Regeneron and Vyriad Announce Strategic Agreement for Discovery and Development of New Oncolytic Virus Treatments for Cancer

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Phase 2 trial will evaluate combination of PD-1 inhibitor Libtayo® (cemiplimab-rwlc) and oncolytic virus Voyager-V1; preclinical research collaboration will explore new oncolytic virus treatments

Vyriad to receive upfront payment and equity investment from Regeneron

Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) and Vyriad, Inc. today announced a research collaboration and option licensing agreement focused on the development of new oncolytic (cancer-killing) virus-based treatments for various forms of cancer. The agreement includes a Phase 2 clinical study, slated to begin in 2020, evaluating Regeneron's PD-1 inhibitor Libtayo® (cemiplimab-rwlc) in combination with Vyriad's oncolytic virus Voyager-V1 in multiple types of cancer, including melanoma, lung, liver and endometrial cancers. The companies will also enter into a five-year research effort that utilizes Regeneron's *VelociSuite*® technologies to jointly design and validate novel Vesicular Stomatitis Virus (VSV)-based oncolytic virus treatments.

Libtayo is a fully-human monoclonal antibody targeting the immune checkpoint receptor PD-1 (programmed cell death protein-1) and is being jointly developed and commercialized by Regeneron and Sanofi under a global collaboration agreement. Libtayo was invented by Regeneron using the company's proprietary *VelocImmune*® technology which uses a unique genetically-humanized mouse to produce optimized fully-human antibodies.

Vyriad's investigational drug candidate Voyager-V1 is a potent VSV programmed to attack cancer cells selectively, while also activating the immune system to kill local and distant cancer cells. Further, it amplifies inflammatory and antitumor immune system responses that help turn "cold" tumors "hot," which potentially enhances anti-PD-1 activity. Voyager-V1 is deliverable by intravenous infusion.

"Vyriad's differentiated oncolytic virotherapy platform helps Regeneron continue to diversify our arsenal of immuno-oncology approaches, which include multiple combinations with our anti-PD-1 backbone, as well as novel delivery and re-targeting mechanisms," said Israel Lowy, M.D., Ph.D., Senior Vice President and Head of Clinical and Translational Sciences, Oncology at Regeneron. "We are eager to explore the combination of Voyager-V1 and Libtayo in patients with different tumor types in the short term, and see long-term promising synergies with our existing areas of strength, particularly in antibody development and viral vector technologies. We look forward to working together to help cancer patients in need."

"We are thrilled to partner with Regeneron in this far-reaching collaboration to develop novel cancer treatments," said Stephen Russell, M.D., Ph.D., President and Chief Executive Officer of Vyriad. "We are optimistic that the clinical combination of Voyager-V1 with Libtayo will result in effective anticancer activity, and we are very excited to join forces with Regeneron scientists to develop a new generation of precision targeted VSV therapies. Through the collaboration, we expect that the emerging power of oncolytic virotherapy can finally integrate with proven capabilities of antibody engineering, with the potential to create life-changing medicines for cancer patients."

Under the agreement, Vyriad will receive an upfront payment and Regeneron will make an equity investment in the company. Regeneron will have an exclusive option to license Voyager-V1 and other collaboration products. Vyriad is eligible to receive additional payments based on the achievement of specified development and commercial milestones, as well as royalties on net sales of potential future VSV-based collaboration products. During the five-year collaboration term, Vyriad will work exclusively with Regeneron to research and develop VSV technologies. Specific financial terms were not disclosed.

More About Voyager-V1
Voyager-V1 is an investigational oncolytic virus that was designed for enhanced safety, efficacy, and traceability through the inclusion of an interferon beta gene, enabling the virus to replicate quickly in cancer cells without damaging healthy cells, recruit cancer-fighting immune cells to the tumor, and secrete a measurable reporter protein into the blood. Voyager-V1 was also engineered to include an iodine transporter NIS gene that facilitates tracking of the virus' spread to cancer cells throughout the body. Voyager-V1 is under evaluation as both a monotherapy and combination therapy in multiple Phase 1-2 studies for metastatic colorectal cancer, endometrial cancer, non-small cell lung cancer, squamous cell carcinoma of the head and neck and various blood cancers.

More About Libtayo
Libtayo is approved in the U.S., European Union, Canada and Brazil for adult patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation. In the U.S., the generic name for Libtayo is cemiplimab-rwlc, with rwlc as the suffix designated in accordance with Nonproprietary Naming of Biological Products Guidance for Industry issued by the U.S. Food and Drug Administration.

Beyond the ongoing EMPOWER-CSCC-1 trial, Libtayo is also being investigated in adjuvant and neoadjuvant trials in CSCC and in potential registrational trials in non-small cell lung cancer, basal cell carcinoma and cervical cancer. Additional studies include trials in squamous cell carcinoma of the head and neck, melanoma, colorectal cancer, prostate cancer, multiple myeloma, Hodgkin's lymphoma and non-Hodgkin's lymphoma. These trials are designed to investigate Libtayo as monotherapy; in combination with conventional treatments like chemotherapy; or in combination with other investigational agents, including vaccines, oncolytic viruses and bispecific antibodies, among others. 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, 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.

For more information, please see 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
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, infectious diseases, pain and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary *VelociSuite*® technologies, including *VelocImmune*® which uses a unique genetically-humanized mouse 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 Vyriad
Vyriad is a clinical-stage company developing proprietary oncolytic virus therapies for the treatment of cancers with significant unmet needs. Founded by scientists at Mayo Clinic and the University of Miami, Vyriad programs viruses to selectively attack cancer cells, thereby igniting antitumor immune responses that can complete the process of tumor destruction and prevent disease recurrence. Our lead platforms, derived from vesicular stomatitis and measles viruses, are being evaluated in ongoing Phase 1-2 clinical trials addressing multiple cancer types. Vyriad is a privately held company based in Rochester, Minnesota. For more information, visit www.vyriad.com.

Regeneron Forward-Looking Statements and Use of Digital Media
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 nature, timing, and possible success and therapeutic applications of Regeneron's or its collaborators' products, product candidates, and research and clinical programs now underway or planned, such as the oncolytic virus-based treatment programs discussed in this press release (including the program evaluating Libtayo® (cemiplimab-rwlc) in combination with Voyager-V1 in multiple types of cancer, including melanoma, lung, liver, and endometrial cancers); the extent to which the results from the research and development programs conducted by Regeneron or its collaborators (including based on the collaboration discussed in this press release) may be replicated in other studies and lead to therapeutic applications; 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), as well as Regeneron's collaboration with Vyriad, Inc. discussed in this press release, to be cancelled or terminated without any product success; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates and new indications for marketed products, such as Libtayo (as a monotherapy or in combination with conventional treatments or other investigational agents (such as oncolytic viruses), as applicable) 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's lymphoma, non-Hodgkin's lymphoma, and other potential indications; 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 or its collaborators' product candidates in clinical trials; ongoing regulatory obligations and oversight impacting Regeneron's marketed products, 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 or its collaborators' ability to continue to develop or commercialize products and product candidates; competing drugs and product candidates that may be superior to Regeneron's or its collaborators' products and product candidates; uncertainty of market acceptance and commercial success of Regeneron's or its collaborators' products and product candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary) on the commercial success of Regeneron's or its collaborators' 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 (as applicable) to perform manufacturing, filling, finishing, packaging, labeling, distribution, and other steps related to Regeneron's products and product candidates; the availability and extent of reimbursement of the Company'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; 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; 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 Dupixent® (dupilumab) and Praluent® (alirocumab), the ultimate outcome of any such 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 year ended December 31, 2018 and its Form 10-Q for the quarterly period ended September 30, 2019. 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, 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).

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