Isis Reports Financial Results and Highlights for Third Quarter of 2008

November 10, 2008

- Isis ends the third quarter profitable with more than $500 million in cash

- Conference Call Webcast Monday, November 10, 8:30 a.m. EST at http://www.isispharm.com

CARLSBAD, Calif., Nov. 10 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today announced its financial results for the third quarter ended September 30, 2008. Isis' positive net income for the third quarters of 2008 and 2007 was $3.2 million and $20.0 million, respectively, driven primarily by significant revenue in each period from Isis' corporate partnerships. Additionally in the last 15 months, Isis has achieved three quarters of pro forma net income, excluding non-cash stock compensation expense.

"We maintained our financial strength, ending the third quarter profitable, while remaining on track to meet our financial guidance with a net operating loss of less than $15 million for the year on a pro forma basis and year-end cash of at least $450 million. In addition to the three quarters of pro forma net income, over the last 15 months, on a pro forma basis, we have had two quarters of net operating income, with our current quarter having a very small loss at the net operating level. Although we reported another quarter of positive net income, we are not yet at the point of sustainable profitability and our quarter-to-quarter performance will continue to fluctuate based on one-time events. However, these positive financial results reflect how we are able to create significant ongoing revenue and how close the successful execution of our business model has brought us to sustainable profitability, an important goal for Isis," commented B. Lynne Parshall, COO and CFO of Isis.

"Our business model is only achievable because of the speed and productivity of our antisense drug discovery platform, which enables us to build a robust and diverse pipeline of drugs that are attractive to our partners. Our financial strength is driven by the successful execution of our business model, creating valuable partnerships allowing us to move many drugs forward with significant financial and other support from our partners, while keeping our operating expenses low," continued Ms. Parshall.

Upcoming Key Milestones
-- Initiate three trials studying mipomersen in apheresis-eligible patients and high-risk high cholesterol patients
-- Report top line data on mipomersen from a Phase 2 liver imaging study in heterozygous Familial Hypercholesterolemia (FH) patients
-- Provide an update on mipomersen from an ongoing open-label extension study in patients with FH
-- Report Phase 2 study data in type 2 diabetics treated with ISIS 113715 and sulfonylureas
-- Initiate a Phase 1 study on ISIS 333611, Isis' first CNS drug targeting SOD1 for the treatment of ALS
-- Potential acquisition of Ibis by Abbott

Financial Results

For the first nine months of 2008, Isis had a pro forma net operating loss (NOL) of only $4.5 million, excluding compensation expense related to stock options, compared to a pro forma NOL of $23.3 million for the same period in 2007. On a GAAP basis, Isis' loss from operations was $16.3 million and $30.5 million for the first nine months of 2008 and 2007, respectively. The considerable improvement in the Company's financial performance was driven primarily by the significant increase in revenue in 2008 from Isis' corporate partnerships. The strategic alliances that Isis entered into over the past year have strengthened its financial position and have created a continuing revenue base from license fees, augmented by sublicensing fees and milestone payments for these and earlier partnerships.

Revenue

Total revenue for the first nine months of 2008 and 2007 was $86.5 million and $44.9 million, respectively. Isis' revenue almost doubled in 2008 compared to 2007 as a result of Isis' new collaborations including its strategic alliances with Genzyme, Ortho-McNeil and Bristol-Myers Squibb. Also contributing to the increase was the revenue Regulus earned from its strategic alliance with GlaxoSmithKline (GSK). In addition to revenue from its pharmaceutical alliances, Isis' satellite company strategy has made significant contributions to Isis' revenue. For example, in the third quarter of 2007, Isis earned $26.5 million of sublicensing revenue from Alnylam. In 2008, Isis continued to earn substantial revenue from its satellite companies, including $6.1 million in sublicensing revenue from Alnylam and Antisense Therapeutics Limited (ATL).

Operating Expenses

On a pro forma basis, operating expenses for the first nine months of 2008 and 2007 were $91.0 million and $68.2 million, respectively. Isis' pro forma operating expenses were $32.5 million for the three months ended September 30, 2008 and were essentially flat compared to $32.1 million for the three months ended June 30, 2008. The higher year to date expenses in 2008 compared to 2007 were primarily due to increased activity levels related to Isis' planned investment to fill its pipeline and the expansion of its clinical development programs, including increased expenses for manufacturing of drug supplies for Isis' corporate partners and its internal drug development programs, an increase in Ibis' operating expenses to support the growth of its commercial business and the activities to achieve the Abbott milestones, and expenses for Regulus, which began operations in September 2007. On a GAAP basis, Isis' operating expenses for the first nine months of 2008 and 2007 were $102.8 million and $75.4 million, respectively, including non-cash compensation expense related to stock options of $11.8 million and $7.2 million, respectively.

Net Loss and Net Loss Applicable to Common Stock

Isis' net loss for the first nine months of 2008 and 2007 was $3.3 million and $4.0 million, respectively. Isis' net loss in 2008 was significantly lower than 2007 primarily due to a decrease in the Company's loss from operations. Isis' loss applicable to common stock for the first nine months of 2008 and 2007 was $3.3 million or $0.04 per share and $129.3 million or $1.57 per share, respectively. In the third quarter of 2007, Isis purchased the equity of Symphony GenIsis. The $125.3 million on Isis' Statement of Operations in a line item called Excess Purchase Price over Carrying Value of Noncontrolling Interest in Symphony GenIsis, Inc. represented a deemed dividend to the previous owners of Symphony GenIsis. This deemed dividend only impacted Isis' net loss applicable to common stock and its net loss per share calculations for 2007 and does not affect Isis' net income (loss).

Balance Sheet

As of September 30, 2008, Isis had cash, cash equivalents and short-term investments of $512.0 million compared to $193.7 million at December 31, 2007. In 2008, Isis received a significant amount of cash from its partners including:

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-- $325.0 million from Genzyme
-- $40.5 million from Abbott (for its transaction with Ibis)
-- $20.0 million from GSK (for its transaction with Regulus)
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As of September 30, 2008, Isis had consolidated working capital of $411.9 million compared to $145.1 million at December 31, 2007. The cash Isis received in the first half of 2008 primarily led to the increase in Isis' consolidated working capital, offset by $68.9 million of deferred revenue from Genzyme and GSK that is included in current liabilities.

Based on Isis' existing and committed cash, not including the cash Isis could receive from Abbott if Abbott completes its purchase of Ibis, Isis remains on track to meet its cash guidance with a 2008 year end cash balance greater than $450 million, which is sufficient to fund the activities of the Company for at least five years.

Ibis Biosciences, Inc.

Ibis' revenue for the first nine months of 2008 and 2007 was $9.0 million and $8.1 million, respectively. The increase in Ibis' year to date 2008 revenue compared to the same period in 2007 was primarily a result of the government contracts awarded in late 2007 and 2008 and the increased number of Ibis' T5000(TM) Biosensor System placements. So far in 2008, Ibis has been awarded up to $11.6 million of new contracts that support Ibis' continued revenue growth by expanding the applications for the Ibis T5000 Biosensor System. Ibis' revenue in 2008 also included revenue from the distribution agreement Ibis and Abbott entered into in March 2008.

Excluding non-cash compensation expense related to stock options, operating expenses for Ibis were $22.4 million and $14.1 million for the first nine months of 2008 and 2007, respectively. The increase in operating expenses primarily reflects an increase in costs to support the growth of Ibis' commercial business and the costs to achieve milestones as part of the Abbott transaction. Ibis generated a loss from operations, excluding non-cash compensation expense related to stock options, of $13.4 million and $6.0 million for the first nine months of 2008 and 2007, respectively.

Regulus Therapeutics LLC

Regulus' revenue for the first nine months of 2008 and 2007 was $1.4 million and $41,000, respectively. The increase was primarily related to revenue from its collaboration with GSK.

Excluding non-cash compensation expense related to stock options, operating expenses for Regulus were $4.5 million and $49,000 for the first nine months of 2008 and 2007, respectively. With the strategic alliance with GSK, it is anticipated that Regulus' expenses will increase over its run rate to date in 2008 as Regulus advances its research and development activities. Regulus generated a loss from operations, excluding non-cash compensation expense related to stock options, of $3.1 million and $8,000 for the first nine months of 2008 and 2007, respectively.

Quarterly Highlights

"We have had a very successful year financially and in the advancement of the drugs in our pipeline with many milestones to look forward to, including the initiation of three additional trials studying mipomersen," continued Ms. Parshall. "Together with Genzyme, we completed enrollment in a pivotal Phase 3 mipomersen study and initiated a second Phase 3 mipomersen study. Tonight data will be presented by two of the investigators conducting clinical studies on mipomersen, including top line data from an ongoing Phase 2 study showing that mipomersen did not cause steatosis or fatty liver. Additionally, we will provide an update on our open-label extension study where we have patients who have been exposed to mipomersen from three to 23 months with a median continuous exposure of 16 months."

"Building on the success of mipomersen, we have bolstered our cardiovascular franchise with the addition of a new drug targeting PCSK9 and the initiation of clinical trials on our CRP inhibitor. This year we and our partners have presented encouraging Phase 2 data on our antisense drugs in cardiovascular disease, cancer and multiple sclerosis, advanced two new drugs into the pipeline and initiated clinical studies on two exciting antisense drugs. We continue to make progress in every element of our business and look forward to another strong year in 2009," concluded Ms. Parshall.

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Cardiovascular Program
-- Initiated a Phase 3 mipomersen study in heterozygous FH subjects with
   coronary artery disease
-- Completed enrollment of the pivotal Phase 3 mipomersen study in
   homozygous FH subjects
-- Granted broad patent coverage for the therapeutic use of antisense
   compounds targeting apolipoprotein B, U.S. Patent No. 7,407,943
   entitled "Antisense modulation of apolipoprotein B expression"
-- Initiated a Phase 1 study of ISIS 353512, an antisense drug that
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targets C-reactive protein

Other Drug Programs
-- ATL and Teva Pharmaceutical Industries Ltd. reported encouraging Phase 2 results for ATL/TV1102 at the World Congress on Treatment and Research in Multiple Sclerosis
-- Atlantic Healthcare received U.S. orphan drug designation for alicaforsen for the treatment of pouchitis
-- Excaliard Pharmaceuticals, Inc. selected a development compound, EXC001, for the local treatment of fibrosis and scarring
-- iCo Therapeutics Inc. reported interim data from an ongoing Phase 1 study of iCo-007 in patients with diffuse diabetic macular edema that showed that iCo-007 appears to be well tolerated
-- OncoGenex Pharmaceuticals Inc. was granted Fast Track Designation from the U.S. Food & Drug Administration (FDA) for OGX-011 in combination with docetaxel for progressive metastatic prostate cancer
-- OncoGenex Pharmaceuticals Inc. reached an agreement with the FDA on the design of a Phase 3 registration trial of OGX-011 in patients with hormone refractory prostate cancer, via the Special Protocol Assessment process

Ibis Biosciences
-- Received an additional $20 million investment from Abbott in June 2008 for a total investment of $40 million and 18.6 percent equity in Ibis, retaining Abbott's exclusive option to purchase the remaining equity in Ibis
-- Awarded up to $8.4 million in government grants and contracts to fund the expansion of applications of the Ibis technology
-- Presented seven research studies highlighting the power of the Ibis T5000 to rapidly and accurately detect and characterize pathogens at the International Conference on Antimicrobial Agents and Chemotherapy (ICAAC) and the Annual Infectious Disease Society of America
-- Provided development plan for the next-generation instrument platform, which will build upon Ibis' current technology and be tailored for use in a clinical diagnostic setting

Regulus Therapeutics (microRNA Joint Venture)
-- Published research in Molecular and Cellular Biology demonstrating that the microRNA, miR-21, plays a key role in the regulation of certain cancer cells, including an aggressive form of brain cancer
-- Published research in Cancer Cell showing that the microRNA, miR-296, is involved in promoting the formation of new blood vessels in cancer cells
-- Added Stelios Papadopoulos to its Board of Directors and appointed Garry Menzel as Executive Vice President

Additional Highlights
-- Granted patents that significantly expand the scope of Isis' "Crooke" patent estate. U.S. Patent No. 7,432,250 and U.S. Patent No. 7,432,249 add broad claims that cover RNA-based product compositions and methods of treatment

Conference Call

At 8:30 a.m. Eastern Time today, November 10, Isis will conduct a live webcast conference call to discuss this earnings release and related activities. Interested parties may access the webcast at http://www.isispharm.com or listen to the call by dialing 877-795-3604. A webcast replay will be available for a limited time at the same address.

About Isis Pharmaceuticals, Inc.

Isis is exploiting its expertise in RNA to discover and develop novel drugs for its product pipeline and for its partners. The Company has successfully commercialized the world's first antisense drug and has 19 drugs in development. Isis' drug development programs are focused on treating

cardiovascular and metabolic diseases. Isis' partners are developing antisense drugs invented by Isis to treat a wide variety of diseases. Ibis Biosciences, Inc., Isis' majority-owned subsidiary, is developing and commercializing the Ibis T5000(TM) Biosensor System, a revolutionary system to identify infectious organisms. Isis is a joint owner of Regulus Therapeutics LLC, a joint venture focused on the discovery, development and commercialization of microRNA therapeutics. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of over 1,500 issued patents worldwide. Additional information about Isis is available at http://www.isispharm.com.

This press release includes forward-looking statements regarding Isis Pharmaceuticals' business, the financial position and outlook for Isis as well as its Ibis Biosciences subsidiary and its Regulus joint venture, and the therapeutic and commercial potential of the Company's technologies and products in development. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as Isis' goals or projections. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, in developing and commercializing systems to identify infectious organisms that are effective and commercially attractive, and in the endeavor of building a business around such products. Isis' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Isis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Isis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' programs are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2007, and its most recent quarterly report on Form 10-Q, which are on file with the SEC. Copies of these and other documents are available from the Company.

In this press release, unless the context requires otherwise, "Isis," "Company," "we," "our," and "us" refers to Isis Pharmaceuticals and its subsidiaries and joint venture.

ISIS PHARMACEUTICALS, INC.
SELECTED FINANCIAL INFORMATION

Condensed Consolidated Statements of Operations
(In Thousands, Except Per Share Data)

	Three months ended, September 30,		Nine months ended, September 30,	
	2008	2007	2008	2007
	(unaudited)		(unaudited)	
Revenue:				
Research and development revenue under collaborative agreements	$31,240	$11,921	$78,739	$17,404
Licensing and royalty revenue	975	26,710	7,790	27,489
Total revenue	32,215	38,631	86,529	44,893
Expenses:				
Research and development	31,968	24,296	89,611	64,629
Selling, general and administrative	4,571	4,278	13,206	10,769
Total operating expenses	36,539	28,574	102,817	75,398
Income (loss) from operations	(4,324)	10,057	(16,288)	(30,505)
Other income (expense):				
Investment income	7,546	2,603	13,061	9,058
Interest expense	(1,509)	(1,488)	(4,297)	(6,132)
Gain on investments, net	-	-	-	3,510
Loss on early retirement of debt	-	-	-	(3,212)
Loss attributed to noncontrolling interest in Symphony GenIsis, Inc.	-	8,748	-	23,157
Loss attributed to noncontrolling interest in Regulus Therapeutics LLC	1,208	87	3,056	87
Loss attributed to noncontrolling interest in Ibis Biosciences, Inc.	267	-	1,163	-
Net income (loss)	3,188	20,007	(3,305)	(4,037)
Excess purchase price over carrying value of noncontrolling interest in Symphony GenIsis, Inc.	-	(125,311)	-	(125,311)
Net income (loss) applicable to				

common stock	$3,188	$(105,304)	$(3,305)	$(129,348)
Basic and diluted net income (loss) per share	$0.03	$(1.25)	$(0.04)	$(1.57)
Shares used in computing basic net income (loss) per share	95,863	83,942	93,786	82,650
Shares used in computing diluted net income (loss) per share	100,181	83,942	93,786	82,650

Isis Pharmaceuticals, Inc.
Reconciliation of GAAP to Pro Forma Basis:
Condensed Consolidated Operating Expenses and Loss From Operations
(In Thousands)

	Three months ended, September 30,		Nine months ended, September 30,	
	2008 (unaudited)	2007	2008 (unaudited)	2007
As reported operating expenses according to GAAP	$36,539	$28,574	$102,817	$75,398
Excluding compensation expense related to stock options pursuant to SFAS 123(R)	(4,050)	(2,455)	(11,815)	(7,208)
Pro forma operating expenses	$32,489	$26,119	$91,002	$68,190
As reported income (loss) from operations according to GAAP	$(4,324)	$10,057	$(16,288)	$(30,505)
Excluding compensation expense related to stock options pursuant to SFAS 123(R)	(4,050)	(2,455)	(11,815)	(7,208)
Pro forma income (loss) from operations	$(274)	$12,512	$(4,473)	$(23,297)

Reconciliation of GAAP to Pro Forma Basis

As illustrated in the Selected Financial Information in this press release, pro forma operating expenses and pro forma income (loss) from operations were adjusted from GAAP to exclude compensation expense related to stock options, which are non-cash. Isis has regularly reported non-GAAP measures for operating expenses and income (loss) from operations as pro forma results. These measures are provided as supplementary information and are not a substitute for financial measures calculated in accordance with GAAP. Isis reports these pro forma results to better enable financial statement users to assess and compare its historical performance and project its future operating results and cash flows. Further, the presentation of Isis' pro forma results is consistent with how Isis' management internally evaluates the performance of its operations.

Ibis Biosciences, Inc.
Statements of Operations
(In Thousands)

	Three months ended, September 30,		Nine months ended, September 30,	
	2008 (unaudited)	2007	2008 (unaudited)	2007
Revenue:				
Commercial revenue (1)	$624	$1,049	$2,917	$2,490
Research and development revenue under collaborative agreements	2,128	3,589	6,072	5,615
Total revenue	2,752	4,638	8,989	8,105

Expenses:

Cost of commercial revenue (2) 203 767 1,751 2,004

Research and development 6,313 3,791 16,788 10,002

Selling, general and administrative	1,666	1,328	5,193	3,351
Total operating expenses	8,182	5,886	23,732	15,357
Loss from operations	$(5,430)	$(1,248)	$(14,743)	$(7,252)

(1) Ibis' commercial revenue has been classified as research and

development revenue under collaborative agreements on Isis' condensed

consolidated statement of operations.

(2) Ibis' cost of commercial revenue has been classified as research and

development expenses on Isis' condensed consolidated statement of operations.

Regulus Therapeutics LLC
Statements of Operations
(In Thousands)

	Three months ended, September 30,		Nine months ended, September 30,	
	2008	2007	2008	2007
	(unaudited)		(unaudited)	

Revenue:

Research and development revenue

under collaborative agreements $681 $41 $1,429 $41

Total revenue	681	41	1,429	41

Expenses:

Research and development 2,374 99 5,292 99

General and administrative 517 30 1,328 30

Total operating expenses	2,891	129	6,620	129
Loss from operations	$(2,210)	$(88)	$(5,191)	$(88)

Isis Pharmaceuticals, Inc.
Condensed Consolidated Balance Sheets
(In Thousands)

	September 30, 2008 (unaudited)	December 31, 2007
Assets:		
Cash, cash equivalents and short-term investments	$512,023	$193,719
Other current assets	17,520	13,598
Property, plant and equipment, net	14,019	7,131
Other assets	41,130	44,410

Total assets	$584,692	$258,858
Liabilities, noncontrolling interest and		
stockholders' equity:		
Other current liabilities	17,889	$29,000
Current portion of deferred contract revenue	99,794	33,205
2 5/8% convertible subordinated notes	162,500	162,500
Long-term obligations, less current portion	5,478	362
Long-term deferred contract revenue	191,279	23,548
Noncontrolling interest in Regulus Therapeutics LLC	6,315	9,371
Noncontrolling interest in Ibis Biosciences, Inc.	33,359	-
Stockholders' equity	68,078	872
Total liabilities, noncontrolling interest		
and stockholders' equity	$584,692	$258,858

SOURCE Isis Pharmaceuticals, Inc.
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(ISIS)

CO: Isis Pharmaceuticals, Inc.; Ibis Biosciences, Inc.; Regulus Therapeutics LLC
ST: California
IN: HEA MTC BIO
SU: ERN CCA

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