
Responder rate	4/15 (27%)	4/11 (36%)

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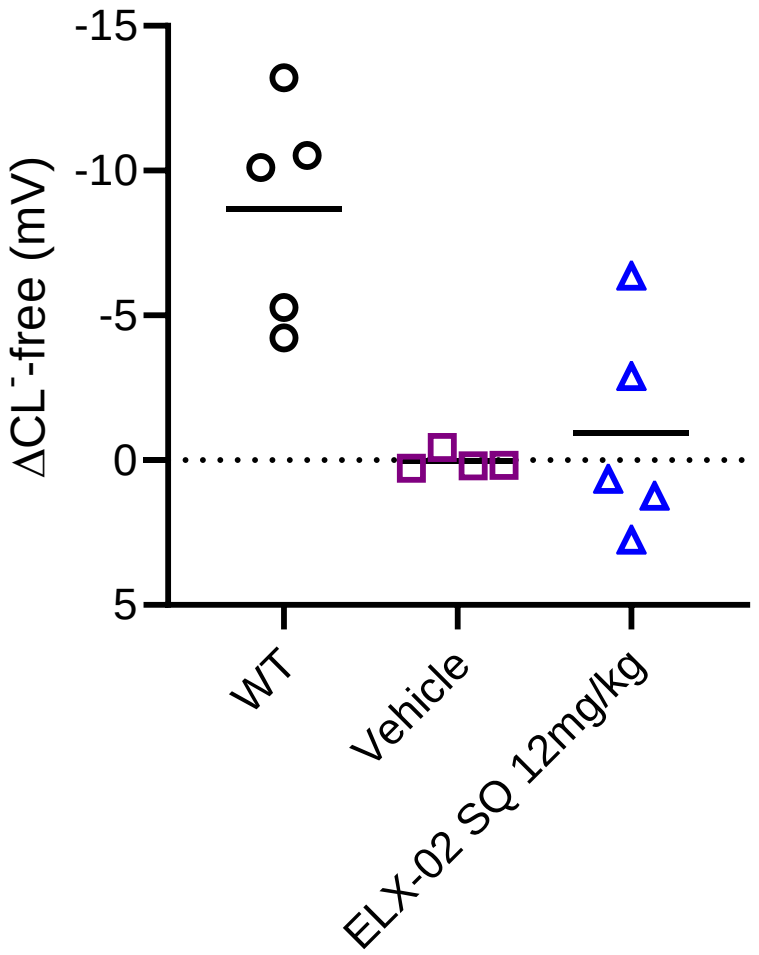
High variability also in G542X rats after SC ELX-02 treatment

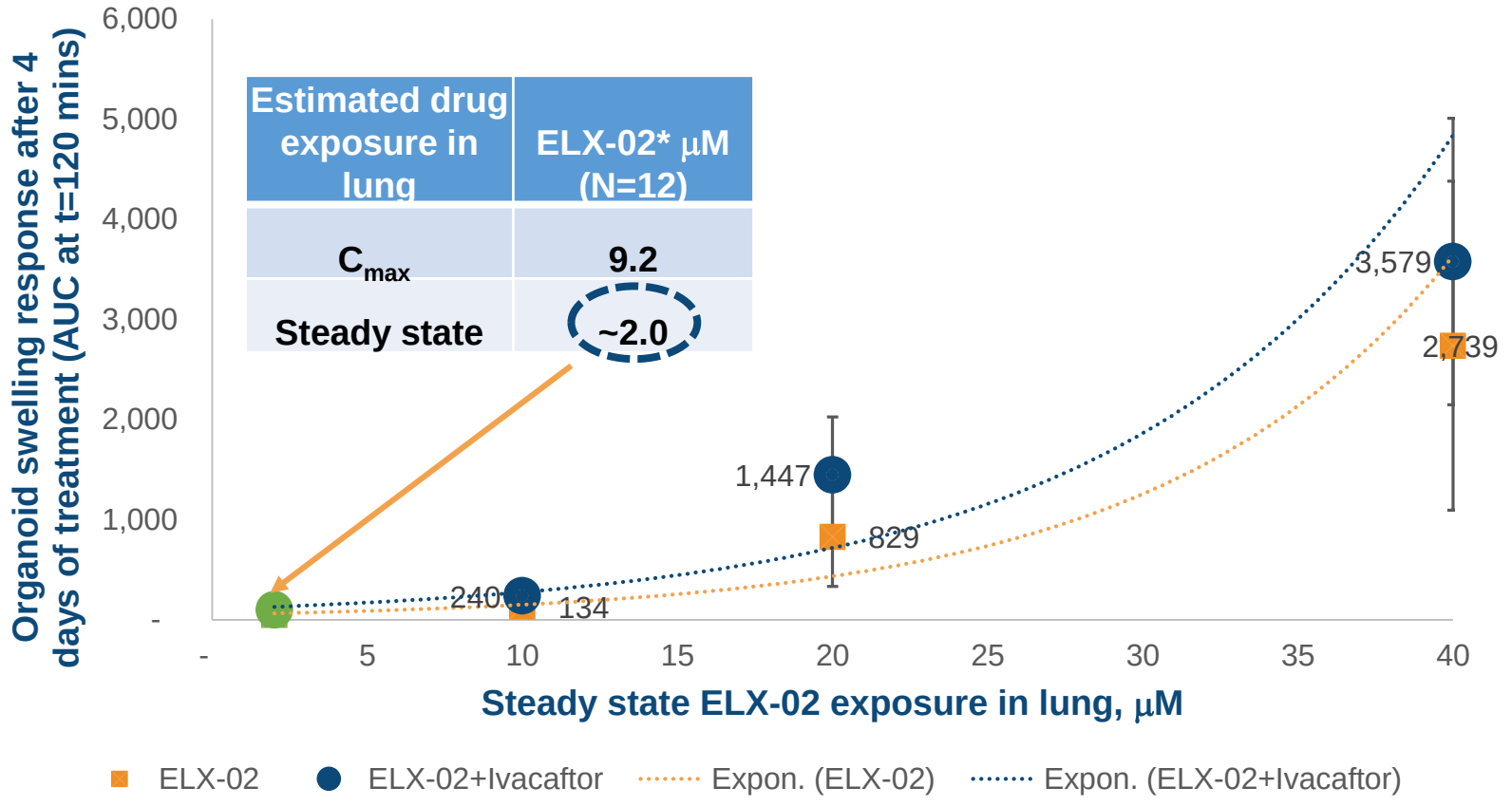
Nasal potential difference in G542X rats after 7 days of SC ELX-02 treatment at 12 mg/kg (human equivalent dose of 1.5 mg/kg)



Data from Dr. Susan Birket – UAB

Higher drug exposure in lung needed to generate therapeutic benefit

Swelling response in CF patient organoids to ELX-02 treatment with and without ivacaftor*



Expect to safely achieve steady state exposure of ~200µM in the airway with Inhaled ELX-02 at 0.075 mg/kg/day

Forskolin concentration: 0.8uM; Swelling adjusted for control. Data generated at HUB across multiple experiments. Values represent mean and standard deviation across multiple experiments

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Key takeaways

Evidence of activity for ELX-02 observed and shown to be well tolerated with no SAEs

Efficacy signal potentially confounded by variability due to low drug exposure

Path forward in CF to be determined together with the CF Foundation

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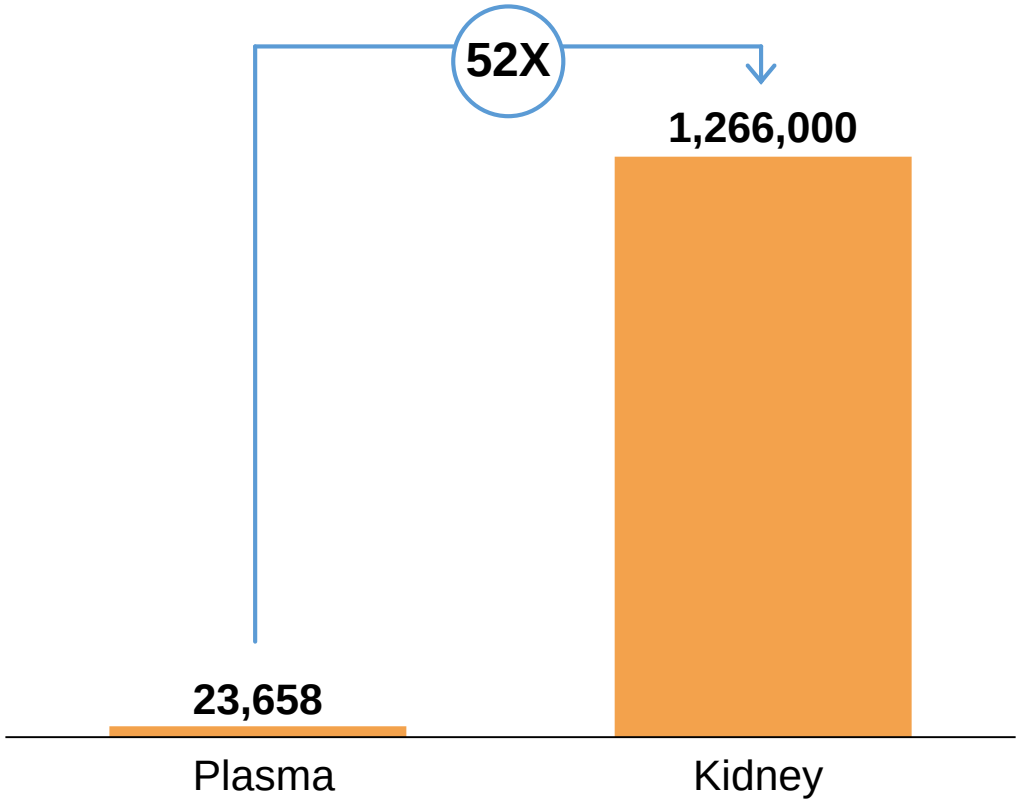
In contrast, high ELX-02 levels can be easily achieved in kidney

Estimated ELX-02 dose to exposure relationship in kidney at 1mg/kg, ng*hour/ml



- **CF results de-risk current Alport Program**
- **Estimated kidney exposure at 0.75 mg/kg 50-100μM**

Significant pipeline milestones expected over next 12 months

Milestones over next 12 months

	2H 2022	1H 2023
Class 1 Cystic Fibrosis (Inhaled ELX-02)	• Inhaled ELX-02 IND submission • Inhaled vs. SC *in vivo* efficacy readout	• TBD (in conjunction with CF Foundation)
Alport Syndrome (SC ELX-02)	• Proof-of-concept trial start	• Topline results
RDEB/JEB (ZKN-013)	• IND submission • Phase 1 (SAD) start	• Phase 1 (MAD) start
FAP (ZKN-013)		• IND submission preparation

Cash, including CFF award, expected to be sufficient to fund operations into 4Q23

* RDEB/JEB: Recessive Dystrophic/Junctional Epidermolysis Bullosa; FAP: Familial adenomatous polyposis

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Questions?

Answers.

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