Enzon Presents Data at 2010 EORTC-NCI-AACR Meeting

Third-Generation mRNA-Targeting Compounds Show Potent Anti-Tumor Activity

BRIDGEWATER, N.J.--(BUSINESS WIRE)-- Enzon Pharmaceuticals, Inc. (Nasdaq: ENZN) today presented data from preclinical studies of three investigational messenger RNA (mRNA) antagonists. These antagonists are based on the locked nucleic acid (LNA) technology platform targets licensed from Santaris Pharma A/S. The data were presented in poster sessions at EORTC-NCI-AACR International Symposium on Molecular Targets and Cancer Therapeutics, which is being held November 16-19 in Berlin, Germany.

"The robust anti-tumor activity in these preclinical studies underscores the therapeutic potential of our third-generation mRNA antagonists to inhibit key tumor targets that are generally inaccessible to antibodies and small molecules," said Ivan Horak, MD, Enzon's President of Research and Development and Chief Scientific Officer. "The Locked Nucleic Acid technology on which these novel compounds are based provides significant advantages over earlier RNA-targeting agents, including greater stability, affinity, and potency. We look forward to further investigating the safety and efficacy of these compounds in the clinical setting."

LNA-Based mRNA Compound Poster Presentations

"Down-modulation of the androgen receptor with EZN-4176 inhibits the growth of prostate tumor and potentiates the inhibitory effect of MDV-3100, a novel anti-androgen," Yixian Zhang et al. Poster No. 218

- EZN-4176 offers a new strategy for treating castration-resistant prostate cancer (CRPC), either alone or in combination with MDV-3100. MDV3100 is a novel androgen receptor antagonist currently in Phase III testing in patients with advanced prostate cancer.
- *In vitro,* EZN-4176 specifically inhibited the growth of prostate tumor cells that were responsive or resistant to hormone deprivation, which correlated with down-modulation of the androgen receptor (AR), as well as AR transactivation.
- *In vivo*, EZN-4176 demonstrated tumor inhibition comparable to MDV-3100 and bicalutamide (Casodex®) in CWR22 tumor xenografts, which was accompanied by down-modulation of mRNA.
- Combination with anti-androgens (MDV3100 or bicalutamide) showed much-improved inhibitory effect in growth assays compared to MDV3100 alone. *In vivo,* The combinatorial effect with MDV3100 was synergistic.

"Down-regulation of β-catenin mRNA by a locked nucleic acid oligonucleotide antagonist inhibits tumor growth in experimental models of human cancer," Melissa Dumble et al. Poster No. 53

- EZN-3892 may provide a targeted, effective method of inhibiting tumor growth through down-regulation of β-catenin, a transcriptional regulator that is critical in the development of numerous human cancers.
- In mice bearing tumors derived from human colon and lung cancers, EZN-3892 produced 71% and 76% tumor-growth inhibition, respectively.
- Administration of EZN-3892 to mice bearing polyps with sustained β-catenin activity resulted in a 50% reduction in β-catenin mRNA in polyp tissue, while non-related mRNA was unaltered.

"Reduced Expression of HER3 with a specific RNA antagonist is associated with antitumor effects in preclinical models of cancer," Yaming Wu et al. Poster No. 144

- *In vitro,* EZN-3920 potently inhibited HER3 expression and tumor growth in various tumor cells lines, including a lung tumor cell line that was selected for resistance to gefitinib and an ovarian cell line that overexpresses HER2.
- *In vivo,* systemic administration of EZN-3920, prepared in saline, resulted in specific down-modulation of HER3 mRNA and protein expression, as well as blockade in P13K/AKT signaling pathways in the lung and ovarian cancer xenograft models.
- In established Polyomavirus middle T transgenic mammary tumors transplanted into mice, perturbation of HER2/HER3 signaling pathway with EZN-3920 resulted in tumor growth inhibition, reduced expression of HER3, and induction of apoptosis.
- EZN-3920 may provide a novel strategy to overcome resistance to HER1 and HER2 targeted therapies. Furthermore,

down-regulation of HER3 may provide a novel strategy to overcome resistance to HER1 and HER2 targeted therapies.

"An antisense molecule to HER3 sustains growth inhibitory effects in gefitinib resistant cells that are independent of MET overexpression," Zhengxing Qu et al. Poster No. 307

- Down-regulation of HER3 by an LNA antisense molecule is an effective method to inhibit tumor-cell growth both *in vitro* and *in vivo*. Robust *in vivo* activity was observed in 2 distinct models of breast cancer and one model of lung cancer.
- Gefitinib hypersensitivity may indicate that cells are dependent on HER3 and will be inhibited by HER3 antisense molecules.
- Sustained activation of HER3 in the presence of down-regulation of phospho-EGFR may be just as important as HER3 hyperactivation in the gefitinib-resistant cells.
- Pharmacological manipulation to down-regulate HER3 by EZN-3920 could prove to be a translational approach to controlling HER3-mediated tumor growth in cancer patients.

The abstracts and posters can be found on the Company's website at www.enzon.com.

About Enzon

Enzon Pharmaceuticals, Inc. is a biopharmaceutical company dedicated to the development of innovative medicines for patients with cancer. Enzon's drug development programs utilize several approaches, including its cutting-edge proprietary Customized Linker Technology utilizing PEGylation and mRNA antagonists using the Locked Nucleic Acid (LNA) technology. Enzon receives a royalty revenue stream from licensing arrangements for other products developed using the proprietary Customized Linker Technology. Further information about Enzon and this press release can be found on the Company's web site at www.enzon.com.

Forward Looking Statements

There are forward-looking statements contained herein, which can be identified by the use of forward-looking terminology such as the words "believes," "expects," "may," "will," "should," "potential," "anticipates," "plans," or "intends" and similar expressions. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results, events or developments to be materially different from the future results, events or developments indicated in such forward-looking statements. Such factors include, but are not limited to the timing, success and cost of clinical studies for Enzon's product candidates; the ability to obtain regulatory approval of product candidates, Enzon's ability to obtain the funding necessary to develop its product candidates, market acceptance of, and demand for, Enzon's product candidates and the impact of competitive products, pricing and technology. A more detailed discussion of these and other factors that could affect results is contained in our filings with the U.S. Securities and Exchange Commission, including our annual report on Form 10-K for the year ended December 31, 2009. These factors should be considered carefully and readers are cautioned not to place undue reliance on such forward-looking statements. No assurance can be given that the future results covered by the forward-looking statements will be achieved. All information in this press release is as of the date of this press release and Enzon does not intend to update this information.

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