

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

**SCHEDULE 13D**  
Under the Securities Exchange Act of 1934  
**(Amendment No. 4)\***

**AFFIMED N.V.**

(Name of Issuer)

**COMMON STOCK**

(Title of Class of Securities)

**N01045108**

(CUSIP Number)

**OrbiMed Advisors LLC  
OrbiMed Capital GP III LLC  
Samuel D. Isaly**

**601 Lexington Avenue, 54th Floor  
New York, NY 10022  
Telephone: (212) 739-6400**

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

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

**October 15, 2015**

(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 o.

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 ("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. N01045108

1	NAME OF REPORTING PERSONS OrbiMed Advisors LLC	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions) <span style="float: right;">(a) <input type="checkbox"/> (b) <input type="checkbox"/></span>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS (See Instructions) N/A	
5	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) <span style="float: right;"><input type="checkbox"/></span>	
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 4,500,641*
	9	SOLE DISPOSITIVE POWER 0
	10	SHARED DISPOSITIVE POWER 4,500,641*
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 4,500,641*	
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (See Instructions) <span style="float: right;"><input type="checkbox"/></span>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 13.53% <sup>†</sup>	
14	TYPE OF REPORTING PERSON (See Instructions) IA	

\* Includes 326,650 shares that may be transferred pursuant to the Carve-Out Agreements described in Item 6.

<sup>†</sup> This percentage is calculated based upon 33,259,404 shares of the Issuer's Common Stock (as defined below) outstanding, as set forth in the Issuer's final prospectus dated October 15, 2015, filed with the Securities and Exchange Commission (the "SEC") on October 15, 2015.

CUSIP No. N01045108

1	NAME OF REPORTING PERSONS OrbiMed Capital GP III LLC	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions) <span style="float: right;">(a) <input type="checkbox"/> (b) <input type="checkbox"/></span>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS (See Instructions) N/A	
5	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) <span style="float: right;"><input type="checkbox"/></span>	
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 4,458,842*
	9	SOLE DISPOSITIVE POWER 0
	10	SHARED DISPOSITIVE POWER 4,458,842*
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 4,458,842*	
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (See Instructions) <span style="float: right;"><input type="checkbox"/></span>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 13.41% <sup>†</sup>	
14	TYPE OF REPORTING PERSON (See Instructions) OO	

\* Includes 323,623 shares that may be transferred pursuant to the Carve-Out Agreements described in Item 6.

<sup>†</sup> This percentage is calculated based upon 33,259,404 shares of the Issuer's Common Stock (as defined below) outstanding, as set forth in the Issuer's final prospectus dated October 15, 2015, filed with the Securities and Exchange Commission (the "SEC") on October 15, 2015.

CUSIP No. N01045108

1	NAME OF REPORTING PERSONS Samuel D. Isaly	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions) <span style="float: right;">(a) <input type="checkbox"/> (b) <input type="checkbox"/></span>	
3	SEC USE ONLY	
4	SOURCE OF FUNDS (See Instructions) N/A	
5	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEMS 2(d) or 2(e) <span style="float: right;"><input type="checkbox"/></span>	
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 4,500,641*
	9	SOLE DISPOSITIVE POWER 0
	10	SHARED DISPOSITIVE POWER 4,500,641*
11	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 4,500,641*	
12	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (See Instructions) <span style="float: right;"><input type="checkbox"/></span>	
13	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 13.53% <sup>†</sup>	
14	TYPE OF REPORTING PERSON (See Instructions) IN	

\* Includes 326,650 shares that may be transferred pursuant to the Carve-Out Agreements described in Item 6.

<sup>†</sup> This percentage is calculated based upon 33,259,404 shares of the Issuer's Common Stock (as defined below) outstanding, as set forth in the Issuer's final prospectus dated October 15, 2015, filed with the Securities and Exchange Commission (the "SEC") on October 15, 2015.

## Item 1. Security and Issuer

This Amendment No. 4 to Schedule 13D supplements and amends the Statement on Schedule 13D of OrbiMed Advisors LLC, OrbiMed Capital GP III LLC and Samuel D. Isaly originally filed with the Securities and Exchange Commission (the “SEC”) on September 19, 2014 (the “Statement”) and amended by Amendment No. 1 thereto filed with the SEC on February 20, 2015, Amendment No. 2 filed on May 14, 2015, and Amendment No. 3 filed on August 17, 2015. The Statement relates to the common stock, nominal value €0.01 per share (the “Common Stock”), of Affimed N.V. (formerly Affimed Therapeutics B.V.), a public company with limited liability (*naamloze vennootschap*) organized under the laws of the Netherlands (the “Issuer”), with its principal executive offices located at Im Neuenheimer Feld 582, 69120 Heidelberg, Germany. The Common Stock is listed on the Nasdaq Global Market under the ticker symbol “AFMD.” Information given in response to each item shall be deemed incorporated by reference in all other items, as applicable.

On October 15, 2015, the Issuer filed Amendment No. 1 to its registration statement on Form F-3 (the “F-3 Registration Statement”) relating to the offering, issuance and sale of up to \$150,000,000 of the Issuer’s shares of Common Stock (“Shares”), debt securities, warrants, purchase contracts and units and the offering, issuance and sale of up to 12,985,302 Shares which may be sold by certain selling shareholders, including OrbiMed Associates III, LP (“Associates III”) and OrbiMed Private Investments III, LP (“OPI III”). The base prospectus, dated October 15, 2015, included in the F-3 Registration Statement reported that as of October 14, 2015, there were approximately 33,259,404 Shares outstanding. Based on such information, the percentage of outstanding Shares that the Reporting Persons may be deemed to beneficially own was reduced by more than one percent of the Issuer’s Shares outstanding from the percentage reported in Amendment No. 3 to the Statement. The percentage of outstanding Shares that the Reporting Persons may be deemed to beneficially own has also been reduced since the Reporting Persons filed Amendment No. 3 to the Statement by the transactions described in Item 5(c).

## Item 2. Identity and Background

(a) This Amendment No. 4 to the Statement is being filed by OrbiMed Advisors LLC (“Advisors”), a limited liability company organized under the laws of Delaware, OrbiMed Capital GP III LLC (“GP III”), a limited liability company organized under the laws of Delaware, and Samuel D. Isaly (“Isaly”), an individual (collectively, the “Reporting Persons”).

(b) – (c) Advisors, a registered investment adviser under the Investment Advisers Act of 1940, as amended, is the sole general partner of Associates III and the sole managing member of GP III, which is the sole general partner of OPI III. OPI III and Associates III hold Shares, as more particularly described in Item 6 below. Advisors has its principal offices at 601 Lexington Avenue, 54th Floor, New York, New York 10022.

GP III has its principal offices at 601 Lexington Avenue, 54th Floor, New York, New York 10022.

Isaly, a natural person, owns a controlling interest in Advisors.

The directors and executive officers of Advisors and GP III 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;
- (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 Schedule 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 Consideration**

Not applicable.

**Item 4. Purpose of Transaction**

As described more fully in Item 1 above, the obligation of the Reporting Persons to file this Amendment No. 4 arises based on information about the number of Shares outstanding set forth in the F-3 Registration Statement and not by virtue of transactions effected by the Reporting Persons with respect to the Shares. This Amendment No. 4 to the Statement also reports on the transactions by the Reporting Persons more fully described in Item 5 below. The Shares initially had been acquired (and those that continue to be held, are held) by the Reporting Persons for the purpose of making an investment in the Issuer and not with the intention of acquiring control of the Issuer's business.

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 Common Stock 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 Common Stock or otherwise, they may acquire shares 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 in this Amendment No. 4 to the Statement, 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, such as a merger, reorganization or liquidation, 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, including any plans or proposals to change the number or term of directors or to fill any existing vacancies on the board, (e) any material change in the Issuer's capitalization or dividend policy of the Issuer, (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 from a national securities exchange or to cease to be authorized to be quoted in an inter-dealer quotation system of a registered national securities association, (i) a class of equity securities of the Issuer becoming eligible for termination of registration pursuant to Section 12(g)(4) of the Act or (j) any action similar to any of those enumerated above.

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

(a)-(b) As of the date of this filing, Advisors, GP III and Isaly may be deemed, for purposes of Rule 13d-3 of the Act, directly or indirectly, including by reason of their mutual affiliation, to be the beneficial owners of the Common Stock described in Item 6 below. Based upon information contained in the most recent available filing by the Issuer with the SEC, such Common Stock deemed to be indirectly beneficially owned by GP III constitutes approximately 13.41% of the issued and outstanding Common Stock, and such Common Stock deemed to be indirectly beneficially owned by Advisors and Isaly constitutes approximately 13.53% of the issued and outstanding Common Stock. Advisors, pursuant to its authority as the sole managing member of GP III, which is the sole general partner of OPI III, and as the sole general partner of Associates III, may be deemed to indirectly beneficially own the Common Stock held by OPI III and Associates III. GP III, pursuant to its authority as the general partner of OPI III, may be deemed to indirectly beneficially own the Common Stock held by OPI III. Isaly, pursuant to his authority as the managing member of Advisors and owner of a controlling interest in Advisors, pursuant to its limited liability company agreement, may be deemed to also indirectly beneficially own the Common Stock attributable to Advisors. As a result, Isaly, Advisors and GP III share the power to direct the vote and the disposition of the Shares held by OPI III described in Item 6 below, and Isaly and Advisors share the power to direct the vote and the disposition of the Shares held by Associates III described in Item 6 below.

In addition, Advisors and GP III, pursuant to their authority under the limited partnership agreements of OPI III and/or Associates III, as more particularly referred to in Item 6 below, prior to the date of this filing, caused OPI III and Associates III, as applicable, together with certain other shareholders of the Issuer (collectively with OPI III and Associates III, the "Selling Shareholders") to enter into agreements substantially in the form filed as Exhibit 4 to Amendment No. 1 to the Statement (the "Amended and Restated Carve-Out Agreements") with the Issuer's managing directors and certain of the Issuer's supervisory directors and consultants (the "Beneficiaries"), as described in Item 6 below.

(c)

<b>Seller</b>	<b>Date of Transaction</b>	<b>Transaction</b>	<b>Number of Shares</b>	<b>Price Per Share*</b>
OPI III	March 11, 2016	Sold	57,072	\$3.90
Associates III	March 11, 2016	Sold	544	\$3.90
OPI III	March 14, 2016	Sold	24,133	\$3.99
Associates III	March 14, 2016	Sold	226	\$3.99

\*The Price Per Share reported above is a weighted average price. Upon request, the Reporting Persons undertake to provide the Issuer, any security holder of the Issuer, or the SEC full information regarding the Shares purchased at each separate price within the ranges set forth above.

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 Relationship with Respect to Securities of the Issuer**

In addition to the relationships between the Reporting Persons described in Items 2, 3 and 5 above, GP III is the sole general partner of OPI III, pursuant to the terms of the limited partnership agreement of OPI III. Advisors is the sole managing member of GP III, pursuant to the terms of the limited liability company agreement of GP III, and the sole general partner of Associates III, pursuant to the terms of the limited partnership agreement of Associates III. Pursuant to these agreements and relationships, Advisors and GP III have discretionary investment management authority with respect to the assets of OPI III, and Advisors has discretionary investment management authority with respect to the assets of Associates III. Such authority includes the power of GP III and Advisors to vote and otherwise dispose of securities purchased by OPI III, and the power of Advisors to vote and otherwise dispose of securities purchased by Associates III. The number of outstanding Shares held of record by OPI III is 4,458,842, and the number of outstanding Shares held of record by Associates III is 41,799. Advisors may be considered to hold indirectly 4,500,641 Shares, and GP III may be considered to hold indirectly 4,458,842 Shares.

On June 29, 2015, Michael B. Sheffery, a Partner Emeritus of Advisors, retired from the board of directors of the Issuer at the expiration of his term.

### ***Registration Rights Agreement***

The Issuer is party to a registration rights agreement among OPI III, Associates III, SGR Sagittarius Holding AG, BioMed Invest I Ltd., LSP III Omni Investment Coöperatief U.A. and Novo Nordisk A/S dated September 17, 2014 (the "Registration Rights Agreement"), a summary of which is set forth at Item 6 of Amendment No. 3 to the Statement. All of the Shares held by OPI III and Associates III, with the exception of the Shares covered by the Amended and Restated Carve-Out Agreements, were registered on the F-3 Registration Statement.

### ***Amended and Restated Carve-Out Agreements***

In connection with the Issuer's initial public offering, Advisors and GP III, pursuant to their authority under the limited partnership agreements of OPI III and/or Associates III, caused OPI III and Associates III, as applicable, together with the other Selling Shareholders, to enter into the carve-out agreements with the Beneficiaries described in the Statement (the "Original Carve-Out Agreements"). On February 17, 2015, the Selling Shareholders entered into a termination agreement pursuant to which the Selling Shareholders and the Beneficiary agreed to terminate the Original Carve-Out Agreement with such Beneficiary for the future and to replace it by individual Amended and Restated Carve-Out Agreements between each Selling Shareholder and the Beneficiary.

The Amended and Restated Carve-Out Agreements grant each Beneficiary the right to receive a payment equal to a certain percentage of the fair value of the Issuer contingent upon the occurrence of a defined event, including an initial public offering. Following the expiration of applicable lock-up agreements, (i) the obligations of OPI III and Associates III under the Amended and Restated Carve-Out Agreements were satisfied through a transfer to the Beneficiaries of an amount of shares of Common Stock in the aggregate amount of 379,023 shares, and (ii) portions of these shares are sold pursuant to Rule 144 to satisfy withholding taxes triggered by the transfer and delivered to the Beneficiaries with the net amount of shares to which each Beneficiary is entitled to receive pursuant to his or her individual Amended and Restated Carve-Out Agreement.

The foregoing description of the Amended and Restated Carve-Out Agreements does not purport to be complete and is qualified in its entirety by reference to the full text of the form of Amended and Restated Carve-Out Agreement, a copy of which was filed as Exhibit 3 to Amendment No. 1 to the Statement and is incorporated herein by reference. Other than as described in this Amendment No. 3 to the Statement, to the best of the Reporting Persons' knowledge, there are no other contracts, arrangements, understandings or relationships (legal or otherwise) among the persons named in Item 2 and between such persons and any person with respect to any securities of the Issuer.



**Item 7. Materials to Be Filed as Exhibits**

<b>Exhibit</b>	<b>Description</b>
1.	Joint Filing Agreement among OrbiMed Advisors LLC, OrbiMed Capital GP III LLC and Samuel D. Isaly.
2.	Form of Registration Rights Agreement (incorporated by reference to Exhibit 4.1 to Amendment No. 1 to the Issuer's Form F-1 (SEC File No. 333-197097), filed with the SEC on July 17, 2014)
3.	Form of Amended and Restated Carve-Out Agreement (incorporated by reference to Exhibit 4 to Amendment No. 1 to the Reporting Persons' Statement on Schedule 13D, filed with the SEC on February 20, 2015)

**SIGNATURE**

After reasonable inquiry and to the best of each of the undersigned's knowledge and belief, each of the undersigned certifies that the information set forth in this Amendment No. 4 to the Statement is true, complete and correct.

Dated: March 17, 2016

OrbiMed Advisors LLC  
a Delaware Limited Liability Company

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

OrbiMed Capital GP III LLC  
a Delaware Limited Liability Company

By: OrbiMed Advisors LLC  
A Delaware Limited Liability Company and its  
Managing Member

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

Samuel D. Isaly

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 601 Lexington Avenue, 54th Floor, New York, NY 10022.

Name	Position with Reporting Person	Principal Occupation
Samuel D. Isaly	Managing Member	Managing 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 executive officers and directors of its managing member, OrbiMed Advisors LLC, set forth on Schedule I attached hereto.

**EXHIBIT INDEX**

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3.	Form of Amended and Restated Carve-Out Agreement (incorporated by reference to Exhibit 4 to Amendment No. 1 to the Reporting Persons' Statement on Schedule 13D, filed with the SEC on February 20, 2015)

## JOINT FILING AGREEMENT

The undersigned hereby agree that the Statement on this Schedule 13D, dated March 17, 2016 (the "Schedule 13D"), with respect to the Common Stock, of Affimed N.V. 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 17<sup>th</sup> day of March 2016.

OrbiMed Advisors LLC  
a Delaware Limited Liability Company

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

OrbiMed Capital GP III LLC  
a Delaware Limited Liability Company

By: OrbiMed Advisors LLC  
A Delaware Limited Liability Company and its  
Managing Member

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

Samuel D. Isaly

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

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