FDA Approves Libtayo® (cemiplimab-rwlc) as First and Only Treatment for Advanced Cutaneous Squamous Cell Carcinoma

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TARRYTOWN, N.Y. and PARIS, Sept. 28, 2018 /PRNewswire/ --

Libtayo is the third anti-PD-1 approved in the U.S.

CSCC is the second most common skin cancer in the U.S.

Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) and Sanofi today announced that the U.S. Food and Drug Administration (FDA) has approved Libtayo® (cemiplimab-rwlc) for the treatment of patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation. Libtayo is a fully-human monoclonal antibody targeting the immune checkpoint receptor PD-1 (programmed cell death protein-1) and is the first and only treatment specifically approved and available for advanced CSCC in the U.S.

"Today's FDA decision is great news for patients with advanced CSCC, who previously had no approved treatment options. This is especially true because these patients are no longer candidates for curative surgery or radiation," said Michael R. Migden, M.D., a lead investigator in the pivotal CSCC clinical program and Professor in the Departments of Dermatology and Head and Neck Surgery at The University of Texas MD Anderson Cancer Center. "Libtayo is an important new immunotherapy option for U.S. physicians to help address a significant unmet need in this patient group."

CSCC is the second most common form of skin cancer and is responsible for an estimated 7,000 deaths each year in the U.S. It currently accounts for approximately 20% of all skin cancers in the U.S., with the number of newly diagnosed cases expected to rise annually. When CSCC invades deeper layers of the skin or adjacent tissues, it is categorized as locally advanced. Once it spreads to other distant parts of the body, it is considered metastatic.

"By following the science, we identified early on that advanced CSCC was a promising target for investigation with Libtayo," said Israel Lowy, M.D., Ph.D., Vice President of Global Clinical Development and Head of Translational Science and Clinical Oncology, Regeneron. "We are proud to offer patients in the U.S. this first and only treatment for advanced CSCC and remain focused on advancing our clinical research investigating Libtayo as a potential monotherapy and combination therapy in other cancer types."

Libtayo was evaluated by the FDA under Priority Review, which is reserved for medicines that represent significant improvements in safety or efficacy in treating serious conditions, and in 2017 was granted Breakthrough Therapy Designation status for advanced CSCC. Breakthrough Therapy Designation was created to expedite the development and review of drugs that have the potential for substantial improvement in the treatment of serious or life-threatening conditions.

"In the U.S., CSCC accounts for one in five skin cancers, and the number of new diagnoses is increasing," said Olivier Brandicourt, M.D., Chief Executive Officer, Sanofi. "We believe Libtayo has the potential to make a difference for U.S. patients with advanced CSCC, as it helps to fill a critical gap in treatment options. We are committed to bringing this important medicine to patients in other countries around the world as quickly as possible."

The recommended dosage 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.

Libtayo is expected to provide significant value for patients with advanced CSCC and those who care for them. The U.S. list price, or wholesale acquisition cost, is $9,100 per three-week treatment cycle. Actual costs to patients are generally anticipated to be lower as the list price does not reflect insurance coverage, copay support or financial assistance from patient support programs.

Regeneron and Sanofi are committed to helping U.S. patients who have been prescribed Libtayo access their medication. The companies have launched Libtayo Surround™ to help patients understand how Libtayo may be covered by their health insurance plans. Additionally, Libtayo Surround is designed to help eligible patients who need financial assistance with their prescription. For more information, please call 1-877-LIBTAYO (1-877-542-8296), Option 1, or visit www.Libtayo.com.

Regeneron and Sanofi Genzyme, the specialty care global business unit of Sanofi, will market Libtayo jointly in the U.S. Libtayo was invented by Regeneron using the company's proprietary *VelocImmune*® technology that yields optimized fully-human antibodies.

Pivotal Advanced CSCC Clinical Program and Results
The FDA approval of Libtayo was based on a combined analysis of data from an open-label, multi-center, non-randomized Phase 2 trial known as EMPOWER-CSCC-1 (Study 1540) and two advanced CSCC expansion cohorts from a multi-center, open-label, non-randomized Phase 1 trial (Study 1423). Together, the trials represent the largest prospective data set in advanced CSCC.

The major efficacy outcome measures for the integrated analysis of EMPOWER-CSCC-1 and the two CSCC expansion cohorts were confirmed objective response rate (ORR), as assessed by independent central review (ICR), and ICR-assessed duration of response (DOR). The efficacy analysis was conducted when all patients had the opportunity for at least six months of follow-up.

Combined efficacy results (n=108) from EMPOWER-CSCC-1 and the two advanced CSCC expansion cohorts from the Phase 1 trial were as follows:

Efficacy Endpoints*	**Metastatic CSCC**	**Locally Advanced CSCC**	**Combined CSCC**

	(n = 75)	(n= 33)	(n = 108)
Confirmed ORR			
ORR (95% confidence interval [CI])	47% (35, 59)	49% (31, 67)	47% (38, 57)
Complete response rate†	5%	0%	4%
Partial response rate	41%	49%	44%
DOR			
Range in months	3-15+	1-13+	1-15+
Patients with DOR ≥ 6 months, n (%)	21 (60%)	10 (63%)	31 (61%)

+Denotes ongoing at last assessment
*Median duration of follow-up: metastatic CSCC: 8.1 months; locally advanced CSCC: 10.2 months; combined CSCC: 8.9 months
†Only includes patients with complete healing of prior cutaneous involvement; locally advanced CSCC patients in EMPOWER-CSCC-1 required biopsy to confirm complete response.

For the combined safety analysis (n=163) of EMPOWER-CSCC-1 and the two advanced CSCC expansion cohorts, the most common adverse reactions reported were fatigue (29%), rash (25%) and diarrhea (22%). Libtayo was permanently discontinued due to adverse reactions in 5% of patients; adverse reactions resulting in permanent discontinuation were pneumonitis, autoimmune myocarditis, hepatitis, aseptic meningitis, complex regional pain syndrome, cough and muscular weakness. Serious adverse reactions (SAEs) occurred in 28% of patients. SAEs that occurred in at least 2% of patients were cellulitis, sepsis, pneumonia, pneumonitis and urinary tract infection.

Cemiplimab-rwlc Development Program Overview
Cemiplimab-rwlc is being jointly developed by Regeneron and Sanofi under a global collaboration agreement.

In April 2018, the European Medicines Agency (EMA) accepted for review the Marketing Authorization Application for Libtayo for the treatment of patients with metastatic CSCC or with locally advanced CSCC who are not candidates for surgery. The EMA review process is anticipated to be complete in the first half of 2019. There are currently no EMA-approved treatments for advanced CSCC. Regulatory applications in additional countries are also being considered for submission later in 2018.

In addition to advanced CSCC, cemiplimab-rwlc is being investigated in trials in non-small cell lung cancer, basal cell carcinoma, and cervical cancer along with trials in squamous cell carcinoma of the head and neck, melanoma, colorectal cancer, prostate cancer, multiple myeloma, Hodgkin lymphoma and non-Hodgkin lymphoma. These potential uses are investigational, and their safety and efficacy have not been evaluated by any regulatory authority.

IMPORTANT SAFETY INFORMATION AND INDICATION FOR U.S. PATIENTS

What is the most important information I should know about Libtayo?

Libtayo is a medicine that may treat a type of skin cancer by working with your immune system. Libtayo can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. These problems may happen anytime during treatment or even after your treatment has ended.

Call or see your healthcare provider right away if you develop any symptoms of the following problems or these symptoms get worse:

- **Lung problems (pneumonitis).** Signs and symptoms of pneumonitis may include new or worsening cough, shortness of breath, and chest pain.
- **Intestinal problems (colitis) that can lead to tears or holes in your intestine.** Signs and symptoms of colitis may include diarrhea (loose stools) or more frequent bowel movements than usual; stools that are black, tarry, or sticky or that have blood or mucus; and severe stomach-area (abdomen) pain or tenderness.
- **Liver problems (hepatitis).** Signs and symptoms of hepatitis may include yellowing of your skin or the whites of your eyes, severe nausea or vomiting, pain on the right side of your stomach area (abdomen), drowsiness, dark urine (tea colored), bleeding or bruising more easily than normal, and feeling less hungry than usual.
- **Hormone gland problems** (especially the adrenal glands, pituitary, thyroid and pancreas). Signs and symptoms that your hormone glands are not working properly may include headaches that will not go away or unusual headaches, rapid heartbeat, increased sweating, extreme tiredness, weight gain or weight loss, dizziness or fainting, feeling more hungry or thirsty than usual, hair loss, feeling cold, constipation, deeper voice, very low blood pressure, urinating more often than usual, nausea or vomiting, stomach-area (abdomen) pain, and changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness.
- **Kidney problems,** including nephritis and kidney failure. Signs of these problems may include decrease in your amount of urine, blood in your urine, swelling in your ankles, and loss of appetite.
- **Skin problems.** Signs of these problems may include rash, itching, skin blistering, and painful sores or ulcers in the mouth, nose, throat, or genital area.

- **Problems in other organs.** Signs of these problems may include headache, tiredness or weakness, sleepiness, changes in heartbeat (such as beating fast, seeming to skip a beat, or a pounding sensation), confusion, fever, muscle weakness, balance problems, nausea, vomiting, stiff neck, memory problems, seizures (encephalitis), swollen lymph nodes, rash or tender lumps on skin, cough, shortness of breath, vision changes, or eye pain (sarcoidosis), seeing or hearing things that are not there (hallucinations), severe muscle weakness, low red blood cells (anemia), bruises on the skin or bleeding, and changes in eyesight.
- **Rejection of a transplanted organ.** Your doctor should tell you what signs and symptoms you should report and monitor you, depending on the type of organ transplant that you have had.
- **Infusion (IV) reactions that can sometimes be severe and life-threatening.** Signs of these problems may include chills or shaking, itching or rash, flushing, shortness of breath or wheezing, dizziness, fever, feeling of passing out, back or neck pain, and facial swelling.

Getting medical treatment right away may help keep these problems from becoming more serious.

Your healthcare provider will check you for these problems during your treatment with Libtayo. Your healthcare provider may treat you with corticosteroid or hormone replacement medicines. Your healthcare provider may delay or completely stop treatment if you have severe side effects.

Before you receive Libtayo, tell your healthcare provider about all your medical conditions, including if you:

- have immune system problems such as Crohn's disease, ulcerative colitis, or lupus;
- have had an organ transplant;
- have lung or breathing problems;
- have liver or kidney problems;
- have diabetes;
- are pregnant or plan to become pregnant; Libtayo can harm your unborn baby
  Females who are able to become pregnant:
  - Your healthcare provider will give you a pregnancy test before you start treatment.
  - You should use an effective method of birth control during your treatment and for at least 4 months after your last dose of Libtayo. Talk with your healthcare provider about birth control methods that you can use during this time.
  - Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with Libtayo.
- are breastfeeding or plan to breastfeed. It is not known if Libtayo passes into your breast milk. Do not breastfeed during treatment and for at least 4 months after the last dose of Libtayo.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

The most common side effects of Libtayo include tiredness, rash, and diarrhea. These are not all the possible side effects of Libtayo. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Regeneron Pharmaceuticals and Sanofi at 1-877-542-8296.

Please see accompanying full Prescribing Information, including Medication Guide.

What is Libtayo?

Libtayo is a prescription medicine used to treat people with a type of skin cancer called cutaneous squamous cell carcinoma (CSCC) that has spread or cannot be cured by surgery or radiation.

It is not known if Libtayo is safe and effective in children.

About Regeneron Pharmaceuticals, Inc.
Regeneron (NASDAQ: REGN) is a leading biotechnology company that invents life-transforming medicines for people with serious diseases. Founded and led for 30 years by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to seven FDA-approved treatments and numerous product candidates in development, 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, neuromuscular diseases, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary *VelociSuite*® technologies, such as *VelocImmune*® which produces optimized fully-human antibodies, and 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

Regeneron Forward-Looking Statements and Use of Digital Media

This news 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 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 Libtayo® (cemiplimab-rwlc) for the treatment of patients with metastatic cutaneous squamous cell carcinoma ("CSCC") or patients with locally advanced CSCC who are not candidates for curative surgery or curative radiation and other potential indications; the likelihood and timing of achieving any of Regeneron's anticipated clinical development milestones; unforeseen safety issues resulting from the administration of products and product candidates in patients, including serious complications or side effects in connection with the use of Regeneron's product candidates (such as Libtayo) in clinical trials; the likelihood and timing of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates and new indications for marketed products, including without limitation Libtayo for the treatment of non-small cell lung cancer, basal cell carcinoma, cervical cancer, squamous cell carcinoma of the head and neck, melanoma, colorectal cancer, prostate cancer, multiple myeloma, Hodgkin lymphoma, non-Hodgkin lymphoma, and other potential indications; the extent to which the results from the research and development programs conducted by Regeneron or its collaborators may be replicated in other studies and lead to therapeutic applications; ongoing regulatory obligations and oversight impacting Regeneron's marketed products (such as Libtayo), research and clinical programs, and business, including those relating to patient privacy; 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 product candidates; competing drugs and product candidates that may be superior to Regeneron's products and product candidates; uncertainty of market acceptance and commercial success of Regeneron's products and product candidates; 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 to perform filling, finishing, packaging, labeling, distribution, and other steps related to Regeneron's products and product candidates; coverage and reimbursement determinations by third-party payers, including Medicare and Medicaid; 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 or collaboration 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 without any further product success; and risks associated with intellectual property of other parties and pending or future litigation relating thereto, including without limitation the patent litigation proceedings relating to EYLEA® (aflibercept) Injection, Dupixent® (dupilumab) Injection, Praluent® (alirocumab) Injection, the ultimate outcome of any such litigation proceedings, 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 fiscal year ended December 31, 2017 and its Form 10-Q for the quarterly period ended June 30, 2018. 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 any forward-looking statement, 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).

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 regarding the marketing and other potential of the product, or regarding potential future revenues from the product. 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, unexpected regulatory actions or delays, or government regulation generally, that could affect the availability or commercial potential of the product, the absence of guarantee that the product will be commercially successful, the uncertainties inherent in research and development, including future clinical data and analysis of existing clinical data relating to the product, including post marketing, unexpected safety, quality or manufacturing issues, competition in general, risks associated with intellectual property and any related future litigation and the ultimate outcome of such litigation, and volatile economic conditions, as well as those risks 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, 2017. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

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