

SECURITIES AND EXCHANGE COMMISSION

FORM SC 13D/A

Schedule filed to report acquisition of beneficial ownership of 5% or more of a class of equity securities [amend]

Filing Date: **2008-08-29**
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([HTML Version](#) on [secdatabase.com](#))

FILED BY

ISALY SAMUEL D

CIK: **1055949**
Type: **SC 13D/A**

Business Address
787 THIRD AVE
NEW YORK NY 10010
2127396400

SUBJECT COMPANY

NxStage Medical, Inc.

CIK: **1333170** | IRS No.: **043454702** | State of Incorporation: **DE** | Fiscal Year End: **1231**
Type: **SC 13D/A** | Act: **34** | File No.: **005-81212** | Film No.: **081048701**
SIC: **3845** Electromedical & electrotherapeutic apparatus

Mailing Address
439 SOUTH UNION STREET
5TH FLOOR
LAWRENCE MA 01843

Business Address
439 SOUTH UNION STREET
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LAWRENCE MA 01843
978-687-4700

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

SCHEDULE 13D

(Amendment No. 2)

Under the Securities Exchange Act of 1934

NxStage Medical, Inc.

(Name of Issuer)

Common Stock

(Title of Class of Securities)

67072V103

(CUSIP Number)

**OrbiMed Advisors LLC
OrbiMed Capital GP III LLC**

Samuel D. Isaly

767 Third Avenue

New York, NY 10017

Telephone: (212) 739-6400

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

Copy to:

Nathan J. Greene, Esq.

Shearman & Sterling LLP

599 Lexington Avenue

New York, New York 10022

Telephone: (212) 848-4000

August 21, 2008

(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(b) 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 (the "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. 67072V103

Page 3 of 12 Pages

1	NAME 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) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS (See Instructions) WC	
5	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER 0
	8	SHARED VOTING POWER 64,493
	9	SOLE DISPOSITIVE POWER 0
	10	SHARED DISPOSITIVE POWER 64,493
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 64,493	
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 0.14%	
14	TYPE OF REPORTING PERSON (See Instructions) IA	

SCHEDULE 13D

CUSIP No. 67072V103

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1	NAME OF REPORTING PERSONS I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY) OrbiMed Capital GP III LLC	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions) (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS (See Instructions) WC	
5	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER 0
	8	SHARED VOTING POWER 6,764,874
	9	SOLE DISPOSITIVE POWER 0
	10	SHARED DISPOSITIVE POWER 6,764,874
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 6,764,874	
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 14.60%	
14	TYPE OF REPORTING PERSON (See Instructions) OO	

SCHEDULE 13D

CUSIP No. 67072V103

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1	NAME 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) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS (See Instructions) WC	
5	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) <input type="checkbox"/>	
6	CITIZENSHIP OR PLACE OF ORGANIZATION United States	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7	SOLE VOTING POWER 0
	8	SHARED VOTING POWER 6,829,367
	9	SOLE DISPOSITIVE POWER 0
	10	SHARED DISPOSITIVE POWER 6,829,367
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 6,829,367	
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 14.73%	
14	TYPE OF REPORTING PERSON (See Instructions) IN	

Item 1. Security and Issuer.

The class of equity securities to which this Statement on Schedule 13D relates is the Common Stock (the “Shares”) of Nxstage Medical, Inc. (the “Issuer”), a Delaware company with its principal executive offices located at 439 South Union Street, 5th Floor Laurence, MA 01843.

Item 2. Identity and Background.

(a) This Statement is being filed by OrbiMed Advisors LLC, a limited liability company organized under the laws of Delaware, OrbiMed Capital GP III LLC, a limited liability company organized under the laws of Delaware, and Samuel D. Isaly (“Isaly”), an individual (collectively, the “Reporting Persons”).

(b) – (c) OrbiMed Advisors LLC is a registered investment adviser under the Investment Advisers Act of 1940, as amended, that acts as investment adviser or general partner to certain clients which hold Shares of the Issuer, as more particularly described in Item 6 below. OrbiMed Advisors LLC has its principal offices at 767 Third Avenue, 30th Floor, New York, New York 10017.

OrbiMed Capital GP III LLC is a company that acts as investment adviser or general partner to certain limited partnerships as more particularly described in Item 6 below. OrbiMed Capital GP III LLC has its principal offices at 767 Third Avenue, 30th Floor, New York, New York 10017.

Isaly, a natural person, owns a controlling interest in OrbiMed Advisors LLC and OrbiMed Capital GP III LLC.

The directors and executive officers of OrbiMed Advisors LLC and OrbiMed Capital GP III LLC are set forth on Schedules I and II, attached hereto. Schedules I and II set forth the following information with respect to each such person:

- (i) name;
- (ii) business address (or residence address where indicated);
- (iii) present principal occupation or employment and the name, principal business and address of any corporation or other organization in which such employment is conducted;
- (iv) citizenship.

(d) – (e) During the last five years, neither the Reporting Persons nor any Person named in Schedules I or II have been (i) convicted in a criminal proceeding (excluding traffic violations or similar misdemeanors) or (ii) a party to a civil proceeding of a judicial or administrative body of competent jurisdiction and as a result of such proceeding was or is subject to a judgment, decree or final order enjoining future violations of, or prohibiting or mandating activities subject to, federal or state securities laws or finding any violation with respect to such laws.

(f) Isaly is a citizen of the United States.

Item 3. Source and Amount of Funds or Other Considerations.

Prior to the close of August 26, 2008, pursuant to the authority of OrbiMed Advisors LLC and OrbiMed Capital GP III LLC under their respective investment advisory contracts and limited partnership agreements with or relating to Caduceus Private Investments III, LP (“Caduceus”) and OrbiMed Associates III, LP (“Associates”), as more particularly referred to in Item 6 below, caused these clients to purchase 5,718,256 Shares of the Issuer (27,700 Shares purchased on August 26, 2008, 108,900 Shares purchased on August 25, 2008, 26,100 Shares purchased August 21, 2008 and the balance prior thereto) and to enter into a Warrant Purchase Agreement (the “Agreement”) to purchase 1,111,111 Shares of the Issuer exercisable immediately and for the duration of five years.

As a result of the transactions described in this Item 3, the Reporting Persons are beneficial owners of approximately 14.73% of the outstanding Shares of the Issuer. Isaly, as the owner of a controlling interest in both OrbiMed Advisors LLC and OrbiMed Capital GP III LLC, is the beneficial owner of approximately 14.73% of the outstanding Shares of the Issuer. OrbiMed Advisors LLC is the beneficial owner of approximately 0.14% of the outstanding Shares of the Issuer and OrbiMed Capital GP III LLC is the beneficial owner of approximately 14.60% of such Shares.

None of the Reporting Persons have acquired or disposed of any additional Shares of the Issuer since August 26, 2008.

Item 4. Purpose of Transaction.

Prior to the close of July 23, 2008, Jonathan T. Silverstein, a director of the Issuer, who also is a partner of OrbiMed Advisors LLC and of OrbiMed Capital GP III LLC, was the recipient of a grant of stock options of the Issuer (the “Director’s Stock Options”). Pursuant to an agreement with the Reporting Persons, Silverstein is obligated to transfer any Shares issued under the Director’s Stock Options to the Reporting Persons, who will distribute the Shares to Caduceus and Associates on a pro-rata basis.

The following table sets forth the transactions with respect to the Director’s Stock Options and includes the Director’s Stock Options’ exercisable date. As of this filing, none of the Director’s Stock Options have been exercised.

Title	Conversion Price	Date Exercisable	Expiration Date	Number of Shares Underlying Security	Ownership of Shares
Director's Stock Option (right to buy)	\$4.36	07/23/2008	07/22/2013	11,667	The amount shown represents (i) options to purchase 11,557 shares of Common Stock held by Caduceus, and (ii) options to purchase 110 shares of Common Stock held by Associates.

This statement relates to the acquisition of Shares by the Reporting Persons. The Shares acquired by the Reporting Persons were acquired for the purpose of making an investment in the Issuer and not with the intention of acquiring control of the Issuer’s business on behalf of the Reporting Persons’ respective advisory clients.

The Reporting Persons previously were granted the right to appoint a representative to the Board of Directors (the “Board”) of the Issuer, so as to permit active monitoring of the operations of the Issuer. As mentioned above, Jonathan T. Silverstein currently serves as the Reporting Person’s representative on the Board.

The Reporting Persons from time to time intend to review their investment in the Issuer on the basis of various factors, including the Issuer’s business, financial condition, results of operations and prospects, general economic and industry conditions, the securities markets in general and those for the Issuer’s Shares in particular, as well as other developments and other investment opportunities. Based upon such review, the Reporting Persons will take such actions in the future as the Reporting Persons may deem appropriate in light of the circumstances existing from time to time. If the Reporting Persons believe that further investment in the Issuer is attractive, whether because of the market price of the Issuer’s Shares or otherwise, they may acquire shares of Common Stock or other securities of the Issuer either in the open market or in privately negotiated transactions. Similarly, depending on market and other factors, the Reporting Persons may determine to dispose of some or all of the Shares currently owned by the Reporting Persons or otherwise acquired by the Reporting Persons either in the open market or in privately negotiated transactions.

Except as set forth above, the Reporting Persons have not formulated any plans or proposals which relate to or would result in: (a) the acquisition by any person of additional securities of the Issuer or the disposition of securities of the Issuer, (b) an extraordinary corporate transaction involving the Issuer or any of its subsidiaries, (c) a sale or transfer of a material amount of the assets of the Issuer or any of its subsidiaries, (d) any change in the present Board of Directors or management of the Issuer, (e) any material change in the Issuer's capitalization or dividend policy, (f) any other material change in the Issuer's business or corporate structure, (g) any change in the Issuer's charter or bylaws or other instrument corresponding thereto or other action which may impede the acquisition of control of the Issuer by any person, (h) causing a class of the Issuer's securities to be deregistered or delisted, (i) a class of equity securities of the Issuer becoming eligible for termination of registration or (j) any action similar to any of those enumerated above.

Item 5. Interest in Securities of the Issuer.

(a)-(b) As of this date of this filing, OrbiMed Advisors LLC, OrbiMed Capital GP III LLC and Samuel D. Isaly may be deemed directly or indirectly, including by reason of their mutual affiliation, to be the beneficial owners of the Shares described in Item 3. Based upon information contained in the most recent available filing by the Issuer with the SEC, such Shares constitute approximately 14.73% of the issued and outstanding Shares. As described above in Item 2, Isaly owns, pursuant to the terms of the limited liability company agreement of each of OrbiMed Advisors LLC and OrbiMed Capital GP III LLC, a controlling interest in the outstanding limited liability company interests of such entity. As a result, Isaly, OrbiMed Advisors LLC and OrbiMed Capital GP III LLC share power to direct the vote and to direct the disposition of the Common Stock described in Item 3.

(c) Except as disclosed in Item 3, the Reporting Persons have not effected any transactions in the Shares during the past sixty (60) days.

(d) Not applicable.

(e) Not applicable.

Item 6. Contracts, Arrangements, Understandings or Relationships with Respect to Securities of the Issuer.

In addition to the relationships between the Reporting Persons described in Item 5, OrbiMed Capital GP III LLC is the general partner of Caduceus, pursuant to the terms of its limited partnership agreement. OrbiMed Advisors LLC acts as investment manager of Associates, pursuant to the terms of its investment advisory agreement. Pursuant to these agreements and relationships, OrbiMed Advisors LLC and OrbiMed Capital GP III LLC have discretionary investment management authority with respect to the assets of these investment accounts. Such authority includes the power to vote and otherwise dispose of securities purchased by Caduceus and Associates. The number of outstanding Shares of the Issuer attributable to Caduceus is 5,664,245 Shares and 1,100,629 Warrants and to Associates 54,011 Shares and 10,482 Warrants. OrbiMed Advisors LLC, pursuant to its authority under its

investment advisory contracts with Associates, may be considered to hold indirectly 54,011 Shares and 10,482 Warrants and OrbiMed Capital GP III LLC, pursuant to its authority under its investment advisory contract with Caduceus, may be considered to hold indirectly 5,664,245 Shares and 1,100,629 Warrants. As noted above under Item 4, Jonathan T. Silverstein, a partner of OrbiMed Advisors LLC and OrbiMed Capital GP III LLC has been appointed to the Board of the Issuer and, accordingly, the Reporting Persons may have the ability to effect and influence control of the Issuer.

Also as noted in Item 4, Silverstein has been granted a number of Director's Stock Options and is obligated to transfer any Shares issued pursuant to such Options to the Reporting Persons, who will distribute the Shares to Caduceus and Associates on a pro-rata basis. Accordingly, the number of Director's Stock Options attributable to Caduceus and Associates is 11,557 and 110, respectively. Of these OrbiMed Advisors LLC and OrbiMed Capital GP III LLC may be considered to hold indirectly 110 and 11,557 Director's Stock Options, respectively.

Other than the agreements and the relationships mentioned above, to the best knowledge of the Reporting Persons, there are no contracts, arrangements, understandings or relationships (legal or otherwise) among the persons named in Item 2 and between such persons and any persons with respect to any securities of the Issuer, including, but not limited to, transfer or voting of any of the Shares, finder's fees, joint ventures, loan or option arrangements, puts or calls, guarantees of profits, division of profits or loss, or the giving of withholding of proxies.

Item 7. Materials to be Filed as Exhibits.

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

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.

Dated: August 29, 2008

OrbiMed Advisors LLC

By: /s/ Samuel D. Isaly

Name: Samuel D. Isaly

Title: Managing Partner

OrbiMed Capital GP III LLC

By: /s/ Samuel D. Isaly

Name: Samuel D. Isaly

Title: Managing Partner

By: /s/ Samuel D. Isaly

Name: Samuel D. Isaly

Schedule I

The name and present principal occupation of each of the executive officers and directors of OrbiMed Advisors LLC are set forth below. Unless otherwise noted, each of these persons are United States citizens and have as their business address 767 Third Avenue, New York, NY 10017.

Name	Position with Reporting Person	Principal Occupation
Samuel D. Isaly	Managing Partner	Partner OrbiMed Advisors LLC
Michael Sheffery	Partner	Partner OrbiMed Advisors LLC
Carl L. Gordon	Partner	Partner OrbiMed Advisors LLC
Sven Borho German and Swedish Citizen	Partner	Partner OrbiMed Advisors LLC
Jonathan T. Silverstein	Partner	Partner OrbiMed Advisors LLC
W. Carter Neild	Partner	Partner OrbiMed Advisors LLC
Eric A. Bittelman	Chief Financial Officer and Chief Compliance Officer	CFO/CCO OrbiMed Advisors LLC

Schedule II

The name and present principal occupation of each of the executive officers and directors of OrbiMed Capital GP III LLC are set forth below. Unless otherwise noted, each of these persons are United States citizens and have as their business address 767 Third Avenue, New York, NY 10017.

Name	Position with Reporting Person	Principal Occupation
Samuel D. Isaly	Managing Partner	Partner OrbiMed Capital GP III LLC
Michael Sheffery	Partner	Partner OrbiMed Capital GP III LLC
Carl L. Gordon	Partner	Partner OrbiMed Capital GP III LLC
Sven Borho German and Swedish Citizen	Partner	Partner OrbiMed Capital GP III LLC
Jonathan T. Silverstein	Partner	Partner OrbiMed Capital GP III LLC
W. Carter Neild	Partner	Partner OrbiMed Capital GP III LLC
Eric A. Bittelman	Chief Financial Officer and Chief Compliance Officer	CFO/CCO OrbiMed Capital GP III LLC

EXHIBIT INDEX

Exhibit	Description	Page No.
A.	Joint Filing Agreement among OrbiMed Advisors LLC, OrbiMed Capital GP III LLC and Samuel D. Isaly	A-1

JOINT FILING AGREEMENT

The undersigned hereby agree that the Statement on this Schedule 13D, dated August 29, 2008 (the "Schedule 13D"), with respect to the Common Stock, par value \$.001 per share, of NxStage Medical, 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 Exchange Act of 1934, as amended, and that this Agreement shall be included as an Exhibit to this Schedule 13D. Each of the undersigned agrees to be responsible for the timely filing of the Schedule 13D, 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 29th day of August, 2008.

OrbiMed Advisors LLC

By: /s/ Samuel D. Isaly

Name: Samuel D. Isaly

Title: Managing Partner

OrbiMed Capital GP III LLC

By: /s/ Samuel D. Isaly

Name: Samuel D. Isaly

Title: Managing Partner

By: /s/ Samuel D. Isaly

Name: Samuel D. Isaly