

**PROSPECTUS SUPPLEMENT NO. 4**

**A.P. PHARMA, INC.**

**69,600,669 shares of Common Stock**

This prospectus supplement amends the prospectus dated April 2, 2012 (as supplemented on May 10, 2012, August 9, 2012 and November 5, 2012) to allow certain stockholders or their pledgees, donees, transferees, or other successors in interest (the "Selling Stockholders"), to sell, from time to time, up to 69,600,669 shares of our common stock (the "Common Stock"), all of which are issuable upon the conversion of our Senior Secured Convertible Notes due 2021 or the "Notes" (such underlying shares being referred to herein as the "Shares"). The number of shares registered in the Registration Statement is based upon the shares potentially issuable under the Notes at maturity in May 2021 (based on the initial outstanding principal balance of \$1,500,000 and assuming all interest payments are made in-kind). We note that the actual number of Shares that may be issued under the Notes may be less, if the Notes are converted prior to maturity or if the Note holders elect to receive interest payments in cash.

We would not receive any proceeds from any such sale of these Shares.

This prospectus supplement is being filed to include the information set forth in the Current Report on Form 8-K filed on March 28, 2013, which is set forth below. This prospectus supplement should be read in conjunction with the prospectus dated April 2, 2012 and any supplements thereto, which are to be delivered with this prospectus supplement.

Our Common Stock is quoted on the OTC Bulletin Board under the symbol "APPA.OB". On March 27, 2013, the last reported sale price per share of our Common Stock on the OTC Bulletin Board was \$0.58. Our principal executive offices are located at 123 Saginaw Drive, Redwood City, California 94063, and our telephone number is (650) 366-2626.

**Investing in our securities involves risks. You should carefully consider the risk factors beginning on page 2 of the prospectus before you make an investment in our securities.**

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**

**THE DATE OF THIS PROSPECTUS SUPPLEMENT NO. 4 IS MARCH 28, 2013**

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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

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**FORM 8-K**

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**CURRENT REPORT**

**Pursuant to Section 13 or 15(d) of  
the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported) March 28, 2013**

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**A.P. Pharma, Inc.**

(Exact name of registrant as specified in its charter)

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**Delaware**  
(State or other jurisdiction  
of incorporation)

**001-33221**  
(Commission  
File Number)

**94-2875566**  
(I.R.S. Employer  
Identification No.)

**123 Saginaw Drive**  
**Redwood City, CA**  
(Address of principal executive offices)

**94063**  
(Zip Code)

**Registrant's telephone number, including area code (650) 366-2626**

**N/A**  
(Former name or former address, if changed since last report)

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Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
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**ITEM 8.01 Other Events.**

On March 28, 2013, A.P. Pharma, Inc. announced that it received a Complete Response Letter from the U.S. Food and Drug Administration regarding its lead candidate, APF530, for the prevention of Chemotherapy-induced nausea and vomiting. The Complete Response Letter describes certain issues that must be addressed by the company prior to approval of APF530, as described in the press release attached hereto as Exhibit 99.1 and incorporated herein by reference.

**ITEM 9.01. Financial Statements and Exhibits.**

(d) Exhibits.

<u>Exhibit No.</u>	<u>Description</u>
99.1	Press Release, Dated March 28, 2013

**SIGNATURE**

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 hereunto duly authorized.

A.P. Pharma, Inc.

Date: March 28, 2013

/s/ John B. Whelan

John B. Whelan

President and Chief Executive Officer

**For Immediate Release**

A.P. Pharma Receives FDA Complete Response Letter for APF530

*- Company Revises Projected Launch Timing from 2H 2013 to 1H 2014 -*

*- Conference Call to Be Held at 8:30 a.m. Eastern Time -*

REDWOOD CITY, Calif. – March 28, 2013 – A.P. Pharma, Inc. (OTCBB: APPA.OB), a specialty pharmaceutical company, today announced that it has received a Complete Response Letter (CRL) from the U.S. Food and Drug Administration (FDA) regarding its New Drug Application (NDA) for its lead product candidate, APF530, for the prevention of chemotherapy-induced nausea and vomiting (CINV). The CRL describes the following issues that must be addressed.

- With respect to chemistry, manufacturing and controls (CMC), the FDA has requested the refinement of one product quality analytical test method, and that certain deficiencies identified during facility pre-approval inspections be addressed.
- The FDA has requested that a human factors validation study evaluating the usability of the APF530 syringe system together with its proposed product labeling and instructions for use be conducted with product assembled using a validated, commercial process.
- With respect to clinical, the FDA has requested a re-analysis of the existing Phase 3 clinical data that reclassifies patients into those receiving moderately emetogenic chemotherapy (MEC) and highly emetogenic chemotherapy (HEC) according to the recently modified ASCO 2011 Guideline. The FDA did not request any new clinical studies.

“We appreciate the FDA’s thorough review of the APF530 NDA,” stated John B. Whelan, A.P. Pharma’s president and chief executive officer. “While disappointed in today’s notification, we believe that the issues raised in the CRL are addressable, and we remain firmly committed to the successful development of APF530, which we believe will fulfill an important unmet need and improve the lives of patients suffering from CINV. In order to allow us time to carefully address the issues raised in the CRL, we are now projecting product launch for the first half of 2014, versus our prior guidance of the second half of 2013.”

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**Conference Call Details**

A.P. Pharma will host a conference call on Thursday, March 28, 2013 at 8:30 a.m. Eastern Time (5:30 a.m. Pacific Time). Interested investors may participate in the conference call by dialing (877) 856-1964 (domestic) or (719) 386-0001 (international) and use participant code 135738. In addition, the live conference call is being webcast and can be accessed on the “Calendar of Events” page of the “Investors” section of the Company’s website at [www.appharma.com](http://www.appharma.com). A replay of the webcast will be posted to this same section of the website available approximately two hours after the call.

**About APF530**

A.P. Pharma’s lead product, APF530, is being developed for the prevention of both acute- and delayed-onset chemotherapy-induced nausea and vomiting (CINV). One of the most debilitating side effects of cancer chemotherapy, CINV is a leading cause of premature discontinuation of treatment. There is only one injectable 5-HT3 antagonist approved for the prevention of delayed-onset CINV, so this indication represents an area of particular unmet medical need. APF530 contains the 5-HT3 antagonist granisetron formulated in the Company’s proprietary Biochronomer™ drug delivery system, which allows therapeutic drug levels to be maintained for five days with a single subcutaneous injection. Currently available intravenous and oral formulations of granisetron are approved only for the prevention of acute-onset CINV. Granisetron was selected for APF530 because it is widely prescribed by physicians based on a well-established record of safety and efficacy.

**About A.P. Pharma**

A.P. Pharma is a specialty pharmaceutical company developing products using its proprietary Biochronomer™ polymer-based drug delivery platform. This drug delivery platform is designed to improve the therapeutic profile of injectable pharmaceuticals by converting them from products that must be injected once or twice per day to products that need to be injected only once every one or two weeks. The Company’s lead product, APF530, is being developed for the prevention of both acute- and delayed-onset chemotherapy-induced nausea and vomiting. A.P. Pharma resubmitted its New Drug Application (NDA) for APF530 to the U.S. Food and Drug Administration (FDA) in September 2012 and received a Complete Response Letter in March 2013. For further information, please visit the Company’s web site at [www.appharma.com](http://www.appharma.com).

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**Forward-looking Statements**

This news release contains “forward-looking statements” as defined by the Private Securities Litigation Reform Act of 1995. These forward-looking statements involve risks and uncertainties, including uncertainties associated with the potential approval of APF530 and the potential timing for such approval, if approved at all, the projected timing for the commercial launch of APF530, if approved, as well as risks relating to capital resources and liquidity, satisfactory completion of clinical studies, progress in research and development programs, successful launch and acceptance of new products and other risks and uncertainties identified in the Company’s filings with the Securities and Exchange Commission. We caution investors that forward-looking statements reflect our analysis only on their stated date. We do not intend to update them except as required by law.

**Contacts**

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and

**Corporate Contact:**

John B. Whelan, President and Chief Executive Officer

Office Phone: 650-366-2626

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