Unlocking protein production with translational read-through for rare genetic diseases
Certain statements included in this presentation are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These include statements of management’s intentions, belief, plans and future expectations and, therefore, you are cautioned not to place undue reliance on them. Such forward-looking statements involve risks and uncertainties and actual results could differ materially from any forward-looking statements expressed or implied herein. The risks and uncertainties that could result in actual results to differ materially from those forward-looking statements express or implied herein include, but are not limited to: the Company's ability to continue as a going concern; the ability of the Company to consummate additional financings; the development of the Company's technology; the approval of the Company's patent applications; the Company's ability to successfully defend its intellectual property or obtain the 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 success of the Company's license agreements; the timing and success of the Company's preliminary studies, preclinical research, clinical trials and related regulatory filings; if approved, the acceptance by the market of the Company's products and the continued quotation of the Company's common stock on the over-the-counter securities market, as well as other factors expressed from time to time in the Company's 10-K, 10-Qs and other filings with the SEC. The forward-looking statements contained herein are made only as of the date of this presentation, and the Company undertakes no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstances.
Eloxx Pharmaceuticals Highlights

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<thead>
<tr>
<th>Leading Read Through Company</th>
<th>Clinical stage biopharmaceutical company developing novel small molecule medicines designed to treat genetic diseases by restoring the production of proteins from genes with nonsense mutations</th>
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Highly Experienced Leadership Team

Robert Ward
Chairman and CEO

Pedro Huertas, MD, PhD
CMO

Gregory Weaver
CFO

John van Duzer, Ph.D.
VP CMC

Barbara Ryan
Investor Relations

Neil Sharpe, Ph.D.
VP Translational Sci.
The Promise of Read-Through

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

Translational read through restores the production of full length proteins by overcoming the premature stop codon and nonsense mediated decay.

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

Aminoglycosides first showed read-through activity in nonsense mediated diseases.

Aminoglycosides tolerability profile has limited suitability for read through treatment of serious genetic diseases.

>1,800 genetic diseases involve nonsense mutations.

- Cystic Fibrosis
- Cystinosis
- MPS I Syndrome
- Rett Syndrome
- Duchenne Muscular Dystrophy
Eloxx read-through program is pursuing product candidates with the following characteristics:

- Activity independent of gene size or complexity of genetic disorder
- Molecular scaffold with defined ribosomal effect
- Active at all three premature stop codons
- Reduces rate of nonsense mediated decay
- Restores protein production to a clinically significant level
- Acceptable tolerability profile
- Suitable for chronic administration
Aminoglycoside Ribosomal Interaction

- 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)
Discovery of ELX-02

- Novel compounds derived from aminoglycoside scaffold
- Screened for read-through activity on known disease related nonsense mutations
- Reduced mitochondrial inhibition (range 12-140X)
- Reduced prokaryotic ribosomal inhibition

ELX-02 Preclinical Development

- IND Enabling Studies
  - Functional and anatomic hearing studies
    - No observation of ototoxicity
  - Histopathology and functional renal studies
    - Indication of improved NOAEL margin
    - Currently anticipate dosing without adjustment for renal impairment
  - On track for mid-year submission
- Initiated regulatory pre-IND review of CMC to support planned clinical program
ELX-02 Clinical Development

ClinicalTrials.gov Identifier: NCT03292302  Completed

A Phase 1a, Randomized, Double-blinded, Placebo-Controlled, Single Dose Escalation Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of ELX-02 in Healthy Adult Volunteers

To Date:
No SAE Observed
No renal or otoacoustic SAE
Generally well tolerated

ClinicalTrials.gov Identifier: NCT03309605  Ongoing

A Phase 1, Randomized, Double-Blinded, Placebo-Controlled, Third Party Open, Multiple Dose Escalation, Single Center Study to Evaluate the Safety, Tolerability and Pharmacokinetics of Subcutaneously Administered ELX-02 in Independent Consecutive Cohorts of Healthy Subjects

Planned Enrollment 45
Cystinosis Development Program

- Ultra-rare lysosomal storage disease
- Caused by mutations in cystinosin (CTNS)
  - Cysteine efflux channel
- Cystine lysosomal accumulation causes manifestations of disease
- It is generally recognized that the current standard of care (cysteamine administration) stimulates alternative transport pathway
- W138X most common nonsense mutation represents 1/3 of patient population
- ELX-02 currently available data indicate the potential to:
  - Increase translational read-through
  - Reduce NMD
  - Restore CTNS mRNA to near normal levels
  - Lower cystine accumulation \textit{in vitro} and \textit{in vivo}
In vitro model indicates ELX-02 reduces nonsense mediated decay (NMD)

In vitro model indicates ELX-02 restores Cystinosin transporter function

In vitro model
CTNS<sup>W138X/W138X</sup> fibroblasts

CTNS/GAPDH mRNA level

Cystine Accumulation
ELX-02 Animal Model Cystinosis

CTNS^{Y226X/Y226X} knock-in
Dr Paul Goodyer
McGill University

Cystine Accumulation

21 Days of Biweekly ELX-02 Administration
Significantly Reduced Kidney Cystine Levels
ELX-02 Cystinosis Next Steps

- Dec 2017 Pre-IND FDA Discussion
  - On track for mid-2018 IND Submission in US
  - Targeting 4Q 2018 for FPFV Phase 2 Study
Cystic Fibrosis Development Program

- Systemic rare disease
- Caused by mutations in transmembrane conductance regulator (CFTR)
  - Chloride channel
- Mutations lead to dysregulation in multiple organ systems
- Current standard of care based on molecular chaperones for trafficking and conformation
- G542X most common nonsense mutation represents 5% of patient population
- ELX-02 currently available data indicates the potential to:
  ✓ Increase translational read-through
  ✓ Improve chloride currents in HBEs and organoids
  ✓ Demonstrate synergy with correctors and potentiators in heterozygous population
Cystic Fibrosis
CFTR Molecular Defect

- Premature stop codons or nonsense mutations are Class 1
- There are currently no approved therapies for Class 1
- G542X represents approximately 5% of the total CF patient population
- Eloxx’s development path for read-through therapeutics will be focused on the patient subset with diagnosed nonsense mutations

<table>
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<th>Mutation examples</th>
<th>Rescue synthesis</th>
<th>Rescue traffic</th>
<th>Restore channel activity</th>
<th>Correct splicing</th>
<th>Promote stability</th>
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<tr>
<td>G542X (a)</td>
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<td>W1282X (b)</td>
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<th>Corrective therapy</th>
<th>Drug approved (Yes/No)</th>
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Novel personalized therapies for cystic fibrosis: Treating the basic defect in all patients. Journal of Internal Medicine 277(2) · September 2014
Goals of Cystic Fibrosis Personalized Medicine Approach

- Development path focused on individual’s genetic background (ie, CFTR mutation)

- Today most patients have genetic sequence data that could enable personalized treatment
Cystic Fibrosis: First Organoid Clinical Success

First 6 patients successfully treated based on organoid diagnosis.

Does not refer to ELX-02

CF patient
Organoids For Cystic Fibrosis Screening

A CF assay on cystic fibrosis patient organoids

Healthy CFTR activation:
Swelling of Organoids

CF mutated CFTR activation:
No-Swelling of Organoids
Organoids Pre-clinical Patient Stratification Can Be Used To Define Clinical Trial Populations

A CF swelling assay on cystic fibrosis patient organoids

Patient Organoid without drug treatment: No Swelling of Organoids

Patient Organoid with drug treatment: Swelling of Organoids
ELX-02 Example Organoid Results

4-points dose titration of ELX-02 compound at 5μM Forskolin after 48h incubation in absence or presence of VX-770 (added acutely or incubated for 48h) in F508del/G542X organoid cultures. Combination VX-809/ VX770 (added acutely or incubated for 48h) was performed as control.
ELX-02 Cystic Fibrosis Next Steps

☑ Jan 2018 Pre-CTA (Belgium) Regulatory Meeting

- On track for mid-2018 CTA (Belgium) Submission
- Targeting 4Q2018 for FPFV Phase 2 Study
Our Current Development Pipeline

ELX-02

2017 2018 2019 2020

Phase 1a Phase 1b MAD

Submission CTA (Belgium) IND (FDA)

Cystic Fibrosis Cystinosis

Phase 2

ELX Library Compounds

Preclinical Mutational Profiling Candidate Nomination

ELX-02 and the ELX Library Compounds are investigational agents and have not been approved for use by any regulatory agency.
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March 20 FY2017 Earnings Call

Suntrust 4th Annual Orphan Drug Day Feb 13, 2018
Cowen 38th Annual Health Care Conference March 12, 2018
Thank you!