

EPIX Pharmaceuticals, Inc.

Form 424B3

November 14, 2006

**Filed Pursuant to Rule 424(b)(3)
Registration No. 333-117925**

**PROSPECTUS SUPPLEMENT NO. 4 DATED NOVEMBER 14, 2006
(TO PROSPECTUS DATED NOVEMBER 5, 2004)**

EPIX PHARMACEUTICALS, INC.

\$100,000,000 3.00% CONVERTIBLE SENIOR NOTES DUE 2024

2,239,000 SHARES OF COMMON STOCK ISSUABLE UPON CONVERSION OF THE NOTES

This Prospectus Supplement No. 4 supplements and amends the Prospectus dated November 5, 2004, as amended by Prospectus Supplement No. 1 dated December 23, 2004, Prospectus Supplement No. 2 dated February 16, 2005 and Prospectus Supplement No. 3 dated April 1, 2005 (as amended, the Prospectus), relating to the resale from time to time by holders of our 3.00% Convertible Senior Notes Due 2024 (the Notes) and shares of our common stock issuable upon the conversion of the Notes. Such information has been obtained from the selling holders. This Prospectus Supplement should be read in conjunction with the Prospectus, which is to be delivered with this Prospectus Supplement.

Our common stock is quoted on The Nasdaq Global Market under the symbol EPIX. The last reported sale price of our common stock on November 13, 2006 was \$4.28 per share.

FOR A DISCUSSION OF SIGNIFICANT MATTERS THAT SHOULD BE CONSIDERED BEFORE BUYING THE NOTES OR OUR COMMON STOCK, SEE PART II, ITEM 1A. RISK FACTORS IN OUR QUARTERLY REPORT ON FORM 10-Q FOR THE PERIOD ENDED SEPTEMBER 30, 2006.

Neither the Securities and Exchange Commission, any state securities commission nor any other regulatory authority, has approved or disapproved these securities nor have any of the foregoing authorities passed upon or endorsed the merits of this offering or the accuracy or adequacy of this Prospectus Supplement or the Prospectus or the documents incorporated by reference therein. Any representation to the contrary is a criminal offense.

On August 16, 2006, we completed our acquisition of Predix Pharmaceuticals Holdings, Inc. (Predix) pursuant to the terms of that certain Agreement and Plan of Merger, dated as of April 3, 2006 as amended on July 10, 2006, by and among us, EPIX Delaware, Inc., our wholly-owned subsidiary, and Predix, as amended. Pursuant to the merger agreement, Predix merged with and into EPIX Delaware, Inc. and became a wholly-owned subsidiary of us. The merger with Predix was primarily a stock transaction valued at approximately \$125 million, including the assumption of net debt at closing. As part of the merger, we also assumed all outstanding options and warrants to purchase capital stock of Predix. The purchase price includes a \$35 million payment to the holders of Predix stock, options and warrants payable in cash, stock or a combination of both based on Predix having achieved a certain strategic milestone. Pursuant to the terms of the merger agreement, \$20 million of the milestone was paid in cash on October 29, 2006. The remaining \$15 million of the milestone payment will be paid in shares of EPIX common stock on October 29, 2007, except to the extent that such shares would exceed 49.99% of outstanding shares immediately after such milestone payment when combined with all shares of EPIX common stock issued in the merger and issuable upon exercise of all Predix options and warrants that we assumed in the merger. The portion of the remaining milestone payment that can not be paid in EPIX common stock will be paid in cash with interest accrued at a rate of 10%. In addition, in connection with the merger, we effected a 1-for-1.5 reverse stock split of our outstanding common stock.

Following the merger, EPIX is a biopharmaceutical company focused on discovering, developing and commercializing novel pharmaceutical products through the use of proprietary technologies to better diagnose, treat and manage patients. We have a blood-pool imaging agent (Vasovist) approved in the European Union, Canada, Iceland, Norway, Switzerland and Australia, and five internally-discovered therapeutic and imaging drug candidates currently in clinical trials. Vasovist is currently being marketed in Europe. These drug candidates are targeting conditions such as depression, Alzheimer's disease, cardiovascular disease and obesity. We also have collaborations with leading organizations, including Amgen, Cystic Fibrosis Foundation Therapeutics, and Schering AG (Germany).

The focus of our therapeutic drug discovery and development efforts is on the two classes of drug targets known as G-protein Coupled Receptors (GPCRs) and ion channels. GPCRs and ion channels are classes of proteins embedded

in the

surface membrane of all cells and are responsible for mediating much of the biological signaling at the cellular level. We believe that our proprietary drug discovery technology and approach addresses many of the inefficiencies associated with traditional GPCR and ion channel-targeted drug discovery. By integrating computer-based, or *in silico*, technology with in-house medicinal chemistry, we believe that we can rapidly identify and optimize highly selective drug candidates. We focus on GPCR and ion channel drug targets whose role in disease has already been demonstrated in clinical trials or in preclinical studies. In each of our four clinical-stage therapeutic programs, we used our drug discovery technology and approach to optimize a lead compound into a clinical drug candidate in less than ten months, synthesizing fewer than 80 compounds per program. We moved each of these drug candidates into clinical trials in less than 18 months from lead identification. We believe our drug discovery technology and approach enables us to efficiently and cost-effectively discover and develop GPCR and ion channel-targeted drugs.

In the merger, Predix stockholders received .826702 shares of our common stock for each share of Predix capital stock for an aggregate of approximately 13,621,452 shares of our common stock, or approximately 47% of the outstanding shares of our common stock, after giving effect to the merger and to our 1-for-1.5 reverse stock split. The shares of our common stock issued to the Predix stockholders were registered with the Securities and Exchange Commission on a Registration Statement on Form S-4 (Reg. No. 333-133513). Approximately 29,152,220 shares of our common stock were outstanding immediately after the merger and giving effect to the 1-for-1.5 reverse stock split. The impact of the 1-for-1.5 reverse stock split on our previously filed financial statements included in our Annual Report of Form 10-K for the year ended December 31, 2005, as incorporated by reference to this Prospectus, is as follows:

| Our previously filed selected financial data: | December 31, 2005 | December 31, 2004 | December 31, 2003 |
|---|----------------------------------|----------------------------------|----------------------------------|
| Shares outstanding at year-end | 23,284,810 | 23,190,154 | 22,318,642 |
| Basic and diluted net loss per share | \$ (1.05) | \$ (0.89) | \$ (1.09) |
| Weighted average common shares used in computing basic and diluted net loss per share | 23,258,187 | 22,888,673 | 19,055,698 |

| Selected financial data for a 1-for-1.5 reverse stock split made effective August 16, 2006: | December 31, 2005 | December 31, 2004 | December 31, 2003 |
|--|----------------------------------|----------------------------------|----------------------------------|
| Shares outstanding at year-end | 15,523,206 | 15,460,102 | 14,818,642 |
| Basic and diluted net loss per share | \$ (1.57) | \$ (1.34) | \$ (1.09) |
| Weighted average common shares used in computing basic and diluted net loss per share | 15,505,458 | 15,259,115 | 19,055,698 |

As a result of the reverse stock split, the Prospectus is hereby supplemented and amended to reflect the effect of the reverse stock split on our outstanding common stock and the adjustment, effective August 17, 2006, of the conversion rate from 33.5909 shares of common stock to 22.39 shares of common stock per each U.S. \$1,000 principal amount of the Notes. The conversion rate of 22.39 shall apply to the information regarding the number of shares of common stock that may be sold under the table appearing under the heading "Selling Holders" in the Prospectus.

The information appearing in the table below, as of the date hereof, further supplements and amends the information in the table appearing under the heading **Selling Holders** in the Prospectus, and, where the name of a selling holder identified in the table below also appears in the table in the Prospectus, the information set forth in the table below regarding that selling holder supersedes the information in the Prospectus:

| <u>Name</u> | Principal Amount Of Notes Beneficially Owned That May Be Sold (\$)(1) | Shares of Common Stock That May be Sold (2) | Principal Amount Of Notes Owned After Completion of Offering (\$) | Shares of Common Stock Beneficially Owned After Completion of Offering (\$) |
|----------------------------------|--|--|--|--|
| Pioneer U.S. High Yield Corp. | 3,400,000 | 76,126 | 0 | 0 |
| ING Pioneer High Yield Portfolio | 500,000 | 11,195 | 0 | 0 |

(1) Amounts indicated may be in excess of the total amount registered due to sales or transfers exempt from the registration requirements of the Securities Act since the date upon which the selling holders provided to us the information regarding their Notes and common stock.

(2) Reflects adjusted conversion rate of 22.39 shares of common stock per each U.S. \$1,000 principal amount of the Notes. Unless otherwise noted, represents shares of common stock issuable upon conversion of Notes.

The selling holders identified above may have sold, transferred or otherwise disposed of all or a portion of their Notes since the date on which they provided the information about their Notes in transactions exempt from the registration requirements of the Securities Act.