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): November 17, 2021

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 Global 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 November 17, 2021, Eloxx Pharmaceuticals, Inc. (the "Company") issued a press release announcing data from its Phase 2 Clinical Trials of ELX-02 in Class 1 Cystic Fibrosis Patients and will be holding a conference call to discuss these results. A copy of the press release and a copy of the presentation materials to be discussed during the call 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.

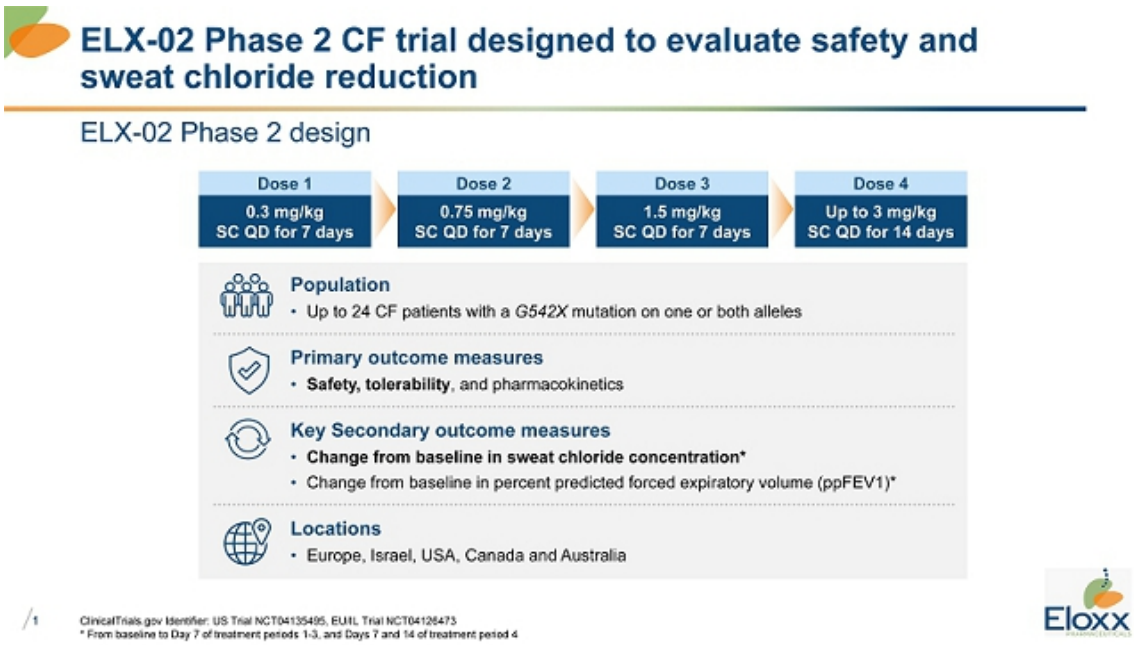
Item 8.01 Other Events.

We are providing the following business update.

Recent Developments

On November 17, 2021 the Company announced topline results from the monotherapy arms of its Phase 2 clinical trial of ELX-02 in Class 1 cystic fibrosis (CF) patients with at least one G542X nonsense allele mutation. ELX-02 was well tolerated and achieved a statistically significant 5.4 mmol/L reduction in sweat chloride in patients at the 1.5 mg/kg/day dose. The intra-patient dose escalation stage of the trial has successfully identified 1.5 mg/kg/day as the dose for further development. Based on the statistically significant monotherapy results observed at the 1.5 mg/kg/day dose, planning for the advancement of ELX-02 into Phase 3 clinical development has started. The Company conducted the study in the United States and Israel under substantially similar protocols and the data reported reflects the results across both geographic regions.

The corporate update also included the following information:



ELX-02 safety summary

- No ELX-02 related serious adverse events seen
- Drug related discontinuations
  - Tinnitus (mild-moderate) 1 patient at 0.3 mg/kg
    - Occurred in patient with pre-existing tinnitus after exposure to loud music
    - Reported after first dose and resolved during follow-up
    - Case was reviewed by Audiology and SRC – did not have a safety concern
  - Injection site reaction in 3 patients
    - 1 at 0.75 mg/kg
    - 2 at the highest dose level of up to 3 mg/kg
- Injection site reactions were the most common finding across the patients
  - Mild erythema or redness
  - Mild-moderate Injection pain
- Ivacaftor combination amendment is approved in all participating countries with no significant safety concerns

Eloxx

Sweat chloride secondary endpoint analysis performed using standard criteria

Key statistical assessment to ensure appropriate baseline values

Sweat chloride levels collected on both arms*
- Values with difference >15 mmol/L excluded

Average baseline calculated:
- Sweat chloride collected on screening and prior to drug administration
- Values with difference > 15 mmol/L between values excluded**
- Baseline based on the average of the above two values

Sweat chloride collected at the end of each treatment period

Drug response evaluated based on difference between end of the treatment period to the average baseline for each patient

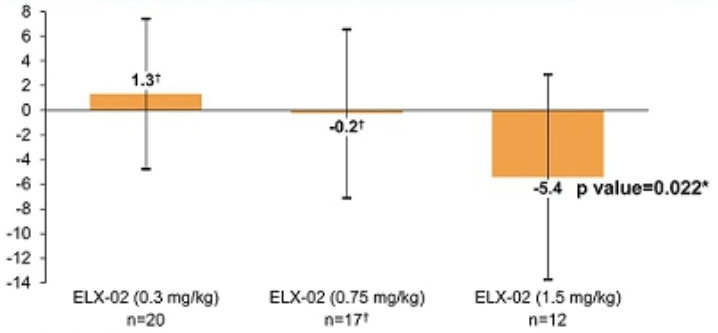
*CLSI. Sweat Testing: Third Edition. CLSI document C34-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2009
** Am J Respir Crit Care Med Jun 3 2016

Eloxx

CF patients receiving 1.5mg/kg/day had statistically significant sweat chloride reduction of 5.4mmol/L after 1 week

Activity in Phase 2 of ELX-02 treated Class 1 CF patients

Mean sweat chloride changes in Hom and Het G542X CF patients on 1 week treatment with ELX-02 (mmol/L)*



Plan to advance to Phase 3

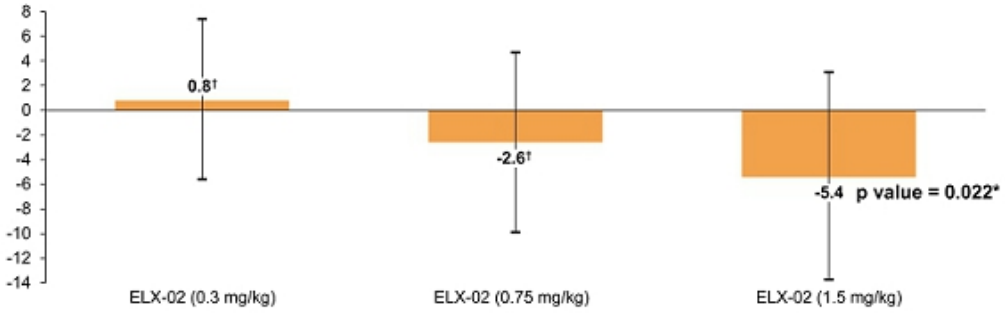
- **Biologic signal detected at 1.5 mg/kg/day dose**** despite short duration and small sample size. Suggests likely improvement in FEV1 after longer treatment duration
- **Trend towards dose response**

† p value did not reach significance
* p value one-sided t-test =0.022 non-parametric =0.026
** Results for patients receiving variable doses up to 3.0 mg/kg were not significant. Moreover, inconsistent dosing (as seen in pharmacokinetic results) and fewer completers among patients at these variable dose levels limited the interpretability of the related data and the ability to draw meaningful conclusions. Based on these findings, Eloxx does not plan to continue evaluation of doses above 1.5mg/kg and up to a 3.0 mg/kg

Stronger evidence of dose response in subset analysis of 1.5mg/kg dose completers

Post-hoc subset analysis of sweat chloride change in 1.5mg/kg/day completers

Sweat chloride changes (mmol/L) in Hom and Het G542X CF patients on 1 week treatment with ELX-02 at 1.5mg/kg dose (n=12)



† p value did not reach significance
* p value one-sided t-test =0.022 non-parametric =0.026

Forward-looking Statements

This current report 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 September 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 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	Eloxx Pharmaceuticals, Inc. Press Release, November 17, 2021
99.2	Eloxx Pharmaceuticals, Inc. Presentation, November 17, 2021
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: November 17, 2021

ELOXX PHARMACEUTICALS, INC.

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

Exhibit 99.1

Eloxx Pharmaceuticals Reports Positive Topline Results from Monotherapy Arms of Phase 2 Clinical Trial of ELX-02 in Class 1 Cystic Fibrosis Patients

ELX-02 monotherapy dosed at 1.5mg/kg/day demonstrated a statistically significant 5.4mmol/L mean sweat chloride reduction, an established surrogate for restoration of CFTR biological activity

ELX-02 monotherapy results support advancement of ELX-02 into Phase 3 clinical development

First patient dosed in Phase 2 ELX-02 expansion treatment arms evaluating combination with ivacaftor; topline data expected by the end of the first half of 2022

Company to host conference call and webcast Wednesday, November 17, 2021 at 8:30 am ET

WATERTOWN, MA – Nov 17, 2021 – Eloxx Pharmaceuticals, Inc. (NASDAQ: ELOX), a leader in ribosomal RNA-targeted genetic therapies for rare diseases, today announced positive topline results from the monotherapy arms of its Phase 2 clinical trial of ELX-02 in Class 1 cystic fibrosis (CF) patients with at least one G542X nonsense allele mutation. ELX-02 was well tolerated and achieved a statistically significant 5.4mmol/L reduction in sweat chloride in patients at the1.5mg/kg/day dose.

The intra-patient dose escalation stage of the trial has successfully identified 1.5 mg/kg/day as the dose for further development. Based on the statistically significant monotherapy results observed at the 1.5mg/kg/day dose, planning for the advancement of ELX-02 into Phase 3 clinical development has started. The U.S. Food and Drug Administration (FDA) has granted Fast Track designation for ELX-02. 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 Medicines Agency

“We are highly encouraged with the topline results from the monotherapy arms of our Phase 2 trial, and believe that ELX-02, if approved, has potential to transform the lives of Class 1 CF patients with nonsense mutations, who do not have any available therapies,” said Sumit Aggarwal, President and Chief Executive Officer of Eloxx.

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

The Phase 2 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. Topline results for the intra-patient dose escalation monotherapy arms are summarized below:

- ELX-02 was generally well tolerated in the trial, with no treatment-related serious adverse events noted.

- The study met a key secondary endpoint by showing a statistically significant reduction in mean sweat chloride **of 5.4 mmol/L (p value=0.0218, n=12 patients) after one week of therapy** for ELX-02 dosed at 1.5mg/kg/day.

    - Short term reductions in sweat chloride have been shown to correlate with biologic activity of the CFTR protein and translate to lung function improvement over the long term.

    - A potential dose response trend was also seen in mean sweat chloride reduction, with a stronger dose response trend in the subset of patients (post-hoc) that completed the 1.5mg/kg/day dosing.

    - The reduction in mean sweat chloride in Class 1 CF patients with nonsense mutations who received 1.5mg/kg/day in the trial is similar to the activity in Class 1 CF patient organoids treated with ELX-02 in preclinical experiments.

    - As expected, no change was observed in forced expiratory volume (FEV1) due to short treatment duration.

- While the trial was not designed as a longer-term efficacy study and did not compare ELX-02 to any other agent, results from prior Phase 2 trials with FDA-approved agents for CF can serve as a contextual reference for the level of sweat chloride reduction observed and its potential clinical relevance.

    - Results of a Phase 2 study with lumacaftor and lumacaftor/ivacaftor combination (Orkambi), an FDA-approved combination CF agent, demonstrated 4.1mmol/L to 5.1 mmol/L reductions in sweat chloride over two- and three-week study durations in Class 2 CF patients with HomF50del mutations.

    - Results of a phase 2 study with tezacoftor/ivacaftor combination (Symdeko, an FDA-approved combination CF agent, demonstrated a 1.8mmol/L to 5.2 mmol/L reduction in sweat chloride over 28 days in Class 2 CF patients with HomF50del mutations.

    - Treatment with both these agents resulted in improved lung function as measured by forced expiratory volume FEV1 with longer treatment duration in subsequent Phase 3 trials with Orkambi and Symdeko.

“These significant results for sweat chloride, a surrogate for CFTR protein function in patients, are very exciting. I look forward to working with Eloxx on future development of ELX-02.” said Prof. Eitan Kerem, Head of The Division of Pediatrics Hadassah Medical Center.

Planned Next Steps for ELX-02 CF Program

ELX-02 in combination with other CF therapies.

First patient dosing has occurred in the expansion arm of the Phase 2 trial, which includes a combination of ELX-02 and Kalydeco (ivacaftor), a CFTR protein potentiator. In preclinical studies, Class 1 CF patient organoids had a 2- to 3-fold higher swelling response with a combination of ELX-02 and Kalydeco than with ELX-02 as a monotherapy. Topline results are expected by the end of the first half of 2022.

“With dosing of the first patient, we have now advanced ELX-02 into the Phase 2 combination study and have begun preparations for Phase 3 clinical development,” said Vijay Modur MD, PhD, Head of Research & Development of Eloxx.

Inhaled delivery of ELX-02

Eloxx has also begun evaluation of inhaled (nebulizer-based) delivery of the current subcutaneous formulation of ELX-02. Eloxx believes that inhaled delivery has the potential to further improve the activity of ELX-02 as a single agent and in combination with other drugs given potential for increased drug exposure in the lung versus plasma. Prior animal studies have shown a 19-fold increase in ELX-02 exposure at a similar dose when administered as an inhalation agent versus subcutaneously. We expect to submit an Investigational New Drug application the second half of 2022.

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 8:30 a.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 (866) 913-8546 for domestic participants and (210) 874-7715 for international participants, with Conference ID # 2393967. 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-ZM^{TM} 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. 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, 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 September 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 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

Exhibit 99.2

RARE Thinking for RARE Solutions

Topline ELX-02 Phase 2 Cystic Fibrosis Results

November 17, 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 September 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.

Opening Remarks

Sumit Aggarwal
President and CEO

Today's agenda

Topic	Speaker
Opening Remarks	Sumit Aggarwal, President & CEO
Remaining Unmet Need in Cystic Fibrosis & ELX-02 Topline Phase 2 Results	Dr. Eitan Kerem
ELX-02 Next Steps &Program Expansion	Dr. Vijay Modur, Head of R&D
Key Takeaways & Closing Remarks	Sumit Aggarwal, President & CEO

ELX-02 is 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
- **Fast Track Designation from FDA** for treatment of CF patients with nonsense mutations
- **Phase 2 monotherapy trial** designed to **evaluate** safety and **biological activity**

Eloxx PHARMACEUTICALS

Key takeaways from ELX-02 Phase 2 monotherapy trials

- Significant unmet need remains for Class 1 CF patients
- ELX-02 well-tolerated with no treatment-related serious adverse events
- Statistically significant mean sweat chloride reduction of 5.4mmol/L (p=0.022*) at 1.5mg/kg/day
- Evidence of stronger dose response in patients that completed 1.5/mg/kg/day dosing
- Results support continued development of ELX-02 and advancement into Phase 3 clinical development

* p value one-sided t-test =0.022 non-parametric =0.026

Eloxx PHARMACEUTICALS

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.

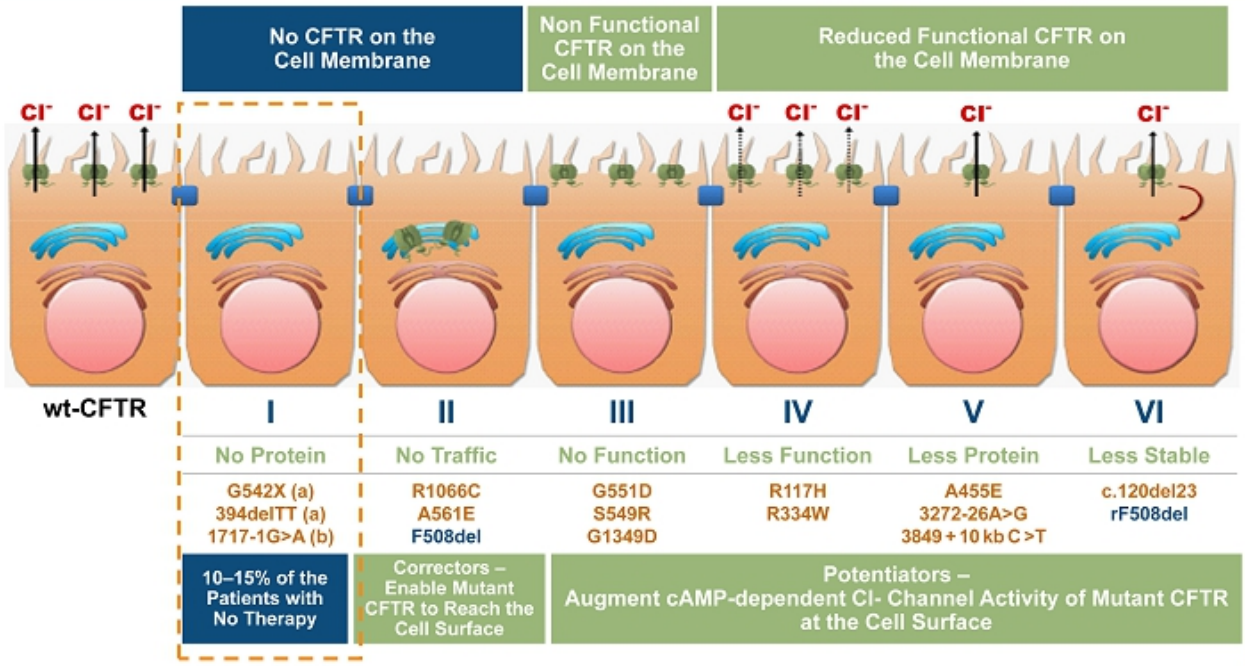
- **Selected awards:**
  - 2014: ECFS Award acknowledging his substantial and remarkable contribution to cystic fibrosis research
  - 2016: Honorary Fellowship of the Royal College of Pediatrics and Child Health, UK.
- **Education**
  - Hebrew University – Hadassah Medical School
  - Pediatric residency 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 & ELX-02 Top-line Results

Dr. Eitan Kerem

Eloxx PHARMACEUTICALS

No available treatments for Class 1 CF patients with CFTR nonsense mutations



CF patients carrying nonsense mutations have most severe phenotype

Early presentation – usually at the first weeks of life

Pancreatic insufficiency with poor nutritional state

More severe lung disease

- Higher rate of FEV1 decline
- Higher rate of respiratory infection with pseudomonas aeruginosa and other pathogenic bacteria

Expected shorter life span

Eloxx PHARMACEUTICALS

Established 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

Eloxx PHARMACEUTICALS

ELX-02 Phase 2 CF trial designed to evaluate safety and sweat chloride reduction

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

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

Locations
- Europe, Israel, USA, Canada and Australia

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

ELX-02 safety summary

No ELX-02 related serious adverse events seen

Drug related discontinuations
- Tinnitus (mild-moderate) 1 patient at 0.3 mg/kg
  - Occurred in patient with pre-existing tinnitus after exposure to loud music
  - Reported after first dose and resolved during follow-up
  - Case was reviewed by Audiology and SRC – did not have a safety concern
- Injection site reaction in 3 patients
  - 1 at 0.75 mg/kg
  - 2 at the highest dose level of up to 3 mg/kg

Injection site reactions were the most common finding across the patients
- Mild erythema or redness
- Mild-moderate Injection pain

Ivacaftor combination amendment is approved in all participating countries with no significant safety concerns

Eloxx PHARMACEUTICALS

Sweat chloride secondary endpoint analysis performed using standard criteria

Key statistical assessment to ensure appropriate baseline values

Sweat chloride levels collected on both arms*
- Values with difference >15 mmol/L excluded

Average baseline calculated:
- Sweat chloride collected on screening and prior to drug administration
- Values with difference > 15 mmol/L between values excluded**
- Baseline based on the average of the above two values

Sweat chloride collected at the end of each treatment period

Drug response evaluated based on difference between end of the treatment period to the average baseline for each patient

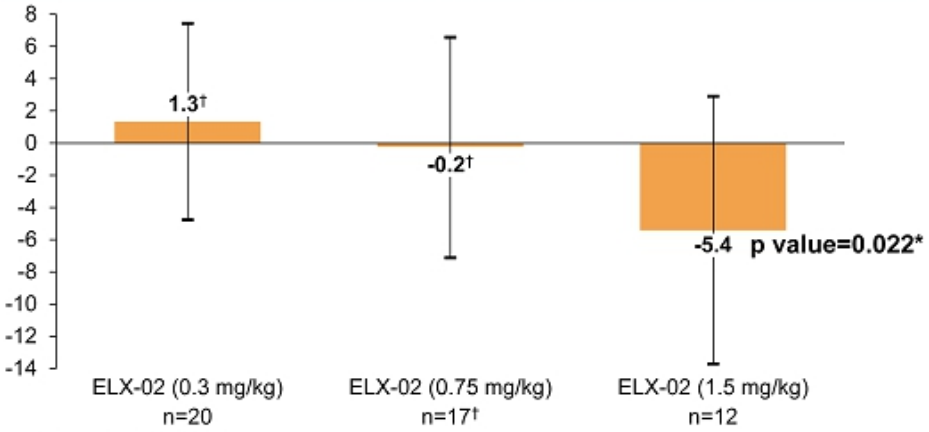
*CLSI. Sweat Testing: *Third Edition. CLSI document C34-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2009*
** *Am J Respir Crit Care Med* Jun 3 2016

Eloxx PHARMACEUTICALS

CF patients receiving 1.5mg/kg/day had statistically significant sweat chloride reduction of 5.4mmol/L after 1 week

Activity in Phase 2 of ELX-02 treated Class 1 CF patients

Mean sweat chloride changes in Hom and Het G542X CF patients on 1 week treatment with ELX-02 (mmol/L)*



Plan to advance to Phase 3

- **Biologic signal detected at 1.5 mg/kg/day dose**** despite short duration and small sample size. Suggests likely improvement in FEV1 after longer treatment duration
- **Trend towards dose response**

† p value did not reach significance

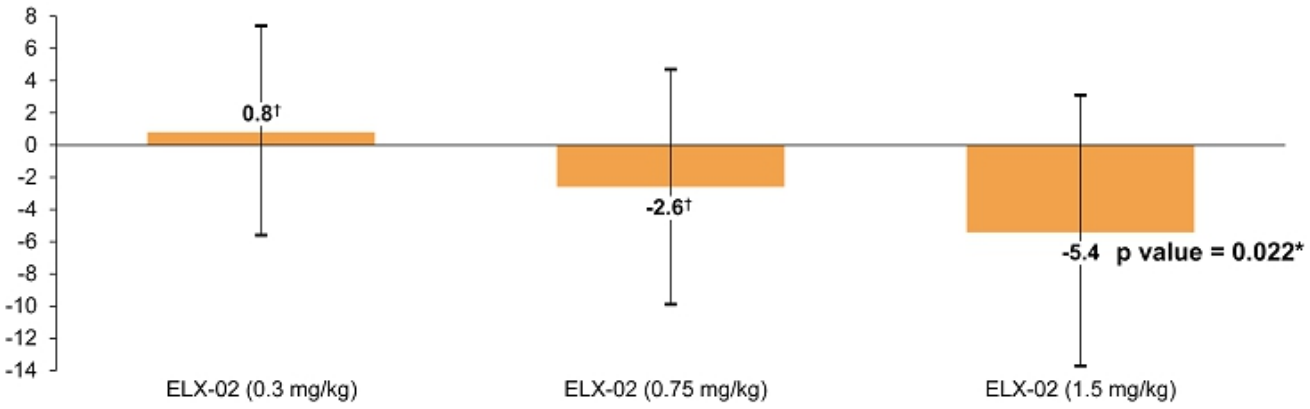
* p value one-sided t-test =0.022 non-parametric =0.026

** Results for patients receiving variable doses up to 3.0 mg/kg were not significant. Moreover, inconsistent dosing (as seen in pharmacokinetic results) and fewer completers among patients at these variable dose levels limited the interpretability of the related data and the ability to draw meaningful conclusions. Based on these findings, Eloxx does not plan to continue evaluation of doses above 1.5mg/kg and up to a 3.0 mg/kg.

Stronger evidence of dose response in subset analysis of 1.5mg/kg dose completers

Post-hoc subset analysis of sweat chloride change in 1.5mg/kg/day completers

Sweat chloride changes (mmol/L) in Hom and Het G542X CF patients on 1 week treatment with ELX-02 at 1.5mg/kg dose (n=12)

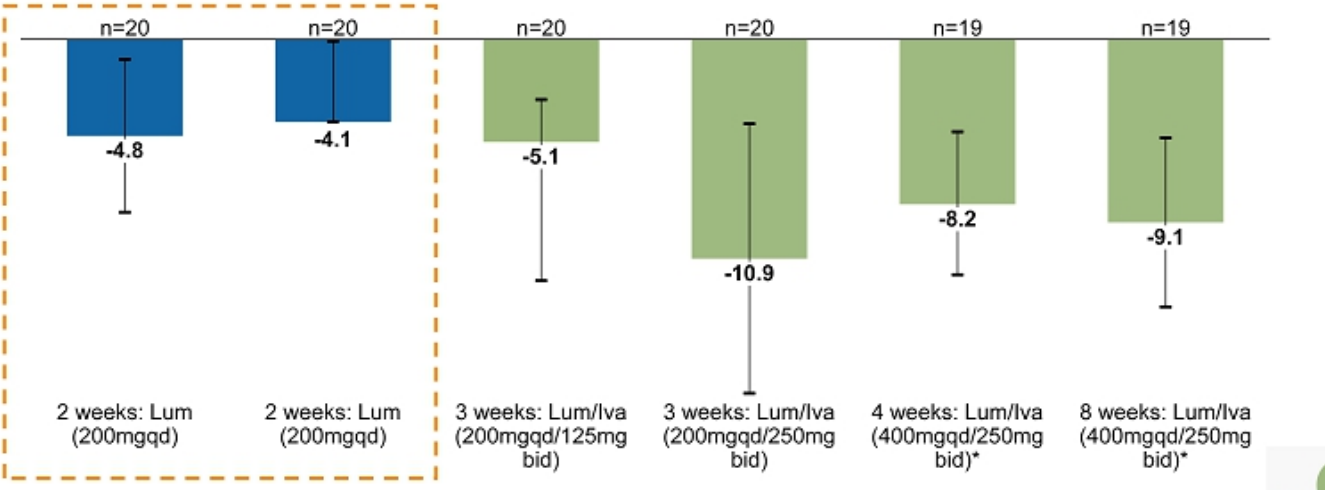


† p value did not reach significance
* p value one-sided t-test =0.022 non-parametric =0.026

Class 2 CF patients on Lumcaftor had a 4.1 to 4.8 mmol/L mean sweat chloride reduction at 2 weeks in Phase 2

Activity in Class 2 Hom delF508 patients in Phase 2 Orkambi trials

Mean sweat chloride changes in Class 2 Hom F508del CF Patients treated with Lumacaftor and Lumcaftor/Ivacaftor combination (Orkambi)

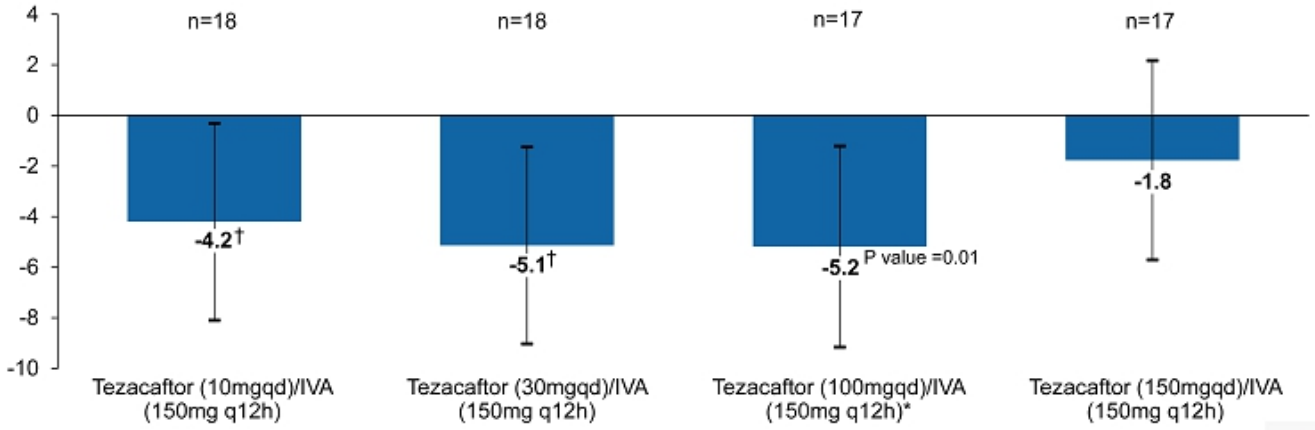


Data from *Lancet Respir Med.* 2014 Jul;2(7):527-38
* Approved Orkambi dose

Class 2 CF patients on Symdeko had a 1.8 to 5.2 mmol/L mean sweat chloride reduction at 4 weeks in Phase 2

Activity in Class 2 Hom delF508 patients in Phase 2 Symdeko trials

Mean sweat chloride changes in Class 2 Hom F508del CF Patients treated with Tezacaftor/Ivacaftor (Symdeko) from baseline through day 28



Data from Am J Respir Crit Care Med. 2018 Jan 15;197(2):214-224
† p value did not reach significance
* Approved Symdeko dose

Summary: ELX-02 monotherapy was well tolerated and met the key secondary endpoint of sweat chloride reduction

Class 1 nonsense mutation CF patients with the most severe phenotype have no approved disease modifying therapies

Statistically significant sweat chloride reduction at 1.5mg/kg ELX-02 in G542X Class 1 CF patients of 5.4 mmol/L reduction (p value <0.05, n=12)

Strong activity with high responder proportion despite short treatment duration and small sample size

Biological activity suggests potential **FEV1 improvement with longer treatment duration**

Similar to short-term treatment activity in Class II patients with Orkambi and Symdeko (approved agents*)

ELX-02 generally well tolerated

*Note no head-to-head comparison has been conducted between ELX-02 and these agents

Eloxx PHARMACEUTICALS

ELX-02 Next Steps & Program Expansion

Dr. Vijay Modur
Head of R&D

Eloxx PHARMACEUTICALS

ELX-02 Phase 2 monotherapy results support planned combination trial with Ivacaftor and Phase 3 planning

Phase 2 extension study initiated evaluating combination of ELX-02 and ivacaftor:

2–3 fold higher activity observed in Class 1 nonsense CF preclinical models **with ELX-02 and ivacaftor** combination*

Current results with 1 week therapy suggest **potential for stronger effect with ivacaftor** for a longer treatment duration

First patient in combination therapy dosed
(Topline data expected by end of 1H 2022)

On Track for end of Phase 2 meeting in 2H 2022 and start of Phase 3 in late 2022/1H 2023

*Oral Sessions / Journal of Cystic Fibrosis WS03 - 18S1 (2019) S1–S38

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

Key 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

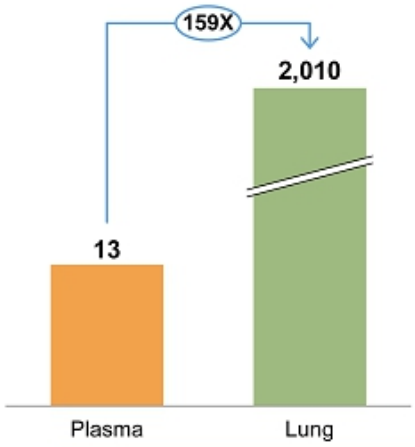
Topline data expected by end of 1H 2022

Eloxx PHARMACEUTICALS

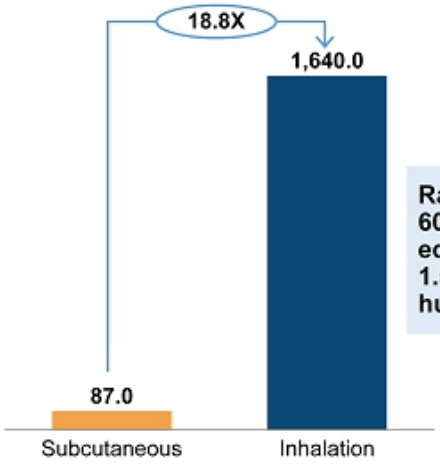
Phase 2 results support potential for higher efficacy with inhaled delivery of ELX-02

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

Eloxx PHARMACEUTICALS

ELX-02 Class 1 CF program milestones

Anticipated ELX-02 Class 1 CF program milestones

- ✓ 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
- ✓ Initiated IND-enabling studies for inhalation

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

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

Eloxx PHARMACEUTICALS

Key Takeaways & Closing Remarks

Sumit Aggarwal
President and CEO

Key takeaways from ELX-02 Phase 2 monotherapy trials

- Significant unmet need remains for Class 1 CF patients
- ELX-02 well-tolerated with no treatment-related serious adverse events
- Statistically significant mean sweat chloride reduction of 5.4mmol/L (p=0.022*) at 1.5mg/kg/day
- Evidence of stronger dose response in patients that completed 1.5/mg/kg/day dosing
- Results support continued development of ELX-02 and advancement into Phase 3 clinical development

* p value one-sided t-test =0.022 non-parametric =0.026

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

Eloxx PHARMACEUTICALS

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

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

Three rare disease programs with over $5B market potential

Statistically significant sweat chloride reduction in CF patients with ELX-02 confirms drug potential

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

Eloxx PHARMACEUTICALS


Questions?
Answers.

TURBO-ZM™