SKYEPHARMA PLC
Form 6-K
May 19, 2004

**SECURITIES AND EXCHANGE COMMISSION**
**WASHINGTON, D.C. 20549**

**FORM 6-K**

**REPORT OF FOREIGN PRIVATE ISSUER**
**PURSUANT TO RULE 13a - 16 OR 15d - 16 OF**
**THE SECURITIES EXCHANGE ACT OF 1934**

For the month of May, 2004

SkyePharma PLC

(Translation of registrant's name into English)

SkyePharma PLC, 105 Piccadilly, London W1J 7NJ England

(Address of principal executive office)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40F.

Form 20-F X Form 40-F

Indicate by check mark whether the registrant by furnishing the information contained in this Form is also thereby furnishing the information to the Commission pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.

Yes No X

If "Yes" is marked, indicate below the file number assigned to the registrant in connection with Rule 12g3-2(b): 82-
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For Immediate Release 19 May, 2004

**SKYEPHARMA AND ENDO ANNOUNCE FDA**

**APPROVAL OF DEPODUR™**
**(previously referred to as DepoMorphine™)**

Innovative Single Epidural Injection to Provide
48 Hours of Post-Surgical Pain Relief

LONDON, UK, and CHADDS FORD, Pa., USA 19 May 2004 -- SkyePharma PLC (LSE: SKP, Nasdaq: SKYE) and Endo Pharmaceuticals (Nasdaq: ENDP) today announced that the US Food & Drug Administration (FDA) has approved SkyePharma's New Drug Application (NDA) for DepoDur™ for the treatment of pain following major surgery. Previously referred to as DepoMorphine™, DepoDur™ is a novel single dose sustained-release injectable formulation of morphine.

Michael Ashton, Chief Executive of SkyePharma, said: "The FDA's decision to approve DepoDur™ is a tremendous vindication of our faith in the product. DepoDur™ represents the largest single commitment SkyePharma has made to product development, including funding the product through Phase III trials and building and sustaining a purpose-built manufacturing plant. We expect its commercialisation to have a profound effect on the company's future. Our clinical trial programme for DepoDur™ involved over 1000 patients in four different pain models and demonstrated the great potential of the product to improve the control of post-operative pain. We and our partners look forward to the benefits this product will bring for many patients after surgery."

Endo's Chairman and Chief Executive Officer Carol A. Ammon said: "We are delighted with the FDA's decision on DepoDur™. We believe the approval of DepoDur™ is an important step in fulfilling our vision of building our franchise in pain management as well as extending our reach into complementary therapeutic areas such as anaesthesiology." She added that Endo expects to be in a position to commercialize DepoDur™ by the end of 2004 provided SkyePharma is able to provide sufficient inventory to support the launch of the product. "We look forward to the commercialization of DepoDur™ and believe it provides a novel approach to the treatment of post-operative pain benefiting patients undergoing major surgery."

**For further information please contact:**

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**Notes for editors:**

**SkyePharma PLC** develops pharmaceutical products benefiting from world-leading drug delivery technologies that provide easier-to-use and more effective drug formulations. There are now ten approved products incorporating SkyePharma's technologies in the areas of oral, injectable, inhaled and topical delivery, supported by advanced solubilisation capabilities. For more information, visit *www.skyepharma.com.* A wholly owned subsidiary of Endo Pharmaceuticals Holdings Inc. (Nasdaq: ENDP), **Endo Pharmaceuticals** is a fully integrated specialty pharmaceutical company with market leadership in pain management products. The company researches, develops, produces and markets a broad product offering of 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 DepoDur™**

DepoDur™ is a single dose extended-release injectable formulation of morphine sulphate. DepoDur™ employs SkyePharma's proprietary DepoFoam™ technology and is supplied as a ready-to-use suspension. It is given as a single epidural injection before or during surgery and provides pain relief for up to 48 hours following surgery. There is no need for an in-dwelling catheter for continuous infusion, thereby overcoming a major drawback to the otherwise theoretically desirable epidural route of administration for opioid analgesics.

DepoDur™ is designed for the control of pain after major surgery. SkyePharma and Endo expect that its main use will be in control of post-operative pain in hospitalised patients undergoing major surgical procedures requiring general or regional anaesthesia such as major abdominal surgery, orthopaedic surgery and caesarean section. Currently there are an estimated 6 million such procedures every year in the USA and 5 million in Europe.

DepoDur™ is supplied in a 2 ml vial containing a 10 mg/ml suspension in sterile saline and is administered as a single dose epidural injection at the lumbar level prior to surgery (or after clamping of the umbilical cord during caesarean section). The recommended dose is 10 mg for caesarean section, 10-15 mg for lower abdominal surgery and 15 mg for major orthopaedic surgery of the lower extremities. Some patients may benefit from a dose of 20 mg. It should be appreciated that as with all opioids the incidence of serious adverse respiratory events is dose-related. Respiratory depression is the chief hazard of all opioid preparations and occurs more frequently in elderly or debilitated patients. For elderly patients (age >65 years), the low end of the dosing range for DepoDur™ is recommended together with vigilant peri-operative monitoring.

On 16 September 2003 the FDA formally accepted for filing a New Drug Application ("NDA") for DepoDur™, which had been submitted on 18 July 2003. On 20 November 2003 SkyePharma submitted an application for DepoDur™ to the UK Medicines and Healthcare products Regulatory Agency ("MHRA"). After national approval in the UK, SkyePharma intends to seek approval in other European Union countries under the Mutual Recognition procedure. SkyePharma has licensed DepoDur™ to Endo for North America and to Medeus Pharma for Europe.

SkyePharma has completed seven clinical trials of DepoDur™. The Phase IIb and Phase III clinical development programme for DepoDur™ involved four separate pain models and included more than 1000 patients. In the two Phase III trials, in hip surgery and lower abdominal surgery, DepoDur™ demonstrated extended dose-related analgesia and achieved its primary endpoint (superiority over study comparators in terms of total demand for opioid analgesics after surgery) with a high degree of statistical significance ($p<0.0001$ and $p=0.0003$, respectively). DepoDur™ also achieved statistical significance on several secondary endpoints. Importantly, statistical significance was achieved for the current pain intensity scores at rest and with activity over a 48 hour period and for the ratings of overall pain control.

In two related Phase IIb trials, DepoDur™ was significantly better than study comparators in the caesarean section study ($p=0.0209$) and approached statistical significance in the knee arthroplasty study ($p=0.0902$), which used a novel endpoint: time-weighted pain intensity recall score over 48 hours. DepoDur™ achieved a high degree of statistical significance in total demand for opioid analgesics after surgery ($p=0.001$), a secondary endpoint in this trial but the primary endpoint in the three other studies.

In all four of these studies the safety profile of DepoDur™ was typical for an epidural opioid agent. As with all opioid preparations, respiratory depression is the chief hazard associated with DepoDur™. The most common adverse events reported during clinical trials were decreased oxygen saturation, hypotension,

urinary retention, vomiting, constipation, nausea, pruritus, pyrexia, anemia, headache and dizziness.

**About DepoFoam™**

DepoFoam™ is SkyePharma's proprietary extended-release injectable delivery technology. This is fully commercialised and approved by regulatory agencies in both the USA and Europe. DepoFoam™ consists of lipid-based particles containing discrete water-filled chambers dispersed through the lipid matrix. The particles are 10-30 microns in diameter and are suspended in saline. The suspension resembles skimmed milk and can be injected through a fine needle. The water-filled chambers containing active drug account for most of the weight of the particles. The lipids are naturally occurring substances (or close analogues) such as phospholipids and triglycerides. The small amount of lipid is cleared rapidly in the body as the particles deliver their drug payload over a period that can be modified from 1 to 30 days.

**About post-operative pain**

After a major surgical operation, the level of pain is usually very high for the first one to two days but the intensity of pain gradually subsides and by the end of the second day pain can normally be satisfactorily controlled with oral analgesics. For the immediate post-operative period, opioid analgesics like morphine (used alone or in combination with other non-opioid analgesics) are likely to remain the "gold standard" for relief of severe acute pain. However the relatively short duration of pain relief with opioids means that they require either continuous infusion or patient-controlled analgesia ("PCA") in which a pump delivers a series of doses of a short-acting opioid analgesic in response to the patient pressing a button (under computer control to prevent over-dosing). Both of these approaches require the patient to have an in-dwelling epidural or intravenous catheter. Such catheters can fall out or interfere with patient mobility and are a potential source of infections. Epidural catheters are also contra-indicated with concomitant use of anticoagulants because of the risk of bleeding in the spinal column that can potentially result in paralysis. There is a growing trend toward routine use of anticoagulants in patients undergoing orthopaedic surgery in order to prevent the formation of blood clots.

**SkyePharma Forward-Looking Statement**

*Except for the historical information herein, the matters discussed in this news release include forward-looking statements that may involve a number of risks and uncertainties. Actual results may vary significantly based upon a number of factors, which are described in SkyePharma's 20-F and other documents on file with the SEC. These include without limitation risks in obtaining and maintaining regulatory approval for existing, new or expanded indications for its products, other regulatory risks, risks relating to SkyePharma's ability to manufacture pharmaceutical products on a large scale, risks that customer inventory will be greater than previously thought, risks concerning SkyePharma's ability to manage growth, market a pharmaceutical product on a large scale and integrate and manage an internal sales and marketing organization and maintain or expand sales and market share for its products, risks relating to the ability to ensure regulatory compliance, risks related to the research, development and regulatory approval of new pharmaceutical products, risks related to research and development costs and capabilities, market acceptance of and continuing demand for SkyePharma's products and the impact of increased competition, risks associated with anticipated top and bottom line growth and the possibility that upside potential will not be achieved, competitive products and pricing, and risks associated with the ownership and use of intellectual property rights. SkyePharma undertakes no obligation to revise or update any such forward-looking statement to reflect events or circumstances after the date of this release.*

**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. 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; 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 Registration Statement on Form S-3 filed with the SEC on April 30, 2004. Readers should evaluate any statement in light of these important factors.*

END

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

**SkyePharma PLC**

By: /s/ Douglas Parkhill

Name: Douglas Parkhill
Title: Company Secretary

Date: May 19, 2004