Genzyme and Isis Complete Licensing of Mipomersen

June 24, 2008

Conference call to be held today at 10 a.m. EDT

CAMBRIDGE, Mass., and CARLSBAD, Calif., June 24 /PRNewswire-FirstCall/ -- Genzyme Corp. (Nasdaq: GENZ) and Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today announced the finalization of the license and collaboration agreement for mipomersen. The collaboration provides Genzyme with exclusive worldwide rights to mipomersen, a novel lipid-lowering drug discovered and developed by Isis that is in phase 3 clinical development. During the second half of this year, enrollment is expected to be completed in a pivotal study of mipomersen in homozygous familial hypercholesterolemia, and a new trial in apheresis-eligible patients is expected to begin.

As part of the agreement, Isis will receive a $175 million license fee for mipomersen. In February, Isis received a $150 million payment from Genzyme to purchase 5 million shares of Isis common stock at $30 per share.

The companies have updated the deal terms so that Isis will contribute up to $50 million in additional development funding for mipomersen, bringing Isis' development funding commitment up to $125 million. Thereafter Isis and Genzyme will share development costs equally. The initial Isis development funding commitment and the shared funding will end when the program is profitable. In exchange for this additional contribution, Isis has the opportunity to receive $75 million in milestone payments early.

"Mipomersen is an innovative treatment that has the potential to change the standard of care for severely ill patients whose needs cannot be addressed by current cholesterol-lowering therapies," said Henri A. Termeer, Genzyme's chairman and chief executive officer. "This treatment is an important addition to Genzyme's robust late-stage pipeline. We will manage the clinical development of mipomersen within our current R&D budget and financial guidance."

Over the next 30 days, the companies will transition the mipomersen IND and all regulatory authority to Genzyme. As the sponsor of mipomersen, Genzyme will take the lead on discussions with regulatory agencies and filings. In response to guidance received from the FDA, the companies have modified the initial development plan for mipomersen, subject to further discussions with the agency.

The key changes to the plan include:

-- The addition of clinical studies of mipomersen in apheresis-eligible patients.

-- Consolidation of the planned filings for heterozygous FH patients and other high-risk, high cholesterol patients into a single registration in the U.S.

-- Acceleration of the planned outcome study so that it can be used to support the above mentioned consolidated U.S. filing.

"Mipomersen is an important drug that demonstrates the power and precision of antisense drugs. We believe now, as we did in January, that Genzyme is the ideal partner for mipomersen," said Stanley Crooke, Chairman and Chief Executive Officer of Isis. "We will continue to work with Genzyme on a development plan that is responsive to the FDA and other regulatory agencies, and maximizes the value of the drug. In addition, we look forward to exploring new areas of therapeutic opportunity with Genzyme in CNS and certain rare diseases as part of this alliance."

Deal Terms

As a result of the changes in the development plan and consistent with the premise of the transaction in which the companies are sharing the value of mipomersen, the following changes to the original financial terms of the deal have been made:

-- Isis will contribute up to the first $125 million in development funding, reflecting an additional contribution of up to $50 million. Thereafter Isis and Genzyme will share development costs equally. The initial Isis development funding commitment and the shared funding will end when the program is profitable. In exchange for this additional contribution, Isis has the opportunity to receive certain milestone payments early.

-- $75 million of the $150 million milestone associated with the heterozygous FH indication (the portion related to U.S. registration) may be accelerated, to be paid $25 million at annual product revenue of $250 million and $50 million at annual product revenue of $500 million. The $75 million milestone for European approval of the heterozygous FH indication remains the same.

All other financial terms of the transaction remain unchanged. As part of the agreement, Isis will receive a total of $325 million in up-front payments from Genzyme, including the $175 million license fee and the $150 million February 2008 stock purchase.

Isis is eligible to receive up to $750 million in commercial milestone payments, in three increments of $250 million, when annual net revenues meet $3 billion, $4 billion, and $5 billion for two consecutive years.

Isis is also eligible to receive up to $825 million in development and regulatory milestone payments, which are broken out as follows:

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    -- Total milestones related to homozygous FH                $50 million
    -- Total milestones related to heterozygous FH             $150 million
       -$75 million for U.S. approval (may be accelerated
         based on earlier achievement of sales targets)
       -$75 million for E.U. approval

-- Total milestones related to approvals of a first Non-FH indication

                                          $375 million
    -- Total milestones related to approvals of a
follow-on product                                              $250 million
                                                    Total    $825 million
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Isis and Genzyme will allocate responsibility for funding development expenses as described above. Genzyme will be responsible for funding sales and marketing expenses until revenues are sufficient to cover them.

Genzyme and Isis will share mipomersen profits, beginning with a 70/30 Genzyme/Isis split. This split will adjust on a sliding scale, reaching 50/50 when annual revenues reach $2 billion. As part of the strategic relationship, Genzyme will also have preferred access to future Isis drugs for CNS and certain rare diseases.

Mipomersen Development Plan

The initial indication sought for mipomersen will be for patients with homozygous FH, and a phase 3 trial in this patient population is ongoing. A U.S. filing for this indication is expected during the second half of 2010. The companies also plan to study mipomersen's use in other very high risk patient groups, including apheresis-eligible patients. Data from a trial in apheresis-eligible patients is expected before the filing for the initial homozygous FH indication.

LDL apheresis is a blood-filtering procedure that targets "bad" cholesterol, and is indicated for individuals for whom diet and maximum drug therapy has either been ineffective or not tolerated. Specific LDL levels defining apheresis eligibility vary by country. Many patients who are eligible, however, choose not to undergo apheresis due to its negative impact on quality of life. The procedure is painful and inconvenient, requiring patients to go to apheresis centers for treatment once every one to two weeks. Apheresis can cost $75,000 to $150,000 per year.

The trial in apheresis-eligible patients is an important addition to the mipomersen development program. Like homozygous FH patients, apheresis- eligible patients are characterized by extremely high LDL levels and are not able to be managed by existing therapies. There are an estimated 10,000 - 15,000 apheresis-eligible patients in the United States and Europe.

Genzyme and Isis expect to begin three additional trials of mipomersen in high-risk patients during the second half of this year. These trials will include: one for heterozygous FH patients, and two for high-risk, high cholesterol patients. These trials will continue to build the body of clinical evidence around mipomersen's value in managing very high risk patients.

Data from these five trials will also inform the design of the morbidity and mortality outcome study for potential expansion of mipomersen's label to include a larger group of at-risk, high cholesterol patients. In addition to the ongoing discussions with the FDA, plans are underway to engage in discussions with regulatory authorities in Europe, where the development path for mipomersen may differ from that in the U.S.

About Mipomersen

Mipomersen is a second-generation antisense drug that reduces the production of apoB-100, a protein critical to the synthesis and transport of "bad" cholesterol. Mipomersen is currently in phase 3 development for patients with homozygous familial hypercholesterolemia, a disease which creates a greatly increased risk of premature cardiovascular disease (CVD) and CVD-related death. In phase 2 studies, mipomersen, a weekly injectable therapeutic, was observed to reduce cholesterol and other atherogenic lipids beyond reductions achieved with standard lipid-lowering drugs, enabling more patients to achieve LDL-C targets.

About Genzyme

One of the world's leading biotechnology companies, Genzyme is dedicated to making a major positive impact on the lives of

people with serious diseases. Since 1981, the company has grown from a small start-up to a diversified enterprise with more than 10,000 employees in locations spanning the globe and 2007 revenues of $3.8 billion. In 2007, Genzyme was chosen to receive the National Medal of Technology, the highest honor awarded by the President of the United States for technological innovation.

With many established products and services helping patients in nearly 90 countries, Genzyme is a leader in the effort to develop and apply the most advanced technologies in the life sciences. The company's products and services are focused on rare inherited disorders, kidney disease, orthopaedics, cancer, transplant, and diagnostic testing. Genzyme's commitment to innovation continues today with a substantial development program focused on these fields, as well as immune disease, infectious disease, and other areas of unmet medical need.

Genzyme's press releases and other company information are available at http://www.genzyme.com and by calling Genzyme's investor information line at 1-800-905-4369 within the United States or 1-678-999-4572 outside the United States.

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 18 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.

Genzyme Safe Harbor Statement

This press release contains forward-looking statements, including without limitation, statements concerning mipomersen's safety and benefits for patients with high cholesterol, the development plan for mipomersen and FDA's requirements for its approval. These statements are subject to risks and uncertainties that could cause actual results to differ materially from those forecasted. These risks and uncertainties include, among others: the timing of further discussions with FDA regarding the approval of mipomersen; the timing and content of submissions to and decisions made by the FDA relating to mipomersen; further analysis of clinical trial data; the results of other studies; the actual efficacy and safety of mipomersen; and the risks and uncertainties described in Genzyme's SEC reports filed under the Securities Exchange Act of 1934, including the factors discussed under the caption "Risk Factors" in Genzyme's Quarterly Report on Form 10-Q for the quarter ended March 31, 2008. Genzyme cautions investors not to place substantial reliance on the forward-looking statements contained in this press release. These statements speak only as of today's date and Genzyme undertakes no obligation to update or revise the statements.

Isis Safe Harbor Statement

This press release includes forward-looking statements regarding Isis' collaboration with Genzyme Corporation, its financial and business development activities, and the development, activity, therapeutic potential and safety of mipomersen in treating patients with high cholesterol. 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 quarterly report on Form 10-Q for the quarter ended March 31, 2008, which are on file with the SEC. Copies of these and other documents are available from the Company.

Conference Call Information

Genzyme will host a conference call with Isis today at 10:00 a.m. Eastern. To participate in the call, please dial 1-210-234-0010 and use passcode "Genzyme." The replay number for the call is 1-203-369-0239, and the replay will be available until midnight on July 1. Today's call will also be Webcast on the investor events section of http://www.genzyme.com.

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