

Isis Pharmaceuticals Continues to Strengthen Balance Sheet by Prepaying \$19.7 Million of 12% Convertible Debt Held By Elan

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Prepayment Reduces Isis' Potential Dilution by 2.2 Million Shares

CARLSBAD, Calif., July 3 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS), announced today the prepayment of \$19.7 million in 12% convertible debt held by Elan Corporation, plc. of Dublin, Ireland with \$14.7 million in cash. Isis will now fund its portion of the ongoing joint venture research and development, rather than accruing additional convertible debt to Elan. The transaction saves Isis \$12.3 million in interest and allows Isis to avoid 2.2 million shares of potential dilution over the remaining life of the debt. The repayment represents a significant portion of the lines of credit extended by Elan to fund Isis' share of expenses in two joint ventures, Orasense™, Ltd. and HepaSense™, Ltd. Isis is an 80.1% owner in each joint venture and Elan owns 19.9%.

"This repayment of convertible debt is financially beneficial to Isis in multiple ways. Using the low-interest proceeds of our recent convertible debt offering, we are retiring high-interest debt. We are able to do this at a 25% discount to our carrying value for the debt. We are eliminating significant future interest expense and the potential for 2.2 million shares of dilution," said B. Lynne Parshall, Isis' Executive Vice President and CFO. "Consistent with the nature of our collaborations, this agreement is mutually attractive to both companies. We are pleased with the progress made by each of our joint ventures, Orasense and HepaSense, and with Elan's contributions to this progress."

Seamus Mulligan, Executive Vice President of Elan Enterprises, remarked "We were pleased to conclude a transaction that is also beneficial to Elan. Had Elan converted the Isis notes at their higher conversion price, as set forth in the original agreements, Elan's proceeds on the sale of the common shares in today's market would have been less."

"The strength of our financial position now enables us to pay for our share of the ongoing research in these ventures, which helps us avoid associated future debt and dilution," stated Ms. Parshall. "This agreement is another example of our focused effort to steadily improve our financial position. Cumulatively in the last two months, we have reduced our high-interest debt by approximately \$94 million, resulting in interest expense savings of about \$62 million over the remaining terms of those liabilities."

Orasense and HepaSense were created in 1999 and 2000, respectively. Orasense is developing a platform technology for the oral delivery of antisense drugs. ISIS 104838, Isis' antisense inhibitor of tumor necrosis factor -- alpha (TNF-alpha), is the first oral drug the joint venture is developing. ISIS 104838 is being developed to treat rheumatoid arthritis and other inflammatory diseases. HepaSense is focused on the development of an antisense drug, ISIS 14803, to treat patients chronically infected with Hepatitis C virus (HCV). The joint ventures have made significant progress in both the creation of oral antisense formulations and the development of ISIS 14803 for HCV, respectively. Each joint venture is completing its original research plan. Isis and Elan are evaluating ways to maximize the value of each joint venture.

Isis will conduct a live webcast conference call to discuss the company's debt retirement progress on Wednesday, July 3, at 10:00 am Eastern time. To participate over the internet go to www.isispharm.com or to <http://www.firstcallevts.com/service/ajwz361322089gf12.html>. A replay of the webcast will be available at the Isis 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 900 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 Isis' plans regarding the retirement of its debt, the financial position of the company, the potential of its joint ventures with Elan, Orasense and HepaSense, the planned development activities and therapeutic potential for our products in our pipeline, and the potential value of the company's functional genomics and drug discovery technology platform. 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, for the year ended December 31, 2001, which is on file with the U.S. Securities and Exchange Commission, copies of which are available from the company.

HepaSense™ is a trademark of HepaSense, Ltd.

Orasense™ is a trademark of Orasense, Ltd.

Vitravene® is a registered trademark of Novartis AG. GeneTrove™ and Ibis Therapeutics™ are trademarks of Isis Pharmaceuticals, Inc.

Affinitac™, a trademark of Eli Lilly and Company, is an investigational cancer compound being developed through an alliance between Lilly and Isis Pharmaceuticals, Inc. and marketed globally by Lilly.

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