Isis Pharmaceuticals Reports Financial Results and Highlights for the Year 2002

February 11, 2003

Company Achieves Record Revenues in 2002

CARLSBAD, Calif., Feb. 11 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS), today announced its financial results for the year ended December 31, 2002. The company reported revenue of $80.2 million in 2002 compared to $53.3 million in 2001, an increase of 51%. The company's loss from operations for 2002 was $50.8 million compared to $46.1 million in 2001, according to generally accepted accounting principles (GAAP). On a proforma basis the company's loss from operations for 2002 was $52.4 million, which is adjusted from GAAP to exclude the non-cash compensation benefit of $3.0 million and restructuring charges of $1.4 million. This compares to a proforma loss from operations in 2001 of $41.5 million, which excludes $4.6 million in non-cash compensation expense.

The company's revenue for the quarter and year ended December 31, 2002, was $21.9 million and $80.2 million, respectively, compared to $21.7 million and $53.3 million, respectively, for the same periods in 2001. The fluctuation in revenue from quarter-to-quarter reflects timing differences associated with recognition of revenue from corporate collaborations, rather than trends. The increase in revenue for the year was primarily due to the company's collaboration with Eli Lilly and Company and its success in attracting a variety of additional new partners and technology licensees.

Operating expenses for the quarter and year ended December 31, 2002 were $33.1 million and $131.0 million, respectively, compared with $29.4 million and $99.4 million for the same periods in 2001. The increase was primarily a result of increased research and development activity due to the company's investment in its 13 products in development, including costs for the on-going Phase III trial of Affinitak™ and two Phase III trials for alicaforsen (ISIS 2302) in Crohn's disease, as well as costs of increased research efforts to support the collaboration with Lilly.

The operating expenses for the quarters and years ended December 31, 2002 and 2001 included non-cash compensation related to variable stock options. During 2002, the company reversed approximately $3.0 million in compensation expense related to variable stock options due to the decrease in Isis' stock price in 2002 compared to the price in 2001. In comparison, Isis expensed $4.6 million related to variable stock options for the year ended December 31, 2001. In November 2002, Isis recorded a one-time restructuring charge of $1.4 million related to the termination of the GeneTrove™ database product, which resulted in a reduction in its workforce of 25 people and a write-down of certain intellectual property. There were no restructuring charges in 2001.

The company's net loss applicable to common stock for the quarter and year ended December 31, 2002 was $16.0 million, or $0.29 per share and $73.3 million, or $1.35 per share, respectively, compared with $16.0 million, or $0.31 per share, and $75.1 million, or $1.70 per share, for the same periods in 2001. Shares used in computing basic and diluted net loss per share for the quarter and the year ended December 31, 2002 were 55.2 million and 54.5 million, respectively, compared to 51.8 million and 44.1 million for the same periods in 2001. Isis' net loss for the quarter and year ended December 31, 2002 included $2.8 million and $16.0 million, respectively, for Isis' equity in loss of affiliates, compared to $5.5 million and $18.8 million, for the same period of 2001. This decrease reflects Isis' previously announced reacquisition of ISIS 14803 for hepatitis C virus from HepaSense™, the company's joint venture with Elan Corporation, plc. Additionally during 2002, Isis recorded a one-time net gain of $2.7 million on the prepayment of its high interest debt.

The company ended 2002 with $289.4 million in cash and short-term investments and $244.2 million in working capital, compared to $312.0 million in cash and short-term investments and $280.6 million in working capital at the end of December 2001. The decrease in the company's cash balances was the result of day-to-day operating expenses and the prepayment of $74.0 million and $19.7 million of debt in the second and third quarters of 2002, respectively, offset by the net proceeds received from the issuance of $125.0 million of convertible notes, and $42.9 million in proceeds from Lilly loans to support the Lilly research collaboration and to construct the Affinitak manufacturing facility. At December 31, 2002, the company's liabilities were comprised primarily of the following components:

* $125.0 million of 5.5% convertible notes, due 2009, convertible by holder at $16.625
* $47.5 million in drawdowns from the interest-free loan from Lilly for the research collaboration, payable in cash or stock at $40 per share at Isis' option in 2005
* $31.0 million in other corporate partner loans, repayable in cash or stock at Isis' option
* $15.4 million in drawdowns from the Lilly construction loan for the Affinitak manufacturing facility, payable with Affinitak success milestones or other product-related cash inflows
* $10.5 million in ordinary corporate debt, primarily related to facilities and equipment financing

"In 2002 we successfully strengthened our financial position through the preservation of a significant cash balance and the prudent management of our debt. We ended the year with $289 million in cash, even as we continued the aggressive development of our pipeline of 13 products. We reduced future cash outflows by retiring nearly $95 million in expensive debt with proceeds from the issuance of 5.5% convertible notes. As a result, we have a net savings of nearly $40 million in total future interest payments," said B. Lynne Parshall, Isis' Executive Vice President and CFO.

"Throughout 2002 we continued to generate revenue from a variety of sources, including new and existing collaborations, the expansion of partnerships, licensing of intellectual property and the achievement of milestones," stated Ms. Parshall. "In September 2002, Lilly selected Isis to be the commercial manufacturer of launch supplies of Affinitak, a transaction that is of significant value to us. We have already completed the expansion of our manufacturing facility, and we plan to begin manufacturing drug for Lilly in the first quarter of 2003. These activities will be reflected on our P&L

in the coming quarters and we expect them to be an important source of revenue in the coming year, particularly if the results of the Phase III trial of Affinitak in patients with non-small cell lung cancer are positive."

"We will provide financial guidance for 2003 following the announcement of the Affinitak Phase III trial outcome," continued Ms. Parshall. "Based on our current financial strength, we believe we are well-positioned to advance the development of our large and growing pipeline of antisense drugs. We are committed to our goal of establishing antisense as a new sector of the pharmaceutical industry to bring value to patients and shareholders."

Isis' 2002 Highlights

Strengthened Financial Position

In 2002 Isis took the following actions which had the cumulative effect of decreasing future interest payments by a net of $40.0 million:

- Completed a private placement of $125.0 million of 5.5% Convertible Subordinated Notes. The notes are convertible into shares of Isis Common Stock at a conversion price of $16.625 per share and are due May 1, 2009.
- With a portion of the proceeds from the 5.5% Notes:
  - Retired high-interest debt, the 14% Senior Subordinated Notes. The total amount of this debt, including principal plus interest, was approximately $74.0 million. This transaction saved Isis approximately $50.0 million in future interest payments.
  - Prepaid $19.7 million in 12% convertible debt held by Elan with $14.7 million in cash. This transaction saved Isis $12.3 million in future interest and allowed the company to avoid 2.2 million shares of potential dilution over the remaining life of the debt.
- Hybridon and Isis cancelled the remaining reciprocal financial obligations related to the Collaboration and License Agreement entered into in May 2001. For Isis, the transaction eliminated $4.5 million of debt and future shareholder dilution.

Advanced Antisense Drug Discovery

- Advanced the broad antisense drug discovery program with Lilly. To date for the GeneTrove portion of the collaboration, Isis has delivered antisense inhibitors to more than 225 different gene targets. Several genes have been validated as drug targets by the partnership. These genes, which span multiple therapeutic areas, have advanced into antisense drug discovery.
- Expanded the Lilly research collaboration to include select targets in cancer
- Expanded therapeutic potential of antisense technology to cardiovascular disease as demonstrated by data presented on the lipid-regulating target ApoB-100
- Achieved a milestone in the Amgen antisense drug discovery collaboration

Advanced Antisense Drug Development

- Completed enrollment of the 600-patient Phase III Affinitak trial
- Announced positive clinical data from five Phase II programs:
  - In pancreatic cancer, with ISIS 2503
  - In hepatitis C, with ISIS 14803
  - In Crohn's disease with alicaforsen (ISIS 2302)
  - In psoriasis with alicaforsen (ISIS 2302)
  - In non-small cell lung cancer with Affinitak
- Initiated five new clinical trials:
  - Phase III European study of alicaforsen (ISIS 2302) in Crohn's disease: 150 patients
  - Phase II, pivotal-quality study of alicaforsen (ISIS 2302) in ulcerative colitis (UC): 170 patients
  - Phase II trial of ISIS 104838 in rheumatoid arthritis: 160 patients

  * Phase II trial of ISIS 14803 in hepatitis C: 40 patients
  * Phase I trial of OGX-011 in prostate cancer: 30 patients
- Announced positive data of capsule form of ISIS 104838, which demonstrates that antisense drugs can be administered in oral solid form for the first time in human clinical trials
- Progressed in multiple partnerships:
  * Expanded Lilly antisense alliance to include new Affinitak manufacturing agreement and collaboration to discover cancer treatments
  * Achieved a $3.75 million development milestone in HepaSense joint venture with Elan
  * Extended hepatitis C drug discovery collaboration with Merck & Co., Inc. for a second time
- Reacquired rights to ISIS 14803 for hepatitis C as a result of the conclusion of the HepaSense collaboration with Elan

Established New Partnerships for Divisions: GeneTrove and Ibis Therapeutics™

- Initiated GeneTrove collaborations with GlaxoSmithKline, Merck, Pharmacia Corporation, and Amgen
- Licensed patents to Eyetech Pharmaceuticals, Inc. necessary to make, develop and commercialize EYE001, a non-antisense compound for the treatment of ophthalmic diseases
- Awarded $2.4 million three-year contract from U.S. Army Medical Research Institute of Infectious Disease (USAMRIID) to advance Ibis Therapeutics' antibacterial drug discovery program

Strengthened Intellectual Property Estate

- Received grant of 1000th U.S. patent, affirming Isis' position as the leader in antisense technology. As of the date of this release, Isis has nearly 1,200 issued U.S. patents
- Expanded gene-related intellectual property estate to 200 patents
- Received grant of a key U.S. patent covering second-generation antisense
- Settled, on favorable terms to Isis, patent infringement lawsuit against Sequitur, Inc.

Recent Events

- Conclusion of Elan's funding of and scientific participation in the Orasense™ research collaboration at the end of the year in accordance with the terms of the agreement
- Completion of target validation agreement with Pfizer, in which Pfizer obtained access to Isis' antisense inhibitors and acquired a license to specific patents within Isis' intellectual property estate for use in its internal antisense-based functional genomics program
- Completion of functional genomics intellectual property license agreement with atugen
- Achievement of second milestone in Amgen antisense drug discovery collaboration

"In the past two years, Isis has reported positive study results from a total of nine Phase II clinical programs. These data demonstrate antisense drug activity across multiple diseases and multiple formulations," said Stanley T. Crooke, Isis' Chairman and CEO. "We have the opportunity to add to the evidence of antisense clinical activity in 2003, as we have a very full drug development agenda. Most notably, Lilly and we plan to report data from the first Phase III trial of Affinitak in March. We also expect to have results from studies of antisense drugs in the treatment of rheumatoid arthritis, ulcerative colitis/pouchitis and multiple cancer indications. With two Phase III programs, six compounds in Phase II development and more than a decade of experience with antisense technology, Isis is poised to bring this revolutionary technology to its potential."

Isis' 2003 Goals

- Report Phase III trial results of Affinitak in non-small cell lung cancer
- Complete enrollment of two Phase III trials of alicaforsen in Crohn's disease
- Report results of several Phase II trials of antisense drugs, including studies for the treatment of UC/pouchitis, rheumatoid arthritis and multiple cancer indications
- Initiate Phase I trials of at least one preclinical drug
- Add compound to development pipeline
- File IND to support Phase II trials in oral formulations program
- Maintain strong cash position

Webcast Conference Call

Isis will conduct a live webcast conference call to discuss this news on Tuesday, February 11 at 10 a.m. Eastern time. To participate over the Internet go to www.isispharm.com . A replay of the webcast will be available at this address for up to 30 days.

Isis Pharmaceuticals, Inc. is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs. The company has commercialized its first product, Vitravene® (formivirsen), to treat CMV-induced retinitis in AIDS patients. In addition, Isis has 13 antisense products in its development pipeline, with two in late-stage development and six in Phase II human clinical trials. Affinitak™ (formerly called LY900003 and ISIS 3521), an inhibitor of PKC-alpha, is in Phase III trials for non-small cell lung cancer, and alicaforsen (ISIS 2302), an ICAM-1 inhibitor, is in Phase III human clinical trials for Crohn's disease. Isis has a broad patent estate, as the owner or exclusive licensee of nearly 1,200 issued patents worldwide. Isis' GeneTrove™ division uses antisense to assist pharmaceutical industry partners in validating and prioritizing potential gene targets through customized services. Ibis Therapeutics™ is a division focused on the discovery of small molecule drugs that bind to RNA. Additional information about Isis is available at www.isispharm.com .

This press release includes forward-looking statements concerning the financial position of Isis Pharmaceuticals the therapeutic and commercial potential of compounds developed by the company and the potential value of the company's functional genomics and drug discovery technology platforms. Any statement describing a goal, expectation, intention or belief of the company is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as Isis' 2003 goals within the body of this press release. 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 and financing such activities. Actual results could differ materially from those projected in this press release. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' research and development programs are described in additional detail in the company's Annual Report on Form 10-K and quarterly report on Form 10-Q for the periods ended December 31, 2001 and September 30, 2002, respectively, which are on file with the U.S. Securities and Exchange Commission, copies of which are available from the company.

ISIS PHARMACEUTICALS, INC.
SELECTED FINANCIAL INFORMATION
(In Thousands, Except Per Share Data)
Condensed Statements of Operations

	Three months ended, December 31,		Years ended, December 31,	
	2002	2001	2002	2001
	(Unaudited)			
Revenue:				
Research and development revenues under collaborative				

agreements	$18,240	$15,602	$67,820	$40,396
Research and development revenues from joint ventures	3,508	4,053	11,942	10,561
Licensing revenues	111	2,089	417	2,316
Total revenue	21,859	21,744	80,179	53,273
Expenses:				
Research and development	30,091	24,786	124,074	83,741
General and administrative	1,632	3,136	8,547	11,061
Compensation (benefit) related to stock options	9	1,519	(3,002)	4,573
Restructuring activities	1,373	--	1,373	--
Total operating expenses	33,105	29,441	130,992	99,375
Loss from operations	(11,246)	(7,697)	(50,813)	(46,102)
Equity in loss of affiliates	(2,831)	(5,540)	(16,011)	(18,840)
Investment and other income	2,219	1,720	8,462	6,358
Interest expense	(3,971)	(4,108)	(16,562)	(15,248)
Loss on repayment of debt	--	--	(2,294)	--
Gain on repayment of debt	--	--	4,976	--
Net loss	(15,829)	(15,625)	(72,242)	(73,832)
Accretion of dividends on preferred stock	(168)	(331)	(1,060)	(1,299)
Net loss applicable to common stock	$(15,997)	$(15,956)	$(73,302)	$(75,131)
Basic and diluted net loss per share	$(0.29)	$(0.31)	$(1.35)	$(1.70)
Shares used in computing basic and diluted net loss per share	55,155	51,799	54,480	44,109

Condensed Balance Sheets
(In Thousands)

	December 31, 2002	December 31, 2001
Assets:		
Current assets	$320,180	$328,816
Property, plant and equipment, net	59,094	28,245
Other assets	59,409	60,000
Total assets	$438,683	$417,061
Liabilities and stockholders' equity:		
Current liabilities	$75,950	$48,247
5.5% Convertible subordinated notes	125,000	--
Long-term obligations, net of current portion	67,893	125,710
Long-term deferred revenue, net of current portion	14,363	20,005
Stockholders' equity	155,477	223,099
Total liabilities and stockholders' equity	$438,683	$417,061

SOURCE Isis Pharmaceuticals, Inc.