



## **Enzon Presents Clinical and Preclinical Data on mRNA Antagonists at 2011 AACR-NCI-EORTC Meeting**

### **Clinical Study Demonstrates Tolerability and Anti-Tumor Activity of Survivin mRNA Antagonist in Combination With Docetaxel in Solid Tumors; Novel mRNA Antagonists Inhibit Tumor Growth, Oncogenic Proteins in Preclinical Studies**

PISCATAWAY, NJ -- (MARKET WIRE) -- 11/12/11 -- Enzon Pharmaceuticals, Inc. (NASDAQ: ENZN) today announced the presentation of clinical and preclinical data from three messenger ribonucleic acid (mRNA) product candidates based on the Company's locked nucleic acid (LNA) technology platform at the AACR-NCI-EORTC International Conference: Molecular Targets and Cancer Therapeutics in San Francisco, CA.

Enzon's LNA oligonucleotides, which reach their mRNA target without a delivery mechanism, unlike most RNA approaches, target difficult-to-drug pathways with well-established links to cancer survival, proliferation and drug resistance. These unique targets include hypoxia inducible factor-1a (HIF-1a), survivin, androgen receptor, HER3 and  $\beta$ -catenin. "The current data further elucidate the strengths of our third-generation LNA platform, including its ability to safely and effectively target important pathways in oncology using antisense molecules," said Aby Buchbinder, M.D., Enzon's Vice President of Clinical Development.

#### *Phase I study of EZN-3042 targeting Survivin (Poster #A-216)*

Investigators presented data from a Phase I, open-label, dose-escalation study of EZN-3042, an LNA oligonucleotide targeting survivin mRNA, in combination with docetaxel, in 16 patients with advanced solid malignancies. Survivin, an important mediator of cancer cell death and cell proliferation, has demonstrated potential in both solid and liquid tumor models, including highly encouraging results in acute lymphoblastic leukemia. The combination demonstrated good tolerability and antitumor activity in previously treated patients, and established a maximum tolerated dose of 6.5 mg/kg for EZN-3042 combined with the approved dose of docetaxel 75 mg/m<sup>2</sup>. The most common adverse events associated with the combination of EZN-3042 and docetaxel were mostly Grade 1 or 2, included fatigue, alopecia, neutropenia, anorexia, nausea and peripheral sensory neuropathy.

"Survivin is associated with drug resistance and poor outcome in many solid and liquid cancers," said Anthony W. Tolcher, M.D., director of clinical research at South Texas Accelerated Research Therapeutics and the principal investigator of the study. "It is also a challenging protein to target with established therapeutic approaches. By down regulating the mRNA encoding survivin, EZN-3042 inhibits the function of survivin and halts tumor progression in preclinical models when used in combination with chemotherapy. These Phase I results demonstrate the tolerability of such combination therapy in man, and support the validation of this potentially significant new approach in later study."

#### *Preclinical Data of EZN-3920 targeting HER3 (Poster #A147) and EZN-3892 targeting $\beta$ -catenin (Poster #A74)*

Enzon also announced the presentation of preclinical data using two of its other novel LNA-based compounds, EZN-3920, a HER3 mRNA antagonist, and EZN-3892, a  $\beta$ -catenin mRNA antagonist, at the AACR-NCI-EORTC Meeting.

HER3 interacts with EGFR and HER2-directed therapeutics including erlotinib, lapatinib, and trastuzumab used for the treatment of NSCLC and breast cancers. Numerous reports now indicate that increased expression and activation of HER3 is a key resistance mechanism to these marketed agents and, in addition, is a driver of growth in ovarian cancers. Since HER3 cannot be easily inhibited by small molecules, agents that down regulate HER mRNA, such as EZN-3920, may provide an important therapeutic option. The new data demonstrates that EZN-3920 reduces HER3 mRNA and protein expression associated with antitumor effects in animal models where EGFR or HER2 are known to drive tumor growth. The molecule also retains activity in cell lines made resistant to the EGFR inhibitor, gefitinib. Beyond this, combining EZN-3920 with gefitinib or lapatinib results in synergistic activity in tumor models. One mechanism by which EZN-3920 mediates synergistic activity is due to blockade of the lapatinib-induced expression of HER3. These data suggest that the LNA-based antagonist of HER3 may have utility in a wide variety of cancer patients when given alone or in combination with other agents that target the EGFR/HER2 signal transduction axis.

$\beta$ -catenin is an oncogenic transcription factor connected to the Wnt signaling pathway, which is associated with tumor-cell proliferation in several cancers, including multiple myeloma (MM). Currently, there are no effective agents to block the activity of  $\beta$ -catenin. The newly reported data demonstrates that the LNA-based therapeutic has moderate anti-proliferative effects in vitro using 8 different MM cell lines. The growth of tumors derived from one of the most responsive MM cell lines is dramatically inhibited by EZN-3892. The activity of the compound was associated with moderate target down regulation in tumor as well as more robust target down regulation in the cells surrounding the tumor (stroma). These data, combined with previous reports of

the antitumor effect of EZN-3892 in colorectal tumor models, suggest that EZN-3892 may have utility in the treatment of MM and other tumor types where growth is driven by  $\beta$ -catenin.

Collectively, the preclinical findings with the HER3 and  $\beta$ -catenin specific inhibitors, combined with newly published preclinical data on Enzon's LNA-based therapeutic targeting the androgen receptor (Zhang et al. 2011) and survivin (Parks et al., 2011; Morrison et al., 2011), further substantiate clinical evaluation of this new therapeutic approach for cancer treatment.

The full poster presentations are available online at [www.enzon.com/docs/development\\_presentations](http://www.enzon.com/docs/development_presentations).

#### *About Enzon*

Enzon Pharmaceuticals, Inc. is a biotechnology company dedicated to the research and development of innovative therapeutics for cancer patients with high unmet medical needs. Enzon's drug-development programs utilize two platforms -- Customized PEGylation Linker Technology (Customized Linker Technology®) and third-generation mRNA-targeting agents utilizing the Locked Nucleic Acid (LNA) technology. Enzon currently has four compounds in human clinical development and multiple novel LNA targets in preclinical research. Enzon receives royalty revenues from licensing arrangements with other companies related to sales of products developed using its proprietary Customized Linker Technology. Further information about Enzon and this press release can be found on the Company's website at [www.enzon.com](http://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 Enzon's 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 Enzon's filings with the U.S. Securities and Exchange Commission, including Enzon's most recent Annual Report on Form 10-K for the year ended December 31, 2010. 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.

#### Investor Contact:

Andrea Rabney

Argot Partners

212.600.1902

Email Contact

#### Media Contact:

Meghan Feeks

Argot Partners

212.600.1902

Email Contact

Source: Enzon Pharmaceuticals

