OncoGenex and Isis Pharmaceuticals Announce Compelling Data from Phase I Prostate Cancer Study at ASCO Annual Meeting

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Investigational antisense drug OGX-011 achieves greater than 90 percent target reduction in prostate cancer; compound advances into Phase II development

VANCOUVER, BC and CARLSBAD, CA, June 6 /PRNewswire-FirstCall/ - OncoGenex Technologies Inc. and Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today the results of a Phase I study showing that once weekly intravenous administration of OGX-011 is well tolerated, achieves excellent drug concentration in target tissue, and produces a 91 percent dose-dependent down- regulation of its target, clusterin, in prostate cancer. Clusterin is a cell survival protein that, when overproduced, prevents cancer cell death and counters the effectiveness of standard anti-tumor treatments. OGX-011 is a second-generation antisense drug being developed to sensitize tumors resistant to existing treatments such as chemotherapy, hormone ablation therapy and radiation therapy. K. N. Chi, M.D., Study Chair and a medical oncologist at BC Cancer Agency presented the data today at the 40th Annual Meeting of the American Society of Clinical Oncology in New Orleans.

"This study clearly demonstrates the biological effectiveness of OGX-011 at doses that are very well tolerated," said Dr. Chi. "The Phase I study demonstrates, for the first time, the ability of OGX-011 to potently inhibit clusterin expression in primary prostate cancers."

In the Phase I dose escalation trial, which was coordinated by the National Cancer Institute of Canada Clinical Trials Group (NCIC CTG), investigators reported significant, dose-dependent inhibition of clusterin in prostate cancer patients compared to historical controls at several of the doses studied:

- 91 percent target reduction with a 640 mg dose of OGX-011
- 73 percent target reduction with a 480 mg dose of OGX-011
- 66 percent target reduction with a 320 mg dose of OGX-011
- 58 percent target reduction with a 160 mg dose of OGX-011

Based on tissue pharmacokinetic and optimal inhibition of the drug's target in prostate cancer cells and lymph nodes, 640 mg was recommended as the optimal dose for future Phase II studies of OGX-011. Trials of OGX-011 in combination with hormone and chemotherapy are planned to begin in 2004 in patients with prostate, breast and lung cancers.

"OGX-011 is among the first cancer therapeutics to have the data set to prove it is present in sufficient concentrations in target tissue to significantly inhibit its target. This finding gives us confidence in advancing to phase II studies because dose is now known to correlate to biologic activity in humans," said Martin E. Gleave, M.D., Chief Scientific Officer at OncoGenex and an author on the ASCO poster presentation.

OGX-011 works by blocking or inhibiting the production of clusterin, thereby impairing the cancer cells' survival mechanism and enhancing the effectiveness of standard chemotherapy. Numerous preclinical studies have shown that blocking the production of the clusterin protein with OGX-011 facilitates the induction of cell death through standard therapies, enhances tumor regression, and significantly delays disease progression. In each case, this novel combination strategy is considerably better than treating the tumor with standard therapy alone.

"The OGX-011 Phase I data has exceeded our expectations in its ability to reduce clusterin levels," said Scott Cormack, President and Chief Executive Officer of OncoGenex. "OGX-011 is an example of the next generation of antisense chemistry that is characterized by long tissue half life. With strong pre-clinical and phase I data, we plan to develop OGX-011 for a number of major cancers including prostate, lung, breast and other tumor types in which clusterin is known to be over-expressed."

About the Study

25 patients with localized prostate cancer and high-risk features, such as PSA above 10 or high grade disease, and who were candidates for a prostatectomy participated in the study. OGX-011 was given by weekly I.V. infusion across six cohorts with doses starting at 40 mg and escalating up to 640 mg over a 29-day period. Treatment with buserelin acetate and flutamide, standard hormone therapy for the treatment of prostate cancer, started on day 1 and continued throughout the study. Prostatectomy was performed following the 29-day treatment period. OGX-011 plasma pharmacokinetic and prostate tissue concentrations were determined and clusterin expression was assessed in prostate tissues using immunostaining and quantitative real time PCR (QRT-PCR) of laser-captured cancer cells.

The plasma pharmacokinetics analysis showed linear increases in maximum concentration (CMAX) and Area Under the Curve (AUC) with a half-life of approximately two hours. OGX-011 prostate tissue concentrations increased with dose to a mean of 4.80 micrograms/g (~650nM) at 640 mg. Dose-dependent decreases in clusterin expression were observed in prostate cancer cells. At 640 mg dosing, clusterin mRNA was decreased to a mean of eight percent (SD (equal sign) four percent) compared with lower dose levels and historical controls as assessed by QRT-PCR on laser captured micro dissected cancer cells. By immunohistochemistry, mean percent cancer cells staining zero intensity for clusterin protein at 640 mg dosing was 57 percent (SD (equal sign) 24 percent) compared with 2-15 percent for lower dose levels and historical controls, while clusterin mRNA levels decreased by 91 percent using QRT-PCR.

OGX-011 was well tolerated at the doses studied. The most frequently reported side effects were mild (grade 1 or 2) and included fevers, rigors, fatigue and transient elevations of AST and ALT, enzymes used to detect liver damage. No dose limiting toxicities were observed in the trial.

"We are optimistic about the potential of OGX-011 as it has demonstrated the ability to reduce an important target in a tumor type that will affect one out of every six men at some point in their lifetime," said Stanley T. Crooke, M.D., Ph.D., Isis Chairman and Chief Executive Officer. "Additionally, an important outcome of this trial is the selection of a dose for Phase II development. OncoGenex's trial is a further example of our strategy to evaluate second-generation antisense drugs through clinical trials with crisp, measurable endpoints that provide an early read on the doses necessary to result in activity."

This pre-surgery study was supported by a grant from the U.S. Department of Defense Army Medical Research and Material Command Prostate Cancer Research Program and by an unrestricted grant from Aventis Pharma. The study was coordinated by the National Cancer Institute of Canada Clinical Trials Group (NCIC-CTG), which is funded by the Canadian Cancer Society.

A second Phase I study is in progress which is designed to determine recommended dose of OGX-011 in combination with TAXOTERE® in various solid tumors. This study is expected to be completed by the end of Q3, 2004.

The OncoGenex and Isis partnership combines OncoGenex's proprietary antisense position in inhibitors to the target, clusterin, with Isis' proprietary second-generation antisense chemistry called 2'-O-methoxyethyl. Second-generation antisense drugs offer greater potency, enhanced tolerability, and improved dosing convenience compared to first-generation antisense drugs. In 2003, the companies expanded their antisense drug development partnership to include the development of the second-generation antisense anti-cancer drug candidate, OGX-225. The compound is the first bi-specific antisense inhibitor, a single antisense drug designed to inhibit the production of two proteins simultaneously, IGFBP-5 and IGFBP-2, to enter into preclinical development.

About OncoGenex Technologies

OncoGenex Technologies Inc. is a Vancouver-based biotechnology company developing targeted cancer therapeutics designed to inhibit the tumor cells' ability to adapt when treated with conventional therapies. OncoGenex has five products in development and is the exclusive licensee of technologies from the University of British Columbia. The company has working relationships with many institutions worldwide, including the Division of Urology and the Prostate Centre at Vancouver Hospital & Health Sciences Centre. Additional information about OncoGenex is available at www.oncogenex.ca.

About Isis Pharmaceuticals

Isis Pharmaceuticals, Inc. is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs for its pipeline and for 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 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.

Forward Looking Statements

This press release includes forward-looking statements concerning Isis' collaboration with OncoGenex Technologies and the development, therapeutic potential and safety of OGX-011 (ISIS 112989) targeting clusterin, OGX-225, targeting insulin-like growth factor binding protein-5 (IGFBP-5) and insulin-like growth factor binding protein-2 (IGFBP-2), and in treating cancer. 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.

Source: OncoGenex Technologies Inc.