Data Show SuperGen's Multi-Targeted Tyrosine Kinase Inhibitor Suppresses Critical Double-Stranded DNA Repair Protein, Rad51

Other Presentations at AACR Highlight Progress in SuperGen's Oncology-Focused Pre-Clinical Pipeline

LOS ANGELES, April 19 /PRNewswire-FirstCall/ -- SuperGen Inc. (Nasdaq: SUPG) today announced that MP470, its multi-targeted tyrosine kinase inhibitor, suppresses the Rad51 protein, a critical component of double- stranded DNA repair in cancer cells as part of a series of presentations at the 2007 American Association for Cancer Research Annual Meeting (Abstract 4028).

Additional research findings presented by SuperGen scientists and their collaborators included data pertaining to the improved bioavailability and tolerability of the hydrochloride salt of MP470 as compared to the free base (Abstract 1540). Two posters also demonstrated the use of SuperGen's proprietary CLIMB technology and drug discovery process to facilitate lead development and the design of several novel small molecule inhibitors, including Axl kinase (Abstract 2380), as well as inhibitors of Jak2 (Abstract 2387).

The company also presented new animal model studies for small molecule inhibitors of DNMT1 in zebrafish (Abstract 2229), data from its preclinical compound MP529, a selective Aurora A kinase inhibitor (Abstract 3261) and new data exhibiting receptor tyrosine kinase inhibition in combination with an inhibitor of EGFR in mouse xenograft models (Abstract 5421). Finally, a mini- symposium was presented about work conducted at The Ohio State University on SuperGen's novel DNA hypomethylating agents that selectively induced degradation of DNMT1 in human cancer cells (Abstract 4142).

Copies of the poster presentations will be available in the pipeline section of SuperGen's Web site www.supergen.com.

"We are very encouraged by the strength of the preclinical data from our drug discovery and development programs and are awaiting the initiation of the Phase 1 clinical trial of MP470," said Dr. James S. Manuso, SuperGen's Chairman, President and Chief Executive Officer. "Our products and programs were highlighted in seven posters and a mini-symposium. The data presented brings to light important new aspects of our late-stage preclinical compounds and also validates CLIMB as a rapid and powerful process for the identification of a broad range of potent small molecule inhibitors."

Abstract No. 4028

MP470, a potent suppressor of Rad51, improves response to platinum-based anticancer agents

Rad51 is an important protein involved in resistance to cytotoxic/DNA damaging therapies that are commonly used to treat tumors. It acts to repair the double stranded DNA breaks that are caused by therapies, thus limiting their efficacy and increasing dosage requirements. Data indicate that SuperGen's novel compound, MP470, blocks the induction of Rad51 by anticancer platinum agents. MP470, in combination with carboplatin and paclitaxel in small cell and non-small cell lung cancer lines, showed a significant improvement in tumor response over the carboplatin/paclitaxel treatments alone. A combination therapy regimen that includes MP470 in addition to a platinum-based cytotoxic agent could reduce dosage requirements and widen the therapeutic window.

Abstract No. 1540

Hydrochloride salt of MP470, a potent suppressor of Rad51, improves bioavailability and tolerability

Results from this study suggest that the hydrochloride salt of MP470 (MP470.HCl) could lead to improved safety and tolerability of the compound. Data indicate that MP470.HCl exhibits a several-fold improvement in oral bioavailability when compared to the free base. The compound had a wide therapeutic window in rat and dog models. Additionally, no apparent serious toxicities in the expected therapeutic dose range were observed.

Abstract No. 2380

Discovery and characterization of a series of Axl kinase inhibitors using the CLIMB process

Using CLIMB, researchers created a model of Axl kinase to screen a large virtual library of chemical structures from which five chemical lead scaffolds were selected. Structural modifications improved biochemical and cell-based potency that resulted in compounds that exhibit sensitization to apoptosis and down regulation of Axl-dependent signaling pathways. Inhibitor SGI-AXL-277, a pyrrolopyrimidine, demonstrated low micromolar activity against the Axl enzyme and in cell proliferation assays. Lead optimization toward the identification of a clinical candidate is ongoing.

Abstract No. 2387

Discovery and characterization of small molecule inhibitors for Jak2

Janus kinases (JAKs) are critical to a number of intracellular signaling pathways. Failure of Jak2 regulation or mutations that activate Jak2 expression are implicated in leukemias, lymphomas and various solid tumors. Utilizing CLIMB, researchers used a Jak2 crystal structure to build several models that were made into a substrate for screening a large, virtual small molecule library. This process generated a subset of leads based on calculated binding energies. These leads were then screened in silico to determine "druggable" candidates. Cell-based activity was determined in HEL, K562, MO7 and other human cancer cell lines.

Abstract No. 2229

Zebrafish as a model mechanistic screen for small molecule inhibitors of DNMT1

Data suggest that the zebrafish model offers a fast and reliable method to identify small molecule inhibitors of DNA methyltransferase (DNMT). DNMT1 is considered to be the DNA methyltransferase enzyme mainly responsible for maintaining abnormal promoter methylation in various cancer types. Zebrafish embryos are a viable model for cancer drug research because of their close similarity to humans and their fast and easily visible development. Small molecules that inhibit DNMT1 should produce terminal differentiation abnormalities of the gut tube, retina and exocrine pancreas, all of which are easily visualized. This screen allows quick validation of DNMT1 inhibition in vivo, as well as important data on the toxicity of compounds tested.

Abstract No. 3261

Discovery and development of MP529, a new effective and selective inhibitor of Aurora A kinase

MP529 series compounds, such as SGI-498, SGI-503, SGI-1097 and SGI-1215, demonstrate potent nanomolar inhibitory activity against the Aurora-A enzyme in biochemical enzyme-based assays, while exhibiting little to no activity versus the Aurora B kinase. SuperGen developed this series of lead compounds for use in anticancer therapy using rational-based drug design. Extensive in silico screening reduced the number of compounds submitted to physical assays to fewer than 100, saving significant time and resources over standard drug discovery practices. The series of compounds was evaluated in in vivo xenograft models and showed efficacy while maintaining desirable pharmacokinetic properties.

Abstract No. 5421

Dual inhibition of receptor tyrosine kinases of PDGFR and EGFR abolishes prostate cancer cell growth in culture and in a mouse xenograft model by complete dephosphorylation of PKB/Akt

MP470, SuperGen's multi-targeted tyrosine kinase inhibitor, in combination with Tarceva was more effective than either treatment alone in the inhibition of cell proliferation and phosphorylation of Akt in EGF and PDGF pathways. Moreover, in combination with Tarceva, MP470 inhibited Akt phosphorylation in LNCaP prostate cells. Finally, the MP470/Tarceva treatment was shown to abolish prostate tumor growth in an LNCaP xenograft mouse model

Mini-symposium Abstract No. 4142

Novel DNA hypomethylating agents: non-nucleoside compounds that do not incorporate into DNA selectively induce degradation of DNA methyltransferase I (DNMT1) in human cancer cells by the proteasomal pathway and re-express silenced tumor suppressor genes

Researchers have discovered a novel class of quinoline-based compounds that are not incorporated into DNA and cause selective degradation of DNMT1 in human cancer cells with minimal or no effects on DNMT3A and DNMT3B that have been discovered. This addresses an issue with re-activation of silenced tumor suppressor genes by 5-Azacytidine (5-AzaC or Vidaza) and its congener 5-aza- deoxycydinite (5-aza-CdR or Decitabine or Dacogen). These compounds provide a different mechanistic approach to the creation of cancer therapies because they selectively and rapidly induce degradation of maintenance DNA methyltransferase, DMNT1. However, they show some toxicity due to their incorporation into the cell DNA.

One compound in particular, S1027, resulted in complete degradation of DNMT1 within 24 hours of treatments and also blocked degradation as a pre-treatment of cells with proteasomal inhibitors.

About SuperGen

Based in Dublin, Calif., SuperGen is a pharmaceutical company dedicated to the discovery, rapid development and commercialization of therapies for solid tumors and hematological malignancies. SuperGen is developing a number of therapeutic anticancer products focused on inhibitors of aurora-A, tyrosine kinase and DNA methyltransferase. For more information about SuperGen, please visit http://www.supergen.com.

This press release contains "forward-looking" statements within the meaning of Section 21A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, and is subject to the safe harbor created thereby. The actual results could differ materially from those projected in the forward-looking statements as a result of a number of risks and uncertainties. These forward-looking statements include statements regarding the ability of our products to enter clinical trials and the potential validation of our discovery process to produce new compounds. SuperGen's products may not enter clinical trials and even if these products do enter clinical testing there is no assurance that these tests will be successful. Additionally, the early successes in preclinical work may not be a validation of our discovery process and past success may not predict future success. Other factors that could cause actual results to differ materially from expectations include, but are not limited to, the risk factors detailed in the Company's filings with the Securities and Exchange Commission including reports on its most recently filed Form 10-K. These forward-looking statements are made only as of the date hereof, and we disclaim any obligation to update or revise the information contained in any such forward-looking statements, whether as a result of new information, future events or otherwise.

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