



# News Release

*For Immediate Release*

**CONTACT:**  
Bill Newbould  
(610) 558-9800

**ENDO PHARMACEUTICALS TO DEVELOP AND COMMERCIALIZE  
ALEXZA'S AZ-003 STACCATO<sup>®</sup> INHALED FENTANYL PRODUCT  
- Patented Drug/Device System in Development for Treatment of Breakthrough Pain -**

CHADDS FORD, Pa., Dec. 27, 2007 -- Endo Pharmaceuticals Holdings Inc. (Nasdaq: ENDP), a market leader in pain management, today announced that it has entered into a license and development agreement with Alexza Pharmaceuticals, Inc. (Nasdaq: ALXA) for the exclusive clinical development and commercialization rights in North America for Alexza's AZ-003 (Staccato<sup>®</sup> fentanyl). Currently in Phase I clinical development, AZ-003 is a hand-held drug device system that uses Alexza's proprietary *Staccato*<sup>®</sup> system inhalation technology to deliver fentanyl for the treatment of breakthrough pain in cancer and non-cancer patients.

"We are delighted to partner with a leading-edge company such as Alexza to further expand our penetration in the pain market and bring us another step closer to our stated goal of becoming THE leading pain company," said Endo President and Chief Executive Officer Peter A. Lankau. "Clearly, AZ-003 meets our criteria for clinically differentiated, innovative products that fill an unmet medical need. Early clinical data suggest that AZ-003 could potentially have a rapid onset of action comparable to intravenous administration, and we believe that the formulation will be tamper-resistant. We have evaluated many technologies and product opportunities in the pain field and believe that the Alexza *Staccato* technology is 'best in class' for an inhalation approach to pain management." He also noted that AZ-003 is patent protected until 2022.

Under the terms of the agreement, Endo will pay Alexza an upfront fee of \$10 million, with additional payments of approximately \$40 million upon achievement of predetermined regulatory milestones. Endo will also pay undisclosed royalties to Alexza on net sales of AZ-003. Effective immediately, Endo will assume responsibility for, and funding of, all remaining clinical trial development and regulatory filings. Alexza will manufacture the product for Endo and will be responsible for completing development of the device.

## **About AZ-003**

AZ-003 is the combination of Alexza's proprietary *Staccato* system with fentanyl, a drug belonging to the class of compounds known as opioid analgesics. AZ-003 is a hand-held, electrically heated, multiple-dose inhaler designed to generate and deliver excipient-free fentanyl aerosol for deep lung delivery. The current product candidate consists of a disposable dose cartridge containing 25 doses each of 25 mcg fentanyl, which is inserted into a reusable controller. Development of additional dosage strengths and quantities is anticipated. The controller consists of software and hardware designed to allow safe, patient-controlled delivery of the drug. Since the *Staccato* system can be designed to incorporate a variety of lockout and dosing features, Alexza believes that AZ-003 may reduce the potential for abuse and diversion, and facilitate patient-dose titration to the minimum effective drug dose in a simple, convenient and easy-to-use delivery system.

In October 2007, results from the AZ-003 Phase I clinical trial were presented at the 2007 American Society of Anesthesiologists Annual Meeting, in San Francisco. The clinical trial was conducted in 50 opioid-naïve healthy volunteers in two stages. In Stage 1, the arterial pharmacokinetics (PK) of 25 mcg of AZ-003 was compared to a 25 mcg dose of fentanyl administered intravenously (IV). The AZ-003 PK was equivalent to the IV fentanyl PK, with similar peak plasma concentration ( $C_{max}$ ), time to maximum

plasma concentration ( $T_{max}$ ), and area under the curve concentration (AUC). These data suggest complete bioavailability of the inhaled dose. Mean peak arterial plasma concentrations were observed within 30 seconds for both administration routes. In Stage 2 of the clinical trial, ascending doses of AZ-003, controlled by the *Staccato* system, exhibited dose proportionality of fentanyl throughout the dosing range from 50 mcg to 300 mcg, following an AUC analysis.

No serious adverse events were attributable to AZ-003, and the results from the clinical study showed that AZ-003 was generally safe and well tolerated at all doses.

### *About Endo*

Endo Pharmaceuticals Holdings Inc. is a fully integrated specialty pharmaceutical company with market leadership in pain management products. Through its wholly owned Endo Pharmaceuticals Inc. subsidiary, the company researches, develops, produces and markets a broad product offering of both branded and generic pharmaceuticals, meeting the needs of healthcare professionals and consumers alike. More information, including this and past press releases of Endo Pharmaceuticals Holdings Inc., is available online at [www.endo.com](http://www.endo.com).

### **Forward-Looking Statements**

**This press release contains forward-looking statements, within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, as amended, that are based on management's beliefs and assumptions, current expectations, estimates and projections. Statements that are not historical facts, including statements which are preceded by, followed by, or that include, the words "believes," "anticipates," "plans," "expects" or similar expressions and statements are forward-looking statements. Endo's estimated or anticipated future results, product performance or other non- historical facts are forward-looking and reflect Endo's current perspective on existing trends and information. Many of the factors that will determine the Company's future results are beyond the ability of the Company to control or predict. These statements are subject to risks and uncertainties and, therefore, actual results may differ materially from those expressed or implied by these forward-looking statements. The reader should not rely on any forward-looking statement. The Company undertakes no obligation to update any forward-looking statements whether as a result of new information, future events or otherwise. Several important factors, in addition to the specific factors discussed in connection with these forward-looking statements individually, could affect the future results of Endo and could cause those results to differ materially from those expressed in the forward-looking statements contained in this press release. Important factors that may affect future results include, but are not limited to: market acceptance of the Company's products and the impact of competitive products and pricing; dependence on sole source suppliers; the success of the Company's product development activities and the timeliness with which regulatory authorizations and product launches may be achieved; successful compliance with extensive, costly, complex and evolving governmental regulations and restrictions; the availability on commercially reasonable terms of raw materials and other third party manufactured products; exposure to product liability and other lawsuits and contingencies; dependence on third party suppliers, distributors and collaboration partners; the ability to timely and cost effectively integrate acquisitions; uncertainty associated with pre- clinical studies and clinical trials and regulatory approval; uncertainty of market acceptance of new products; the difficulty of predicting FDA approvals; risks with respect to technology and product development; the effect of competing products and prices; uncertainties regarding intellectual property protection; uncertainties as to the outcome of litigation; a determination by a regulatory agency that we are engaging in inappropriate sales or marketing activities, including promoting the "off-label" use of our products; changes in operating results; impact of competitive products and pricing; product development; changes in laws and regulations; customer demand; possible future litigation; availability of future financing and reimbursement policies of government and private health insurers and others; and other risks and uncertainties detailed in Endo's filings with the Securities and Exchange Commission, including its Annual Report on Form 10-K filed with the SEC on March 1, 2007. Readers should evaluate any statement in light of these important factors.**