Isis Pharmaceuticals Reports Third Quarter And Year-To-Date 2002 Financial Results

November 6, 2002

CARLSBAD, Calif., Nov. 6 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS), today announced financial results for the three month and nine month periods ended September 30, 2002, which includes a strong cash position of $292 million, including short-term investments.

Profit and Loss Statement

The company's loss from operations was $39.6 million for the first nine months of 2002, essentially the same as the loss from operations reported for the identical period in 2001.

Revenue for the three and nine months ended September 30, 2002 totaled $20.3 million and $58.3 million, respectively, compared with $19.3 million and $31.5 million, respectively, for the same periods in 2001. The 85% increase in revenue year to date was primarily related to the licensing of Isis' Phase III non-small cell lung cancer compound, Affinitac™ (formerly known as LY900003 or ISIS 3521) to Eli Lilly and Company in August 2001 and to the company's success in attracting a variety of new partners and technology licensees. Revenue during the quarter and nine months ended September 30, 2001 included one-time milestone payments of $4.5 million from partners under drug distribution and licensing agreements.

Operating expenses for the three and nine months ended September 30, 2002 totaled $37.8 million and $97.9 million, respectively, compared with $24.0 million and $69.9 million, respectively, for the same periods in 2001. The increase in operating expenses for the quarter and year to date are primarily the result of costs associated with:

-- Affinitac Phase III clinical trials
-- the development of the 12 other antisense products in the company's pipeline, including the expenses related to Phase III trials of alicaforsen (ISIS 2302) in Crohn's disease
-- the company's $100 million, multi-year research collaboration with Lilly. These research costs are funded through an interest-free loan from Lilly, which provides Isis with cash rather than revenue
-- increased gene functionalization and target validation activities in support of the company's numerous GeneTrove collaborations and database developments

Total operating expenses for the quarter ended September 30, 2002 included approximately $95,000 in compensation expense related to stock options accounted for as variable stock options, compared to $1.8 million for the same period in 2001. For the nine months ended September 30, 2002, the company reversed approximately $3.0 million in compensation expense related to variable stock options expensed in prior years due to the decrease in Isis' stock price in the third quarter of 2002. Variable stock options can result in significant non-cash increases and decreases in compensation expense as a result of the variability in the company's stock price. The majority of these options expire at the end of 2002.

The company's loss from operations, adjusted to exclude non-cash compensation expenses, for the third quarter and nine months ended September 30, 2002 was $17.4 million and $42.6 million, respectively. This compares to a loss from operations, adjusted to exclude non-cash compensation expenses, for the same periods in 2001 of $2.9 million and $35.4 million, respectively.

The company's net loss applicable to common stock for the quarter was $17.8 million, or $0.33 per share, compared with a net loss applicable to common stock of $12.6 million, or $0.29 per share, for the same period last year. The increase in net loss applicable to common stock was a result of the increase in loss from operations offset by the $5.0 million gain reported for the prepayment of the company's 12% convertible debt held by Elan Corporation, plc. of Dublin, Ireland. Isis' net loss applicable to common stock for the year to date was $57.3 million, or $1.06 per share, on revenues of $58.3 million, compared with a loss of $59.2 million, or $1.43 per share, on revenues of $31.5 million for the same period of 2001.

Balance Sheet

Isis maintained a strong balance sheet by ending the quarter with $292.0 million in cash and short-term investments and $260.7 million of working capital. At December 31, 2001, Isis had cash and short-term investments of $312.0 million and working capital of $280.6 million. The decrease in cash and short-term investments and in working capital was primarily due to 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 from the issuance in the second quarter of $125.0 million of convertible notes.

In total this year, Isis has retired more than $90 million in debt, eliminating significant future interest expense. In July 2002, the company prepaid $19.7 million of 12% convertible debt held by Elan with $14.7 million in cash, and avoided potential dilution of 2.2 million shares. This prepayment resulted in a gain on prepayment of debt of $5.0 million recognized in the third quarter of 2002. Previously, in May 2002, approximately $74.0 million of the net proceeds from the sale of $125.0 million in convertible notes was used to prepay the company's 14% Senior Subordinated Notes. The prepayment resulted in a loss on prepayment of debt totaling $2.3 million, which was recorded in the second quarter of 2002.

2002 Business and Financial Outlook

GeneTrove™

Isis' GeneTrove division has been successful in providing pharmaceutical industry partners with antisense-based custom target validation services and licenses to antisense technology intellectual property for internal functional genomics activities. The division has been unsuccessful, however, in generating customers for its database product offering. As a result, Isis has terminated the GeneTrove database product offering and reduced its

workforce by approximately 25 people. During the fourth quarter of 2002, Isis will incur a one-time charge of approximately $1.2 million associated with the restructuring. GeneTrove will continue to market its custom target validation services and intellectual property licenses to pharmaceutical industry partners, as these components of the GeneTrove business are both financially and strategically valuable to the company.

"GeneTrove is a very successful venture for Isis, particularly in the custom target validation arena, where we sell the "by-product" of our antisense drug discovery efforts: information about what genes do. The database product offering is not on the critical path for success for Isis, and we have concluded that it will not be sufficiently successful to continue our investment," said B. Lynne Parshall, Isis' Executive Vice President and CFO. "We are cutting expenses related to the database and reorganizing the division to more efficiently support the drug discovery and development of Isis and our partners."

Collaborations

Earlier today, Isis announced that it has regained ownership of ISIS 14803, an antisense drug for the treatment of Hepatitis C. ISIS 14803 is a valuable asset to Isis. In Phase II studies, the drug has demonstrated promising antiviral activity in patients with genotype 1, drug resistant Hepatitis C. Elan has concluded its participation in the HepaSense collaboration as part of its restructuring activities. There is essentially no cash impact to Isis resulting from the conclusion of the collaboration. However, Isis will not receive all of the revenue from HepaSense that the company had projected for 2002.

Financial Outlook

As a result of the favorable reacquisition of ISIS 14803 from Elan and the consequent loss of revenue from HepaSense, and the decision to exit the database business, Isis has adjusted its guidance for loss from operations for 2002 to the low $50 million range, excluding non-cash compensation expenses and the restructuring charge noted above. The company had previously projected a loss from operations for 2002 in the mid $40 million range, excluding non-cash compensation expenses.

"We have recently completed important transactions in Orasense and HepaSense, as well as established a valuable manufacturing relationship with Lilly," said Ms. Parshall. "The company is strengthened by these strategic accomplishments, and by the decision to terminate our database business. We are very excited about the return of ISIS 14803. Although it results in less revenue to Isis, there is no meaningful effect on cash. This event, combined with the lack of sales from the GeneTrove database, causes us to revise our net operating loss guidance for the year. We are pleased with our strong cash position and with the great progress we've made this year in advancing our technology and our pipeline. We are focused on aggressively developing our 13 antisense products to bring increased value to shareholders."

Isis' Third Quarter 2002 and Recent Highlights
Clinical Development

-- Isis will manufacture Affinitac for the product launch period for Lilly. Isis estimates that the agreement has the potential to generate up to $120 million in revenue to Isis over the next three years, if the Affinitac new drug application is successfully submitted to the FDA in 2003, the drug is approved based on positive results from Isis' Phase III study and its market penetration is in line with the company's projections. Under the terms of the agreement, Lilly has provided a loan of approximately $21 million to fund a new manufacturing suite dedicated to Affinitac. The loan to Isis will be repaid with Affinitac success milestones and other product-related cash inflows.

-- Results of an open-label Phase II clinical trial of alicaforsen (ISIS 2302) in patients with Crohn's disease demonstrated that the antisense drug may produce clinical disease remissions when patients receive appropriate doses of the drug. The encouraging findings, where 59% of 22 patients achieved a response and 41% achieved a clinical remission, were presented at the 67th Annual Scientific Meeting of the American College of Gasteroenterology.

-- Clinical investigators reported that ISIS 14803 demonstrated promising antiviral activity by producing up to 3.8 log reductions in plasma virus levels in drug resistant, genotype 1 patients with chronic hepatitis C virus (HCV), according to data from an ongoing Phase II clinical trial presented this week. Six of 17 patients receiving 6 mg/kg of ISIS 14803 twice a week experienced viral titer reductions of 1.0 - 3.8 logs, with three of these patients experiencing a greater than 3.0 log reduction. These data were presented at the 53rd Annual Meeting of the American Association for the Study of Liver Diseases.

-- Isis has regained rights to its antisense drug for Hepatitis C, ISIS 14803, in connection with the termination of its collaboration with Elan related to the HepaSense joint venture. Additionally, Isis and Elan extended their collaboration in the Orasense joint venture through the end of 2002. The focus of Orasense is to develop an oral delivery platform for antisense drugs, and to develop an oral formulation of ISIS 104838, an antisense inhibitor of TNF-alpha, for the treatment of rheumatoid arthritis.

Antisense Research and Drug Discovery

-- Isis achieved a research milestone in its drug discovery collaboration with Amgen and received an associated milestone payment. The milestone was related to research progress in the companies' three year antisense drug discovery collaboration that was initiated in December 2001.

Development of Intellectual Property

-- Isis announced the issuance of its 1000th patent and 200th gene-related patent, marking a significant milestone in the company's history that symbolizes its innovative spirit. The company's patent portfolio broadly covers RNA-based drug discovery and development, including the use of RNA/DNA antisense inhibitors in gene functionalization and target validation and for drug discovery; chemistries; antisense inhibitor designs called "motifs;" methods of use of antisense inhibitors; mechanisms of action by which antisense inhibitors inactivate an RNA target; and manufacturing and analytical methods.
-- Isis announced the settlement of litigation pending against Sequitur, Inc. Isis had sued Sequitur, in three separate lawsuits, for alleged infringement of U.S. Patent Nos. 6,001,653; 6,326,199; 6,096,543; 5,959,097; and 5,958,773. Isis and Sequitur reached a mutually agreeable business resolution that resulted in the dismissal of the three lawsuits and all counterclaims. Isis has granted Sequitur a license to certain Isis patents for target validation and functional genomics using first generation antisense oligonucleotides (also known as phosporothioate and/or phosphodiester deoxy antisense oligonucleotides) in exchange for undisclosed payments from Sequitur.

Strengthened Financial Position

-- Isis prepaid $19.7 million in 12% convertible debt held by Elan with $14.7 million in cash. The transaction saved the company $12.3 million in interest and allowed Isis 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.

Isis will conduct a live webcast conference call to discuss this earnings release today, Wednesday, November 6 at 8:30 a.m. Eastern time. To participate over the Internet go to www.isispharm.com or to http://www.firstcallevents.com/service/ajwz369610280gf12.html . 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® (fomivirsen), 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. Affinitac™ (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 more than 1000 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 contains forward-looking statements concerning the financial position and potential of Isis Pharmaceuticals, the prospects of Affinitac in non-small cell lung cancer, of alicaforsen (ISIS 2302) in Crohn's disease, of ISIS 14803 in Hepatitis C, of the Orasense oral formulations program and of the other drug products being developed by the company, as well as the company's ability to earn up to $120 million in revenues as the manufacturer of Affinitac for Lilly during the launch period 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. 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 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 June 30, 2002, respectively, which are on file with the U.S. Securities and Exchange Commission. Copies of these and other filings are available from the company.

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

	Three months ended September 30,		Nine months ended, September 30,	
	2002	2001	2002	2001
Revenue:				
Research and development revenues under collaborative agreements	$16,977	$16,892	$49,580	$24,795
Research and development revenues from joint ventures	3,313	2,360	8,434	6,508
Licensing revenues	10	52	306	226
Total revenue	20,300	19,304	58,320	31,529
Expenses:				
Research and development	35,470	19,895	93,983	58,954
General and administrative	2,244	2,333	6,915	7,926
Compensation related to stock options	95	1,783	(3,011)	3,054
Total operating expenses	37,809	24,011	97,887	69,934
Loss from operations	(17,509)	(4,707)	(39,567)	(38,405)
Equity in loss of affiliates	(3,454)	(5,142)	(13,180)	(13,300)
Interest income	2,207	1,554	6,243	4,637
Interest expense	(3,796)	(4,022)	(12,591)	(11,139)
Loss on prepayment of 14% Notes	--	--	(2,294)	--
Gain on prepayment of 12% Notes	4,976	--	4,976	--

Net loss	(17,576)	(12,317)	(56,413)	(58,207)
Accretion of dividends on preferred stock	(222)	(326)	(892)	(968)
Net loss applicable to common stock	$(17,798)	$(12,643)	$(57,305)	$(59,175)
Basic and diluted net loss per share	$(0.33)	$(0.29)	$(1.06)	$(1.43)
Shares used in computing basic and diluted net loss per share	54,708	43,869	54,253	41,517

Condensed Balance Sheets
(In Thousands)

September 30, December 31,

	2002 (Unaudited)	2001
Assets:		
Current assets	$319,644	$328,816
Property, plant and equipment, net	47,211	28,245
Other assets	57,669	60,000
Total assets	$424,524	$417,061
Liabilities and stockholders' equity:		
Current liabilities	$58,898	$48,247
Long-term obligations, net of current portion	178,840	125,710
Long-term deferred revenue, net of current portion	16,220	20,005
Stockholders' equity	170,566	223,099
Total liabilities and stockholders' equity	$424,524	$417,061

SOURCE Isis Pharmaceuticals, Inc.