Enzon Announces the Initiation of Two Phase I Studies in Collaboration with the National Cancer Institute

BRIDGEWATER, N.J.--(BUSINESS WIRE)-- Enzon Pharmaceuticals, Inc. (Nasdaq: ENZN) today announced the initiation of Phase I clinical studies, in collaboration with the National Cancer Institute (NCI), for two of the Company's novel oncology product candidates, EZN-2968 and EZN-2208 (PEG-SN38). Both EZN-2968 and EZN-2208 have been shown to down-modulate HIF-1α, a subunit of HIF-1. HIF-1 is frequently overexpressed in cancer cells, where it is involved in the upregulation of gene products essential for tumor invasion, migration, angiogenesis and production of vascular endothelial growth factor (VEGF). The studies are being sponsored by the NCI under Clinical Trials Agreements with Enzon.

The first study will explore the safety and effectiveness of EZN-2968, an LNA-based antisense oligonucleotide, in patients with solid malignancies predominantly involving the liver. The second study will explore the modulation of HIF-1α in solid tumors after treatment with EZN-2208 combined with Avastin® (bevacizumab, Genentech/Roche), a humanized antibody targeting VEGF-A. Anti-angiogenic agents such as Avastin have limited efficacy, potentially as a result of the induction and up-regulation of hypoxia-inducible factors such as HIF-1α in the hypoxic conditions of the post-treatment tumor. Such effects may be offset by treatment with ENZ-2208, a topoisomerase inhibitor that down regulates HIF-1α in addition to having a cytotoxic effect.

"HIF-1α is a key element of the signaling cascade that promotes tumor growth and metastases in a wide range of cancers," said Ivan Horak, MD, Enzon's President of Research and Development and Chief Scientific Officer. "These two Phase I studies build on a growing body of clinical and preclinical evidence demonstrating the potential of both EZN-2968 and EZN-2208 to inhibit this important target. We look forward to collaborating with the NCI in further understanding the promise demonstrated by these two product candidates."

The EZN-2968 study is expected to enroll 22 patients with solid tumors, predominantly involving the liver. EZN-2968 will be administered as a two-hour intravenous infusion once a week for three consecutive weeks, followed by a three-week period without drug. Tumor biopsies and other correlative imaging and pharmacodynamic studies will be performed at baseline and after drug administration.

The EZN-2208 study is expected to enroll 20 patients with solid tumors whose disease has progressed following standard therapy, or who have no acceptable standard treatment. EZN-2208 will be administered intravenously on days one, eight, and fifteen of a 28-day cycle. Avastin will be administered intravenously every two weeks. Tumor biopsies and other correlative imaging and pharmacodynamic studies will be performed at baseline and after drug administration.

About EZN-2968 (HIF-1a mRNA antagonist)

EZN-2968 is an antisense oligodeoxynucleotide that down regulates the mRNA encoding HIF-1α. The molecule is based on the locked nucleic acid (LNA) technology platform targets licensed from Santaris Pharma A/S. The LNA technology allows the antisense molecule to have high-potency resistance to nuclease destruction, and administration of the molecule intraveneously when prepared in saline (without any delivery vehicle). Reduction in HIF-1α expression would be expected to lead to inhibition of angiogenesis, the inhibition of tumor cell proliferation, and apoptosis. HIF-1α, normally activated in response to hypoxia-induced stress, is a key transcription regulator of a large number of genes important in cellular adaptation to low-oxygen conditions, including angiogenesis, cell proliferation, apoptosis, and cell invasion.

About EZN-2208 (PEG-SN38)

SN38 is the active metabolite of the widely used cancer drug irinotecan, marketed as Camptosar® in the U.S. Although unmodified SN38 is 1,000 times more potent than CPT-11, it has not been converted into a viable drug candidate because of its insolubility. Using Enzon's proprietary customized linker-enhanced PEGylation technology, the Company developed EZN-2208 (PEG-SN38), which results in a compound with excellent pharmaceutical properties as shown in animal models: increased solubility, higher exposure, and longer half-life than unmodified SN38. These properties allow EZN-2208 to outperform CPT-11 in a variety of animal models of human cancers, including tumors that develop resistance to CPT-11. EZN-2208 is currently being evaluated in ongoing Phase II clinical trials in patients with metastatic breast cancer and metastatic colorectal carcinoma, and in a Phase I study in pediatric patients with solid tumors.

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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