Antisense Therapeutics Limited and Isis Pharmaceuticals Announce Positive Results From a Phase 1 Trial of ATL-1102 for Multiple Sclerosis

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ATL Expects to Start Phase 2 Studies of ATL-1102 in Patients With MS This Year

MELBOURNE, Australia and CARLSBAD, Calif., June 8 /PRNewswire-FirstCall/ -- Antisense Therapeutics Limited (ASX: ANP) and Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today the results of a dose-escalating Phase 1 study of ATL-1102. Based on the study's results, 6 mg/kg/week of ATL-1102 appeared well-tolerated and has been selected as the proposed dose for Phase 2 development. A Phase 2 clinical trial is expected to begin in the second half of 2004. ATL-1102 is a second-generation antisense inhibitor of VLA-4 (Very Late Antigen-4). Inhibition of VLA-4 has been shown to have positive effects in multiple animal models of inflammatory diseases, including MS.

"We are pleased with the favorable results of this trial which, along with preclinical data, give us critical dose information allowing us to move confidently to the next stage of clinical development," said Mark Diamond, Antisense Therapeutics, Chief Executive Officer.

The double-blind, randomized, dose-escalation, placebo-controlled Phase 1 study evaluated the pharmacokinetic and safety profile of ATL-1102. In 54 healthy volunteers, ATL-1102 was either delivered in an intravenous (IV) or subcutaneous (SQ) formulation. ATL-1102 was well-tolerated. The most frequently reported side effects included mild "flu-like" symptoms and occasional injection site reactions, which were generally mild and increased in incidence and severity with escalating dose levels, particularly at 12 and 18 mg/kg/week. The trial was conducted at the Charterhouse Clinical Research Unit of the Ravenscourt Park Hospital (formerly Stamford Hospital) in London.

"These data are consistent with the results of other second-generation antisense drugs demonstrating the predictability of the antisense platform," said Stanley T. Crooke, M.D., Ph.D., Chairman and Chief Executive Officer of Isis Pharmaceuticals. "We continue to make excellent progress with our second-generation antisense drugs with results announced from three trials so far this year and we expect to continue that clinical momentum throughout 2004."

Background Information

Multiple Sclerosis (MS) is a life-long chronic, incurable disease that progressively destroys the central nervous system. It is commonly diagnosed between the ages of 20 and 40 years. According to the National Multiple Sclerosis Society, MS is an autoimmune disease that affects the central nervous system (CNS). Approximately 400,000 Americans acknowledge having MS, and every week about 200 individuals are diagnosed. Worldwide, MS may affect more than two million people.

ATL-1102 is an inhibitor of CD49d, a sub-unit of VLA-4 (Very Late Antigen-4). In MS, white blood cells (leukocytes) are pulled into the CNS from the blood. The inhibition of VLA-4 may prevent white blood cells from entering the CNS to stop the progression of MS. Inhibition of VLA-4 in animals has demonstrated positive effects on a number of inflammatory diseases such as MS. Several other VLA-4 inhibitors are in clinical development for inflammatory conditions. Isis discovered this compound and licensed it to Antisense Therapeutics Limited in 2001.

Antisense Therapeutics Limited is an Australian publicly listed biopharmaceutical drug discovery and development company (ASX: ANP). ANP's mission is to create, develop and commercialize novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL-1102), and Psoriasis (ATL-1101). ANP plans to commercialize its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies. The company's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals, Inc., Queensland Investment Corporation and the Murdoch Childrens Research Institute. Further company details are available on the Antisense Therapeutics website at www.antisense.com.au.

Isis Pharmaceuticals, Inc. is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs for its pipeline and its partners. The company has successfully commercialized the world's first antisense drug and has 11 antisense products in development to treat metabolic, cardiovascular, inflammatory and viral diseases and cancer. Through its Ibis Therapeutics® program, Isis is developing a biosensor to identify infectious organisms, and is discovering small molecule drugs that bind to RNA. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of more than 1,300 issued patents worldwide. Additional information about Isis is available at www.isispharm.com.

This press release includes forward-looking statements regarding Isis' collaboration with ATL and the development, therapeutic potential and safety of ATL-1102 (ISIS 107248) targeting VLA-4 and in treating multiple sclerosis. Any statement describing our goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as Isis' clinical goals. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of developing technology and systems used to identify infectious agents, in discovering and commercializing drugs that are safe and effective for use as human therapeutics and in the endeavor of building a business around such products and services. Actual results could differ materially from those discussed 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 Isis' Annual Report on Form 10-K for the year ended December 31, 2003, and quarterly report on Form 10-Q for the quarter ended March 31, 2004, which are on file with the U.S. Securities and Exchange Commission. Copies of these and other documents are available from the company.

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