

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

**SCHEDULE 13D**

**Under the Securities Exchange Act of 1934  
(Amendment No. 4)\***

**Pacira Pharmaceuticals, Inc.**

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(Name of Issuer)

**Common Stock**

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(Title of Class of Securities)

**695127 10 0**

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(CUSP Number)

**OrbiMed Advisors LLC  
OrbiMed Capital GP III LLC  
Samuel D. Isaly  
601 Lexington Avenue, 54<sup>th</sup> Floor  
New York, NY 10022  
Telephone: (212) 739-6400**

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(Name, Address and Telephone Number of Person  
Authorized to Receive Notices and Communications)

**September 25, 2012**

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(Date of Event Which Requires Filing of this Statement)

If the filing person has previously filed a statement on Schedule 13G to report the acquisition that is the subject of this Schedule 13D, and is filing this schedule because of §§240.13d-1(e), 240.13d-1(f) or 240.13d-1(g), check the following box.

**Note:** Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See §240.13d-7 for other parties to whom copies are to be sent.

\* 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 disclosures provided in a prior cover page.

The information required on 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).

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1. Name of Reporting Persons.  
I.R.S. Identification No(s). of above person(s) (entities only)  
OrbiMed Advisors LLC

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

(a)

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(b)

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3. SEC Use Only

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4. Source of Funds (See Instructions)  
AF (See Item 3)

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5. Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)

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6. Citizenship or Place of Organization  
Delaware

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7. Sole Voting Power  
0

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Number of  
Shares  
Beneficially  
Owned by  
Each  
Reporting  
Person With:

8. Shared Voting Power  
1,620,000

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9. Sole Dispositive Power  
0

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10. Shared Dispositive Power  
1,620,000

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11. Aggregate Amount Beneficially Owned by Each Reporting Person  
1,620,000

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12. Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)

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13. Percent of Class Represented by Amount in Row (11)

4.997%(1)

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14. Type of Reporting Person (See Instructions)  
IA

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(1) This percentage is calculated based upon 32,419,407 shares of the Issuer's Common Stock outstanding, as reported in Issuer's quarterly report on Form 10-Q filed on August 9, 2012.

1. Name of Reporting Persons.  
I.R.S. Identification No(s). of above person(s) (entities only)  
OrbiMed Capital GP III LLC

---

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

(a)

---

(b)

---

3. SEC Use Only

---

4. Source of Funds (See Instructions)  
AF (See Item 3)

---

5. Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)

---

6. Citizenship or Place of Organization  
Delaware

---

7. Sole Voting Power  
0

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Number of  
Shares  
Beneficially  
Owned by  
Each  
Reporting  
Person With:

8. Shared Voting Power  
1,604,700

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9. Sole Dispositive Power  
0

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10. Shared Dispositive Power  
1,604,700

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11. Aggregate Amount Beneficially Owned by Each Reporting Person  
1,604,700

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12. Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)

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13. Percent of Class Represented by Amount in Row (11)

4.949%(1)

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14. Type of Reporting Person (See Instructions)  
OO

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(1) This percentage is calculated based upon 32,419,407 shares of the Issuer's Common Stock outstanding, as reported in Issuer's quarterly report on Form 10-Q filed on August 9, 2012.

1. Name of Reporting Persons.  
I.R.S. Identification No(s). of above person(s) (entities only)  
Samuel D. Isaly

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

(a)

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(b)

---

3. SEC Use Only

---

4. Source of Funds (See Instructions)  
AF (See Item 3)

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5. Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)

---

6. Citizenship or Place of Organization  
United States

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7. Sole Voting Power  
0

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Number of  
Shares  
Beneficially  
Owned by  
Each  
Reporting  
Person With:

8. Shared Voting Power  
1,620,000

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9. Sole Dispositive Power  
0

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10. Shared Dispositive Power  
1,620,000

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11. Aggregate Amount Beneficially Owned by Each Reporting Person  
1,620,000

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12. Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)

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13. Percent of Class Represented by Amount in Row (11)

4.997%(1)

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14. Type of Reporting Person (See Instructions)  
IN

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(1) This percentage is calculated based upon 32,419,407 shares of the Issuer's Common Stock outstanding, as reported in Issuer's quarterly report on Form 10-Q filed on August 9, 2012.

**Explanatory Note:** This Amendment No. 4 to Schedule 13D (this “Amendment No. 4”) supplements and amends the Schedule 13D previously filed with the United States Securities and Exchange Commission (the “SEC”) on February 18, 2011, amended by Amendment No. 1 filed December 1, 2011, Amendment No. 2 filed March 19, 2012 and Amendment No. 3 filed June 15, 2012 (as amended, the “Original Schedule 13 D”). The person and entities filing this Amendment No. 4 are OrbiMed Advisors LLC, a limited liability company under the laws of Delaware, OrbiMed Capital GP III LLC, a limited liability company under the laws of Delaware, and Samuel D. Isaly (“Isaly”), an individual (collectively, the “Reporting Persons”). This Amendment No. 3 is being filed to report the open market sales of shares of Common Stock and the private sale of warrants to purchase Common Stock of Pacira Pharmaceuticals, Inc. (the “Company”) by the Reporting Persons and also to report that the beneficial owners have ceased to be five per cent (5%) holders of the Company’s securities.

**Item 4. Purpose of Transaction**

Item 4 of the Original Schedule 13D is hereby amended and supplemented by adding the following paragraph at the end of Item 4:

The Reporting Persons sold an aggregate of 380,000 shares of Common Stock in open market transactions and 79,031 warrants in private sales from August 15, 2012 through September 27, 2012 for gross proceeds of approximately \$7,474,057.

**Item 5. Interest in Securities of the Issuer**

“Item 5. Interest in Securities of the Issuer” of the Original Schedule 13D is hereby amended and restated as follows:

(a) — (b) As of this date of this filing, the Reporting Persons may be deemed, directly or indirectly, including by reason of their mutual affiliation, to be the beneficial owners of the shares of Common Stock held by the OrbiMed Stockholders, OPI III and Associates III. As of the date of this filing, OPI III directly holds 1,604,700 shares of Common Stock and Associates III directly holds 15,300 shares of Common Stock.

OrbiMed Advisors LLC, pursuant to its authority as the sole managing member of OrbiMed Capital GP III LLC, the sole general partner of OPI III, and as the general partner of Associates III, may be deemed to indirectly beneficially own the securities of the Issuer held by OPI III and Associates III, which represent an aggregate of 1,620,000 shares of Common Stock and constitute approximately 4.997% of the Common Stock(1). Isaly, pursuant to his authority as the managing member of, and owner of a controlling interest in, OrbiMed Advisors LLC, may be deemed to also indirectly beneficially own the foregoing securities of the Issuer attributable to OrbiMed Advisors LLC.

OrbiMed Capital GP III LLC, pursuant to its authority as the general partner of OPI III, may be deemed to indirectly beneficially own the securities of the Issuer held by OPI III, which represent an aggregate of 1,604,700 shares of Common Stock and constitute approximately 4.949% of the Common Stock(1).

As a result of the agreements and relationships described in Items 2, 3, and Item 6 of the Original Schedule 13D, the Reporting Persons have shared discretionary power to direct the vote and the disposition of the securities of the Issuer held by OPI III, and OrbiMed Advisors LLC and Isaly have shared discretionary power to direct the vote and the disposition of the securities of the Issuer held by Associates III.

(c)

<u>Entity</u>	<u>Date of Transaction</u>	<u>Number of Shares Sold</u>	<u>Price Per Share</u>
OPI III	August 15, 2012	36,700	\$ 17.03(1)
Associates III	August 15, 2012	300	\$ 17.03(1)
OPI III	August 17, 2012	41,446	\$ 6.00(2)
Associates III	August 17, 2012	394	\$ 6.00(2)
OPI III	August 20, 2012	36,841	\$ 13.89(3)
Associates III	August 20, 2012	350	\$ 13.89(3)
OPI III	August 23, 2012	53,500	\$ 17.55(4)
Associates III	August 23, 2012	500	\$ 17.55(4)
OPI III	August 24, 2012	113,900	\$ 17.41(5)
Associates III	August 24, 2012	1,100	\$ 17.41(5)
OPI III	August 27, 2012	33,700	\$ 17.83(6)
Associates III	August 27, 2012	300	\$ 17.83(6)
OPI III	September 25, 2012	49,500	\$ 18.52(7)
Associates III	September 25, 2012	500	\$ 18.52(7)
OPI III	September 26, 2012	49,600	\$ 17.52(8)
Associates III	September 26, 2012	400	\$ 17.52(8)
OPI III	September 27, 2012	39,600	\$ 17.95(9)
Associates III	September 27, 2012	400	\$ 17.95(9)

(1) Represents the weighted average sales price for the price increments ranging from \$16.95 to \$17.54.

(2) Represents the private sale of warrants at \$6.00 per share underlying the warrant.

(3) Represents the private sale of warrants at \$13.89 per share underlying the warrant.

(4) Represents the weighted average sales price for the price increments ranging from \$17.30 to \$17.72.

(5) Represents the weighted average sales price for the price increments ranging from \$17.25 to \$17.62.

(6) Represents the weighted average sales price for the price increments ranging from \$17.75 to \$17.92.

(7) Represents the weighted average sales price for the price increments ranging from \$18.12 to \$18.88.

(8) Represents the weighted average sales price for the price increments ranging from \$17.50 to \$18.17.

(9) Represents the weighted average sales price for the price increments ranging from \$17.79 to \$18.30.

(d) Not applicable.

(e) The Reporting Persons have ceased to be five per cent (5%) holders of the Common Stock of the Company as of September 27, 2012.

**Item 6. Material to Be Filed as Exhibits**

A. Agreement regarding filing of joint Schedule 13D.

Signatures

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: September 28, 2012

OrbiMed Advisors LLC

By: /s/ Samuel D. Isaly  
Name: Samuel D. Isaly  
Title: Managing Member

OrbiMed Capital GP III LLC

By: OrbiMed Advisors LLC,  
its Managing Member

By: /s/ Samuel D. Isaly  
Name: Samuel D. Isaly  
Title: Managing Member

By: /s/ Samuel D. Isaly  
Name: Samuel D. Isaly

### Schedule I

The name and present principal occupation of each of the persons managing or otherwise controlling OrbiMed Advisors LLC are set forth below. Unless otherwise noted, each of these persons are United States citizens and have as their business address 601 Lexington Avenue, 54<sup>th</sup> Floor, New York, NY10022.

<u>Name</u>	<u>Position with Reporting Person</u>	<u>Principal Occupation</u>
Samuel D. Isaly	Managing Member	Managing Member OrbiMed Advisors LLC
Michael B. Sheffery	Member	Member OrbiMed Advisors LLC
Carl L. Gordon	Member	Member OrbiMed Advisors LLC
Sven H. Borho German and Swedish Citizen	Member	Member OrbiMed Advisors LLC
Jonathan T. Silverstein	Member	Member OrbiMed Advisors LLC
W. Carter Neild	Member	Member OrbiMed Advisors LLC
Geoffrey C. Hsu	Member	Member OrbiMed Advisors LLC
Evan D. Sotiriou	Chief Financial Officer	Chief Financial Officer OrbiMed Advisors LLC

### Schedule II

The business and operations of OrbiMed Capital GP III LLC are managed by the persons controlling its managing member, OrbiMed Advisors LLC, as set forth on Schedule I above.

**Exhibit Index**

A. Joint Filing Agreement among OrbiMed Advisors LLC, OrbiMed Capital GP III LLC and Samuel D. Isaly.

**Exhibit A**

**JOINT FILING AGREEMENT**

I, the undersigned, hereby express my agreement that the attached Schedule 13D (and any amendments thereto) relating to the beneficial ownership by the undersigned of the equity securities of Pacira Pharmaceuticals, Inc. is filed on behalf of each of the undersigned.

Date: September 28, 2012

OrbiMed Advisors LLC

By: /s/ Samuel D. Isaly

Name: Samuel D. Isaly

Title: Managing Member

OrbiMed Capital GP III LLC

By: OrbiMed Advisors LLC,  
its Managing Member

By: /s/ Samuel D. Isaly

Name: Samuel D. Isaly

Title: Managing Member

By: /s/ Samuel D. Isaly

Name: Samuel D. Isaly