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.

Eloxx PHARMACEUTICALS

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

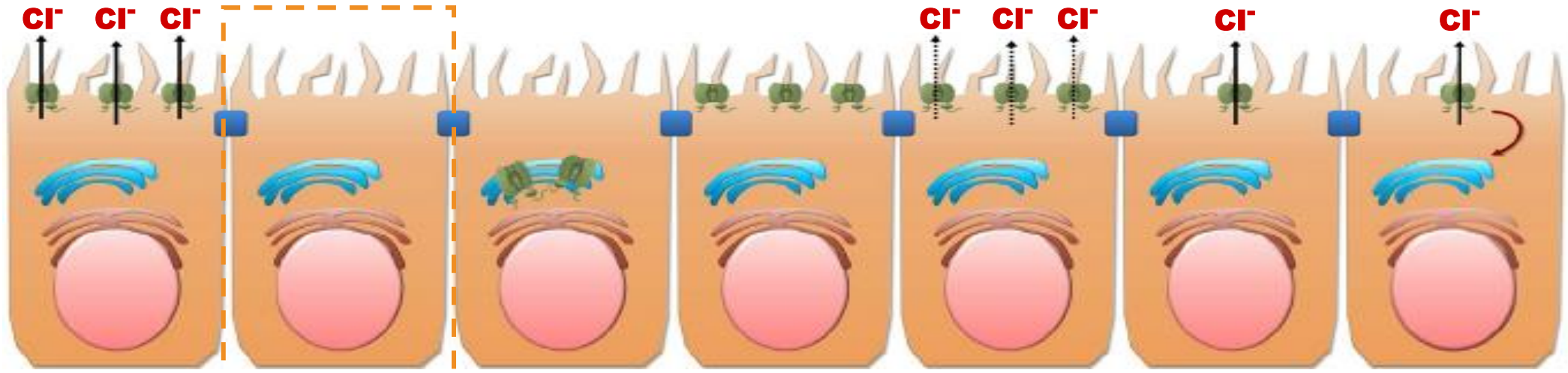
Eloxx PHARMACEUTICALS

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



	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			

Eloxx PHARMACEUTICALS

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

Eloxx PHARMACEUTICALS

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

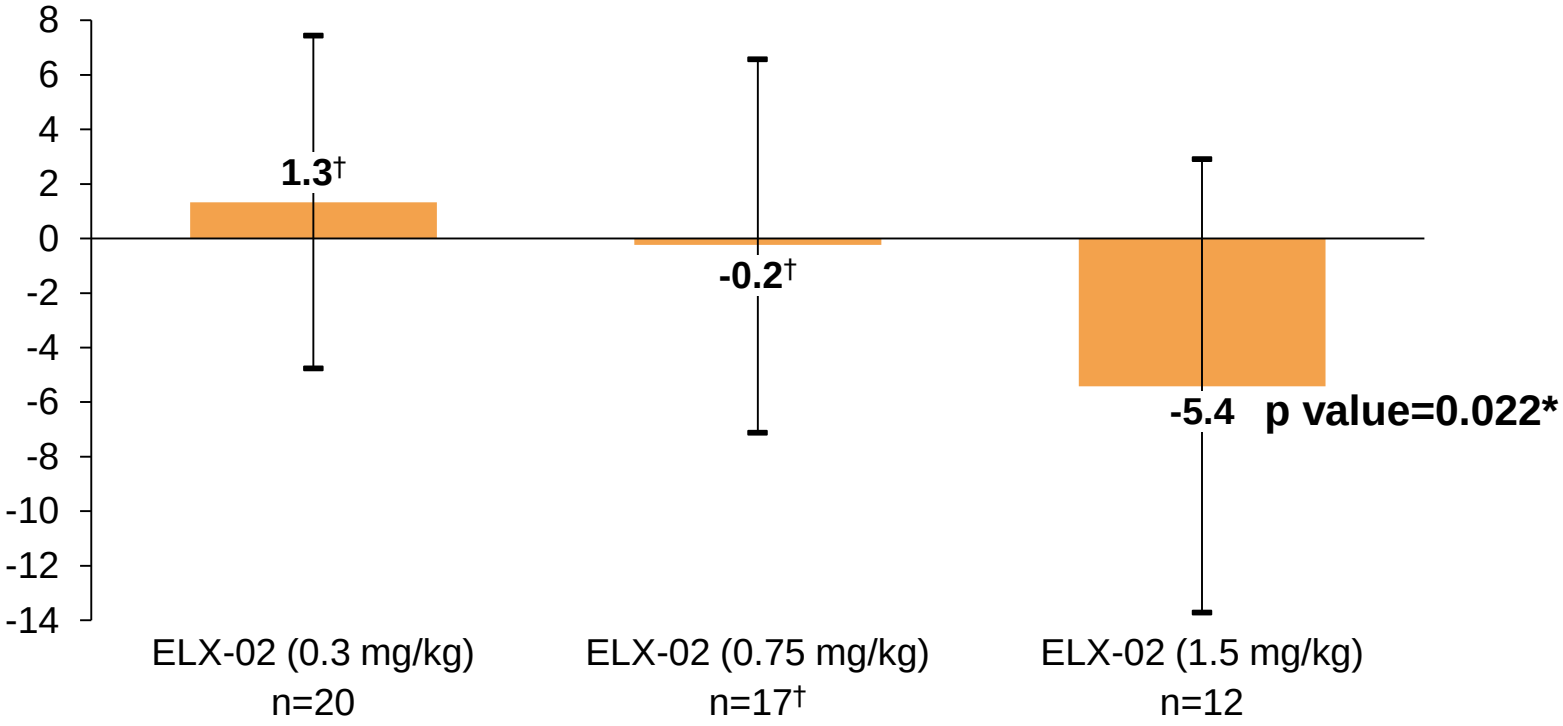
** *Am J Respir Crit Care Med* Jun 3 2016

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

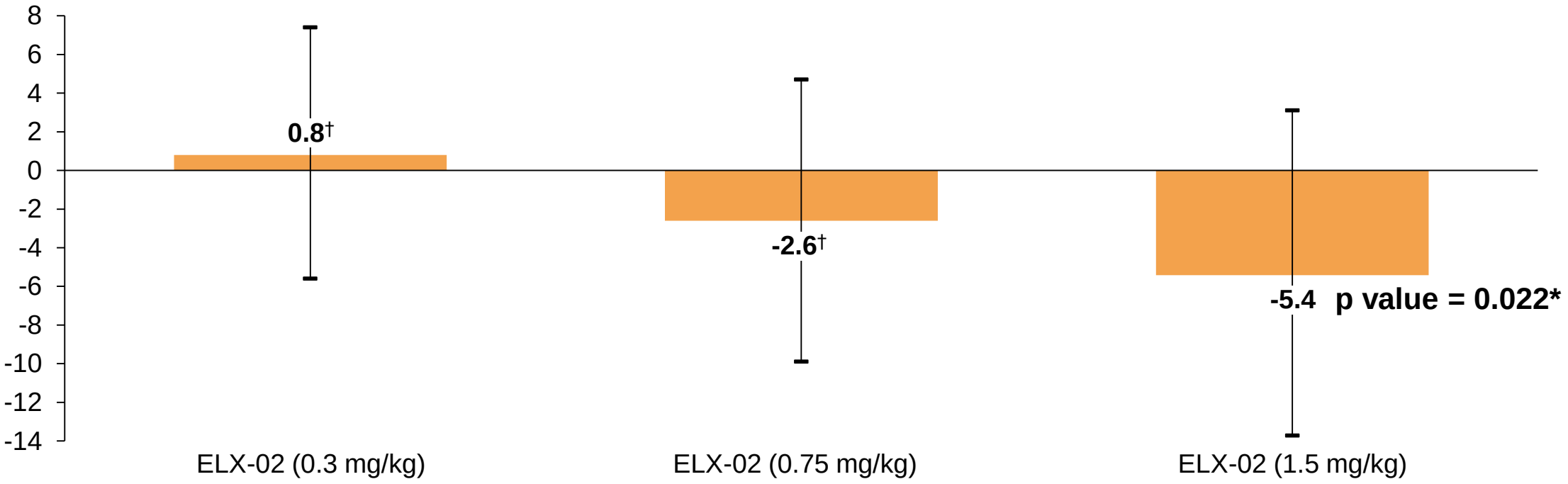
** Results for patients receiving variable doses up to 3.0 mg/kg were not significant. Moreover, inconsistent dosing (as seen in pharmacokinetic results) and fewer completers among patients at these variable dose levels limited the interpretability of the related data and the ability to draw meaningful 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.

Eloxx PHARMACEUTICALS

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)

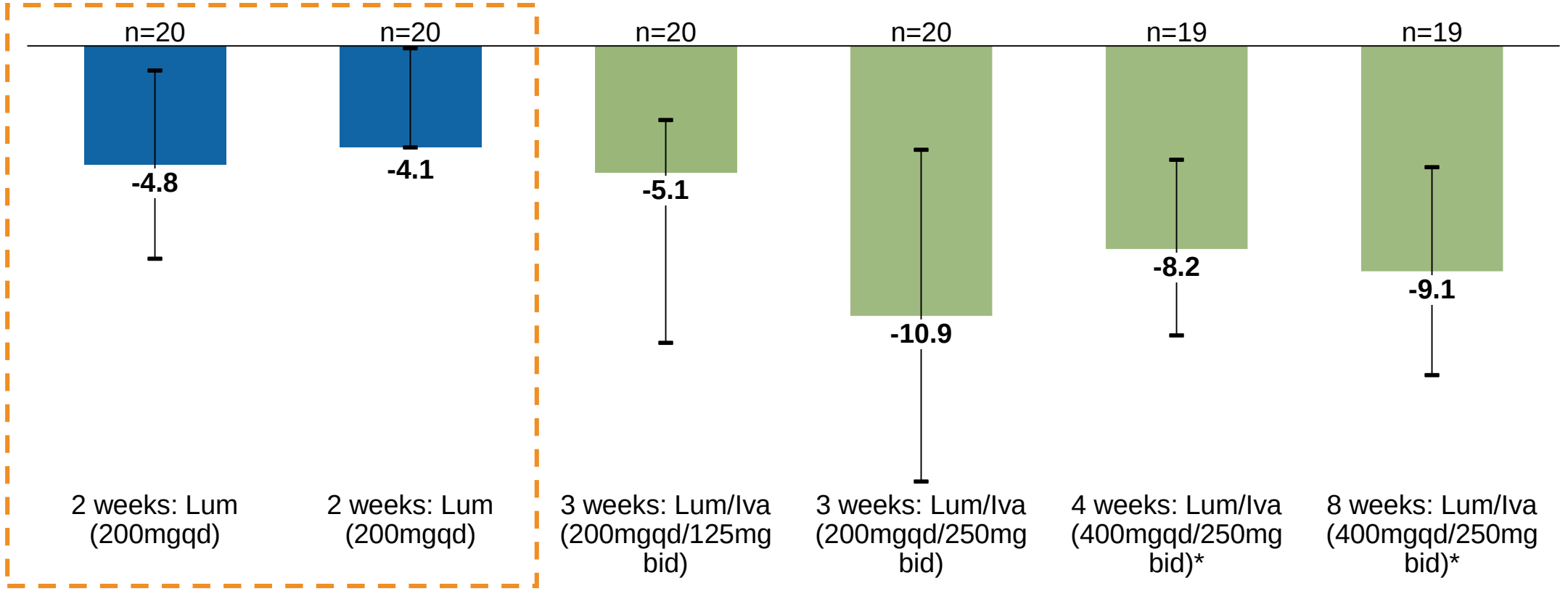


† p value did not reach significance
* p value one-sided t-test =0.022 non-parametric =0.026

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

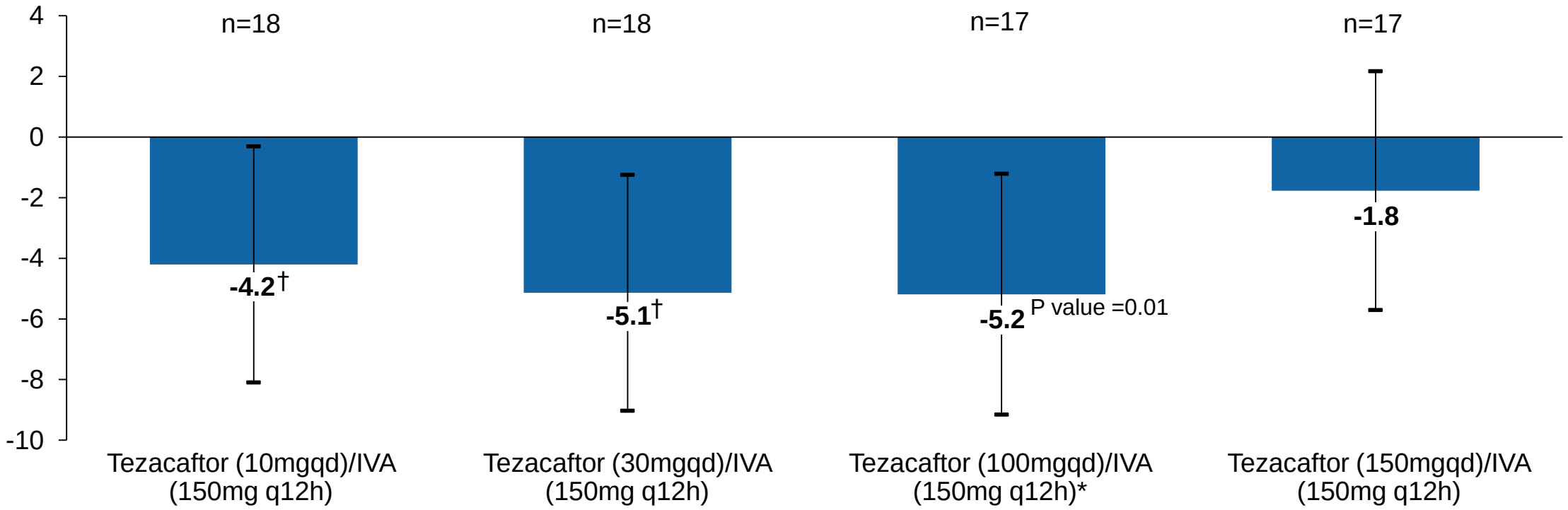
* Approved Orkambi dose

Eloxx PHARMACEUTICALS

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

Eloxx PHARMACEUTICALS

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

Eloxx PHARMACEUTICALS

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

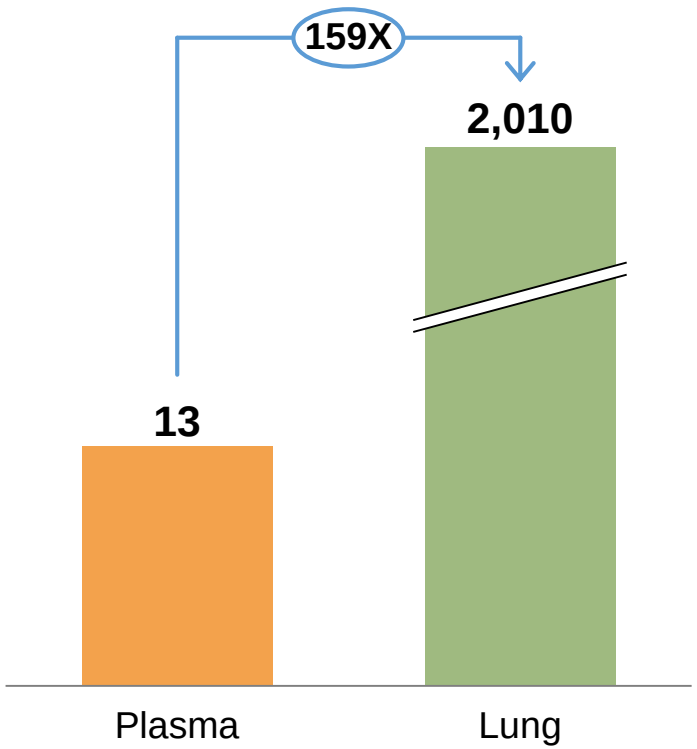
Topline data expected by end of 1H 2022

Eloxx PHARMACEUTICALS

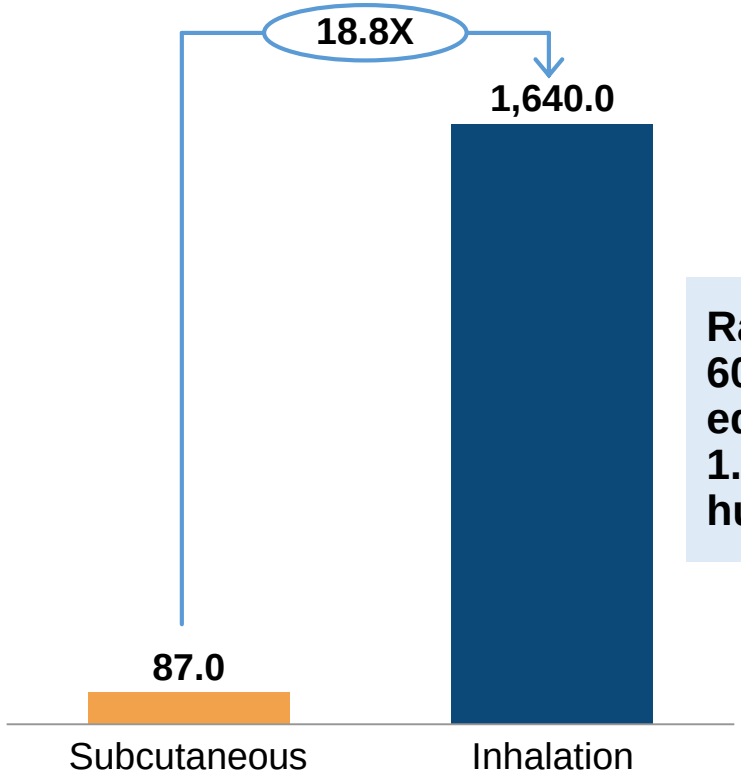
Phase 2 results support potential for higher efficacy with inhaled delivery of ELX-02

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.

Eloxx PHARMACEUTICALS

Eloxx
PHARMACEUTICALS

TURBO-ZM™

Eloxx
PHARMACEUTICALS