

**SECURITIES AND EXCHANGE COMMISSION**

**Washington, D.C. 20549**

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**SCHEDULE 13G**

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

**ISIS PHARMACEUTICALS INC.**

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(Name of Issuer)

COMMON STOCK

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(Title of Class of Securities)

464330109

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(CUSIP Number)

December 31, 2010

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(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 disclosures provided in a prior cover page.

The information required on the remainder of this 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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<b>1</b>	NAMES OF REPORTING PERSONS I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY):  Columbia Wanger Asset Management, LLC 04-3519872	
<b>2</b>	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (SEE INSTRUCTIONS)  (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
<b>3</b>	SEC USE ONLY	
<b>4</b>	CITIZENSHIP OR PLACE OF ORGANIZATION  Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	<b>5</b>	SOLE VOTING POWER  5,629,000
	<b>6</b>	SHARED VOTING POWER  0
	<b>7</b>	SOLE DISPOSITIVE POWER  6,166,000
	<b>8</b>	SHARED DISPOSITIVE POWER  0
<b>9</b>	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  6,166,000	
<b>10</b>	CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS)  <input type="checkbox"/>	
<b>11</b>	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)  6.2%	
<b>12</b>	TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)  IA	

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

ISIS Pharmaceuticals Inc.

**Item 1(b). Address of Issuer's Principal Executive Offices:**

1896 Rutherford Road  
Carlsbad, CA 92008-7326

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

Columbia Wanger Asset Management, LLC

**Item 2(b). Address of Principal Business Office or, if None, Residence:**

227 West Monroe Street, Suite 3000, Chicago, IL 60606.

**Item 2(c). Citizenship:**

Delaware

**Item 2(d). Title of Class of Securities:**

Common Stock

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**Item 2(e). CUSIP Number:**

464330109

**Item 3. If This Statement is Filed Pursuant to Rule 13d-1(b), or 13d-2(b) or (c), Check Whether the Person Filing is a:**

- (a)  Broker or dealer registered under Section 15 of the Exchange Act.
- (b)  Bank as defined in Section 3(a)(6) of the Exchange Act.
- (c)  Insurance company as defined in Section 3(a)(19) of the Exchange Act.
- (d)  Investment company registered under Section 8 of the Investment Company Act.
- (e)  An investment adviser in accordance with Rule 13d-1(b)(1)(ii)(E).
- (f)  An employee benefit plan or endowment fund in accordance with Rule 13d-1(b)(1)(ii)(F).
- (g)  A parent holding company or control person in accordance with Rule 13d-1(b)(1)(ii)(G).
- (h)  A savings association as defined in Section 3(b) of the Federal Deposit Insurance Act.
- (i)  A church plan that is excluded from the definition of an investment company under Section 3(c)(14) of the Investment Company Act.
- (j)  Group, in accordance with Rule 13d-1(b)(1)(ii)(J).

If this statement is filed pursuant to Rule 13d-1(c), check this box.

**Item 4. Ownership:**

With respect to the beneficial ownership of the reporting person, see Items 5 through 11 of the cover pages to this Schedule 13G, which are incorporated herein by reference.

**Item 5. Ownership of 5 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 or More than Five Percent on Behalf of Another Person:**

The shares reported herein include shares held by Columbia Acorn Trust (CAT), a Massachusetts business trust that is advised by the reporting person. CAT holds 5.1% of the shares of the Issuer.

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**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.

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**Item 10. Certification:**

By signing below each of the undersigned certifies that, to the best of such undersigned's 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 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.

**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 8, 2011

**Columbia Wanger Asset Management, LLC**

By: /s/ Bruce H. Lauer

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Bruce H. Lauer

Chief Operating Officer

**EXHIBIT 99.1 — JOINT FILING AGREEMENT**

The undersigned hereby agree that they are filing this statement jointly pursuant to Rule 13d-1(k)(1). Each of them is responsible for the timely filing of such Schedule 13G and any amendments thereto, and for the completeness and accuracy of the information concerning such person contained therein; but none of them is responsible for the completeness or accuracy of the information concerning the other persons making the filing, unless such person knows or has reason to believe that such information is inaccurate.

In accordance with Rule 13d-1(k)(1) promulgated under the Securities and Exchange Act of 1934, as amended, the undersigned hereby agree to the joint filing with each other on behalf of each of them of to such a statement on Schedule 13G with respect to the common stock of beneficially owned by each of them. This Joint Filing Agreement shall be included as an exhibit to such Schedule 13G.

Dated: February 8, 2011

**Columbia Wanger Asset Management, LLC**

By: /s/ Bruce H. Lauer

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Bruce H. Lauer  
Chief Operating Officer

**Columbia Acorn Trust**

By: /s/ Bruce H. Lauer

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Bruce H. Lauer  
Vice President, Treasurer and Secretary