Unlocking protein production with translational read-through for rare genetic diseases
Forward-Looking Statements

This presentation contains forward-looking statements, which are generally statements that are not historical facts. Forward-looking statements can be identified by the words "expects," "anticipates," "believes," "intends," "estimates," "plans," "will," "outlook" and similar expressions. Forward-looking statements are based on management's current plans, estimates, assumptions and projections, and speak only as of the date they are made. We undertake no obligation to update any forward-looking statement in light of new information or future events, except as otherwise required by law. Forward-looking statements involve inherent risks and uncertainties, most of which are difficult to predict and are generally beyond our control. Actual results or outcomes may differ materially from those implied by the forward-looking statements as a result of the impact of a number of factors, including: the development of the Company's read-through technology; the approval of the Company's patent applications; the Company's ability to successfully defend its intellectual property or obtain necessary licenses at a cost acceptable to the Company, if at all; the successful implementation of the Company's research and development programs and collaborations; the Company's ability to obtain applicable regulatory approvals for its current and future product candidates; the acceptance by the market of the Company's products should they receive regulatory approval; the timing and success of the Company's preliminary studies, preclinical research, clinical trials, and related regulatory filings; the ability of the Company to consummate additional financings as needed; as well as those discussed in more detail in our Annual Report on Form 10-K and our other reports filed with the Securities and Exchange Commission.
Eloxx Pharmaceutical Highlights

- Experienced Leadership Team
  - Appointment of Dr. Susan Schneider SVP Ophthalmology

- ELX-02 Clinical Progress
  - EU Cystic Fibrosis Basic Science Meeting March 27th New Data
  - On Track for Completion of Phase 1b MAD 1H2019
  - Expect Topline Cystic Fibrosis Phase 2 in 2019

- Building Ophthalmology Inherited Retinal Disorder Program
  - Association for Research in Vision & Ophthalmology Meeting May New Data
  - IND Enabling Studies Focusing on Usher’s Syndrome
  - Announced Partnership with Foundation Fighting Blindness

- Actively Developing Opportunities for Collaboration to Advance Full Pipeline and Expand Therapeutic Programs
### Eloxx Pipeline

**ELX-02**

<table>
<thead>
<tr>
<th>Phase</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHASE IA SAD</td>
<td>SAD - Single Ascending Dose</td>
</tr>
<tr>
<td>PHASE IB MAD</td>
<td>MAD - Multiple Ascending Dose</td>
</tr>
</tbody>
</table>

**CYSTIC FIBROSIS (CF)**

- CTA (Belgium) | 2019*

**CYSTINOSIS (CYS)**

- IND (United States) | 2019*

**ELX Compounds**

<table>
<thead>
<tr>
<th>Phase</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>MUTATIONAL PROFILING</td>
<td>ONGOING</td>
</tr>
<tr>
<td>OCULAR PRECLINICAL</td>
<td>ONGOING</td>
</tr>
</tbody>
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*Phase II begins following completion of MAD study*
The Potential for Read-Through of Rare Genetic Diseases

Aminoglycosides' tolerability profile historically limited suitability for read-through treatment of serious genetic diseases.

Advances in our understanding of translational read-through enables design of novel small molecules.

In every genetic disease a subset of patients have nonsense mutations that impair the production of essential proteins.

Translational read-through is directed at restoring the production of full length proteins by overcoming the premature stop codon and nonsense mediated decay.

>1,800 Genetic diseases involve nonsense mutations

Cystic Fibrosis, Cystinosis, Retinitis Pigmentosa, Usher’s Syndrome, Primary Ciliary Dyskinesia, Polycystic Kidney Disease

Retinitis Pigmentosa

Cystic Fibrosis

Cystinosis

Retinitis Pigmentosa

Usher’s Syndrome

Primary Ciliary Dyskinesia

Polycystic Kidney Disease
Defined Ribosomal Binding Site

- Well defined molecular interaction with helix 44
- Role in stabilization of tRNA binding at Site A
- Optimizing scaffold by altering interaction with prokaryotic and mitochondrial ribosomes
- Defined tissue penetration and tolerability profile for read-through applications

Aminoglycoside activity observed on single pre-translocation ribosome complexes. Feldman, MB; Terry DS; Altman RB; Blanchard SC. Nature Chemical Biology volume6, pages54–62 (2010)
Novel Compound Library has Demonstrated Activity across Multiple Orphan Diseases
ELOXX Focus on High Unmet Medical Need
  – Nonsense mutations represent important patient segments in over 1,800 diseases
  – Many of these diseases have no approved therapeutics
  – In some diseases the nonsense patient population is appropriate size for traditional clinical development

Developing Novel Therapeutics through Established Pathways
  – Many orphan diseases have existing preclinical assays or animal models with correlations to clinical endpoints
  – Validated Phase 2 endpoints can guide phase transition and design of pivotal trials

Orphan Designation Confers Important Regulatory Considerations
  – Potential for closer collaboration, accelerated development
  – Several economic or exclusivity incentives
  – In the US, Rare Pediatric Disease Priority Review Voucher Program

Ongoing Global Regulatory Interest in Accelerating Development for High Unmet Medical Need
Safety, Tolerability, and Pharmacokinetics of Single Ascending Doses of ELX 02, a Potential Treatment for Genetic Disorders Caused by Nonsense Mutations, in Healthy Volunteers

TO DATE:
• No SAE Observed
• No renal or otoacoustic SAE
• Generally well tolerated

INITIATED 6TH COHORT in Belgium
On track for final Cohort in US
Cystic Fibrosis Nonsense Mutation Patients Represent a Key Unmet Need Population

GLOBAL CYSTIC FIBROSIS PATIENTS BY MUTATION/GENOTYPE

- F508del Mutations
- Other Mutations
- Nonsense Related Mutations

No Currently Approved Drugs To Treat CFTR Nonsense Mutations

CFTR NONSENSE MUTATION SUBTYPES

- G542X
- W1282X
- R553X
- R1162X
- Other Nonsense Mutations

10 - 13%

Source: Eloxx Internal Research/CFTR2 database
Organoid Swelling Assay Demonstrates CFTR Function

Cystic Fibrosis Organoid dose-responsive swelling assay response

Patient Organoid without drug treatment: No Swelling of Organoids

Patient Organoid with ELX-02 treatment: Swelling of Organoids

Swelling quantification of patient organoid with ELX-02 treatment.

AUC G542X/G542X

Vehicle

ELX-02

AUC Cumulative swelling (t=120 min)

0 1000 2000 3000 4000 5000 6000

0 12.5 25 50 100

ELX-02 µg/ml

*** *** *** ***
Nonsense Mutations Can Cause a “Double-Hit”, Loss of mRNA and Functional Protein

CFTR mRNA Comparisons to Healthy, Wild-type Control

Cystic Fibrosis Organoid Responsive to ELX-02 demonstrates elevations above wild-type
Homozygous Nonsense Mutation (G542X)

**SWELLING (FUNCTION) ASSAY**

**NANOSTRING (MRNA) ASSAY**

- **AUC Cumulative swelling (t=120 min)**
  - Vehicle
  - ELX-02 50 µg/mL
  - ELX-02 100 µg/mL

- **CFTR Expression**
  - ELX-02 (µg/mL) 0, 50, 100
New HUB Organoid Data Correlates with Clinical Response

FEV1 response correlates with organoid swelling in samples collected across multiple clinical trials.
- Genistein & Curcumin (circles)
- Ivacaftor (squares)
- Lumacaftor & Ivacaftor (triangles)

Organoid results correlate with sweat chloride change
- \( r = -0.708, p<0.001 \)

ELX-02 Response in Organoids Compares Favorably to Published Results


Eloxx data on file.
Homozygous Nonsense Mutation (G542X)

Cystic Fibrosis Organoid Responsive to ELX-02, Enhanced by Combination

* Source: European Cystic Fibrosis Society 41st Conference, Belgrade, Serbia, June 2018
  - 100 µg/mL ELX-02
  - Error Bars represent SEM
  - $p < 0.0001$ vs Vehicle, Potentiator & Corrector. N.S. vs. ELX-02 + Potentiator & Corrector by Ordinary One Way ANOVA With Sidak’s Multiple Comparison Testing on AUC transformations
Complex Heterozygous Nonsense Mutation (G542X:R1066C missense)

Cystic Fibrosis Organoid Responsive to ELX-02, Enhanced by Combination

*Source: European Cystic Fibrosis Society 41st Conference, Belgrade, Serbia, June 2018

- 100 µg/mL ELX-02
- Error bars represent SEM
- p<0.0001 ELX-02 vs Potentiator & Corrector, Vehicle, p<0.05 ELX-02 vs Triple treatment by One Way Anova with Sidak’s Multiple Comparison Testing on AUC transformations.
Complex Heterozygous Nonsense Mutation (G542X:F508del)

Cystic Fibrosis Organoid Responsive to ELX-02, Enhanced by Combination

*Source: European Cystic Fibrosis Society 41st Conference, Belgrade, Serbia, June 2018

- 100 µg/mL ELX-02
- Error bars represent SEM
- p=0.00012 ELX-02 vs Potentiator & Corrector, p=0.0006 ELX-02 vs Vehicle, ELX-02 vs ELX-02+ Potentiator & Corrector by One Way Anova with Sidak’s Multiple Comparison Testing on AUC transformations.
ELX-02 Organoid Response is Observed Across a Range of CF Genotypes

- G542X; G542X
- G542X; F508del
- G542X; R1066C
- R1162X; F508del
- G542X; W1282X
- W1282X; W1282X
- R553X; F508del
- E60X; F508del

New Genotypes

Eloxx data on file
Data from multiple individuals with the same genotypes also collected.
Clinical Update for ELX-02 Phase 2 in Cystic Fibrosis

- Orphan Drug Designation granted by EMA
- Clinical Trial Application (CTA) for Phase 2 Study received final approved by the FAMHP in Belgium

- Expanding MAD Study
  - 6th cohort initiated in Belgium
    - Completion in 1H2019 with final cohort in US

- Engaging with investigators on a protocol for Phase 2 to insure rapid execution
  - No more than 24 patients
  - Will evaluate changes in sweat chloride at ascending doses
  - Planned enrollment will focus on patients with G542X nonsense mutation on one (complex heterozygote) or both alleles (homozygote)

- Expect Topline Cystic Fibrosis Phase 2 data in 2019
- EU Basic Science Meeting March 27th New Data
Substantial Opportunities in Inherited Retinal Diseases

- **Usher Syndrome**
  - Incidence: 3.2-6.2/100K
  - US Prevalence: 16.3K
  - Nonsense Proportion: 20%

- **Retinitis Pigmentosa**
  - Incidence: 1-5/10K
  - US Prevalence: 67K
  - Nonsense Proportion: 15-50%

- **Choroideremia**
  - Incidence: 1-9/100K
  - US Prevalence: 6.5K
  - Nonsense Proportion: 36%

- **Stickler’s Syndrome**
  - Incidence: 1-9/100K
  - US Prevalence: 66K
  - Nonsense Proportion: 20%

Population values from National Organization for Rare Disorders (NORD) and Orphanet
Inherited Retinal Disease Program Initiated

- Advancing Several Compounds from our Library

- Currently in IND-Enabling Studies
  - Demonstrated positive activity on nonsense mutations across a variety of inherited retinal disorders
  - Favorable tolerability profile
  - Support the use for intravitreal injection

- Development Focus on Ushers Syndrome, Leber’s Congenital Amaurosis, or Other Forms of Retinitis Pigmentosa Caused by Nonsense Mutations

- Wide Ranging Partnership with the Foundation Fighting Blindness
  - Partnership includes broad scientific engagement to support Eloxx’s ocular portfolio development

- ARVO Meeting May 2, 2019 New Data
Usher Syndrome

- No drugs approved or in late-stage development for nonsense variants
- Significant unmet medical need for nonsense forms
  - Over 4,000 patients in North America alone
- Academic collaborations have demonstrated activity with Eloxx Novel Library Compounds
  - Read through protein expression In vitro retinal compatibility
- Encouraging IND enabling studies supporting preservation of electroretinogram (ERG) and retinal histology
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