

## OncoGenex Technologies and Isis Pharmaceuticals Expand Antisense Anti-Cancer Drug Development Collaboration

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VANCOUVER, British Columbia and CARLSBAD, Calif., Sept. 9 /PRNewswire/ -- OncoGenex Technologies Inc., and Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today they have 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-stranded antisense drug designed to inhibit the production of two proteins simultaneously, to enter into preclinical development. OGX-225 targets both insulin-like growth factor binding protein- 5 (IGFBP-5) and insulin-like growth factor binding protein-2 (IGFBP-2), two molecules involved in the development of metastatic disease in hormone- regulated tumors such as prostate and breast cancers. Specific financial terms of the deal were not disclosed.

"IGFBP-2 and IGFBP-5 are exciting drug targets as they facilitate access to a key alternate growth factor which enables tumors to progress in the absence of hormone. By inhibiting both of these proteins, OGX-225 reduces tumor access to the alternate growth factor and thus delays disease progression and metastasis," said Martin E. Gleave, M.D., OncoGenex's Chief Scientific Officer. "This is an area of medical need as we don't have therapies available to treat androgen-independent tumors and this stage of disease is typically associated with very poor survival."

The expansion combines OncoGenex's leading patent position in inhibitors of IGFBP-5 and IGFBP-2 drug targets with Isis' second-generation antisense chemistry, called 2'-O-methoxyethyl, as well as Isis' IGFBP-5 target-specific intellectual property. The companies have already successfully completed initial drug discovery research, which led to the identification of OGX-225. OncoGenex will be solely responsible for the preclinical and clinical development of the drug. Under the financial terms of the agreement, OncoGenex will pay Isis an upfront fee, milestone payments for key clinical and regulatory achievements and royalties on product sales.

"We are pleased to enrich our relationship with OncoGenex and to increase the number of second-generation oncology antisense drug candidates in development," said Brett P. Monia, Ph.D., Vice President, Antisense Drug Discovery at Isis. "This strategic partnership is in alignment with our overall business plan to expand the reach and potential of antisense therapeutics."

"As a product-focused company, it is imperative that we advance our novel therapeutics into preclinical and clinical development quickly and efficiently. By expanding our relationship with Isis, we leverage the strength of both companies to rapidly develop our second product," said Sherry Tryssenaar, Vice President, Operations and Finance at OncoGenex.

Isis and OncoGenex initiated a partnership in December 2001 to co-develop OGX-011 (ISIS 112989) a second-generation antisense drug to the target clusterin. Clusterin is a cell-survival protein that is over-expressed in many human malignancies in response to tumor killing strategies such as chemotherapy, hormone ablation and radiation therapy. OGX-011 is currently in two Phase I clinical trials in combination with chemotherapy for the treatment of prostate cancer and other solid tumors.

### About IGFBP-5 and IGFBP-2

Many tumors rely on hormones to grow. When deprived of hormones, such as with hormone ablation therapy in certain stages of prostate and breast cancers, tumors adapt and substitute growth factors to continue their growth. IGFBP-5 and IGFBP-2 act as switches to regulate cell growth signals; when both IGFBPs are overexpressed (over-produced), evidence suggests a heightened interaction between prostate cells (primarily regulated by IGFBP-2) and bone cells (primarily regulated by IGFBP-5) in a bi-directional fashion. This phenomenon appears to be a key mechanism that accounts for site-specific metastasis to bones and to treatment resistance in hormone refractory prostate cancer. IGFBP-2 has been found to be the most highly over-expressed gene in androgen independent prostate cancer. Preclinical studies conducted by the Prostate Centre at Vancouver General Hospital further demonstrate that over- expression of IGFBP-2 and IGFBP-5 results in significantly more aggressive disease progression. By down-regulating (inhibiting) IGFBP-2 and IGFBP-5 simultaneously the signals and interaction between sites may be blocked, and the progression to refractory disease and metastasis may be delayed. Therefore, OGX-225 could prove effective as a therapeutic to prevent progression of prostate cancer and other tumor types.

### About OncoGenex Technologies Inc.

OncoGenex Technologies Inc. is a Vancouver-based biotechnology company developing targeted cancer therapeutics. OncoGenex has five products in development with its lead product in clinical development for the treatment of various cancers. Additional information about OncoGenex is available at [www.oncogenex.ca](http://www.oncogenex.ca).

### About Isis Pharmaceuticals, Inc.

Isis Pharmaceuticals, Inc., is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs. The company has successfully commercialized the world's first antisense product, and has 11 antisense products in development. In the company's GeneTrove™ program, Isis uses antisense technology as a tool to determine the function of genes and uses that information to direct the Company's internal drug discovery research and that of its corporate partners. Through its Ibis Therapeutics™ program, Isis is developing a novel diagnostic tool to detect infectious organisms and is focused on the discovery of 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 1,200 issued patents worldwide. Additional information about Isis is available at [www.isispharm.com](http://www.isispharm.com)

This press release contains forward-looking statements concerning the clinical development of Isis' cancer program, OGX-011, OGX-225 and their prospects as a treatment for cancer, OncoGenex's drug development program, and the potential of Isis' drug discovery program. There are no guarantees that future clinical trials will confirm the preliminary results referred to in this release or that OGX-225 will receive regulatory approvals or prove to be commercially successful. Any statement describing a goal, expectation, intention or belief of Isis 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 on Form 10-Q for the period ended June 30, 2003, which is on file with the U.S. Securities and Exchange Commission, copies of which are available from the company.

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