



## Enzon's HIF-1 Alpha Antagonist Shows Antitumor Activity

### Innovative and diverse pipeline advances

BRIDGEWATER, N.J., Oct 27, 2008 (BUSINESS WIRE) -- Enzon Pharmaceuticals, Inc. (Nasdaq: ENZN) presented data from its pipeline programs at the 2008 EORTC-NCI-AACR (European Organization for Research and Treatment of Cancer-National Cancer Institute-American Association for Cancer Research) annual meeting in Geneva, Switzerland.

"We are pleased to present data for the first time revealing that our HIF-1 alpha antagonist is well tolerated and demonstrates antitumor activity in previously treated patients with solid tumors," said Jeffrey H. Buchalter, chairman and chief executive officer of Enzon. "Additionally, preclinical studies from our third novel anticancer LNA target, ErbB3 show that it efficiently reduces HER3 expression in preclinical models."

The Posters and Abstracts that were presented included:

#### HIF-1 alpha

Phase I pharmacokinetic (PK), dose-escalation study of EZN-2968, a novel hypoxia-inducible factor-1 alpha (HIF-1 $\alpha$ ) antagonist, administered weekly in patients with solid tumors.

In this Phase I study, the HIF-1 alpha antagonist EZN-2968 was well tolerated in previously treated patients with solid tumors. Patients have received doses of up to 3.5 mg/kg per week, and dose escalation is ongoing. One patient received treatment for 408 days. Prolonged stable disease with clear evidence of tumor shrinkage was observed. This is the first study showing antitumor activity of a messenger RNA targeting agent in patients with solid tumors.

#### PEG-SN38

Pharmacokinetics (PK) of EZN-2208, a novel anticancer agent, in patients with advanced malignancies: a Phase I dose-escalation study.

This Phase I clinical study evaluated PEG-SN38 or EZN-2208 when administered weekly to patients for 3 weeks in each 4 week cycle was well tolerated, and no dose limiting toxicity was observed. Patients have received doses of up to 5 mg/ m<sup>2</sup> per week, and dose escalation is ongoing. The area under the curve appears to increase in a dose proportional manner, with prolonged exposure to SN38 having been achieved. One patient with colorectal cancer who had progressed after prior irinotecan is continuing on therapy beyond 297 days. The weekly schedule of PEG-SN38 has been well tolerated and long-term clinical benefit has been observed in several heavily pretreated patients including patients' refractory to Camptosar.

#### ErbB3 (HER3)

EZN-3920, an ErbB3-locked nucleic acid-based RNA inhibitor, potently silences target gene expression in tumor cells grown in vitro and in vivo.

ErbB3 (HER3) represents a novel target for cancer therapy. EZN-3920 or ErbB3 (HER3) antagonist is a new generation of antisense molecule, Locked Nucleic Acid (LNA) that specifically and efficiently reduces ErbB3 (HER3) expression both in vitro and in vivo in animal studies. Further preclinical studies will examine the antitumor efficacy of EZN-3920.

#### Customized PEG Linker Technology (2 abstracts)

Customized PEG linkers improve tumor delivery of RNA antagonist oligonucleotides.

Enzon used its Customized PEG linker enabling chemistry to examine if it would improve cellular penetration and tumor homing for RNA antagonists. Customized PEG linkers may provide a promising approach for more efficient in vivo delivery of oligonucleotides including LNA oligonucleotides and siRNAs. Enhanced targeting and penetration of oligonucleotides into tumor cells could improve the utility of oligonucleotide based therapy.

Novel Customized releasable polyethylene glycol (PEG) linkers improve tumor delivery and down modulation of target by locked nucleic acid oligonucleotides.

Enzon used its Customized Linker Technology to attach polyethylene glycol (PEG) to LNA oligonucleotides. Releasable PEGylation of LNA enhances accumulation of the oligonucleotide in the tumor and improves down modulation of the target in the tumor. The beneficial effects may be due to the enhanced permeability and retention within the tumor, which has previously been observed with PEGylated molecules. These characteristics may subsequently improve therapeutic efficacy.

#### About ErbB3 (HER3)

ErbB3 or HER3, a member of the HER family is known to be over-expressed in breast, ovarian, and lung cancer, and HER3 over-expression is correlated with a poor prognosis. The development of drugs that antagonize the function of HER3 has been challenging due to the absence of the kinase activity which is unlike other HER members. Therefore, specific targeting of HER3 may require novel strategies such as antisense that down-modulates HER3 receptor expression and disrupts this critical pro-survival pathway.

#### About Enzon

Enzon Pharmaceuticals, Inc. is a biopharmaceutical company dedicated to the development, manufacturing, commercialization of important medicines for patients with cancer and other life-threatening conditions. Enzon has a portfolio of four marketed products, Oncaspar(R), DepoCyt(R), Abecet(R) and Adagen(R). The Company's drug development programs utilize several cutting-edge approaches, including its industry-leading PEGylation technology platform used to create product candidates with benefits such as reduced dosing frequency and less toxicity. Enzon's PEGylation technology was used to develop two of its products, Oncaspar and Adagen, and has created a royalty revenue stream from licensing partnerships for other products developed using the technology. Enzon also engages in contract manufacturing for several pharmaceutical companies to broaden the Company's revenue base. Further information about Enzon and this press release can be found on the Company's web site 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; the ability to obtain regulatory approval of products, market acceptance of, and continuing demand for, Enzon's products and the impact of competitive products and pricing. 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 period ended December 31, 2007. 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.

SOURCE: Enzon Pharmaceuticals, Inc.

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