ENDO PHARMACEUTICALS HOLDINGS INC
Form 424B3
September 27, 2005

QuickLinks -- Click here to rapidly navigate through this document

The information in this prospectus supplement is not complete and may be changed. This prospectus supplement is not an offer to sell these securities and it is not soliciting offers to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION. DATED SEPTEMBER 26, 2005

Filed Pursuant to Rule 424(b)(3)
Registration No. 333-128099
Registration No. 333-115032

PRELIMINARY PROSPECTUS SUPPLEMENT
(To prospectus dated September 26, 2005)

26,000,000 Shares

Endo Pharmaceuticals Holdings Inc.

Common Stock

The selling stockholders are offering 26,000,000 shares of our common stock, $.01 par value per share, by this prospectus supplement and the accompanying prospectus. We will not receive any proceeds from the sale of the shares of common stock by the selling stockholders.

Our common stock is quoted on the Nasdaq National Market under the symbol "ENDP." On September 23, 2005, the last reported sale price of our common stock was $28.81 per share.

Investing in our common stock involves risks. See "Risk Factors" beginning on page 2 of the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public Offering Price	$	$
Underwriting Discount	$	$
Proceeds to Selling Stockholders, Before Expenses	$	$

The selling stockholders have granted to the underwriters a 30-day option to purchase up to an additional 3,900,000 shares of our common stock on the same terms and conditions as set forth above, solely to cover over-allotments, if any.

Delivery of shares of common stock is expected to be made in New York, New York on or about , 2005.

Bear, Stearns & Co. Inc.		**Citigroup**
Morgan Stanley	**SG Cowen & Co.**	**UBS Investment Bank**
C.E. Unterberg, Towbin	**Jefferies & Company, Inc.**	**JPMorgan**

The date of this prospectus supplement is , 2005.

TABLE OF CONTENTS
Prospectus Supplement

Prospectus

This document is in two parts. The first part is the prospectus supplement, which describes the specific terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference. The second part is the accompanying prospectus, which gives more general information, some of which may not apply to this offering.

You should rely only on the information contained in or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not, and the underwriters have not, authorized anyone to provide you with different or additional information. We are not, and the underwriters are not, making an offer of these securities in any state where the offer is not permitted. You should assume that the information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference is accurate only as of its respective date or on the date which is specified in those documents.

FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus may contain or incorporate by reference information that includes or is based on "forward looking statements" within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended. These statements, including estimates of future net sales, future net income and future earnings per share, contained in "Management's Discussion and Analysis of Financial Condition and Results of Operations," which is included in documents incorporated by reference, are subject to risks and uncertainties. Forward-looking statements include the information concerning our possible or assumed results of operations. Also, statements including words such as "believes," "expects," "anticipates," "intends," "estimates," or similar expressions are forward-looking statements. We have based these forward-looking statements on our current expectations and projections about the growth of our business, our financial performance and the development of our industry. Because these statements reflect our current views concerning future events, these forward-looking statements involve risks and uncertainties. Investors should note that many factors, as more fully described in "Risk Factors," beginning on page 2 of the accompanying prospectus and elsewhere in this prospectus supplement, the accompanying prospectus and in documents incorporated by reference, could affect our future financial results and could cause our actual results to differ materially from those expressed in forward-looking statements contained in this prospectus supplement and the accompanying prospectus. Important factors that could cause our actual results to differ materially from the expectations reflected in the forward-looking statements in this prospectus supplement and the accompanying prospectus include, among others:

our ability to successfully develop, commercialize and market new products;

timing and results of pre-clinical or clinical trials on new products;

our ability to obtain regulatory approval of any of our pipeline products;

competition for the business of our branded and generic products, and in connection with our acquisition of rights to intellectual property assets;

significant cash payments we may be required to make to Endo Pharma LLC pursuant to a tax sharing agreement;

market acceptance of our future products;

government regulation of the pharmaceutical industry;

our dependence on a small number of products;

our dependence on outside manufacturers for the manufacture of our products;

our dependence on third-parties to supply raw materials and to provide services for certain core aspects of our business;

new regulatory action or lawsuits relating to our use of narcotics in most of our core products;

our exposure to product liability claims and product recalls and the possibility that we may not be able to adequately insure ourselves;

our ability to protect our proprietary technology;

the successful efforts of manufacturers of branded pharmaceuticals to use litigation and legislative and regulatory efforts to limit the use of generics and certain other products;

our ability to successfully implement our acquisition and in-licensing strategy;

the availability of controlled substances that constitute the active ingredients of some of our products and products in development;

the availability of third-party reimbursement for our products;

the outcome of any pending litigation; and

our dependence on sales to a limited number of large pharmacy chains and wholesale drug distributors for a large portion of our total net sales.

We do not undertake any obligation to update our forward-looking statements after the date of this prospectus supplement for any reason, even if new information becomes available or other events occur in the future.

THE OFFERING

Common Stock Offered by the Selling Stockholders	26,000,000 shares
Nasdaq National Market Symbol	ENDP

USE OF PROCEEDS

All of the shares of common stock offered hereby are being sold by the selling stockholders. We will not receive any proceeds from the sale of shares by the selling stockholders.

THE COMPANY

We are a specialty pharmaceutical company with market leadership in pain management. We are engaged in the research, development, sale and marketing of branded and generic prescription pharmaceuticals used primarily to treat and manage pain. According to IMS Health data, the total U.S. market for pain management pharmaceuticals, excluding over-the-counter products, totaled $18.9 billion in 2004. This represents an approximately 16% compounded annual growth rate since 1999. Our primary area of focus within this market is analgesics and, specifically, opioid analgesics. In 2004, analgesics were the third most prescribed medication in the United States with over 272 million prescriptions written for this classification. Opioid analgesics is a segment that comprised approximately 75% of the analgesics prescriptions for 2004. Total U.S. sales for the opioid analgesic segment were $6.3 billion in 2004, representing a compounded annual growth rate of 20% since 1999.

We have a portfolio of branded products that includes established brand names such as Lidoderm®, Percocet®, Frova®, Percodan®, Zydone® and DepoDur . Branded products comprised approximately 69% of our net sales in 2004. Our non-branded generic portfolio, which accounted for 31% of net sales in 2004, currently consists of products primarily focused in pain management. We focus on selective generics that have one or more barriers to market entry, such as complex formulation, regulatory or legal challenges or difficulty in raw material sourcing.

We have established research and development expertise in analgesics and devote significant resources to this effort so that we can maintain and develop our product pipeline. Our late-stage branded product pipeline includes two filed New Drug Applications, or NDAs, one product in Phase III clinical trials and five products in Phase II clinical trials.

We enhance our financial flexibility by outsourcing certain of our functions, including manufacturing. Currently, our primary suppliers of contract manufacturing services are Novartis Consumer Health, Inc. and Teikoku Seiyaku Co., Ltd.

Through a dedicated sales force of approximately 370 sales representatives in the United States, we market our branded pharmaceutical products to high-prescribing physicians in pain management, neurology, surgery, anesthesiology, oncology and primary care. Our sales force also targets retail pharmacies and other healthcare professionals throughout the United States.

Our wholly-owned subsidiary, Endo Pharmaceuticals Inc., commenced operations in 1997 by acquiring certain pharmaceutical products, related rights and assets of The DuPont Merck Pharmaceutical Company, which subsequently became DuPont Pharmaceuticals Company and was thereafter purchased by the Bristol-Myers Squibb Pharma Company in 2001. Endo Pharmaceuticals Inc. was formed by some members of the then-existing management of DuPont Merck and an affiliate of Kelso & Company who were also parties to the purchase agreement, under which we acquired these initial assets. We were incorporated in Delaware as a holding company on November 18, 1997. Our common stock is quoted on the Nasdaq National Market under the symbol "ENDP."

Our executive offices are located at 100 Endo Boulevard, Chadds Ford, Pennsylvania 19317. Our telephone number is (610) 558-9800. The address of our website is www.endo.com (this is an inactive textual reference only). The information on our website is not part of this prospectus supplement or the accompanying prospectus.

Recent Developments

Oxymorphone ER Trials

On October 20, 2003, we announced that the Food and Drug Administration, or the FDA, had issued an approvable letter for oxymorphone extended-release (ER) tablets. In the letter, the FDA requested that we address certain questions and provide additional clarification and information, including some form of an additional clinical trial to further confirm the safety and efficacy of this product. We have undertaken two additional Phase III clinical trials of oxymorphone ER to provide the

FDA with additional safety and efficacy data. On August 22, 2005, we reported the results from one of the oxymorphone ER Phase III clinical trials that was conducted under the special protocol assessment (SPA) process of the FDA. In this multi-center, randomized, double-blind, parallel group trial, the safety and efficacy of oxymorphone ER were compared with placebo in 205 opioid-naïve patients with moderate-to-severe chronic low back pain. This study demonstrated a statistically significant ($p<0.0001$) difference in pain scores between oxymorphone ER and placebo during a 12-week treatment period. This study will supplement the previously submitted Phase III trial that the company believes the FDA already has accepted as demonstrating efficacy in the intended patient population. We believe we will be in a position to submit the complete response to the approvable letter to the FDA in early 2006 and expect an "action letter" from the FDA approximately six months following our complete response submission. There is no certainty that the FDA will accept this study or what, if any, additional information the FDA will require for final approval of oxymorphone ER. We expect the results of the second oxymorphone Phase III clinical trial in opioid-experienced patients to be completed and announced early in the fourth quarter of 2005. See "Risk Factors The pharmaceutical industry is heavily regulated, which creates uncertainty about our ability to bring new products to market and imposes substantial compliance costs on our business" in the accompanying prospectus.

Oxymorphone IR Trial

On October 20, 2003, we announced that the FDA had issued an approvable letter for oxymorphone immediate release (IR) tablets. In the letter, the FDA requested that we address certain questions and provide additional clarification and information, including some form of an additional clinical trial to further confirm the safety and efficacy of this product. We have undertaken an additional Phase III clinical trial of oxymorphone IR to provide the FDA with additional safety and efficacy data. In September 2005, we completed the oxymorphone IR Phase III clinical trial that was conducted under the SPA process of the FDA. In this randomized, double-blind, single and multiple dose trial of the analgesic efficacy and safety of oxymorphone IR tablets in patients with moderate-to-severe pain following abdominal surgery, the result demonstrated a statistically significant difference in pain scores between oxymorphone IR and placebo both following a single-dose and repeat doses. We believe we will be in a position to submit the complete response to the approvable letter to the FDA in early 2006 and expect an "action letter" from the FDA approximately six months following our complete response submission. There is no certainty that the FDA will accept this study or what, if any, additional information the FDA will require for final approval of oxymorphone IR. See "Risk Factors The pharmaceutical industry is heavily regulated, which creates uncertainty about our ability to bring new products to market and imposes substantial compliance costs on our business" in the accompanying prospectus.

Launch of Generic OxyContin®

On June 7, 2005, we announced that the U.S. Court of Appeals for the Federal Circuit in Washington, D.C., affirmed the Opinion and Order issued in Endo's favor by the U.S. District Court for the Southern District of New York on January 5, 2004. This affirmance by the Federal Circuit Court dismisses the claims that Endo's oxycodone extended-release tablets, 10mg, 20mg, 40mg, and 80mg, a bioequivalent version of The Purdue Frederick Company's, or Purdue's, OxyContin®, infringe certain of Purdue's patents and permanently enjoins Purdue from enforcing these patents. The U.S. Food and Drug Administration had previously granted final approval of Endo's abbreviated new drug application (ANDA) for all four strengths of the product in 2004. Endo's oxycodone ER tablets are AB-rated bioequivalent versions of OxyContin®, a product that is indicated for the management of moderate-to-severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time. According to IMS Retail Provider Perspective data, all OxyContin® strengths, as well as generics of the 80 mg strength, had combined 2004 U.S. sales of approximately $2 billion. The FDA has confirmed that Endo has 180 days of marketing exclusivity with respect to the 10mg, 20mg and 40mg strengths of this product, since the company was the first applicant to file an ANDA containing a

Paragraph IV certification for these oxycodone extended-release strengths. Under the Medicare Prescription Drug Improvement and Modernization Act of 2003, this marketing exclusivity commences upon the appellate court decision affirming the district court's decision. On June 7, 2005, we began commercial sale of our oxycodone ER tablets, 10mg, 20mg, 40mg and 80mg strengths. See "Risk Factors We were successful in our patent challenge against Purdue for our generic OxyContin® product, both at trial and on appeal. Purdue has petitioned the Court of Appeals for a rehearing, and if we receive an unfavorable ruling by the appeals court, we may be liable for damages and the price of our common stock may decline" in the accompanying prospectus.

Our Strategy

Our business strategy is to continue to strengthen our position as a market leader in pain management while also pursuing other markets, especially those with complementary therapeutic or physician bases. The elements of our strategy include:

Capitalizing on our established brand names and brand awareness through focused marketing and promotional efforts. Lidoderm®, the first FDA-approved product for the treatment of the pain of post-herpetic neuralgia, continues to increase market penetration due to our ongoing promotional and educational efforts. We consider two of our brands, Percocet® and Percodan®, to be "gold standards" of pain management. Percocet® has been prescribed by physicians since 1976, while Percodan® has been prescribed since 1950. We believe that we have established credibility with physicians as a result of these products' history of demonstrated effectiveness and safety. We plan to continue to capitalize on this brand awareness to market new products and explore new indications for existing products as well as market new formulations and dosages of our existing branded products. During 2004, we launched Frova®, indicated for the acute treatment of migraine attacks in adults, which we believe has differentiating features from other migraine products, including the longest half-life in the triptan class and a very low reported recurrence rate in its clinical program. We believe these distinct characteristics have yet to be fully exploited in the market and that we will be able to capitalize on Frova®'s clinical benefits and commercial potential by targeting the specialty physician audience and effectively leveraging the relationships and reputation that we have built with the neurology and pain specialist community over the years. During 2004, we also began our educational efforts to physicians including advocacy development for DepoDur , the first and only single-dose epidural injection that can provide up to 48 hours of pain control to help ease pain for people undergoing major surgery in the United States. We began commercial shipments of DepoDur in December 2004. We believe that our strong corporate and product reputation leads to more rapid adoption of our new products by physicians.

Leveraging our pain management expertise by developing proprietary products and generic products with significant barriers to market entry. To capitalize on our expertise in pain management, we are developing new products to address acute, chronic and neuropathic pain conditions. Specifically, we are developing new patent-protected products that may substantially improve the treatment of pain. We are co-developing an oral extended-release, or ER, version of oxymorphone with Penwest Pharmaceuticals Co. See "Recent Developments Oxymorphone ER Trials." In addition, in May 2004, we and SkyePharma, Inc., our collaboration partner, announced that the FDA had approved SkyePharma's NDA for DepoDur for the treatment of pain following major surgery. DepoDur is a novel single dose sustained-release injectable formulation of morphine. We launched DepoDur in December 2004. We have also developed an extended-release oxycodone, an AB-rated generic version of OxyContin®, a product of Purdue that is indicated for the management of moderate-to-severe pain when continuous, around-the-clock analgesic is needed for an extended period of time. On June 7, 2005, we began commercial sale of our oxycodone extended-release tablets, 10mg, 20mg, 40mg and 80mg strengths. See " Recent Developments Launch of Generic OxyContin®."

Acquiring and in-licensing complementary products, compounds and technologies. We look to continue to enrich our product line through selective product acquisitions and in-licensing, or acquiring licenses to products, compounds and technologies from third parties. In February 2004, we entered into an

agreement for the exclusive U.S. and Canadian marketing and distribution rights to Noven Pharmaceuticals, Inc.'s developmental transdermal fentanyl patch intended to be the generic equivalent of Johnson & Johnson's Duragesic® (fentanyl transdermal system), which had U.S. sales of approximately $1.6 billion in 2004. The agreement also establishes an ongoing collaboration between the two companies for the development of additional prescription transdermal products. In August 2004, we entered into a license agreement with Vernalis Development Limited, or Vernalis, under which Vernalis agreed to exclusively license to us rights to market Frova® (frovatriptan) in North America. Launched in the U.S. in June 2002, Frova® is indicated for the acute treatment of migraine headaches in adults. In August 2004, we entered into an agreement granting us the exclusive rights to develop and market Orexo AB's (a privately held Swedish company) patented sublingual muco-adhesive fentanyl product (Rapinyl) in North America. Rapinyl is a sub-lingual, fast-dissolving tablet of fentanyl being studied for the treatment of breakthrough pain. The benefits of Rapinyl are believed to include both a fast onset of action and patient convenience. In March 2005, we entered into an agreement with ProEthic Pharmaceuticals, Inc. for the U.S. and Canadian rights to develop and commercialize a once-daily ketoprofen-containing topical patch. Ketoprofen is a non-steroidal anti-inflammatory drug, or NSAID, generally used for the treatment of inflammation and pain and available in the U.S. only in oral form. Also in March 2005, we entered into an agreement that will give us the exclusive license to develop and commercialize DURECT's sufentanil-containing transdermal patch in the U.S. and Canada. The sufentanil patch, which is in the early stage of clinical development, employs DURECT's proprietary TRANSDUR drug-adhesive matrix formulation and is intended to provide relief of moderate-to-severe chronic pain for up to seven days.

Our Competitive Strengths

We believe that we have established a position as a market leader among specialty pharmaceutical companies by capitalizing on our following core strengths:

Established portfolio of branded products. We have assembled a portfolio of branded pharmaceutical products to treat and manage pain. These products include Lidoderm®, a topical patch containing lidocaine, which is the first FDA-approved product to treat the pain associated with post-herpetic neuralgia. The FDA has granted Lidoderm® orphan drug status, which means, generally, that no other lidocaine-containing product can be approved for this indication until March 2006. Additionally, Lidoderm® is protected by certain patents until 2015. Net sales of Lidoderm® increased 73% from $178.3 million in 2003 to $309.2 million in 2004. We consider Percocet®, our oxycodone/acetaminophen combination product and Percodan®, our oxycodone/aspirin combination product, which have been marketed since 1976 and 1950, respectively, to be "gold standards" of pain management based on their long history of demonstrated product safety and effectiveness. In 2004, according to IMS Health data, approximately 77% of prescriptions written for oxycodone with acetaminophen are in fact written as "Percocet." We believe our close relationships with physicians who are considered to be pain management "thought leaders" in pain centers, hospitals, and other pain management institutions enable us to improve our market penetration. During 2004, we added Frova® to our portfolio of branded products, which we believe has differentiating features from other migraine products, including the longest half-life in the triptan class and a very low reported recurrence rate in its clinical program. We believe these distinct characteristics have yet to be fully exploited in the North American market and that we will be able to capitalize on Frova®'s clinical benefits and commercial potential by targeting the specialty physician audience and effectively leveraging the relationships and reputation that we have built with the neurology and pain specialist community over the years. We believe this interaction with the thought leaders and our track record of developing and launching new products has enabled us to pursue, through in-licensing and acquisitions, novel products for the treatment of pain and complementary therapeutic areas.

Substantial pipeline focused on pain management with a balanced focus on complementary therapeutic areas. As a result of our focused research and development efforts, we filed two NDAs with the FDA

in December 2002 for oxymorphone ER tablets and oxymorphone IR tablets. On October 20, 2003, we announced that the FDA had issued an approvable letter for oxymorphone ER. In the letter, the FDA requested that we address certain questions and provide additional clarification and information, including some form of an additional clinical trial to further confirm the safety and efficacy of this product. We have undertaken two additional clinical trials of oxymorphone ER to provide the FDA with additional safety and efficacy data. On August 22, 2005, we reported the results from one of the oxymorphone ER Phase III clinical trials that was conducted under the special protocol assessment (SPA) process of the FDA. In this multi-center, randomized, double-blind, parallel group trial, the safety and efficacy of oxymorphone ER were compared with placebo in 205 opioid-naïve patients with moderate-to-severe chronic low back pain. This study demonstrated a statistically significant ($p<0.0001$) difference in pain scores between oxymorphone ER and placebo during a 12-week treatment period. This study will supplement the previously submitted Phase III trial that the company believes the FDA already has accepted as demonstrating efficacy in the intended patient population. We believe we will be in a position to submit the complete response to the approvable letter to the FDA in early 2006 and expect an "action letter" from the FDA approximately six months following our complete response submission. There is no certainty that the FDA will accept this study or what, if any, additional information the FDA will require for final approval of oxymorphone ER. We expect the results of the second oxymorphone Phase III clinical trial in opioid-experienced patients to be completed and announced early in the fourth quarter of 2005. In addition, we currently have one product in Phase III clinical trials and five products in Phase II clinical trials.

Research and development expertise. Our research and development effort is focused on expanding our product portfolio by capitalizing on our core expertise with analgesics. We have assembled an experienced and multi-disciplined research and development team of scientists and technicians with proven expertise working with analgesics and complex formulations. We believe this expertise allows for timely FDA approval of our products. We have demonstrated our ability to commercialize our research and development efforts during the last eight years through the launch of a number of new products and product line extensions since August 1997.

Targeted national sales and marketing infrastructure. We market our products directly to physicians through an internal sales force of approximately 300 specialty and office-based representatives and approximately 70 hospital-based representatives. Through our sales force, we market our branded pharmaceutical products to approximately 50,000 physicians, which include both specialists and primary care physicians.

Selective focus on generic products. Our generic product portfolio includes products focused on pain management. Development of these products involves barriers to entry such as complex formulation, regulatory or legal challenges or difficulty in raw material sourcing. We believe products with these characteristics will face a lesser degree of competition and therefore provide longer product life cycles and higher profitability than commodity generic products. We have executed our generic product development strategy successfully to date with products such as morphine sulfate extended-release tablets, which we introduced in November 1998 as a bioequivalent version of MS Contin®, a product of Purdue. In addition, we are the first company to have filed an ANDA with the FDA for the bioequivalent version of the 10mg, 20mg and 40mg strengths of Purdue's OxyContin®. For several reasons, including potential marketing exclusivity, we believe it is a significant advantage to be the first successful filer of an ANDA for a generic drug. On June 7, 2005, we began commercial sale of our oxycodone ER tablets, 10mg, 20mg, 40mg and 80mg strengths. See "Risk Factors We were successful in our patent challenge against Purdue for our generic OxyContin® product, both at trial and on appeal. Purdue has petitioned the Court of Appeals for a rehearing, and if we receive an unfavorable ruling by the appeals court, we may be liable for damages and the price of our common stock may decline" in the accompanying prospectus.

Experienced and dedicated management team. Our senior management team has a proven track record of building our business through internal growth as well as through acquisitions and licensing. Members of our senior management led the purchase of the company from The DuPont Merck Pharmaceutical Company in August 1997 as well as the licensing of Lidoderm®, DepoDur and many of the products in our development pipeline. Management has received FDA approval on more than fifteen new products and product line extensions since 1997, and as a result of several successful product launches, has grown our net sales from approximately $108.4 million in 1998 to approximately $615.1 million in 2004.

Product Overview

The following table summarizes select products in our marketed portfolio as well as selected products in development:

Product	Active ingredient(s)	Branding	Status
Lidoderm®	lidocaine 5%	Branded	Marketed
Percocet®	oxycodone and acetaminophen	Branded	Marketed
Percodan®	oxycodone and aspirin	Branded	Marketed
Zydone®	hydrocodone and acetaminophen	Branded	Marketed
Frova®(1)	frovatriptan	Branded	Marketed
DepoDur (2)	morphine sulfate	Branded	Marketed
Endocet®	oxycodone and acetaminophen	Generic	Marketed
Morphine Sulfate ER	morphine sulfate	Generic	Marketed
Oxycodone ER	oxycodone hydrochloride	Generic	Marketed
Oxymorphone ER(3)	oxymorphone hydrochloride	Branded	Approvable Letter
Oxymorphone IR	oxymorphone hydrochloride	Branded	Approvable Letter
Frova® (menstrually related migraine)(1)	frovatriptan	Branded	Phase III
Lidoderm® (chronic low back pain)	lidocaine 5%	Branded	Phase II
LidoPAIN® BP(4)	lidocaine	Branded	Phase II
Propofol IDD-D (2)	propofol	Branded	End of Phase II
Rapinyl (oral, fast dissolving)(5)	fentanyl	Branded	Phase II
Topical Ketoprofen Patch(6)	ketoprofen	Branded	Phase II
CHRONOGESIC (7)	sufentanil	Branded	Early Stage
Transdermal Sufentanil Patch(8)	sufentanil	Branded	Early stage
Transdermal Fentanyl Patch(9)	fentanyl	Generic	ANDA filed; under FDA review

(1) Licensed marketing rights from Vernalis Development Limited.

(2) Licensed marketing rights from SkyePharma, Inc.

(3) Co-developed with Penwest Pharmaceuticals Co.

(4) Licensed marketing rights from EpiCept Corporation.

(5) Licensed marketing and development rights from Orexo AB.

(6) Licensed marketing and development rights from ProEthic Pharmaceuticals, Inc.

(7) Licensed marketing rights from DURECT Corporation.

(8) Licensed marketing and development rights from DURECT Corporation.

(9) Licensed marketing rights from Noven Pharmaceuticals, Inc.

Branded Products

Lidoderm®. Lidoderm® was launched in September 1999. A topical patch product containing lidocaine, it is the first FDA-approved product for the relief of the pain associated with post-herpetic neuralgia. There are approximately 200,000 patients per year who suffer from this condition in the United States, the majority of whom are elderly. The FDA has granted Lidoderm® orphan drug status, generally meaning that no other lidocaine-containing patch product can be approved for this indication until March 2006. Certain exceptions apply (for example, a product shown to be clinically superior may be approved); however, we are unaware that any such product has been, or is being, developed. Lidoderm® is also currently protected by patents for, among other things, a method of treating post-herpetic neuralgia and the composition of the lidocaine-containing patch. The last of these patents will expire in 2015. In 2002, 2003 and 2004, Lidoderm® net sales were $83.2 million, $178.3 million and $309.2 million, respectively, and $164.6 million for the six months ended June 30, 2005. Lidoderm® accounted for approximately 50% of our 2004 net sales and approximately 49% of our net sales for the six months ended June 30, 2005.

In addition, we are currently exploring potential new indications for Lidoderm® and have initiated a Phase II clinical trial in chronic low back pain.

Percocet®. We consider Percocet® to be a "gold standard" of pain management. Launched in 1976, Percocet® is approved for the treatment of moderate-to-moderately severe pain. Although Percocet® has faced generic competition for nearly 20 years, in 2004, according to the IMS National Prescription Audit, approximately 17.9 million new prescriptions for this combination of oxycodone hydrochloride and acetaminophen were written for the brand name "Percocet," of which, due to generic substitution, only approximately 7% were filled by pharmacists with our brand Percocet®.

During the fourth quarter of 2001, we launched two new formulations: Percocet® 7.5/325 and Percocet® 10.0/325. These new dosage strengths allow physicians the flexibility of increasing the dose of opioid while still maintaining a low level of acetaminophen. In October 2003, a competitor announced that it was launching its generic versions of Percocet® 7.5/325 and Percocet® 10.0/325. The Percocet® family of products had net sales of $144.6 million, $214.2 million and $86.5 million in the years 2002, 2003 and 2004, respectively, and $52.2 million for the six months ended June 30, 2005. The Percocet® franchise accounted for approximately 14% of our 2004 net sales and approximately 16% of our net sales for the six months ended June 30, 2005.

Frova®. We began shipping Frova® upon closing of the license agreement with Vernalis in mid-August 2004 and initiated our promotional efforts in September. We believe that Frova® has differentiating features from other migraine products, including the longest half life in the triptan class and a very low reported recurrence rate in its clinical program. We believe these distinct characteristics have yet to be fully exploited in the market and that we will be able to capitalize on Frova®'s clinical benefits and commercial potential by targeting the specialty physician audience and effectively leveraging the relationships and reputation that we have built with the neurology and pain specialist community over the years. We believe we can create an advocacy base among thought leaders who treat patients with the most intractable migraines. Further, we believe that Frova®'s potential future application for the prevention of menstrually related migraine makes it one of our most promising products. Net sales of Frova® were $11.4 million in 2004 and $14.8 for the six months ended June 30, 2005.

Frova® is also being studied in Phase III clinical trials as a potential prophylactic treatment for Menstrually Related Migraine (MRM). If approved for this indication, we believe that Frova® would be the first triptan to be indicated for the prevention of any type of migraine. We anticipate filing a supplemental New Drug Application (sNDA) for this indication in the first half of 2006, following the completion by our partner Vernalis of the second of two Phase III clinical trials.

DepoDur . We began commercial shipments of DepoDur in December of 2004. DepoDur is FDA-approved for the treatment of pain following major surgery. DepoDur is the first and only single-dose epidural injection that can provide up to 48 hours of pain control to help ease pain for people undergoing major surgery in the United States.

Percodan®. Launched in 1950 for the treatment of moderate-to-moderately severe pain, we also consider Percodan® to be a "gold standard" of pain management. According to the IMS National Prescription Audit, in 2004, approximately 283,000 prescriptions for oxycodone hydrochloride and oxycodone terephthalate in combination with aspirin were written for the brand name "Percodan." Due to generic substitution, only approximately 17% of these prescriptions were filled by pharmacists with our brand Percodan®.

Zydone®. In February 1999, we launched Zydone® tablets, branded hydrocodone/acetaminophen products for the relief of moderate-to-moderately severe pain. Zydone® is available in three strengths, 5.0mg, 7.5mg and 10.0mg, each in combination with 400mg acetaminophen. There is currently no generic equivalent available for this product.

Other. The balance of our branded portfolio consists of a number of products, none of which accounted for more than 5% of our total net sales in the 2004 fiscal year or for the six months ended June 30, 2005.

Generic Products

When a branded pharmaceutical product is no longer protected by any relevant patents, normally as a result of a patent's expiration, or by other, non-patent "market exclusivity," third parties have an opportunity to introduce generic counterparts to such branded product. Generic pharmaceutical products are therapeutically equivalent to their brand-name counterparts and are generally sold at prices significantly less than the branded product. Accordingly, generic pharmaceuticals may provide a safe, effective and cost-effective alternative to users of branded products.

Our generic portfolio is currently comprised of products that cover a range of indications, most of which are focused in pain management. One of our generic products is morphine sulfate extended-release tablets, which accounted for approximately 10% of our total net sales in 2004 and approximately 6% of our total net sales for the six months ended June 30, 2005. In addition, we have a generic oxycodone hydrochloride and acetaminophen product, Endocet®, which accounted for approximately 19% of our total net sales in 2004 and approximately 11% of our total net sales for the six months ended June 30, 2005. We also offer a generic of Sinemet® (carbidopa/levodopa) for the treatment of the symptoms of idiopathic Parkinson's disease.

We have also developed an extended-release oxycodone, an AB rated generic version of OxyContin®, a product of Purdue. According to IMS Retail Provider Perspective data, OxyContin® generated U.S. sales of approximately $1.8 billion in 2004. We have received final approval from the FDA for bioequivalent versions of the 10mg, 20mg, 40mg and 80mg strengths of OxyContin®. We currently are in litigation with Purdue regarding our generic version of OxyContin®. See "Risk Factors We were successful in our patent challenge against Purdue for our generic OxyContin® product, both at trial and on appeal. Purdue has petitioned the Court of Appeals for a rehearing, and if we receive an unfavorable ruling by the appeals court, we may be liable for damages and the price of our common stock may decline" in the accompanying prospectus. We are the first company to have filed an ANDA with the FDA for the bioequivalent versions of the 10mg, 20mg and 40mg strengths of OxyContin®, thereby entitling us to 180 days of generic product ANDA marketing exclusivity with respect to these strengths of this product. Under the Medicare Prescription Drug Improvement and Modernization Act of 2003, this marketing exclusivity begins to run upon the appellate court decision affirming the district court's decision. We launched all four strengths of the product on June 7, 2005 and had net sales of $29.2 million for the six months ended June 30, 2005. Our bioequivalent version of OxyContin® (oxycodone extended-release tablets) accounted for approximately 9% of our total net sales for the six months ended June 30, 2005.

The balance of our generic portfolio consists of a few other products, none of which accounted for more than 5% of our total net sales for 2004 or for the six months ended June 30, 2005.

We principally pursue the development and marketing of generic pharmaceuticals that have one or more barriers to entry. The characteristics of the products that we may target for generic development may include:

complex formulation or development characteristics;

regulatory or legal challenges; or

difficulty in raw material sourcing.

We believe products with these characteristics will face a lesser degree of competition, therefore providing longer product life cycles and/or higher profitability than commodity generic products.

Products in Development

Our pipeline portfolio contains products intended to address acute pain, chronic pain and neuropathic pain conditions as well as products in complementary therapeutic areas. We cannot predict when or if any of these products will be approved by the FDA.

Oxymorphone ER. We are co-developing an oral extended-release version of oxymorphone with Penwest Pharmaceuticals. If approved, we expect oxymorphone ER will compete in the approximately $4.2 billion U.S. long-acting strong opioid market. See " Recent Developments Oxymorphone ER Trials."

Oxymorphone IR. In December 2002, we filed an NDA for oxymorphone IR with the FDA. If approved, oxymorphone IR is intended to treat acute moderate-to-severe pain. See " Recent Developments Oxymorphone IR Trial."

LidoPAIN® BP. Currently in Phase II clinical trial development, LidoPAIN® BP is a patent-protected, adhesive-backed, high-concentration lidocaine-based patch product, intended for the treatment of acute lower back pain. LidoPAIN® BP is being developed by EpiCept.

Propofol IDD-D . Currently in the end of Phase II clinical trial development, Propofol IDD-D is an intravenous, or IV, formulation of propofol as the sole active ingredient using SkyePharma's patented Insoluble Drug Delivery (IDD-D) technology. Propofol IDD-D is intended for the maintenance of anesthesia in adults during surgery and for sedation of adults hospitalized in an intensive-care setting.

Rapinyl . Currently in Phase II clinical trial development, Rapinyl is a sub-lingual, fast-dissolving tablet of fentanyl intended for the treatment of breakthrough pain. We believe the benefits of Rapinyl include rapid absorption of the active substance, a fast onset of action and patient convenience, which we believe will improve compliance in patients who experience breakthrough pain. We anticipate that we will commence Phase III clinical trials in 2005.

Topical Ketoprofen Patch. Currently in Phase II clinical trials in the U.S., the ketoprofen patch is being developed for the localized treatment of acute pain associated with soft-tissue injuries such as tendonitis or joint sprains and strains. Two Phase III placebo-controlled studies in soft-tissue injury and ankle sprains have been completed in Europe by ProEthic Pharmaceuticals, Inc.'s European partner APR Applied Pharma Research AG, with statistically significant results. Ketoprofen is a non-steroidal anti-inflammatory drug (NSAID) generally used for the treatment of inflammation and pain and currently available in the U.S. only in oral form. We anticipate that we will commence Phase III clinical trials of this product in the first-half of 2006.

CHRONOGESIC . Currently in early-stage clinical development, CHRONOGESIC is intended to treat 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. CHRONOGESIC is a self-driven titanium implant that is placed just under the skin, similar in size to a matchstick, from which drug is released by the natural process of osmosis at a controlled rate. The CHRONOGESIC clinical development program is on temporary hold pending DURECT's

implementation of some necessary design and manufacturing enhancements to the CHRONOGESIC product. DURECT anticipates that the implementation of these design and manufacturing enhancements will continue to delay the restart of clinical trials.

Transdermal Sufentanil Patch. The sufentanil patch, which is in early-stage clinical development, employs DURECT's proprietary TRANSDUR drug-adhesive matrix formulation and is intended to provide relief of moderate-to-severe chronic pain for up to seven days.

Transdermal Fentanyl Patch. Currently under FDA review, the ANDA for a transdermal fentanyl patch was accepted for filing as of October 1, 2003. This product was developed by Noven Pharmaceuticals, Inc. If approved, this product would be the generic equivalent of Johnson & Johnson's Duragesic® (fentanyl transdermal system) which had U.S. sales of approximately $1.6 billion in 2004. In February 2005, the FDA approved a Supplemental New Drug Application filed by Johnson & Johnson for new labeling for its Duragesic® product. Noven has been advised by the FDA that all pending ANDAs relating to the Duragesic® product, including its ANDA, will be required to be amended prior to approval to reflect recent changes in the Duragesic® label. Noven is currently working with the FDA with respect to a revised label for the fentanyl patch. Once finalized, existing inventory will be repackaged to reflect the revised labeling. We are unable to predict the timing or impact of all ANDAs' required labeling changes, nor the timing of approval of any of the ANDAs relating to the Duragesic® product.

Other. We also have other undisclosed analgesic products addressing the broad spectrum of pain management in various stages of development, and we are currently exploring potential new indications for Lidoderm®.

SUMMARY HISTORICAL CONSOLIDATED FINANCIAL DATA

The summary historical consolidated financial data for the six months ended June 30, 2004 and 2005 have been derived from our unaudited interim condensed consolidated financial statements. All other summary historical consolidated financial data presented below have been derived from our audited consolidated financial statements. The summary historical consolidated financial data presented below should be read in conjunction with the audited consolidated financial statements, unaudited interim condensed consolidated financial statements and accompanying notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" incorporated by reference in this prospectus supplement and the accompanying prospectus. The summary data in this section is not intended to replace the consolidated financial statements.

	Year Ended December 31,			Six Months Ended June 30,	
	2002	2003	2004	2004	2005
	(in thousands, except per share data)				
Statement of Operations Data:					
Net sales	$ 398,973	$ 595,608	$ 615,100	$ 297,457	$ 334,134
Cost of sales	98,857	135,671	140,989	61,788	71,843
Gross profit	300,116	459,937	474,111	235,669	262,291
Selling, general and administrative	110,907	155,827	180,200	81,759	109,675
Research and development	56,823	51,024	50,546	29,001	47,972
Depreciation and amortization	3,142	6,272	10,630	4,089	7,294
Loss on disposal of other intangible			3,800	3,800	
Compensation related to stock options (primarily selling, general and administrative)	34,659	144,524			
Purchased in-process research and development	20,300	(6,966)			
Manufacturing transfer fee	9,000				
Operating income	65,285	109,256	228,935	117,020	97,350
Interest expense (income), net	4,391	258	(2,161)	(218)	(3,968)
Income before income tax	60,894	108,998	231,096	117,238	101,318
Income tax	30,081	39,208	87,787	44,516	38,457
Net income(1)	$ 30,813	$ 69,790	$ 143,309	$ 72,722	$ 62,861
Net income per share					
Basic	$ 0.30	$ 0.54	$ 1.09	$ 0.55	$ 0.48
Diluted(2)	$ 0.30	$ 0.53	$ 1.08	$ 0.55	$ 0.47
Shares used to compute net income per share					
Basic	102,064	128,417	131,805	131,786	131,922
Diluted	102,126	132,439	132,718	132,759	132,879

(footnotes on following page)

(1) Net income includes charges, net of tax, as follows:

	Year Ended December 31,			Six Months Ended June 30,	
	2002	2003	2004	2004	2005
			(in thousands)		
Net income	$ 30,813	$ 69,790	$ 143,309	$ 72,722	$ 62,861
Upfront and milestone payments to partners		3,079	8,062	6,203	12,409
Termination of development agreement			2,356	2,357	
Compensation related to stock options	21,819	88,989			
Manufacturing costs of oxycodone ER	5,059	15,131			
Manufacturing transfer costs	2,230	3,540			
Manufacturing transfer fee	5,666				
Purchased in-process research and development	20,300	(6,966)			

(2) Diluted net income per share includes charges, net of tax, as follows:

	Year Ended December 31,			Six Months Ended June 30,	
	2002	2003	2004	2004	2005
Net income	$ 0.30	$ 0.53	$ 1.08	$ 0.55	$ 0.47
Upfront and milestone payments to partners		0.02	0.06	0.04	0.10
Termination of development agreement			0.02	0.02	
Compensation related to stock options	0.21	0.67			
Manufacturing costs of oxycodone ER	0.05	0.11			
Manufacturing transfer costs	0.02	0.03			
Manufacturing transfer fee	0.06				
Purchased in-process research and development	0.20				