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

Cantor Global Healthcare, October 2, 2018
This press release 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

- ELX-02 Clinical Progress
  - Phase 1a SAD Submitted for Publication
  - Phase 1b MAD Ongoing
  - Final Approval CTA for Cystic Fibrosis Phase 2 in Belgium
  - Open IND for Cystinosis Phase 2 in US

- Expect to Complete MAD and Reach Top Line Phase 2 Data in 2019

- Upcoming ELX-02 Presentation at the North American Cystic Fibrosis Society Meeting on October 18
  - “Measuring mRNA Levels in Cystic Fibrosis Organoids with Nonsense Mutations Following Treatment with ELX-02”

- Progressing Novel Library Molecules Toward IND
  - Existing Data Support Activity on Nonsense Mediated Ocular Orphan Targets
  - Supportive Preclinical Studies Have been Initiated
  - On Track for Advancing Pipeline in 2018

- Well Funded to 2020
  - Cash and Cash Equivalents of $63.4 million at June 30, 2018
Built a Highly Experienced Leadership Team

Robert Ward
CHAIRMAN AND CEO

Greg Williams, PhD
COO

David Snow
CBO

Greg Weaver
CFO

Neil Belloff, Esq.
GENERAL COUNSEL

John van Duzer, PhD
VP CMC

Neal Sharpe, PhD
VP TRANSLATIONAL SCIENCE

Barbara Ryan
INVESTOR RELATIONS
The Potential for Read-Through of Rare Genetic Diseases

Aminoglycosides first showed read-through activity in nonsense mediated 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
- MPS I Syndrome
- Rett Syndrome
- Duchenne Muscular Dystrophy

Aminoglycosides' tolerability profile historically limited suitability for read-through treatment of serious genetic diseases.
Eloxx read-through program is pursuing product candidates with the following characteristics:

<table>
<thead>
<tr>
<th>Activity independent of gene size or complexity of genetic disorder</th>
<th>Molecular scaffold with defined ribosomal effect</th>
<th>Active at all three premature stop codons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduces rate of nonsense mediated decay</td>
<td>Restores protein production to a clinically significant level</td>
<td>Acceptable tolerability profile</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suitable for chronic administration</td>
</tr>
</tbody>
</table>
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 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

Increased Selectivity towards Cytoplasmic versus Mitochondrial Ribosome Confers Improved Efficiency of Synthetic Aminoglycosides in Fixing Damaged Genes: A Strategy for Treatment of Genetic Diseases Caused by Nonsense Mutation.

Substantial Advantages for Orphan Drug Development

- 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
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

CFTR Nonsense mutation subtypes

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

10 - 13%

No Currently Approved Drugs To Treat CFTR Nonsense Mutations

Source: Eloxx Internal Research/CFTR2 database
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
Homozygous Nonsense Mutation (G542X)

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

- As presented at the European Cystic Fibrosis Society 41st Conference, Belgrade, Serbia, June 2018
- 100 µg/mL ELX-02 As previously presented
Complex Heterozygous Nonsense Mutation (G542X:R1066C missense)

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Homozygous Deletion Mutation (F508del)

Cystic Fibrosis Organoids Without Nonsense Mutations are Not Responsive to ELX-02

As presented at the European Cystic Fibrosis Society 41st Conference, Belgrade, Serbia, June 2018

- 100 µg/mL ELX-02 As previously presented
ELX-02 Clinical Development – Phase 1 Studies

CLINICALTRIALS.GOV Identifier: NCT03292302
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

Submitted for Publication

CLINICALTRIALS.GOV Identifier: NCT03309605
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

Completed 4th Cohort
Revising protocol for additional cohorts

TO DATE:
• No SAE Observed
• No renal or otoacoustic SAE
• Generally well tolerated
Clinical Update for ELX-02 Phase 2 in Cystic Fibrosis

√ Submitted Orphan Drug Application to EMA

√ Clinical Trial Application (CTA) for Phase 2 Study received final approved by the FAMHP in Belgium

• Expanding MAD Study
  √ 4th Cohort Completed
  • Additional Cohorts to Evaluate Drug Concentrations

• Engaging with investigators on a protocol for Phase 2 to insure rapid execution
  • 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 top line data in 2019
Eloxx Presentation

“Measuring mRNA Levels in Cystic Fibrosis Organoids with Nonsense Mutations Following Treatment with ELX-02”

October 18
Clinical Update for ELX-02 Phase 2 in Cystinosis

- FDA granted ELX-02 orphan drug status in cystinosis
- IND for ELX-02 in cystinosis is open in the US
- Engaging Investigators on Phase 2 protocol
  - Will evaluate changes in cysteine levels in white blood cells
  - Study will be posted on clintrials.gov
- Expect top line data on cysteine levels in 2019

- Data previously reported showed that ELX-02 decreases the cysteine content in cellular and animal models*  

* Dr. Paul Goodyer at the 14th Annual WORLDSymposium on Lysosomal Diseases in a presentation titled “Translational read through of CTNS nonsense mutations and attenuation of CTNS nonsense-mediated mRNA decay by ELX-02”
On Track for Advancing Pipeline in 2018

Multiple Novel Compounds Are Advancing To IND Enabling Studies

Extensive Intellectual Property Portfolio

Eloxx holds global rights on these library compounds ELX-02 Composition of Matter 2031 without extensions Library Composition of Matter from 2027-2038 or later Library Use Patents Expire 2036 or later
Novel Compound Library has Demonstrated Activity across Multiple Orphan Diseases
Substantial Potential Ocular Orphan Opportunity

Population values from National Organization for Rare Disorders (NORD)
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
In Vitro Retinal Biocompatibility

- Studies in retinal culture have demonstrated distinct biocompatibility profile, ie, no change in retinal staining or structure\(^1\)
- Multiple Library Compounds\(^2\) have been evaluated to date
- Additional supportive preclinical studies ongoing

\(^1\)Goldmann et al. EMBO Mol Med 2012, 4(11):1186-1199

\(^2\) ELX compounds, NB84, NB122, NB124 and NB127, but not gentamicin and G418, elicit comparable biocompatibility in vitro effect [Möller et al. 2016 The Annual Meeting of the Association for Research in Vision and Ophthalmology (ARVO)]
Demonstration of Usher Protein Production

<table>
<thead>
<tr>
<th>Usher Patient Mutation</th>
<th>Healthy Control</th>
<th>Vehicle</th>
<th>Gentamycin</th>
<th>NB84</th>
<th>NB122</th>
<th>NB124</th>
<th>NB127</th>
</tr>
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<tbody>
<tr>
<td>Harmonin (USH1C)</td>
<td>harm a4_wt</td>
<td>harm a4_p.R155X +DMSO</td>
<td>harm a4_p.R155X +Gentamycin</td>
<td>harm a4_p.R155X +NB84</td>
<td>harm a4_p.R155X +NB122</td>
<td>harm a4_p.R155X +NB124</td>
<td>harm a4_p.R155X +NB127</td>
</tr>
<tr>
<td>Cell mask</td>
<td>harm a4_wt</td>
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- Collaborations with the Ben-Yosef and Nagel-Wolfrum labs demonstrate potential:
  - Favorable safety profile in the retina
  - Readthrough of relevant eye-disorder mutations
  - Production of missing protein
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Thank you.