



**REGENERON**

## **ZALTRAP<sup>®</sup> (afibercept) Approved in the EU for Patients with Previously Treated Metastatic Colorectal Cancer**

**- First and only agent to statistically significantly improve survival in combination with FOLFIRI chemotherapy after an oxaliplatin regimen -**

**Paris, France and Tarrytown, NY – February 5, 2013** – Sanofi (EURONEXT: **SAN** and NYSE: **SNY**) and Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) today announced that the European Commission (EC) granted marketing authorization in the European Union for ZALTRAP<sup>®</sup> (afibercept) 25mg/ml concentrate for solution for infusion in combination with irinotecan/5-fluorouracil/folinic acid (FOLFIRI) chemotherapy in adults with metastatic colorectal cancer (mCRC) that is resistant to or has progressed after an oxaliplatin-containing regimen. This decision was based on the efficacy and safety results of the VELOUR Phase III trial.

*“ZALTRAP is an important addition to the metastatic colorectal cancer treatment landscape and helps to fill a critical treatment gap,”* said Eric Van Cutsem, M.D., Ph.D., University Hospitals Leuven, Belgium and lead investigator of the VELOUR study. *“ZALTRAP is the first and only agent to demonstrate a statistical survival improvement in a Phase III trial in patients previously treated with an oxaliplatin-based regimen who are being treated with FOLFIRI for their metastatic disease.”*

In Europe, colorectal cancer is the most common cancer in both men and women and is the second leading cause of cancer death. In 2008, there were 436,000 new cases diagnosed and 212,000 deaths from colorectal cancer.<sup>1</sup>

*“I would like to thank the physicians, patients and their families for their support in moving ZALTRAP through the clinical trial process leading to approval in Europe,”* said Debasish Roychowdhury, M.D., Senior Vice President and Head, Sanofi Oncology. *“We are thrilled to provide a new therapy that further extends the lives of patients with metastatic colorectal cancer and look forward to working with European health authorities to ensure patients have access to ZALTRAP.”*

Commenting on the marketing authorization, George D. Yancopoulos, M.D., Ph.D., Chief Scientific Officer of Regeneron and President of Regeneron Research Laboratories, added: *“The European approval of ZALTRAP provides a new option to address the unmet medical need in this patient population. There continues to be a need to develop new cancer therapies, and Regeneron and Sanofi are committed to finding novel investigational treatments and combinations.”*

ZALTRAP received approval from the U.S. Food and Drug Administration (FDA) in August 2012 after a Priority Review, and marketing authorization applications for ZALTRAP are under review with other regulatory agencies worldwide.

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<sup>1</sup> ESMO Consensus Guidelines for management of patients with colon and rectal cancer. A personalized approach to clinical decision making. *Annals of Oncol.* 2012; 23: 2470-2516



### **About the VELOUR Phase III Study**

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 of the trial was overall survival. Secondary endpoints included progression-free survival, overall response rate, and safety.

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 percent relative risk reduction, was also observed. The overall response rate in the ZALTRAP plus FOLFIRI arm was 19.8% vs. 11.1% for FOLFIRI alone (p=0.0001).

The most common adverse reactions (all grades,  $\geq 20\%$  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 ( $\geq 5\%$ ) 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® (aflibercept)**

ZALTRAP is a recombinant fusion protein which acts as a decoy receptor that binds to Vascular Endothelial Growth Factor-A (VEGF-A), VEGF-B and placental growth factor (PlGF), as shown in preclinical studies. VEGF-A is one of the mediators contributing to angiogenesis. VEGF-B and PlGF, related growth factors in the VEGF family, may contribute to tumor angiogenesis as well. In the US, ZALTRAP is a registered trademark of Regeneron Pharmaceuticals, Inc.

In the US ZALTRAP is approved with the US proper name ziv-aflibercept. The World Health Organization (WHO) recommended international non-proprietary name for ZALTRAP is aflibercept. Marketing authorization applications for ZALTRAP are under review other regulatory agencies worldwide.

### **About Colorectal Cancer**

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. According to the American Cancer Society, 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.

### **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 leading science-based biopharmaceutical company based in Tarrytown, New York that discovers, invents, develops, manufactures, and commercializes medicines for the treatment of serious medical conditions. Regeneron markets medicines for eye diseases, colorectal cancer, and a rare inflammatory condition and has product candidates in development in other areas of high unmet medical need, including hypercholesterolemia, rheumatoid arthritis, asthma and atopic dermatitis. For additional information about the company, please visit [www.regeneron.com](http://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<sup>®</sup> (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 September 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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