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## Geron Announces Publication Demonstrating Activity of Imetelstat Against Cancer Stem Cells From Pediatric Neural Tumors

MENLO PARK, Calif.--(BUSINESS WIRE)--Geron Corporation (Nasdaq:GERN) today announced the publication of preclinical data demonstrating that the company's telomerase inhibitor drug, imetelstat (GRN163L), currently in Phase 2 clinical trials, selectively targets cancer stem cells in pediatric tumors of neural origin.

"Cancers of the brain and nervous system are the most common solid tumors in children and the leading cause of morbidity and death from pediatric cancers. These preclinical data show that imetelstat specifically targets the cancer stem cells in pediatric neural tumors, which we believe may be responsible for progression and recurrence of the disease," said Stephen M. Kelsey, M.D., Geron's executive vice president and chief medical officer, oncology. "The findings are important and support the rationale for conducting a clinical trial in pediatric tumors."

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Telomerase activity has previously been linked to progression and poor patient survival in childhood cancers of the central and peripheral nervous system, such as gliomas and neuroblastomas. Cancer stem cells are believed to be responsible for the growth, recurrence and metastasis of tumors. Cancer stem cells are rare populations of malignant cells with the capacity for endless self-renewal found in many types of cancer including neural tumors. Their resistance to chemotherapy and conventional anti-cancer agents make them important targets for novel therapies.

The data in the current study showed that telomerase activity was confined to the cancer stem cell population in the pediatric neural tumors studied. Gliomas removed from fourteen patients showed high telomerase activity in the cancer stem cell fraction, but not in the bulk tumor cells. Glioma and neuroblastoma cancer stem cells grown in culture were also found to have high telomerase activity. These cancer stem cells were found to have extremely short telomeres, which along with high telomerase levels, might render them particularly sensitive to telomerase inhibition by imetelstat.

Treatment of glioma and neuroblastoma cancer stem cell lines with imetelstat for five to 15 weeks *in vitro* led to telomerase inhibition, telomere attrition, growth arrest and loss of self-renewal capacity (a characteristic of stem cells) compared to untreated controls. Furthermore, growth rate and self-renewal capacity did not recover after imetelstat treatment was discontinued for seven weeks despite rapid restoration of telomerase activity. This is significant because many brain tumors recur after cessation of standard therapy.

*In vivo*, tumors failed to develop when neuroblastoma cancer stem cells were pre-treated with imetelstat *in vitro* for four weeks and subsequently implanted in mice given no further treatment. Tumors developed if neuroblastoma stem cells that had not been pre-treated were implanted in mice given imetelstat at the time of implanting. However, the resulting tumors were approximately 2-3 times smaller than controls and survival of these animals was improved. These xenograft data demonstrate activity of imetelstat against neuroblastoma stem cells *in vivo*. A third group of mice were treated with imetelstat once tumors were already established.

Although no survival benefit was observed in these animals, importantly, cells isolated from those tumors formed 4-5 fold fewer colonies *in vitro* compared to controls, showing a decreased self-renewal capacity. Self-renewal of cancer stem cells is thought to be a key driver of tumor recurrence. These data provide non-clinical support for the use of imetelstat in combination with tumor de-bulking agents or as maintenance therapy after tumor de-bulking.

In the past, the feasibility of targeting telomerase in children has been questioned due to speculation on possible detrimental effects on nervous system development and maintenance if telomerase activity was required by normal tissue stem cells in the pediatric nervous system. However, evaluation of normal stem cells from human fetal or pediatric tissues of neural origin in this study showed no detectable telomerase activity. Furthermore, normal pediatric neural tissue stem cells have very long telomeres. Treatment with imetelstat did not affect the proliferative capacity of these cells even after prolonged exposure. These significant non-clinical observations support the use of a telomerase inhibitor to treat childhood cancers.

The research was published online on January 5, 2011 in the journal *Clinical Cancer Research* and featured in the journal's editorial CCR Translation section. The study was co-authored by Dr. Uri Tabori and colleagues at The Hospital for Sick Children and the University of Toronto, Canada in collaboration with Geron scientists. The publication is freely available on the journal's website at <http://clincancerres.aacrjournals.org/content/17/1/111.full>.

### About Telomerase

Telomerase is a critical and broadly applicable tumor target. The enzyme is expressed in a wide range of malignant tumors, and its activity is essential for the indefinite replicative capacity of cancer that enables malignant cell growth. Telomerase has now also been shown to be a target for cancer stem cells. Telomerase is absent or expressed only transiently at low levels in most normal adult tissues.

### About Imetelstat (GRN163L)

Imetelstat is a lipidated short chain oligonucleotide that binds with high affinity and specificity to the catalytic site of telomerase, resulting in competitive inhibition of enzyme activity. Proprietary manufacturing chemistry and the addition of a 5' lipid chain have enabled the molecule to penetrate cells and tissues throughout the body.

Imetelstat has demonstrated anti-tumor effects in a wide range of preclinical xenograft models of human solid and hematological tumors, and potent activity against cancer stem cells derived from primary patient samples or cancer cell lines from multiple tumor types.

Imetelstat has been tested in six Geron-sponsored Phase 1 clinical trials at 22 U.S. medical centers treating over 180 patients examining the safety, tolerability, pharmacokinetics and pharmacodynamics of the drug, alone or in combination with other standard therapies, in patients with different hematological and solid tumors.

Two randomized Phase 2 clinical trials of imetelstat have been initiated; the first in non-small cell lung cancer and a second was recently initiated in breast cancer. Single arm Phase 2 clinical trials are open in multiple myeloma and essential thrombocythemia. All are malignancies in which cancer stem cells are believed to play an important role in relapse after standard therapy. For further information about clinical trials using imetelstat, please visit <http://clinicaltrials.gov/ct2/results?term=imetelstat>.

### About Geron

Geron is developing first-in-class biopharmaceuticals for the treatment of cancer and chronic degenerative diseases. The company is advancing anti-cancer therapies through multiple Phase 2 clinical trials in different cancers by targeting the enzyme telomerase and with a compound designed to penetrate the blood-brain barrier (BBB). The company is developing cell therapy products from differentiated human embryonic stem cells for multiple indications, including central nervous system (CNS) disorders, heart failure, diabetes and osteoarthritis, and has initiated a Phase 1 clinical trial in spinal cord injury. For more information, visit [www.geron.com](http://www.geron.com), visit [www.geron.com](http://www.geron.com).

This news release may contain forward-looking statements made pursuant to the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Investors are cautioned that statements in this press release regarding potential applications of Geron's telomerase and oncology technology constitute forward-looking statements that involve risks and uncertainties, including, without limitation, risks inherent in the development and commercialization of potential products, uncertainty of clinical trial results or regulatory approvals or clearances, need for future capital, dependence upon collaborators and protection of our intellectual property rights. Actual results may differ materially from the results anticipated in these forward-looking statements. Additional information on potential factors that could affect our results and other risks and uncertainties are detailed from time to time in Geron's periodic reports, including the quarterly report on Form 10-Q for the quarter ended September 30, 2010 and the annual report on Form 10-K for the year ended December 31, 2009.

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