

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, DC 20549

SCHEDULE 13G/A

Under the Securities Exchange Act of 1934  
(Amendment No. 1)\*

**ProQR Therapeutics N.V.**

(Name of Issuer)

**Ordinary Shares**

(Title of Class of Securities)

**N71542109**

(CUSIP Number)

**December 31, 2015**

(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).

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1	NAME OF REPORTING PERSONS I.R.S. IDENTIFICATION NO. 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	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5	SOLE VOTING POWER 0
	6	SHARED VOTING POWER 961,820
	7	SOLE DISPOSITIVE POWER 0
	8	SHARED DISPOSITIVE POWER 961,820
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 961,820	
10	CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>	
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) 4.12%	
12	TYPE OF REPORTING PERSON (See Instructions) IA	

1	NAME OF REPORTING PERSONS I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY) OrbiMed Capital 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	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5	SOLE VOTING POWER 0
	6	SHARED VOTING POWER 1,309,680
	7	SOLE DISPOSITIVE POWER 0
	8	SHARED DISPOSITIVE POWER 1,309,680
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 1,309,680	
10	CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>	
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) 5.61%	
12	TYPE OF REPORTING PERSON (See Instructions) IA	

1	NAME OF REPORTING PERSONS I.R.S. IDENTIFICATION NO. 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	CITIZENSHIP OR PLACE OF ORGANIZATION United States	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5	SOLE VOTING POWER 0
	6	SHARED VOTING POWER 2,271,500
	7	SOLE DISPOSITIVE POWER 0
	8	SHARED DISPOSITIVE POWER 2,271,500
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 2,271,500	
10	CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>	
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) 9.73%	
12	TYPE OF REPORTING PERSON (See Instructions) HC	

**Item 1. (a) Name of Issuer:**

ProQR Therapeutics N.V.

**(b) Address of Issuer's Principal Executive Offices:**

Darwinweg 24  
2333 CR Leiden  
The Netherlands

**Item 2. (a) Name of Person Filing:**

OrbiMed Advisors LLC  
OrbiMed Capital LLC  
Samuel D. Isaly

**(b) Address of Principal Business Office:**

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

**(c) Citizenship:**

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

**(d) Title of Class of Securities:**

Ordinary Shares

**(e) CUSIP No.:**

N71542109

**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.

**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 9.73% (4.12% in the case of OrbiMed Advisors LLC and 5.61% in the case of OrbiMed Capital LLC) of the shares on behalf of other persons who have the right to receive or the power to direct the receipt of dividends from, or proceeds from the 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.

**Item 7. Identification and Classification of the Subsidiary which Acquired the Security Being Reported on by the Parent Holding Company or Control Person.**

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.

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.

Dated: February 11, 2016

OrbiMed Advisors LLC

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

OrbiMed Capital LLC

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

Samuel D. Isaly

Samuel D. Isaly  
Name: Samuel D. Isaly





**EXHIBIT A  
JOINT FILING AGREEMENT**

The undersigned hereby agree that the Statement on this Schedule 13G/A dated February 11, 2016 (the "Schedule 13G/A"), with respect to the Ordinary Shares of ProQR Therapeutics 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 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 February 11, 2016.

OrbiMed Advisors LLC

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

OrbiMed Capital LLC

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

Samuel D. Isaly

Samuel D. Isaly  
Name: Samuel D. Isaly

The Statement on this Schedule 13G/A dated February 11, 2016 with respect to the Ordinary Shares of ProQR Therapeutics N.V. 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).