SANOFI

Press Release

Source: Sanofi (EURONEXT: SAN) (NASDAQ: SNY)

FDA approves Libtayo® (cemiplimab-rwlc) monotherapy for patients with first-line advanced non-small cell lung cancer with PD-L1 expression of ≥50%

- Libtayo was superior in extending overall survival compared to chemotherapy in a pivotal trial that allowed for certain disease characteristics frequently underrepresented in advanced NSCLC trials

- This is the third approval for Libtayo in the U.S.

PARIS and TARRYTOWN, N.Y. – February 22, 2021 - The U.S. Food and Drug Administration (FDA) has approved the PD-1 inhibitor Libtayo® (cemiplimab-rwlc) for the first-line treatment of patients with advanced non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression (tumor proportion score ≥50%), as determined by an FDA-approved test. Patients must either have metastatic or locally advanced tumors that are not candidates for surgical resection or definitive chemoradiation, and the tumors must not have EGFR, ALK or ROS1 aberrations.

> *"The approval of Libtayo to treat first-line advanced non-small cell lung cancer with high PD-L1 expression means physicians and patients have a potent new treatment option against this deadly disease,"* said Naiyer Rizvi, M.D., Price Family Professor of Medicine, Director of Thoracic Oncology and Co-director of Cancer Immunotherapy at Columbia University Irving Medical Center, as well as a steering committee member of the trial. *"Notably, Libtayo was approved based on a pivotal trial where most chemotherapy patients crossed over to Libtayo following disease progression, and that allowed for frequently underrepresented patients who had pretreated and clinically stable brain metastases, or who had locally advanced disease and were not candidates for definitive chemoradiation. This gives doctors important new data when considering Libtayo for the varied patients and situations they treat in daily clinical practice."*

This is the third approval for Libtayo and follows a Priority Review by the FDA, which is reserved for medicines that represent significant improvements in safety or efficacy in treating serious conditions. Earlier this month, Libtayo was approved as the first immunotherapy indicated for patients with advanced basal cell carcinoma (BCC) previously treated with a hedgehog pathway inhibitor (HHI) or for whom an HHI is not appropriate, with full approval granted for locally advanced disease and accelerated approval granted for metastatic disease. In 2018, Libtayo was the first systemic treatment approved for adults with advanced cutaneous squamous cell carcinoma (CSCC) that is locally advanced or metastatic and who are not candidates for curative surgery or

curative radiation. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue during or after treatment with Libtayo.

> *"Libtayo has demonstrated an impressive level of efficacy in advanced NSCLC with at least 50% PD-L1expression in its pivotal trial,"* said Ahmet Sezer, M.D., Professor in the Department of Medical Oncology at Başkent University in Adana, Turkey and a trial investigator. *"As published in The Lancet, a prespecified analysis in the subset of patients proven to have PD-L1 expression of at least 50%, Libtayo reduced the risk of death by 43% compared to chemotherapy. This was achieved with a greater than 70% crossover rate to Libtayo following disease progression on chemotherapy, as well as the largest population of patients with pretreated and clinically stable brain metastases among advanced NSCLC pivotal trials to date."*

The data supporting the Libtayo approval are based on an analysis of 710 patients who were randomized to receive treatment in a Phase 3 trial; eligible patients were intended to have PD-L1 expression of ≥50%. In this patient population, Libtayo reduced the risk of death by 32% compared to chemotherapy, with additional efficacy results as follows:

Endpoints	***Libtayo*** ***350 mg every 3 weeks*** *N=356*	***Chemotherapy*** *N=354*
Overall Survival (OS)		
Median (95% Confidence Interval [CI])[a]	22 months (18 months to not evaluable)	14 months (12 to 19 months)
Hazard ratio (95% CI)[b]	0.68 (0.53-0.87)	
p-value	0.0022	
Progression-free Survival (PFS) per Blinded Independent Central Review (BICR)		
Median (95% CI)[a]	6.2 months (4.5 to 8.3 months)	5.6 months (4.5 to 6.1 months)
Hazard ratio (95% CI)[b]	0.59 (0.49-0.72)	
p-value	<0.0001	

a Based on Kaplan-Meier method
b Based on stratified proportional hazards model

An additional prespecified analysis was performed in 563 patients with proven PD-L1 expression of ≥50%, according to the FDA-approved assay, and is described in the updated labeling of the FDA-approved assay (and also recently published in *The Lancet).* This analysis showed that Libtayo reduced the risk of death by 43% compared to chemotherapy, with additional efficacy results as follows:

Endpoints	***Libtayo*** ***350 mg every 3 weeks*** *N=283*	***Chemotherapy*** *N=280*

OS		
Median (95% CI)[a]	not reached (18 months to not evaluable)	14 months (11 to 18 months)
Hazard ratio (95% CI)[b]	0.57 (0.42-0.77)	
p-value	0.0002	
PFS		
Median (95% CI)[a]	8 months (6 to 9 months)	6 months (5 to 6 months)
Hazard ratio (95% CI)[b]	0.54 (0.43-0.68)	
p-value	<0.0001	

NOTE: The analysis was conducted in a subset of the randomized population that excluded 147 patients whose tumors could not be retested or were later found to have <50% PD-L1 expression.
a Based on Kaplan-Meier method
b Based on stratified proportional hazards model

Safety was assessed in 355 patients in the Libtayo group (median duration of exposure: 27 weeks; range: 9 days to 115 weeks) and 342 patients in the chemotherapy group (median duration of exposure: 18 weeks; range: 18 days to 87 weeks). Adverse reactions that occurred more commonly in the Libtayo group and in at least 10% of patients were rash (15% Libtayo, 6% chemotherapy) and cough (11% Libtayo, 8% chemotherapy). The most frequent serious adverse reactions in at least 2% of patients were pneumonia (5% Libtayo, 6% chemotherapy) and pneumonitis (2% Libtayo, 0% chemotherapy). Treatment was permanently discontinued due to adverse reactions in 6% of Libtayo patients; adverse reactions resulting in permanent discontinuation in at least 2 patients were pneumonitis, pneumonia, ischemic stroke and increased aspartate aminotransferase. No new Libtayo safety signals were observed.

> *"With this third approval for Libtayo, we are proud to deliver on our ambition to bring our PD-1 inhibitor to patients in need with difficult-to-treat cancers, such as advanced non-small cell lung cancer,"* said Peter C. Adamson, M.D., Global Development Head, Oncology and Pediatric Innovation at Sanofi. *"As the leading cause of cancer deaths globally, the need for additional therapeutic options in advanced NSCLC is clear. Libtayo allows physicians to further optimize treatment of these patients whose tumors have high expression of PD-L1. We thank all of the trial investigators, patients and their caregivers who helped make this milestone possible."*

Lung cancer is the leading cause of cancer death worldwide. In 2020, an estimated 2.2 million and 225,000 new cases were diagnosed worldwide and in the U.S, respectively. Approximately 84% of all lung cancers are NSCLC, with 75% of these cases diagnosed in advanced stages and an estimated 25% to 30% of cases expected to test positive for PD-L1 in ≥50% of tumor cells.

"We developed Libtayo to deliver clinically meaningful benefits to patients suffering from a diverse range of cancers and to establish a foundation for potential future immunotherapy combinations. Today's approval continues to support this vision," said Israel Lowy, M.D., Ph.D., Senior Vice President, Translational and Clinical Sciences, Oncology at Regeneron*. "Libtayo has already changed the treatment paradigm for certain patients with advanced cutaneous squamous cell carcinoma and is poised to do the same for advanced basal cell carcinoma. Now, Libtayo has the opportunity to make a meaningful difference for the many U.S. patients battling advanced non-small cell lung cancer. Libtayo is being investigated in a variety of settings, and we hope to share updates later this year on our pivotal trials in cervical cancer and in combination with chemotherapy in advanced non-small cell lung cancer."*

About the Phase 3 Trial Supporting Approval

The open-label, randomized, multi-center Phase 3 trial, called EMPOWER-Lung 1, was designed to investigate the first-line treatment of Libtayo monotherapy compared to platinum-doublet chemotherapy in patients with advanced NSCLC who tested positive for PD-L1 in ≥50% of tumor cells and without EGFR, ALK or ROS1 aberrations. PD-L1 expression was confirmed using the Agilent Dako PD-L1 IHC 22C3 pharmDx kit. The primary endpoints were OS and PFS, and secondary endpoints included overall response rate, duration of response and quality of life.

The trial randomized 710 patients with either previously untreated metastatic NSCLC (Stage IV) or locally advanced NSCLC (Stage IIIB/C) who were not candidates for surgical resection or definitive chemoradiation or who had progressed after treatment with definitive chemoradiation. Enrolled patients included those with disease characteristics frequently underrepresented in pivotal advanced NSCLC trials. Among them, 12% had pre-treated and clinically stable brain metastases and 16% had locally advanced NSCLC that was not a candidate for definitive chemoradiation.

Importantly, patients whose disease progressed in the trial were able to change their therapy: those assigned to chemotherapy were allowed to crossover to Libtayo treatment following disease progression, while those assigned to Libtayo monotherapy were allowed to combine Libtayo treatment with 4 to 6 cycles of chemotherapy following disease progression. There was a >70% crossover rate to Libtayo following disease progression on chemotherapy.

About Libtayo

Libtayo is a fully-human monoclonal antibody targeting the immune checkpoint receptor PD-1 on T-cells. By binding to PD-1, Libtayo has been shown to block cancer cells from using the PD-1 pathway to suppress T-cell activation.

Across all of its approved indications, the recommended dose of Libtayo is 350 mg administered as an intravenous infusion over 30 minutes every three weeks, until disease progression or unacceptable toxicity. Libtayo is available as a single-dose 350 mg vial.

In the U.S., the generic name for Libtayo in its approved indication is cemiplimab-rwlc, with rwlc as the suffix designated in accordance with Nonproprietary Naming of Biological Products Guidance for Industry issued by the FDA. Outside of the U.S., the generic name for Libtayo in its approved indication is cemiplimab.

About the Libtayo Development Program

The European Medicines Agency is assessing regulatory submissions for Libtayo in advanced NSCLC with ≥50% PD-L1 expression and locally advanced BCC following treatment with an HHI. Decisions by the European Commission on these submissions are expected by mid-2021.

The extensive clinical program for Libtayo is focused on difficult-to-treat cancers. In skin cancer, this includes trials in adjuvant and neoadjuvant CSCC. Libtayo is also being investigated in pivotal trials in NSCLC (in combination with chemotherapy) and cervical cancer, as well as in trials combining Libtayo with either conventional or novel therapeutic approaches for both solid tumors and blood cancers. These potential uses are investigational, and their safety and efficacy have not been evaluated by any regulatory authority.

Libtayo is being jointly developed by Sanofi and Regeneron under a global collaboration agreement.

About Regeneron

Regeneron (NASDAQ: REGN) is a leading biotechnology company that invents life-transforming medicines for people with serious diseases. Founded and led for over 30 years by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to nine FDA-approved treatments and numerous product candidates in development, almost all of which were homegrown in our laboratories. Our medicines and pipeline are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, pain, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary *VelociSuite*® technologies, such as *VelocImmune*®, which uses unique genetically-humanized mice to produce optimized fully-human antibodies and bispecific antibodies, and through ambitious research initiatives such as the Regeneron Genetics Center, which is conducting one of the largest genetics sequencing efforts in the world.

For additional information about the company, please visit www.regeneron.com or follow @Regeneron on Twitter.

About Sanofi

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.

Sanofi, Empowering Life

Sanofi Media Relations Contact
Sally Bain
Tel.: +1 (781) 264-1091
sally.bain@sanofi.com

Sanofi Investor Relations Contacts Paris
Eva Schaefer-Jansen
Arnaud Delepine
Yvonne Naughton

Sanofi Investor Relations Contacts North America
Felix Lauscher
Fara Berkowitz
Suzanne Greco

Sanofi IR main line:
Tel.: +33 (0)1 53 77 45 45
investor.relations@sanofi.com
https://www.sanofi.com/en/investors/contact

Regeneron Media Relations Contact
Daren Kwok
Tel: +1 (914) 847-1328
daren.kwok@regeneron.com

Regeneron Investor Relations Contact
Vesna Tosic
Tel: +1 (914) 847-5443
vesna.tosic@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 fact that product candidates if approved may not be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities, to complete related transactions and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic and market conditions, cost containment initiatives and subsequent changes thereto, and the impact that COVID-19 will have on us, our customers, suppliers, vendors, and other business partners, and the financial condition of any one of them, as well as on our

employees and on the global economy as a whole. Any material effect of COVID-19 on any of the foregoing could also adversely impact us. This situation is changing rapidly and additional impacts may arise of which we are not currently aware and may exacerbate other previously identified risks. The risks and uncertainties also include the uncertainties 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, 2019. 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 press release includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron Pharmaceuticals, Inc. ("Regeneron" or the "Company"), and actual events or results may differ materially from these forward-looking statements. Words such as "anticipate," "expect," "intend," "plan," "believe," "seek," "estimate," variations of such words, and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. These statements concern, and these risks and uncertainties include, among others, the impact of SARS-CoV-2 (the virus that has caused the COVID-19 pandemic) on Regeneron's business and its employees, collaborators, and suppliers and other third parties on which Regeneron relies, Regeneron's and its collaborators' ability to continue to conduct research and clinical programs, Regeneron's ability to manage its supply chain, net product sales of products marketed or otherwise commercialized by Regeneron and/or its collaborators (collectively, "Regeneron's Products"), and the global economy; the nature, timing, and possible success and therapeutic applications of Regeneron's Products and product candidates being developed by Regeneron and/or its collaborators (collectively, "Regeneron's Product Candidates") and research and clinical programs now underway or planned, including without limitation Libtayo® (cemiplimab) for the first-line treatment of patients with advanced non-small cell lung cancer ("NSCLC") whose tumors have high PD-L1 expression; uncertainty of market acceptance and commercial success of Regeneron's Products and Regeneron's Product Candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary), including the studies discussed or referenced in this press release, on the commercial success of Regeneron's Products (such as Libtayo) and Regeneron's Product Candidates; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's Product Candidates and new indications for Regeneron's Products, such as Libtayo for the treatment of adjuvant and neoadjuvant cutaneous squamous cell carcinoma, NSCLC (in combination with chemotherapy), and cervical cancer (as well as in combination with either conventional or novel therapeutic approaches for both solid tumors and blood cancers); safety issues resulting from the administration of Regeneron's Products (such as Libtayo) and Regeneron's Product Candidates in patients, including serious complications or side effects in connection with the use of Regeneron's Products and Regeneron's Product Candidates in clinical trials; 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 Regeneron's Product Candidates; ongoing regulatory obligations and oversight impacting Regeneron's Products, research and clinical programs, and business, including those relating to patient privacy; the availability and extent of reimbursement of Regeneron's Products from third-party payers, including private payer healthcare and insurance programs, health maintenance organizations, pharmacy benefit management companies, and government programs such as Medicare and Medicaid; coverage and reimbursement determinations by such payers and new policies and procedures adopted by such payers; competing drugs and product candidates that may be superior to, or more cost effective than, Regeneron's Products and Regeneron's Product Candidates; the extent to which the results from the research and development programs conducted by Regeneron and/or its collaborators may be replicated in other studies and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; the ability of Regeneron to manufacture and manage supply chains for multiple products and product candidates; the ability of Regeneron's collaborators, suppliers, or other third parties (as applicable) to perform manufacturing, filling, finishing, packaging, labeling, distribution, and other steps related to Regeneron's Products and Regeneron's Product Candidates; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its financial projections or guidance and changes to the assumptions underlying those projections or guidance; the potential for any license, collaboration, or supply agreement, including Regeneron's agreements with Sanofi, Bayer, and Teva Pharmaceutical Industries Ltd. (or their respective affiliated companies, as applicable), to be cancelled or terminated; and risks associated with intellectual property of other parties and pending or future litigation relating thereto (including without limitation the patent litigation and other related proceedings relating to EYLEA® (aflibercept) Injection, Dupixent® (dupilumab), Praluent® (alirocumab), and REGEN-COV™ (casirivimab and imdevimab)), other litigation and other proceedings and government investigations relating to the Company and/or its operations, the ultimate outcome of any such proceedings and investigations, and the impact any of the foregoing may have on Regeneron's business, prospects, operating results, and financial condition. A more complete description of these and other material risks can be found in Regeneron's filings with the U.S. Securities and Exchange Commission, including

its Form 10-K for the year ended December 31, 2020. Any forward-looking statements are made based on management's current beliefs and judgment, and the reader is cautioned not to rely on any forward-looking statements made by Regeneron. Regeneron does not undertake any obligation to update (publicly or otherwise) any forward-looking statement, including without limitation any financial projection or guidance, whether as a result of new information, future events, or otherwise.

Regeneron uses its media and investor relations website and social media outlets to publish important information about the Company, including information that may be deemed material to investors. Financial and other information about Regeneron is routinely posted and is accessible on Regeneron's media and investor relations website (http://newsroom.regeneron.com) and its Twitter feed (http://twitter.com/regeneron).