

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

SCHEDULE 13G/A
Under the Securities Exchange Act of 1934
Amendment No. 2

A.P. Pharma, Inc.
(Name of Issuer)

Common Stock
(Title of Class of Securities)

00202J203
(CUSIP Number)

December 31, 2008

(Date of Event Which Requires Filing of this Statement)

Check the appropriate box to designate the rule pursuant to which this Schedule is filed:

Rule 13d-1(b)

Rule 13d-1(c)

Rule 13d-1(d)

*The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter the disclosures provided in a prior cover page.

The information required in the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

CUSIP No. 00202J203

1. Names of Reporting Persons.
I.R.S. Identification Nos. of above persons (entities only).

OrbiMed Advisors LLC
2. Check the Appropriate Box if a Member Of a Group (See Instructions)

 (a)
 (b)
3. SEC Use Only
4. Citizenship or Place of Organization

Delaware
5. Sole Voting Power: 0
6. Shared Voting Power: 1,165,100
7. Sole Dispositive Power: 0
8. Shared Dispositive Power: 1,165,100
9. Aggregate Amount Beneficially Owned by Each Reporting Person
1,165,100
10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares
(See Instructions)
11. Percent of Class Represented by Amount in Row (9) 3.77%
12. Type of Reporting Person (See Instructions) IA

Number of
Shares
Beneficially
Owned by
Each Reporting
Person With

CUSIP No. 00202J203

1. Names of Reporting Persons.
I.R.S. Identification Nos. of above persons (entities only).

OrbiMed Capital LLC
 2. Check the Appropriate Box if a Member of a Group (See Instructions)

 (a)
 (b)
 3. SEC Use Only
 4. Citizenship or Place of Organization

Delaware
 5. Sole Voting Power: 0
- Number of
Shares
Beneficially
Owned by
Each Reporting
Person With
6. Shared Voting Power: 1,028,300
 7. Sole Dispositive Power: 0
 8. Shared Dispositive Power: 1,028,300
9. Aggregate Amount Beneficially Owned by Each Reporting Person
1,028,300
 10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares
(See Instructions)
 11. Percent of Class Represented by Amount in Row (9) 3.32%
 12. Type of Reporting Person (See Instructions) IA

CUSIP No. 00202J203

1. Names of Reporting Persons.
I.R.S. Identification Nos. of above persons (entities only).

Samuel D. Isaly
 2. Check the Appropriate Box if a Member of a Group (See Instructions)

 (a)
 (b)
 3. SEC Use Only
 4. Citizenship or Place of Organization

United States
 5. Sole Voting Power: 0
- Number of
Shares
Beneficially
Owned by
Each Reporting
Person With
6. Shared Voting Power: 2,193,400
 7. Sole Dispositive Power: 0
 8. Shared Dispositive Power: 2,193,400
9. Aggregate Amount Beneficially Owned by Each Reporting Person:
2,193,400
 10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares
(See Instructions)
 11. Percent of Class Represented by Amount in Row (9) 7.09%

Item 1. (a) Issuer: A.P. Pharma, Inc.

1. Address:
123 SAGINAW DRIVE
REDWOOD CITY CA 94063

Item 2. (a) Name of Person Filing:

OrbiMed Advisors LLC
OrbiMed Capital LLC
Samuel D. Isaly

(b) Address of Principal Business Offices:

767 Third Avenue, 30th Floor
New York, New York 10017

(c) Citizenship:

Please refer to Item 4 on each cover sheet for each filing person

(d) Title of Class of Securities

Common stock

(e) CUSIP Number: 00202J203

Item 3. OrbiMed Advisors LLC and OrbiMed Capital LLC are investment advisors in accordance with ss.240.13d-1(b)(1)(ii)(E). Samuel D. Isaly is a control person in accordance with ss.240.13d-1(b)(1)(ii)(G).

Item 4. Ownership

Please see Items 5 - 9 and 11 for each cover sheet for each filing separately

Item 5. Ownership of Five Percent or Less of a Class

Not Applicable

Item 6. Ownership of More than Five Percent on Behalf of Another Person.

Reporting persons are holding 7.09% (3.77% in the case of OrbiMed Advisors LLC and 3.32% in the case of OrbiMed Capital LLC) of the securities on behalf of other persons who have the right to receive or the power to direct the receipt of dividends from, or proceeds from sale of, such securities. No one such other person's interest in the securities whose ownership is reported here relates to more than five percent of the class.

OrbiMed Advisors LLC and OrbiMed Capital LLC hold shares on behalf of Caduceus Capital Master Fund Limited (816,000 shares), Caduceus Capital II, L.P. (547,200 shares), UBS Eucalyptus Fund, LLC (551,900 shares), PW Eucalyptus Fund, Ltd. (66,000 shares), and Summer Street Life Sciences Hedge Fund Investors LLC (212,300 shares)

Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on By the Parent Holding Company

Not Applicable

Item 8. Identification and Classification of Members of the Group

Not Applicable

Item 9. Notice of Dissolution of Group

Not Applicable

Item 10. Certification

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were acquired and held in the ordinary course of business and were not acquired and are not held for the purpose of or

with the effect of changing or influencing the control of the issuer of the securities and were not acquired and are not held in connection with or as a participant in any transaction having that purpose or effect.

SIGNATURE

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

Date: February 9, 2009

OrbiMed Advisors LLC

By: /s/ Samuel D. Isaly

Name: Samuel D. Isaly

Title: President

OrbiMed Capital LLC

By: /s/ Samuel D. Isaly

Name: Samuel D. Isaly

Title: Managing Member

By: /s/ Samuel D. Isaly

Name: Samuel D. Isaly

JOINT FILING AGREEMENT

The undersigned hereby agree that the Statement on this Schedule 13G/A, dated February 9, 2009, (the "Schedule 13G/A"), with respect to the Common Stock, par value \$.001 per share, of A.P. Pharma, Inc. is filed on behalf of each of us pursuant to and in accordance with the provisions of Rule 13d-1(k) under the Securities and Exchange Act of 1934, as amended, and that this Agreement shall be included as an Exhibit to this Schedule 13G/A. Each of the undersigned agrees to be responsible for the timely filing of the Schedule 13G/A, and for the completeness and accuracy of the information concerning itself contained therein. This Agreement may be executed in any number of counterparts, all of which taken together shall constitute one and the same instrument.

IN WITNESS WHEREOF, the undersigned have executed this Agreement as of the 9th day of February 2009.

OrbiMed Advisors LLC

By: /s/ Samuel D. Isaly

Name: Samuel D. Isaly

Title: Managing Member

OrbiMed Capital LLC

By: /s/ Samuel D. Isaly

Name: Samuel D. Isaly

Title: Managing Member

By: /s/ Samuel D. Isaly

Name: Samuel D. Isaly

Statement of Control Person

The Statement on this Schedule 13G/A dated February 9, 2009 with respect to the common stock, \$.001 par value per share, of A.P. Pharma, Inc. is filed by Samuel D. Isaly in accordance with the provisions of Rule 13d-1(b) and Rule 13d-1(k), respectively, as control person (HC) of OrbiMed Advisors LLC and OrbiMed Capital LLC.

OrbiMed Advisors LLC and OrbiMed Capital LLC file this statement on Schedule 13G/A in accordance with the provisions of Rule 13d-1(b) and Rule 13d-1(k), respectively, as investment advisors (IA).