

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

OMB APPROVAL  
OMB Number: 3235-0145  
Expires: December 31, 2009  
Estimated average burden  
hours per response 10.4

**SCHEDULE 13G**

**Under the Securities Exchange Act of 1934  
(Amendment No. 2)**

**Amicus Therapeutics, Inc.**

\_\_\_\_\_  
(Name of Issuer)

**Common Stock**

\_\_\_\_\_  
(Title of Class of Securities)

**03152W109**

\_\_\_\_\_  
(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).

**Potential persons who are to respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB control number.**

1. Names of Reporting Persons.

**William Leland Edwards**

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 **U.S.A.**

Number of Shares Beneficially Owned by Each Reporting Person With:	5. Sole Voting Power	<b>0</b>
	6. Shared Voting Power	<b>3,014,998</b>
	7. Sole Dispositive Power	<b>0</b>
	8. Shared Dispositive Power	<b>3,014,998</b>

9. Aggregate Amount Beneficially Owned by Each Reporting Person **3,014,998**

10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions) \_\_\_\_\_

11. Percent of Class Represented by Amount in Row (9) **13.3%**

12. Type of Reporting Person (See Instructions) **IN, HC**

1. Names of Reporting Persons.

**Anthony Joonkyoo Yun, MD**

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

(a) \_\_\_\_\_

(b)  X

3. SEC Use Only \_\_\_\_\_

4. Citizenship or Place of Organization **U.S.A.**

Number of Shares Beneficially Owned by Each Reporting Person With:	5. Sole Voting Power	<b>0</b>
	6. Shared Voting Power	<b>3,014,998</b>
	7. Sole Dispositive Power	<b>0</b>
	8. Shared Dispositive Power	<b>3,014,998</b>

9. Aggregate Amount Beneficially Owned by Each Reporting Person **3,014,998**

10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions)

11. Percent of Class Represented by Amount in Row (9) **13.3%**

12. Type of Reporting Person (See Instructions) **IN, HC**

1. Names of Reporting Persons.

**Palo Alto Investors**

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 **California**

Number of Shares Beneficially Owned by Each Reporting Person With:	5. Sole Voting Power	<b>0</b>
	6. Shared Voting Power	<b>3,014,998</b>
	7. Sole Dispositive Power	<b>0</b>
	8. Shared Dispositive Power	<b>3,014,998</b>

9. Aggregate Amount Beneficially Owned by Each Reporting Person **3,014,998**

10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions)

11. Percent of Class Represented by Amount in Row (9) **13.3%**

12. Type of Reporting Person (See Instructions) **CO, HC**

1. Names of Reporting Persons.

**Palo Alto Investors, 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 **California**

Number of Shares Beneficially Owned by Each Reporting Person With:	5. Sole Voting Power	<b>0</b>
	6. Shared Voting Power	<b>3,014,998</b>
	7. Sole Dispositive Power	<b>0</b>
	8. Shared Dispositive Power	<b>3,014,998</b>

9. Aggregate Amount Beneficially Owned by Each Reporting Person **3,014,998**

10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions) \_\_\_\_\_

11. Percent of Class Represented by Amount in Row (9) **13.3%**

12. Type of Reporting Person (See Instructions) **OO, IA**

1. Names of Reporting Persons.

**Palo Alto Healthcare Master Fund, L.P.**

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

(a) \_\_\_\_\_

(b)   X  

3. SEC Use Only \_\_\_\_\_

4. Citizenship or Place of Organization **Cayman Islands**

Number of Shares Beneficially Owned by Each Reporting Person With:	5. Sole Voting Power	<b>0</b>
	6. Shared Voting Power	<b>1,627,606</b>
	7. Sole Dispositive Power	<b>0</b>
	8. Shared Dispositive Power	<b>1,627,606</b>

9. Aggregate Amount Beneficially Owned by Each Reporting Person **1,627,606**

10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions) \_\_\_\_\_

11. Percent of Class Represented by Amount in Row (9) **6.7%**

12. Type of Reporting Person (See Instructions) **PN**

1. Names of Reporting Persons.

**Palo Alto Healthcare Fund, L.P.**

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

(a) \_\_\_\_\_

(b)   X  

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	<b>0</b>
	6. Shared Voting Power	<b>1,204,917</b>
	7. Sole Dispositive Power	<b>0</b>
	8. Shared Dispositive Power	<b>1,204,917</b>

9. Aggregate Amount Beneficially Owned by Each Reporting Person **1,204,917**

10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions) \_\_\_\_\_

11. Percent of Class Represented by Amount in Row (9) **5.3%**

12. Type of Reporting Person (See Instructions) **PN**

**Item 1.**

- (a) Name of Issuer

**Amicus Therapeutics, Inc.**

—

- (b) Address of Issuer's Principal Executive Offices

**6 Cedar Brook Drive, Cranbury, NJ 08512**

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**Item 2.**

- (a) The names of the persons filing this statement are:

**Palo Alto Investors, LLC ("PAI")**

—

**Palo Alto Investors**

—

**William Leland Edwards**

—

**Anthony Joonkyoo Yun, MD**

—

**Palo Alto Healthcare Master Fund, L.P. ("Healthcare Master")**

—

**Palo Alto Healthcare Fund, L.P. ("Healthcare")**

—

(collectively, the "Filers").

- (b) The principal business office of the Filers except Healthcare Master is located at:

**470 University Avenue, Palo Alto, CA 94301**

The principal business address of Healthcare Master is:

**c/o Citco Fund Services (Bermuda) Limited**

**Washington Mall West, 2nd Floor**

**7 Reid Street**

**Hamilton HM 11**

**Bermuda**

- (c) For citizenship of Filers, see Item 4 of the cover sheet for each Filer.

- (d) This statement relates to shares of Common Stock of the Issuer (the "Stock").

- (e) The CUSIP number of the Issuer is: **03152W109**



**Item 3. If this statement is filed pursuant to rule 240.13d-1(b) or 240.13d-2(b) or (c), check whether the person filing is a:**

- (a)  Broker or dealer registered under section 15 of the Act (15 U.S.C. 78o).
- (b)  Bank as defined in section 3(a)(6) of the Act (15 U.S.C. 78c).
- (c)  Insurance company as defined in section 3(a)(19) of the Act (15 U.S.C. 78c).
- (d)  Investment company registered under section 8 of the Investment Company Act of 1940 (15 U.S.C. 80a-8).
- (e)  An investment adviser in accordance with section 240.13d-1(b)(1)(ii)(E) (as to PAI).
- (f)  An employee benefit plan or endowment fund in accordance with section 240.13d-1(b)(1)(ii)(F).
- (g)  A parent holding company or control person in accordance with 240.13d-1(b)(1)(ii)(G) (as to Palo Alto Investors, Mr. Edwards and Dr. Yun).
- (h)  A savings association as defined in section 3(b) of the Federal Deposit Insurance Act (12 U.S.C. 1813).
- (i)  A church plan that is excluded from the definition of an investment company under section 3(c)(14) of the Investment Company Act of 1940 (15 U.S.C. 80a-3).
- (j)  A non-U.S. institution in accordance with §240.13d-1(b)(ii)(J).
- (k)  Group, in accordance with Rule 13d-1(b)(1)(ii)(K).

If filing as a non-U.S. institution in accordance with §240.13d-1(b)(1)(ii)(J), please specify the type of institution

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**Item 4. Ownership.**

See Items 5-9 and 11 of the cover page for each Filer.

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

If this statement is being filed to report the fact that as of the date hereof the reporting person has ceased to be the beneficial owner of more than five percent of the class of securities, check the following .

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

PAI is a registered investment adviser and is the general partner and investment adviser of Healthcare Master and other investment limited partnerships, and is the investment adviser to other investment funds. PAI's clients have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, the Stock. No individual client, other than Healthcare Master and Healthcare separately hold more than five percent of the outstanding Stock.

**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.**

Palo Alto Investors is the manager of PAI. Mr. Edwards is the controlling shareholder of Palo Alto Investors. Dr. Yun is the President of PAI and Palo Alto Investors. The Filers are filing this Schedule 13G jointly, but not as members of a group, and each of them expressly disclaims membership in a group. Each of PAI, Palo Alto Investors, Mr. Edwards and Dr. Yun disclaims beneficial ownership of the Stock except to the extent of that Filer's pecuniary interest therein. In addition, the filing of this Schedule 13G on behalf of Healthcare Master and Healthcare should not be construed as an admission that they are, and they disclaim that they are, beneficial owners, as defined in Rule 13d-3 under the Securities Exchange Act of 1934, of any of the Stock covered by this Schedule 13G.

**Item 9. Notice of Dissolution of Group**

Not applicable.

**Item 10. Certification.**

**Certification of PAI, Palo Alto Investors, Mr. Edwards and Dr. Yun:**

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were acquired and are 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.

**Certification of Healthcare Master and Healthcare:**

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above 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.

**Exhibits**

Exhibit A Joint Filing Agreement.

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: February 13, 2009

**PALO ALTO INVESTORS**

**PALO ALTO INVESTORS, LLC**

By:

Mark Shamia, Chief Operating Officer

**PALO ALTO HEALTHCARE MASTER FUND, L.P.**

By: Palo Alto Investors, LLC, General Partner

By: Palo Alto Investors, Manager

By:

Mark Shamia, Chief Operating Officer

By:

Mark Shamia, Chief Operating Officer

**PALO ALTO HEALTHCARE FUND,  
L.P.**

By: Palo Alto Investors, LLC, General  
Partner

By: Palo Alto Investors, Manager

By:

Mark Shamia, Chief Operating  
Officer

William L. Edwards

Anthony Joonkyoo Yun, MD

EXHIBIT A

AGREEMENT REGARDING JOINT FILING  
OF STATEMENT ON SCHEDULE 13D OR 13G

The undersigned agree to file jointly with the Securities and Exchange Commission (the "SEC") any and all statements on Schedule 13D or Schedule 13G (and any amendments or supplements thereto) required under section 13(d) of the Securities Exchange Act of 1934, as amended, in connection with purchases and sales by the undersigned of the securities of any issuer until such time as the undersigned file with the SEC a statement terminating this Agreement Regarding Joint Filing of Statement on Schedule 13D or 13G. For that purpose, the undersigned hereby constitute and appoint Palo Alto Investors, LLC, a California limited liability company, as their true and lawful agent and attorney-in-fact, with full power and authority for and on behalf of the undersigned to prepare or cause to be prepared, sign, file with the SEC and furnish to any other person all certificates, instruments, agreements and documents necessary to comply with section 13(d) and section 16(a) of the Securities Exchange Act of 1934, as amended, in connection with said purchases and sales, and to do and perform every act necessary and proper to be done incident to the exercise of the foregoing power, as fully as the undersigned might or could do if personally present, until such time as the undersigned file with the SEC a statement terminating this Agreement Regarding Joint Filing of Statement on Schedule 13D or 13G.

Dated: February 13, 2009

**PALO ALTO INVESTORS**

**PALO ALTO INVESTORS, LLC**

By: Mark Shamia, Chief Operating Officer  
**PALO ALTO HEALTHCARE MASTER FUND, L.P.**  
By: Palo Alto Investors, LLC, General Partner  
By: Palo Alto Investors, Manager  
By: Mark Shamia, Chief Operating Officer

By: Mark Shamia, Chief Operating Officer  
**PALO ALTO HEALTHCAR FUND, L.P.**  
By: Palo Alto Investors, LLC, General Partner  
By: Palo Alto Investors, Manager  
By: \_\_\_\_\_  
Mark Shamia, Chief Operating Officer

William L. Edwards

Anthony Joonkyoo Yun, MD