UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 14, 2022

Eloxx Pharmaceuticals, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-31326**	**84-1368850**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

480 Arsenal Way, Suite 130, Watertown, MA	**02451**
(Address of principal executive offices)	**(Zip Code)**

(Registrant's telephone number, including area code): (781) 577-5300

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.01 par value per share	ELOX	The Nasdaq Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On September 14, 2022, Eloxx Pharmaceuticals, Inc. (the "Company") issued a press release announcing topline results from its Phase 2 combination clinical trial of ELX-02 in Class 1 Cystic Fibrosis ("CF") patients. A copy of the press release and presentation are attached hereto as Exhibit 99.1 and Exhibit 99.2, respectively, and incorporated under this Item 7.01 by reference.

The information in this Item 7.01 of this Current Report on Form 8-K (including Exhibits 99.1 and 99.2 hereto) shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that Section, nor shall it be deemed to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01 Other Events

We are providing the following business update.

Recent Developments

On September 14, 2022, the Company announced topline results from the Phase 2 clinical trial of ELX-02 in combination with ivacaftor in Class 1 CF patients with at least one nonsense mutation. The combination trial of ELX-02 with ivacaftor was well tolerated but did not achieve statistical significance for efficacy endpoints, including changes from baseline in sweat chloride concentration (SCC) and percent forced expiratory volume (FEV1).

The Phase 2 combination clinical trial of ELX-02 was designed to evaluate safety and assess biological activity in G542X nonsense mutation Class 1 CF patients as monotherapy and in combination with ivacaftor. The trial included a 1-week monotherapy period (1.5 mg/kg daily subcutaneous) followed by a four week combination period (1.5 mg/kg daily subcutaneous and 150 mg ivacaftor twice daily).

ELX-02 was generally well tolerated in the trial, with no treatment-related serious adverse events noted. Overall, the study did not achieve statistical significance for efficacy endpoints in the Phase 2 study in Class 1 CF for efficacy endpoints, including changes from baseline in SCC and FEV1. No incremental improvement was observed with ivacaftor combination. Evidence of activity for ELX-02 was observed, as patients with higher baseline sweat chloride levels demonstrated increased responses as indicated by SCC ($p=0.00013$ at Day 35). Trial results were potentially confounded by high variability in sweat chloride and lung function measurement. The Company believes this variability could have been caused by very low drug exposures in the lung. Steady state lung drug levels in patients from this trial were on average 20%, or 2μM, of the lowest levels at which drug activity has previously been seen in preclinical testing. Lung drug exposure with inhaled delivery of ELX-02 is expected to be at least 50-fold greater than with subcutaneous delivery.

Forward-looking Statements

This Current Report on Form 8-K 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 current report, including without limitation, statements regarding 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 quarterly period 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/financial-information/sec-filings.

All forward-looking statements speak only as of the date of this Current Report on Form 8-K 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.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release of Eloxx Pharmaceuticals, Inc., dated September 14, 2022
99.2	Presentation of Eloxx Pharmaceuticals, Inc., dated September 14, 2022
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: September 15, 2022

ELOXX PHARMACEUTICALS, INC.

By: /s/ Sumit Aggarwal
Name: Sumit Aggarwal
Title: President and Chief Executive Officer

Exhibit 99.1

Eloxx Pharmaceuticals Reports Topline Results from Phase 2 Combination Clinical Trial of ELX-02 in Class 1 Cystic Fibrosis (CF) Patients

Combination of subcutaneous ELX-02 with ivacaftor did not achieve statistical significance for efficacy endpoints in Phase 2 study in Class 1 CF

ELX-02 was well tolerated with no drug-related serious adverse events observed

Evidence of activity for ELX-02 observed; efficacy signal potentially confounded by variability due to low drug exposure

Path forward for ELX-02 for the treatment of Class 1 CF to be determined together with CF Foundation

Company to host conference call and webcast today, September 14, 2022, at 4:30 p.m. ET

WATERTOWN, MA – September 14, 2022 – Eloxx Pharmaceuticals, Inc. (NASDAQ: ELOX), a leader in ribosomal RNA-targeted genetic therapies for rare diseases, today announced topline results from the Phase 2 clinical trial of ELX-02 in combination with ivacaftor in Class 1 cystic fibrosis (CF) patients with at least one nonsense mutation. The combination trial of ELX-02 with ivacaftor was well tolerated but did not achieve statistical significance for efficacy endpoints, including changes from baseline in sweat chloride concentration (SCC) and percent forced expiratory volume (FEV1).

"We are disappointed that ELX-02 failed to achieve statistical significance for its key efficacy endpoints in this Phase 2 trial in combination with ivacaftor for the treatment of Class 1 CF. Despite this setback, we were pleased to observe that ELX-02 was well tolerated and demonstrated additional evidence of activity in this underserved patient population. We will work closely with the CF Foundation, as it has generously supported this trial, to determine the next steps in the development of ELX-02 for CF," said Sumit Aggarwal, President and Chief Executive Officer of Eloxx.

Mr. Aggarwal continued, "Given the safety and evidence of activity we have observed to date with ELX-02, including in this trial, we look forward to initiating a proof-of-concept trial for ELX-02 in Alport syndrome, a rare kidney disease, later this year. Given the likelihood of increased drug exposure, as ELX-02 is preferentially taken up in the kidneys, we believe ELX-02 is well suited to potentially deliver transformative results in these patients."

Topline Results of ELX-02 Phase 2 Combination Trial in Class 1 CF Patients

The Phase 2 combination clinical trial of ELX-02 was designed to evaluate safety and assess biological activity in G542X nonsense mutation Class 1 CF patients as monotherapy and in combination with ivacaftor. The trial included a 1-week monotherapy period (1.5 mg/kg daily subcutaneous) followed by a four week combination period (1.5 mg/kg daily subcutaneous and 150 mg ivacaftor twice daily). Topline results are summarized below:

- ELX-02 was generally well tolerated in the trial, with no treatment-related serious adverse events noted.
- Overall, the study did not achieve statistical significance for efficacy endpoints in the Phase 2 study in Class 1 CF for efficacy endpoints, including changes from baseline in SCC and FEV1.
    - No incremental improvement was observed with ivacaftor combination.
- Evidence of activity for ELX-02 was observed, as patients with higher baseline sweat chloride levels demonstrated increased responses as indicated by SCC (p=0.00013 at Day 35).
- Trial results were potentially confounded by high variability in sweat chloride and lung function measurement.
- Eloxx believes this variability could have been caused by very low drug exposures in the lung. Steady state lung drug levels in patients from this trial were on average 20%, or 2mM, of the lowest levels at which drug activity has previously been seen in preclinical testing.
    - Lung drug exposure with inhaled delivery of ELX-02 expected to be at least 50-fold greater than with subcutaneous delivery.

About Class 1 CF

CF patients with a Class 1 nonsense mutation remain highly underserved with no approved disease modifying therapies. An estimated 10-12% of CF patients are Class 1 patients with one or both alleles harboring nonsense mutations, leading to less than full length CFTR proteins on the cell membrane in these patients.

Conference Call and Webcast

Eloxx's management will host a conference call and webcast today at 4:30 p.m. ET. A live webcast of the conference call can be accessed through the "Investors" tab on the Eloxx website, and a replay will be available online after the call. For those planning to ask a question, the dial-in number for the conference call is (888) 672-2415 for domestic participants and (646) 307-1963 for international participants, with Conference ID # 7410846. Please dial in at least 15 minutes in advance to ensure a timely connection to the call.

About Eloxx Pharmaceuticals

Eloxx Pharmaceuticals, Inc. is engaged in the science of ribosome modulation, leveraging its innovative TURBO-ZMTM chemistry technology platform in an effort to develop novel Ribosome Modulating Agents (RMAs) and its library of Eukaryotic Ribosome Selective Glycosides (ERSGs). Eloxx's lead investigational product candidate, ELX-02, is a small molecule drug candidate designed to restore production of full-length functional proteins. The U.S. Food and Drug Administration (FDA) has granted Fast Track designation for ELX-02 for the treatment of CF patients with nonsense mutations. In addition, ELX-02 has also been granted Orphan Drug Designation for the treatment of CF patients with nonsense mutations by the FDA and orphan medicinal product designation by the European Commission. ELX-02 is in clinical development, focusing on cystic fibrosis (US Trial NCT04135495, EU/IL Trial NCT04126473). Eloxx also has preclinical programs focused on select rare diseases, including inherited diseases, cancer caused by nonsense mutations, kidney diseases, including autosomal dominant polycystic kidney disease, as well as rare ocular genetic disorders.

For more information, please visit www.eloxxpharma.com.

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.

Contact

Investors
John Woolford
john.woolford@westwicke.com
443.213.0506

Media
Laureen Cassidy
laureen@outcomescg.com

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 Ac statements other than statements of present and historical facts contained in this press release, including without limitati expected timing of trials of our product candidates and the potential of our product candidate to treat nonsense mutation forward-looking statements. Forward-looking statements can be identified by the words “aim,” “may,” “will,” “would,” “sho “expect,” “explore,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “seeks,” or “continue” or the negative of these terms similar expressions, although not all forward-looking statements cor words. Forward-looking statements are based on management's current plans, estimates, assumptions and projections information currently available to us. Forward-looking statements are subject to known and unknown risks, uncertainties assumptions, and actual results or outcomes may differ materially from those expressed or implied in the forward-lookin due to various important factors, including, but not limited to: our ability to progress any product candidates in preclinical trials; the uncertainty of clinical trial results and the fact that positive results from preclinical studies are not always indica positive clinical results; the scope, rate and progress of our preclinical studies and clinical trials and other research and activities; the competition for patient enrollment from drug candidates in development; the impact of the global COVID-1 on our clinical trials, operations, vendors, suppliers, and employees; our ability to obtain the capital necessary to fund ou the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights; our ability financial in the future through product licensing, public or private equity or debt financing or otherwise; general business regulatory environment, competition and market for our products; and business ability and judgment of personnel, and th of qualified personnel and other important factors discussed under the caption “Risk Factors” in our Quarterly Report on for the quarter ended June 30, 2022, as any such factors may be updated from time to time in our other filings with the S 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, obligation to update or revise any forward-looking statements contained herein, whether as a result of any new informati events, changed circumstances or otherwise.

Summary of Phase 2 results

Combination treatment did not achieve statistical significance for efficacy endpo

Assessment of responders shows drug activity for ELX-02

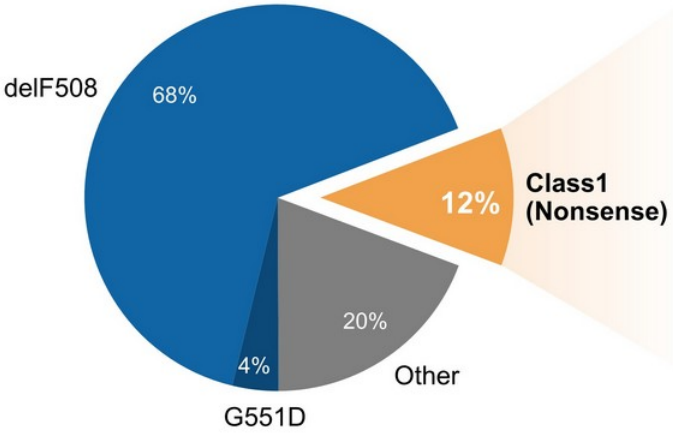
Higher drug exposure in lung needed to generate therapeutic benefit

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

Class 1 CF patients carrying nonsense mutations have t 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 D** by FDA

CYSTIC FIBROSIS FOUNDATION

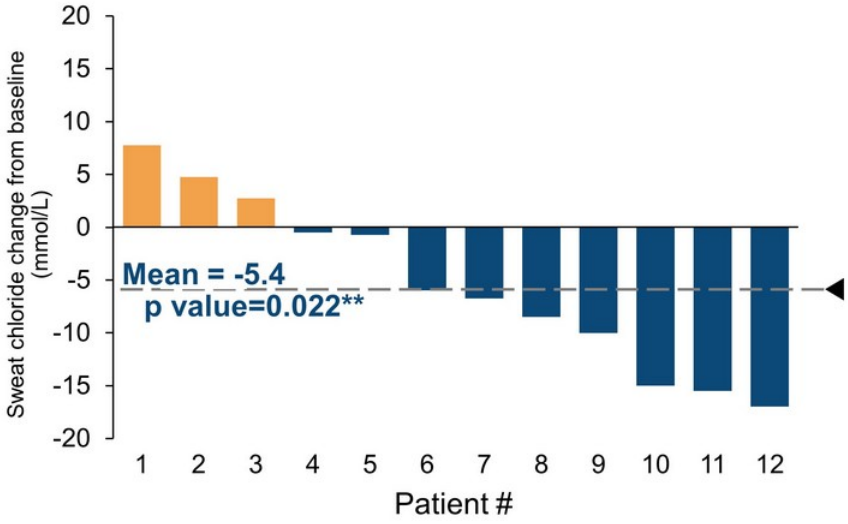
CF Foundation committed to additional funding of up to $15.9 milli for ELX-02 clinical program in March 2022

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

Recap: Significant reduction in sweat chloride observed 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 ch change (S mmol
Responders (mean)	-8.9
Response rate	9/12 (75

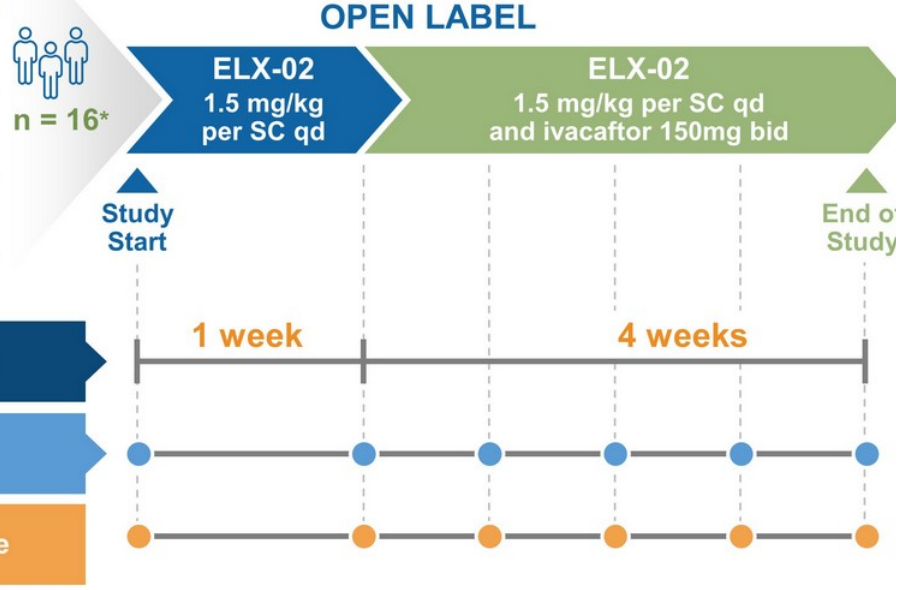
*Drug response evaluated based on difference between end of the treatment period to the average baseline for each patient excluding patients that had a greater than 15mmol/L variability sweat chloride between right and left arms or between screening and day 1

** 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

Expanded 5-week Phase 2 trial to evaluate FEV1 and saf 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)

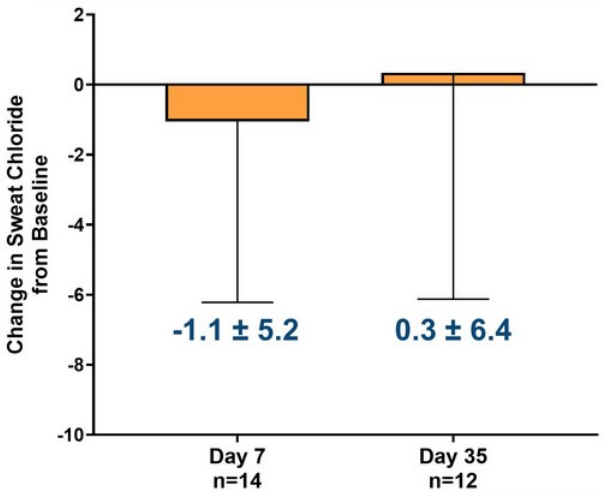
- Combination therapy at 1.5 mg/kg showed drug related discontinuation
  - 2 patients discontinued due to injection site reactions (mild to moderate)
  - 1 patient withdrew from trial due to injection burden prior to dosing
  - 1 patient with tinnitus*

* Patient had an undisclosed history of tinnitus

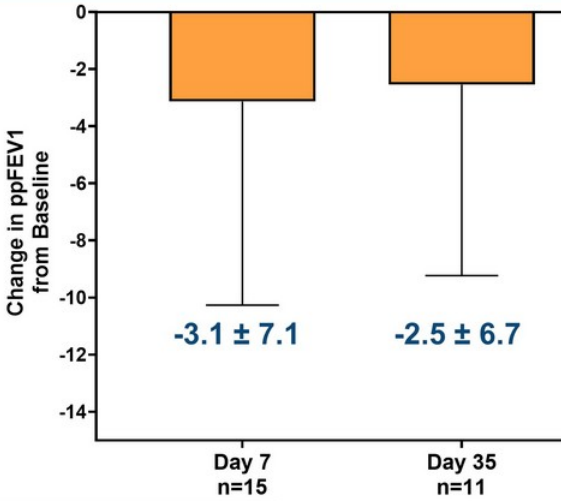
Combination of ELX-02 with ivacaftor did not achieve statistical significance for efficacy endpoints

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

Mean SCC from baseline



Mean FEV1 change from basel

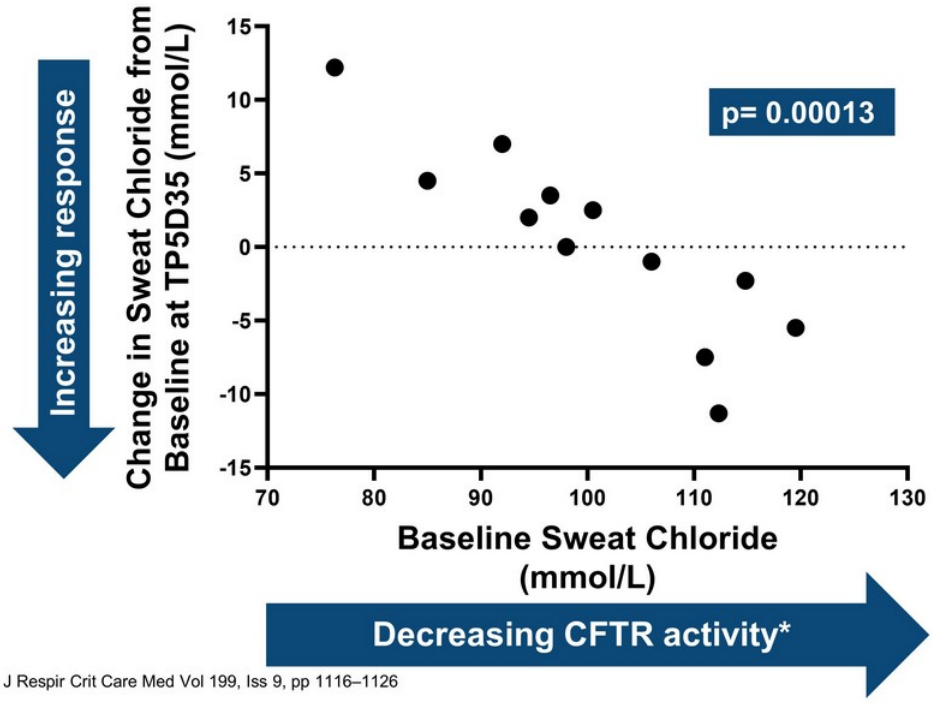


No incremental benefit observed with ivacaftor combination

Error bars: Standard deviation

Responder assessment showed drug activity

Baseline sweat chloride vs. SCC at Day 35

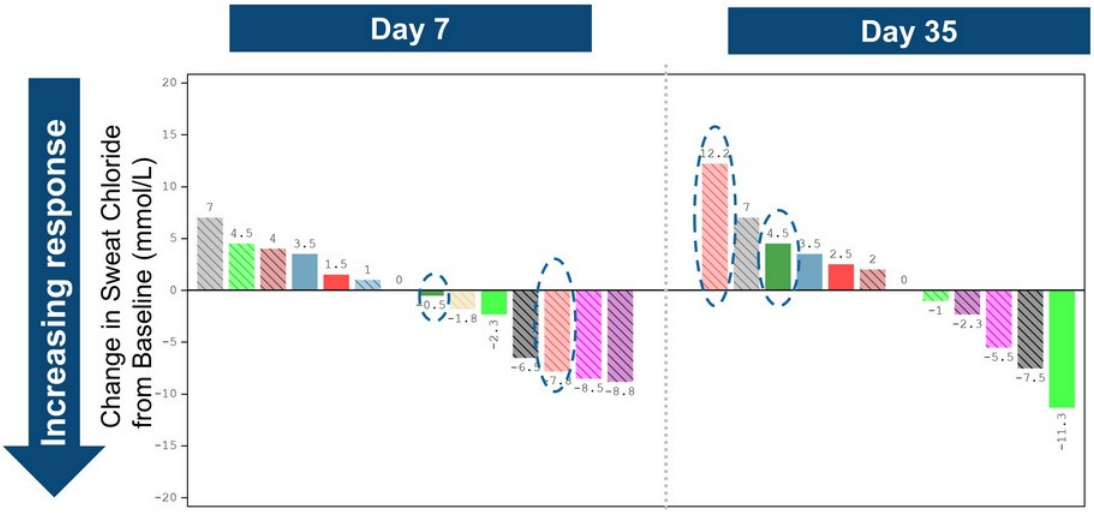


Prior Phase
monotherapy sh
similar relationsh
treatment resp

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

High sweat chloride variability confounded activity signa responders

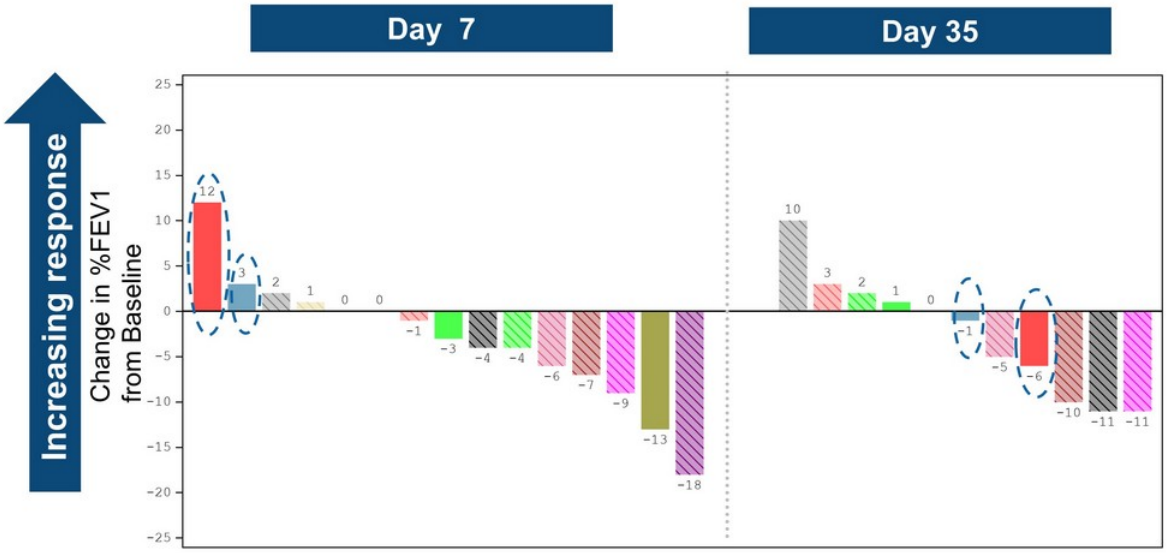
SCC at Day 7 and Day 35 by patient



	SCC a Day 7 Mean (SD)
Responder	-5.2 (3.5)
Responder rate	7/14 (50%

Similar variability in lung function measurement confou activity signal in responders

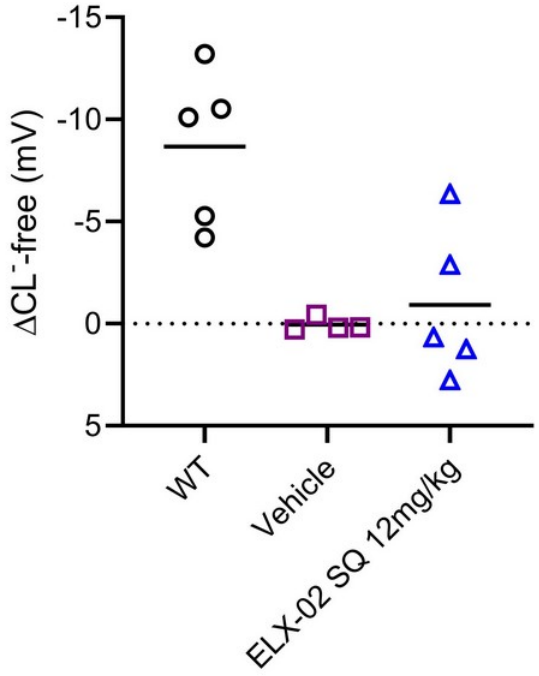
Change in FEV1 from baseline at Day 7 and Day 35 by patient



	FEV chan at D 7 Mea (SD
Responder	+4. (5.
Responder rate	4/1 (27

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

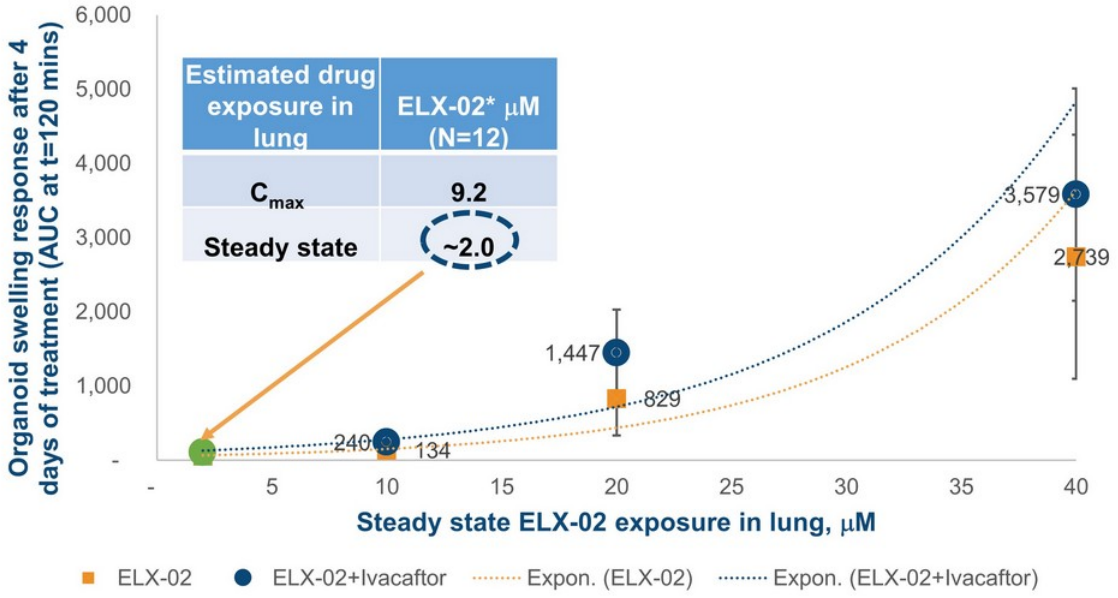
Nasal potential difference in G542X rats after 7 days of SC ELX-02 treatm 12 mg/kg (human equivalent dose of 1.5 mg/kg)



Data from Dr. Susan Birket – UAB

Higher drug exposure in lung needed to generate therap benefit

Swelling response in CF patient organoids to ELX-02 treatment with and v ivacaftor*



Ex a sta ~2 Inh 0.(

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

Key takeaways

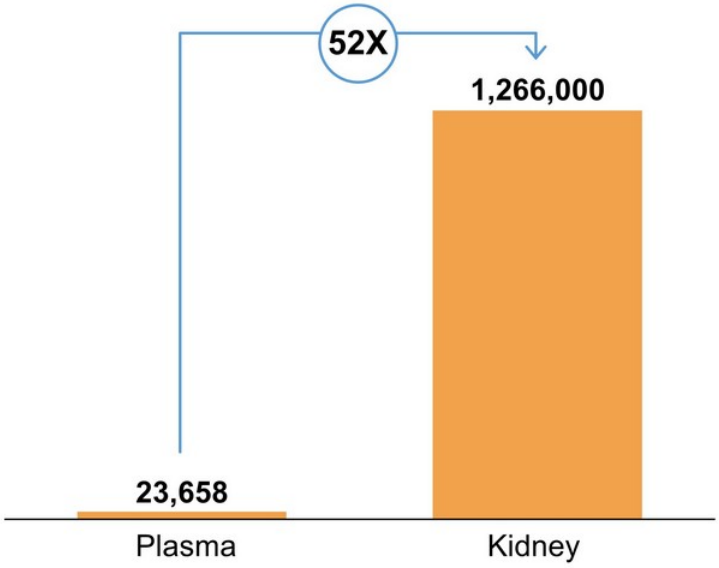
Evidence of activity for ELX-02 observed and shown to be well tolerated with no

Efficacy signal potentially confounded by variability due to low drug exposur

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

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*



- CF results de-risk curren Alport Program
- Estimated kidney exposure at 0.75 mg/kg 5 100μM

Significant pipeline milestones expected over next 12 m

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

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


Questions?
Answers


Eloxx
PHARMACEUTICALS