Endo Pharmaceuticals and DURECT Corporation Agree To Collaborate on Treatment in Pain Management

CHADDS FORD, Pa. and CUPERTINO, Calif., Nov. 11 /PRNewswire-FirstCall/ — Endo Pharmaceuticals Holdings Inc. (Nasdaq: ENDP) and DURECT Corporation (Nasdaq: DRRX), announced today that they have signed an agreement to collaborate on the development and commercialization of DURECT's CHRONOGESIC(TM) (sufentanil) Pain Therapy System for the U.S. and Canada. The companies believe CHRONOGESIC has significant potential to treat patients with chronic pain resulting from a variety of malignant and non-malignant causes. If approved, the product would represent the first systemic medication that provides patients with uninterrupted pain treatment for three months from a single application.

"Endo looks for innovative medicines to help patients and physicians in need of treatment options for pain, and CHRONOGESIC represents one of the most important potential advances in pain management," stated Carol A. Ammon, Chairman and Chief Executive Officer of Endo. "The collaboration with DURECT demonstrates our continued commitment to execute our strategies for growth. We are very excited about this opportunity and look forward to a successful partnership with DURECT."

"With an established commercial infrastructure, a number of gold standard pain products and over 200 sales representatives focused on promoting therapies for pain management, Endo is a well-established player in the pain management arena," stated Dr. James Brown, President and Chief Executive Officer of DURECT. "CHRONOGESIC attracted high interest from a number of potential partners. In the end, we selected Endo as our partner because of their strong commitment to be a focused leader in the pain field. They have commercial, sales and marketing executives with established track records for successfully launching and building new ethical pharmaceutical product businesses. Endo is a major player in the specialty pharmaceuticals business, and CHRONOGESIC(TM) only adds to their leadership position in the pain management arena."

In previous clinical trials, CHRONOGESIC was shown to have an acceptable safety and efficacy profile in over 80 patients. The CHRONOGESIC clinical development program is on temporary hold pending agreement between DURECT and the Food and Drug Administration (FDA) regarding additional monitoring and data collection. These protocol changes requested by the FDA were not in relation to any observed safety issue or adverse event. In addition, DURECT is implementing some necessary design and manufacturing enhancements to the CHRONOGESIC product. DURECT anticipates that the changes to the existing clinical protocol, and the implementation of these design and manufacturing enhancements, will delay the restart of clinical trials until the second half of 2003.

Under the terms of the agreement, DURECT will be responsible for the CHRONOGESIC product's design and development. In connection with the execution

of the agreement, Endo will purchase $5.0 million of newly issued common shares of DURECT. Once the clinical trials are restarted, Endo will fund 50% of the ongoing development costs and will reimburse DURECT for a portion of prior development costs upon the achievement of certain milestones. Milestone payments made by Endo under this agreement could total up to $52 million. The agreement also contains terms and conditions customary for this type of arrangement, including representations, warranties, indemnities and termination rights. For a full description of the arrangement, please see the companies' public filings with the Securities and Exchange Commission, including Endo's Form 8-K.

In addition, under the agreement, Endo has licensed exclusive promotional rights to CHRONOGESIC in the U.S. and Canada. Endo will be responsible for marketing, sales and distribution, including providing specialty sales representatives dedicated to supplying technical and training support for CHRONOGESIC therapy. DURECT will be responsible for the manufacture of CHRONOGESIC. Endo and DURECT will share profits equally, based on projected financial performance of CHRONOGESIC.

CHRONOGESIC is intended to target patients with opioid responsive chronic pain that results from a variety of causes. CHRONOGESIC is designed to deliver sufentanil continuously for three months of pain therapy. Sufentanil is an opioid that is currently used in hospitals as an analgesic agent.

CHRONOGESIC(TM) is a miniature, self-driven titanium capsule that is placed just under the skin, similar in size to a matchstick, from which drug is dispensed by the natural process of osmosis at a highly controlled rate. CHRONOGESIC is designed to address the potential problems of peaks (too much medication) and troughs (too little medication) associated with currently available chronic pain therapies. If approved, CHRONOGESIC will allow physicians to prescribe, and continuously administer to patients, a fixed, clinically meaningful baseline dose of sufentanil for moderate to severe chronic pain for three months and may provide for less risk of potential misuse, abuse and diversion than alternative currently available therapies for chronic pain.

Chronic pain is a significant problem associated with chronic diseases, including cancer and various neurological and skeletal disorders. Chronic nonmalignant pain affects as many as 34 million Americans annually. In addition, the National Cancer Institute estimates that 8.4 million Americans alive today have a history of cancer. Sales of opioids for the treatment of malignant and nonmalignant pain currently exceed $3 billion.

Endo and DURECT will conduct a joint conference call to discuss this press release on Monday, November 11, 2002 at 5:00 p.m. EST (2:00 p.m. PST). The call will be webcast live through DURECT's corporate website and available for 30 days following the call. To access the webcast, please log on to the Investor Relations site of www.www.durect.com. The domestic call-in number is 1-800-360-9865. The international call-in number is 1-973-694-6836. A rebroadcast of the call will be available by phone for 24 hours beginning approximately one hour after the close of the call and can be accessed at 1-800-428-6051 (passcode: 268774).

About Endo

Endo Pharmaceuticals Holdings Inc. is a fully integrated specialty pharmaceutical company with market leadership in pain management products.

Through its 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.

About DURECT Corporation

DURECT Corporation (www.www.durect.com) is pioneering the development and commercialization of pharmaceutical systems for the treatment of chronic debilitating diseases and enabling biotechnology-based pharmaceutical products. DURECT's goal is to deliver the right drug to the right site in the right amount at the right time. DURECT's lead product in development, the CHRONOGESIC(TM) (sufentanil) Pain Therapy System, is a 3-month product for the treatment of chronic pain. DURECT owns three proprietary drug delivery platform technologies, including the SABER(TM) Delivery System (a patented and versatile depot injectable useful for protein delivery), the MICRODUR(TM) Biodegradable Microparticulates (microspheres injectable system) and the DURIN(TM) Biodegradable Implant (drug-loaded implant system).

NOTE:
CHRONOGESIC(TM) is a trademark of DURECT Corporation. SABER(TM), MICRODUR(TM) and DURIN(TM) are trademarks of Southern BioSystems, Inc., a wholly owned subsidiary of DURECT Corporation. Other trademarks referred to belong to their respective owners.

Endo Forward Looking Statement

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. 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. Forward-looking statements are not historical facts and include information regarding the Company's possible or assumed results of operations. Also, statements or expressions that are preceded by, followed by, or that include, the words "believes," "anticipates," "plans," "expects," "intends," "estimates" or similar expressions 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. The reader should not rely on any forward-looking statement. The Company undertakes no obligations 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 the Endo and could cause those results to differ materially from those expressed in the forward-looking statements contained herein. 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; 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 Registration Statement on Form S-4 filed with the Securities and Exchange Commission on June 9, 2000, as amended, and in Endo's Registration Statement on Form S-3 dated October 17, 2001. Readers should evaluate any statement in light of these important factors.

DURECT Forward Looking Statement

The statements in this press release regarding DURECT's products in development, expected or potential product benefits, product development and clinical trials plans and anticipated financial results or benefits are forward-looking statements involving risks and uncertainties that can cause actual results to differ materially from those in such forward-looking statements. Potential risks and uncertainties include, but are not limited to, DURECT's ability to complete the design and manufacturing process development of its products, commercialize its products, obtain product and manufacturing approvals from regulatory agencies, timely enroll patients and clinical sites in connection with its clinical studies, effectively administer its clinical trials, manage its growth and expenses, finance its activities and operations, as well as marketplace acceptance of DURECT's products. Further information regarding these and other risks is included in DURECT's Annual Report on Form 10-K for the fiscal year ended December 31, 2001 filed with the SEC on March 28, 2002, under the heading "Factors that may affect future results," and other periodic reports filed with the SEC. CHRONOGESIC is under development by DURECT and has not been submitted or approved for commercialization by the US Food and Drug Administration or other health authorities.

SOURCE DURECT Corporation; Endo Pharmaceuticals Holdings Inc.

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