Eloxx Pharmaceuticals Presents Positive New Data for Lead Investigational Drug, ELX-02, at the European Cystic Fibrosis Society (ECFS) Basic Science Conference

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ELX-02 shows significant increases in CFTR protein expression and localization correlating with functional activity in Cystic Fibrosis patient-derived organoids bearing CFTR nonsense mutations

In previous studies, the increased CFTR functional activity associated with ELX-02 was shown to correlate with increases in CFTR mRNA with elevations to wild-type levels

ELX-02 appears to increase CFTR mRNA stability, suggesting that ELX-02 may be modulating nonsense mediated decay

WALTHAM, Mass., March 27, 2019 (GLOBE NEWSWIRE) -- **Eloxx Pharmaceuticals, Inc. ("Eloxx"),** (NASDAQ: ELOX), a clinical-stage biopharmaceutical company dedicated to the discovery and development of novel therapeutics to treat cystic fibrosis, cystinosis, inherited retinal disorders, and other diseases caused by nonsense mutations limiting production of functional proteins, today announced positive data demonstrating, for the first time in organoids, that ELX-02 significantly increases CFTR protein expression and localization on the apical surface in organoids with nonsense mutations. These findings were presented today at the ECFS Basic Science Conference in Croatia.

"ELX-02 is the first read-through agent to demonstrate significant increases in CFTR protein expression, localization on the apical surface, and functional activity in a dose responsive manner in organoids derived from cystic fibrosis patients with nonsense mutations" said Dr. Matthew Goddeeris, Research Director at Eloxx Pharmaceuticals. Robert Ward, Chairman and CEO, added, "We believe these ground-breaking new data establish a solid basis for understanding the activity of ELX-02 and it's potential for development in the treatment of the high unmet medical need cystic fibrosis patients with nonsense mutations. We look forward to reporting top line data in 2019 from our planned Phase 2 cystic fibrosis clinical trial."

Recent work with cystic fibrosis patient-derived organoids have extended the potential applications of the FIS assay to include use in stratifying patient disease severity (1) and as a potential predictor of CF patient response to drug therapy (2). On February 26, 2019, Eloxx announced it had joined the consortium agreement of the European HIT-CF project, a European Union funded preclinical and clinical research program evaluating the efficacy and safety of several disease modifying drug candidates in Cystic Fibrosis (CF) patients with rare genetic mutations. The goal of the European HIT-CF project is to investigate whether a positive response to therapies in a patient derived organoid can be predictive of clinical response in a controlled trial.

Eloxx is on track to report top line results in 2019 from a Phase 2 study in cystic fibrosis patients carrying at least one *G542X* mutation in the U.S., and Europe. The European Cystic Fibrosis Society-Clinical Trial Network has reviewed the program and assigned a "high priority" rating.

In a Poster presentation at the ECFS Basic Science Conference titled: "**CFTR protein detection in organoids from healthy and CF patients with nonsense mutations support using organoid model to test ELX-02 mediated CFTR read-through restoration"**, presented by Dr. Shira Landskroner-Eiger, Sr. Principal Scientist, Translational Sciences at Eloxx, it was reported that:

- Consistent with increased CFTR activity observed in the organoid swelling assay, ELX-02 mediates a significant restoration of CFTR protein expression as measured via a capillary-based immunoassay approach in multiple *G542X* or *W1282X* nonsense carrying organoids.

- *G542X* organoids treated with ELX-02 demonstrate proper cell surface CFTR localization on the apical surface, which is consistent with increased CFTR, mRNA, and CFTR function in the swelling assay.

While ELX-02 mediated protein increases have been previously demonstrated, this is the first demonstration reported in cystic fibrosis patient organoids. Within this translational CF organoid model, ELX-02 dose-dependent increases in *CFTR* mRNA stability and function can now be extended to the demonstration of accompanying increases of CFTR protein.

Previously, Eloxx presented positive data for ELX-02 at the North American Cystic Fibrosis Conference in October 2018 in Denver, Colorado in a poster presentation titled: **"Measuring mRNA levels in cystic fibrosis organoids with nonsense mutations following treatment with ELX-02,"** which demonstrated ELX-02 mediated dose responsive increases in CFTR function, as measured by FIS swelling activity, which was found to correlate with increases in *CFTR* mRNA, as measured by NanoString™ technology, with elevations above wild-type. ELX-02 appears to increase the steady state concentrations of *CFTR* mRNA suggesting that ELX-02 may be modulating nonsense mediated decay.

These data demonstrate that ELX-02 promotes translation of functional CFTR and we believe, de-risks our planned Phase 2 clinical trial of ELX-02 in cystic fibrosis patients with the *G542X* CFTR mutation on one or both alleles, which is the second most common mutation globally and accounts for about 5% of the cystic fibrosis population.

Eloxx has continued to generate new data for ELX-02 activity from a growing number of patient-derived organoids which represent multiple nonsense mutations across a variety of genotypes representing the top 5 nonsense mutations in the cystic fibrosis population, which cover over 75% of the nonsense bearing cystic fibrosis patients.

ELX-02 is an investigational agent not approved by any regulatory agency for therapeutic use.

About Eloxx Pharmaceuticals

Eloxx Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company developing novel RNA-modulating drug candidates (designed to be eukaryotic ribosomal selective glycosides) that are designed to treat rare and ultra-rare premature stop codon diseases. Premature stop codons are point mutations that disrupt protein synthesis from messenger RNA. As a consequence, patients with premature stop codon diseases have reduced or eliminated protein production from the mutation bearing allele accounting for some of the most severe phenotypes in these genetic diseases. These premature stop codons have been identified in over 1,800 rare and ultra-rare diseases. Read-through therapeutic development is focused on extending mRNA half-life and increasing protein synthesis by enabling the cytoplasmic ribosome to read through premature stop codons to produce full-length proteins. 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 moving to Phase 2 clinical development focusing on cystic fibrosis and cystinosis. ELX-02 is an investigational drug that has not been approved by any global regulatory body. Eloxx's preclinical candidate pool consists of a library of novel drug candidates designed to be eukaryotic ribosomal selective glycosides identified based on read-through potential. Eloxx is also advancing a new program focused on rare ocular genetic disorders. Eloxx is headquartered in Waltham, MA, with R&D operations in Rehovot, Israel. For more information, please visit www.eloxxpharma.com.

Forward-Looking Statements

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.

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