U.S. FDA Approves ZALTRAP® (ziv-aflibercept) After Priority Review for Previously Treated Metastatic Colorectal Cancer

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PARIS and TARRYTOWN, N.Y., Aug. 3, 2012 /PRNewswire/ -- Sanofi (EURONEXT: **SAN** and NYSE: SNY) and Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) today announced that the U.S. Food and Drug Administration (FDA) approved ZALTRAP® (ziv-aflibercept) Injection for Intravenous Infusion, in combination with 5-fluorouracil, leucovorin, irinotecan (FOLFIRI), for patients with metastatic colorectal cancer (mCRC) that is resistant to or has progressed following an oxaliplatin-containing regimen.

To view the multimedia assets, please click: http://www.multivu.com/mnr/57253-sanofi-fda-approves-zaltrap-ziv-aflibercept

"There are limited treatment options for metastatic colorectal cancer patients who are resistant to or whose disease has progressed after an oxaliplatin-containing regimen," said Edith Mitchell, M.D., Clinical Professor of Medicine and Medical Oncology at Jefferson Medical College of Thomas Jefferson University and an investigator of the VELOUR pivotal study. *"The approval of ZALTRAP in combination with a FOLFIRI chemotherapy regimen offers another treatment option and is welcome news for metastatic colorectal patients and their physicians."*

ZALTRAP was approved following a Priority Review by the FDA. A priority review is a designation given to therapies that offer major advances in treatment or provide a treatment where no adequate therapy exists. Marketing authorization applications for ZALTRAP are also under review by the European Medicines Agency (EMA) and other regulatory agencies worldwide.

"Colorectal cancer is one of the deadliest cancers and is responsible for more than half a million deaths globally each year," said Debasish Roychowdhury, M.D., Senior Vice President and Head, Sanofi Oncology. *"Sanofi looks forward to making ZALTRAP available as soon as possible to patients with metastatic colorectal cancer previously treated with an oxaliplatin-containing regimen."*

The ZALTRAP approval was based on data from the pivotal Phase III VELOUR trial, a multinational, randomized, double-blind trial comparing FOLFIRI in combination with either ZALTRAP or placebo in the treatment of patients with mCRC. The study randomized 1,226 patients with mCRC who previously had been treated with an oxaliplatin-containing regimen. Twenty-eight percent of patients in the study received prior bevacizumab therapy. The primary endpoint was overall survival. Secondary endpoints included progression-free survival, overall response rate, and safety.

"The approval of the novel angiogenesis inhibitor ZALTRAP provides a new option to address the unmet medical need in this patient population," said George D. Yancopoulos, M.D., Ph.D., Chief Scientific Officer of Regeneron and President of Regeneron Research Laboratories. *"However, there continues to be a need to develop new cancer therapies. Regeneron and Sanofi continue to devote resources to finding novel investigational treatments and combinations."*

VELOUR Trial Results
The VELOUR trial showed that in patients previously treated with an oxaliplatin containing regimen, adding ZALTRAP to FOLFIRI significantly improved median survival from 12.06 months to 13.50 months (HR=0.817 (95% CI 0.714 to 0.935; p=0.0032), an 18 percent relative risk reduction. A significant improvement in progression-free survival from 4.67 months to 6.90 months (HR=0.758 95% CI 0.661 to 0.869; p=0.00007), a 24% relative risk reduction, was also observed. The overall response rate in the ZALTRAP plus FOLFIRI arm was 19.8% vs. 11.1% for FOLFIRI (p=0.0001).

The most common adverse reactions (all grades, ≥20% incidence) reported at a higher incidence (2% or greater between-arm difference) in the ZALTRAP/FOLFIRI arm, in order of decreasing frequency, were leukopenia, diarrhea, neutropenia, proteinuria, AST increased, stomatitis, fatigue, thrombocytopenia, ALT increased, hypertension, weight decreased, decreased appetite, epistaxis, abdominal pain, dysphonia, serum creatinine increased, and headache. The most common Grade 3-4 adverse reactions (≥5%) reported at a higher incidence (2% or greater between-arm difference) in the ZALTRAP/FOLFIRI arm, in order of decreasing frequency, were neutropenia, diarrhea, hypertension, leukopenia, stomatitis, fatigue, proteinuria, and asthenia.

About ZALTRAP® (ziv-aflibercept) Injection for Intravenous Infusion
ZALTRAP is a recombinant fusion protein, which acts as a soluble receptor that binds to Vascular Endothelial Growth Factor-A (VEGF-A), VEGF-B and placental growth factor (PIGF). Inhibition of these factors can result in decreased neovascularization and decreased vascular permeability. Sanofi plans to make ZALTRAP available in the U.S. in the third quarter of 2012. Under the terms of their collaboration agreement, Sanofi and Regeneron share equally the global profits of ZALTRAP after Regeneron's obligation to repay its share of development expenses. In the U.S., ZALTRAP is a registered trademark of Regeneron Pharmaceuticals, Inc.

Important Safety Information for ZALTRAP®

WARNING: HEMORRHAGE, GASTROINTESTINAL PERFORATION, COMPROMISED WOUND HEALING

Severe and sometimes fatal hemorrhage, including gastrointestinal (GI) hemorrhage, has been reported in the patients who have received ZALTRAP in combination with FOLFIRI. Monitor patients for signs and symptoms of GI bleeding and other severe bleeding. Do not administer ZALTRAP to patients with severe hemorrhage.

GI perforation including fatal GI perforation can occur in patients receiving ZALTRAP. Discontinue ZALTRAP therapy in patients who experience GI perforation.

Severe compromised wound healing can occur in patients receiving ZALTRAP/FOLFIRI. Discontinue ZALTRAP in patients with

compromised wound healing. Suspend ZALTRAP for at least 4 weeks prior to elective surgery, and do not resume ZALTRAP for at least 4 weeks following major surgery and until the surgical wound is fully healed.

WARNINGS AND PRECAUTIONS

- Patients treated with ZALTRAP have an increased risk of hemorrhage, including severe and sometimes fatal hemorrhagic events.
  - Monitor patients for signs and symptoms of bleeding.
  - Do not initiate ZALTRAP to patients with severe hemorrhage.
  - Discontinue ZALTRAP in patients who develop severe hemorrhage.
- GI perforation including fatal GI perforation can occur in patients receiving ZALTRAP.
  - Monitor patients for signs and symptoms of GI perforation.
  - Discontinue ZALTRAP in patients who experience GI perforation.
- Discontinue ZALTRAP in patients with compromised wound healing.
  - Suspend ZALTRAP for at least 4 weeks prior to elective surgery
  - Do not initiate/resume ZALTRAP until at least 4 weeks after surgery and surgical wound is fully healed.
- Fistula formation involving GI and non-GI sites occurs at a higher incidence in patients treated with ZALTRAP. Discontinue ZALTRAP therapy in patients who develop fistula.
- An increased risk of Grade 3-4 hypertension has been observed in patients receiving ZALTRAP.
  - Monitor blood pressure every two weeks or more frequently and treat with appropriate anti-hypertensive therapy during treatment with ZALTRAP.
  - Temporarily suspend ZALTRAP until hypertension is controlled, and reduce ZALTRAP dose to 2 mg/kg for subsequent cycles.
  - Discontinue ZALTRAP in patients with hypertensive crisis.
- Arterial thromboembolic events (ATE), including transient ischemic attack, cerebrovascular accident, and angina pectoris, occurred more frequently in patients who have received ZALTRAP. Discontinue ZALTRAP in patients who experience an ATE.
- Severe proteinuria, nephrotic syndrome, and thrombotic microangiopathy (TMA) occurred more frequently in patients treated with ZALTRAP.
  - Suspend ZALTRAP when proteinuria ≥2 grams/24 hours and resume ZALTRAP when proteinuria &< 2 grams/24 hours.
  - If recurrent, suspend until proteinuria &< 2 grams/24hours and then reduce ZALTRAP dose to 2 mg/kg.
  - Discontinue ZALTRAP if nephrotic syndrome or TMA develops.
- A higher incidence of neutropenic complications (febrile neutropenia and neutropenic infection) occurred in patients receiving ZALTRAP.
  - Delay administration of ZALTRAP/FOLFIRI until neutrophil count is ≥1.5 x 10^9/L.
- Incidence of severe diarrhea and dehydration is increased in patients treated with ZALTRAP/FOLFIRI.
  - The incidence of diarrhea is increased in patients ≥65 years of age. Monitor closely.
- Discontinue ZALTRAP in patients who develop reversible posterior leukoencephalopathy syndrome.

ADVERSE REACTIONS

- The most common adverse reactions (all grades, ≥20% incidence) reported at a higher incidence (2% or greater between-arm difference) in the ZALTRAP/FOLFIRI arm, in order of decreasing frequency, were leukopenia, diarrhea, neutropenia, proteinuria, AST increased, stomatitis, fatigue, thrombocytopenia, ALT increased, hypertension, weight decreased, decreased appetite, epistaxis, abdominal pain, dysphonia, serum creatinine increased, and headache.
- The most common Grade 3-4 adverse reactions (≥5%) reported at a higher incidence (2% or greater between-arm difference) in the ZALTRAP/FOLFIRI arm, in order of decreasing frequency, were neutropenia, diarrhea, hypertension, leukopenia, stomatitis, fatigue, proteinuria, and asthenia.
- Infections occurred at a higher frequency in patients receiving ZALTRAP/FOLFIRI (46%, all grades; 12%, Grade 3-4) than in patients receiving placebo/FOLFIRI (33%, all grades; 7%, Grade 3-4), including urinary tract infection, nasopharyngitis, upper respiratory tract infection, pneumonia, catheter site infection, and tooth infection.
- In patients with mCRC, venous thromboembolic events (VTE), consisting primarily of deep venous thrombosis and pulmonary embolism, occurred in 9% of patients treated with ZALTRAP/FOLFIRI and 7% of patients treated with placebo/FOLFIRI.

Please click here for full Prescribing Information for ZALTRAP (ziv-aflibercept) Injection for Intravenous Infusion, including Boxed WARNING, and visit: www.ZALTRAP.com

About Colorectal Cancer

According to the American Cancer Society, it is estimated that more than 143,000 new cases of colorectal cancer will be diagnosed in 2012, and more than 51,000 people will die from it. Approximately 60 percent of colorectal cancer cases are diagnosed at the locally advanced or metastatic stage.

Although survival for early stage disease is relatively high, once colorectal cancer metastasizes to distant organs, five-year survival is estimated to be 12 percent.

Worldwide, colorectal cancer is the third most commonly diagnosed cancer in males and the second most in females, with more than 1.2 million new cases diagnosed in 2008. One of the deadliest cancers, colorectal cancer was responsible for more than 600,000 deaths globally in 2008 alone.

About Sanofi Oncology

Based in Cambridge, Massachusetts, USA and Vitry, France, Sanofi Oncology is dedicated to translating science into effective therapeutics that address unmet medical needs for cancer and organ transplant patients. Starting with a deep understanding of the disease and the patient, Sanofi Oncology employs innovative approaches to drug discovery and clinical development, with the ultimate goal of bringing the right medicines to the right patients to help them live healthier and longer lives. We believe in the value of partnerships that combine our internal scientific expertise with that of industry and academic experts. Our portfolio includes 10 marketed products and more than 15 investigational compounds in clinical development, including small molecules and biological agents.

About Sanofi

Sanofi, a global and diversified healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients' needs. Sanofi has core strengths in the field of healthcare with seven growth platforms: diabetes solutions, human vaccines, innovative drugs, consumer healthcare, emerging markets, animal health and the new Genzyme. Sanofi is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY).

About Regeneron Pharmaceuticals, Inc.

Regeneron is a fully integrated biopharmaceutical company that discovers, invents, develops, manufactures, and commercializes medicines for the treatment of serious medical conditions. Regeneron markets three products in the United States, EYLEA® (aflibercept) Injection, ZALTRAP® (ziv-aflibercept) Injection for Intravenous Infusion, and ARCALYST® (rilonacept) Injection for Subcutaneous Use. Regeneron has filed a regulatory application with the U.S. Food and Drug Administration (FDA) for a second indication for EYLEA. Phase 3 studies are in progress with EYLEA in two additional indications and with product candidates sarilumab and REGN727. Regeneron has active research and development programs in many disease areas, including ophthalmology, inflammation, cancer, and hypercholesterolemia. Additional information and recent news releases are available on the Regeneron web site at www.regeneron.com.

Sanofi Forward Looking Statements

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 projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, 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's 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, 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 EMA, 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 product candidates, the absence of guarantee that the product candidates if approved will be commercially successful, the future approval and commercial success of therapeutic alternatives, the Group's ability to benefit from external growth opportunities, trends in exchange rates and prevailing interest rates, the impact of cost containment policies and subsequent changes thereto, the average number of shares outstanding as well as those discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in Sanofi's annual report on Form 20-F for the year ended December 31, 2011. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

Regeneron Forward-Looking Statements

This news release includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron, and actual events or results may differ materially from these forward-looking statements. These statements concern, and these risks and uncertainties include, among others, the nature, timing, and possible success and therapeutic applications of Regeneron's products, product candidates and research and clinical programs now underway or planned, including without limitation ZALTRAP® (ziv-aflibercept), unforeseen safety issues resulting from the administration of products and product candidates in patients, the likelihood and timing of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates, determinations by regulatory and administrative governmental authorities which may delay or restrict Regeneron's ability to continue to develop or commercialize Regeneron's products and drug candidates, competing drugs that may be superior to Regeneron's products and drug candidates, uncertainty of market acceptance of Regeneron's product and drug candidates, unanticipated expenses, the costs of developing, producing, and selling products, the potential for any license or collaboration agreement, including Regeneron's agreements with the Sanofi Group and Bayer HealthCare, to be canceled or terminated without any product success, and risks associated with third party intellectual property and pending or future litigation relating thereto. 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, including its Form 10-K for the year ended December 31, 2011 and its Form 10-Q for the quarter ended June 30, 2012. 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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