

May 21, 2008

Sanofi-aventis and Regeneron Update Aflibercept (VEGF Trap) Clinical Development Program in Oncology

PARIS & TARRYTOWN, N.Y.--(BUSINESS WIRE)--May 21, 2008--Sanofi-aventis (Euronext: SAN and NYSE: SNY) and Regeneron Pharmaceuticals, Inc. (Nasdaq: REGN) today provided an update on the clinical development program for aflibercept, including results from a Phase 2 study in advanced ovarian cancer.

The companies also announced that six abstracts describing the results of clinical trials with aflibercept will be presented at the upcoming annual meeting of the American Society of Clinical Oncology (ASCO) and an additional two abstracts were summarized in the ASCO proceedings. All of the abstracts can be accessed on the ASCO website at www.asco.org. Aflibercept, an innovative fusion protein targeting Vascular Endothelial Growth Factor (VEGF), is being developed by sanofi-aventis and Regeneron for the treatment of several types of cancer.

Phase 3 Studies of Aflibercept in Combination with Chemotherapy

Sanofi-aventis and Regeneron currently are enrolling approximately 4000 patients in the U.S., Europe, and other countries around the world, in four Phase 3 studies that combine aflibercept with standard chemotherapy regimens:

- 2nd-line treatment for metastatic colorectal cancer in combination with folinic acid, 5-FU, and irinotecan.
- 1st-line treatment for metastatic pancreatic cancer in combination with gemcitabine.
- 1st-line treatment for metastatic androgen-independent prostate cancer in combination with docetaxel and prednisone.
- 2nd-line treatment for metastatic non-small cell lung cancer in combination with docetaxel.

A Phase 2 1st-line study of aflibercept in metastatic colorectal cancer in combination with folinic acid, 5-FU, and oxaliplatin is expected to begin later this year.

Phase 2 Study of Single-Agent Aflibercept in Advanced Ovarian Cancer

The companies reported results of a randomized, double-blind, Phase 2 study of 215 women with advanced ovarian cancer who were treated with aflibercept at a dose of either 2 milligrams per kilogram (mg/kg) or 4 mg/kg every two weeks. Response to treatment was assessed both by the clinical investigators and an independent review committee (IRC). As assessed by the investigators, RECIST (Response Evaluation Criteria in Solid Tumors) response rates were 7.3 percent with the 4 mg/kg dose and 3.8 percent with the 2 mg/kg dose. As assessed by the IRC, patients achieved a response rate according to RECIST criteria of 4.6 percent in the 4 mg/kg arm and 0.9 percent in the 2 mg/kg arm. The study did not achieve its primary endpoint of demonstrating that patients in either arm of the study achieved a RECIST response rate as assessed by the IRC that was statistically significantly greater than 5 percent. The results were consistent with the interim data of the same trial reported at the 2007 ASCO meeting.

CA-125 response, an important marker of disease activity in ovarian cancer, was a key secondary endpoint of the study. Response rates, defined as at least a 50 percent reduction in CA-125 protein levels, were 11.6 percent in the evaluable patients treated with 4 mg/kg and 11.5 percent in the evaluable patients treated with 2 mg/kg. Eighteen (13.8 percent) of the 130 patients evaluable for CA-125 response from the combined groups had either a RECIST (as assessed by the IRC) or CA-125 response.

In the entire study population, as assessed by the IRC, median progression-free survival was 13.3 and 13.0 weeks with the 4 mg/kg and 2 mg/kg doses, respectively. Median overall survival was 49.3 and 55.4 weeks with the 4 mg/kg and 2 mg/kg doses, respectively.

Of the 40 patients in both dose groups who had evaluable ascites at baseline, 77.5 percent had either a complete disappearance or stabilization of their ascites over the study period, as assessed by the investigators.

Side effects of treatment with aflibercept were typical of this class of anti-angiogenic agents, with hypertension being the most common grade 3/4 adverse event. Other grade 3/4 adverse events occurring in at least 5 percent of patients included

abdominal pain, anorexia, arthralgia, asthenia, diarrhea, dysphonia, fatigue, headache, proteinuria, and vomiting. Bowel perforations were observed in 1.8 percent of patients. There were no significant differences in safety between the dose groups.

"We are encouraged by the results reported with the use of single-agent aflibercept in this advanced ovarian cancer patient population for whom few therapeutic options are available," stated Dr. Marc Cluzel, Senior Vice President, R&D of sanofi-aventis.

"We and sanofi-aventis are continuing to evaluate the data from this trial in order to determine the next steps for aflibercept in advanced ovarian cancer," commented George D. Yancopoulos, M.D., Ph.D., President of Regeneron Research Laboratories.

Phase 2 Studies of Aflibercept in Symptomatic Malignant Ascites (SMA)

One of the early-stage clinical studies of aflibercept summarized in the published ASCO abstracts (abstract # 14598) is a non-blinded study of patients with advanced ovarian cancer and SMA who were treated with aflibercept dosed 4 mg/kg every 2 weeks. In that study, 8 out of the 10 evaluable patients achieved a repeat paracentesis response rate, the primary endpoint of the study, defined as at least a doubling of time to first paracentesis compared to baseline average. Grade 3/4 adverse events included bowel obstruction, nausea, vomiting, anorexia, edema, general health deterioration, and one case of bowel perforation.

A double-blind, placebo-controlled Phase 2 trial of 54 advanced ovarian cancer patients with SMA is about two-thirds enrolled. The primary endpoint of the study is time to repeat paracentesis.

Phase 1 Studies of Aflibercept in Combination with Chemotherapy

Results from four Phase 1 dose-escalation studies of aflibercept in combination with chemotherapy in solid tumors will be presented at ASCO. Aflibercept was studied in combination with two standard regimens in the treatment of colorectal cancer: FOLFOX-4 (abstract # 3556) and irinotecan, 5-fluorouracil, and leucovorin (I-LV5FU2) (abstract # 3557). Aflibercept was also studied in combination with docetaxel (abstract # 3599) and gemcitabine (abstract # 3558), both widely used in the treatment of several types of solid tumors.

Results from these studies highlight the rationale for the tumor types, the chemotherapy combinations, and the doses selected for the Phase 3 combination studies currently underway.

NCI-Sponsored Studies

More than 12 studies are currently being sponsored by the National Cancer Institute (NCI) Cancer Therapy Evaluation Program (CTEP) under a Clinical Trials Agreement with sanofi-aventis evaluating aflibercept as a single agent or in combination with chemotherapy regimens in a variety of cancer indications. Preliminary results from two of these studies will be presented as posters at ASCO demonstrating the activity of single-agent aflibercept in metastatic colorectal cancer (abstract # 4027) and glioblastoma/anaplastic glioma (abstract # 2020).

Notably, investigators reported preliminary results of a study of 48 patients with either relapsed or first recurrence temozolomide-resistant glioblastoma multiforme or anaplastic glioma. Responses were achieved in 50 percent of patients with anaplastic glioma and 30 percent of patients with glioblastoma. Grade 3 adverse events included fatigue, hypertension, hand-foot syndrome, lymphopenia, thrombosis, and proteinuria.

About Aflibercept (VEGF Trap) in Oncology

Aflibercept is a fully human soluble VEGF receptor fusion protein with a unique mechanism of action. It is a potent angiogenesis inhibitor, which binds VEGF-A more tightly than monoclonal antibodies. It blocks all VEGF-A isoforms plus placental growth factor (PlGF), another angiogenic growth factor that appears to play a role in tumor angiogenesis. Aflibercept has a relatively long half-life of approximately two weeks. Other anti-VEGF drugs have been approved for certain cancer indications and neovascular age-related macular degeneration.

About sanofi-aventis

Sanofi-aventis, a leading global pharmaceutical company, discovers, develops, and distributes therapeutic solutions to improve the lives of everyone. Sanofi-aventis is listed in Paris (EURONEXT PARIS: SAN) and in New York (NYSE: SNY).

Forward Looking Statement

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as

amended. Forward-looking statements are statements that are not historical facts. These statements include product development, product potential projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future events, operations, products and services, and statements regarding future performance. Forward-looking statements are generally identified by the words "expects," "anticipates," "believes," "intends," "estimates," "plans" and similar expressions. Although sanofi-aventis' management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of sanofi-aventis, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMEA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such products candidates, the absence of guarantee that the products candidates if approved will be commercially successful, the future approval and commercial success of therapeutic alternatives as well as those discussed or identified in the public filings with the SEC and the AMF made by sanofi-aventis, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in sanofi-aventis' annual report on Form 20-F for the year ended December 31, 2007. Other than as required by applicable law, sanofi-aventis does not undertake any obligation to update or revise any forward-looking information or statements.

About Regeneron Pharmaceuticals, Inc.

Regeneron is a fully integrated biopharmaceutical company that discovers, develops, and commercializes medicines for the treatment of serious medical conditions. In addition to ARCALYST™ (rilonacept) Injection for Subcutaneous Use, its first commercialized product, Regeneron has therapeutic candidates in clinical trials for the potential treatment of cancer, eye diseases, and inflammatory diseases, and has preclinical programs in other diseases and disorders. Additional information about Regeneron and recent news releases are available on Regeneron's web site at www.regeneron.com.

Forward Looking Statement

This news release discusses historical information and includes forward-looking statements about Regeneron and its products, development programs, finances, and business, all of which involve a number of risks and uncertainties, such as risks associated with preclinical and clinical development of Regeneron's drug candidates, determinations by regulatory and administrative governmental authorities which may delay or restrict Regeneron's ability to continue to develop or commercialize its product and drug candidates, competing drugs that are superior to Regeneron's product and drug candidates, uncertainty of market acceptance of Regeneron's product and drug candidates, unanticipated expenses, the availability and cost of capital, the costs of developing, producing, and selling products, the potential for any collaboration agreement, including Regeneron's agreements with the sanofi-aventis Group and Bayer HealthCare, to be canceled or to terminate without any product success, risks associated with third party intellectual property, and other material risks. A more complete description of these and other material risks can be found in Regeneron's filings with the United States Securities and Exchange Commission (SEC), including its Form 10-Q for the quarter ended March 31, 2008. Regeneron does not undertake any obligation to update publicly any forward-looking statement, whether as a result of new information, future events, or otherwise, unless required by law.

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SOURCE: Regeneron Pharmaceuticals, Inc. / Sanofi-aventis