REGENERON

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Regeneron and ISA Pharmaceuticals Announce Strategic Immuno-Oncology Collaboration

TARRYTOWN, N.Y. and LEIDEN, The Netherlands, Dec. 18, 2017 /PRNewswire/ -- Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) and ISA Pharmaceuticals B.V., a clinical-stage immunotherapy company, today announced a clinical collaboration to advance ISA101, an immunotherapy targeting human papillomavirus type 16 (HPV16)-induced cancer, in combination with cemiplimab (REGN2810), a PD-1 (programmed cell death protein 1) antibody. Regeneron and ISA will jointly fund and conduct clinical trials of the combination treatment in cervical cancer and head-and-neck cancer.

Expression of HPV oncoproteins contributes to the development of cervical and head-and-neck cancers, and approximately 55 percent of cervical cancers and over 60 percent of head-and-neck cancers are HPV16 positive.[1]

Regeneron and ISA will share clinical trial costs and exchange product supply. In addition, Regeneron will provide an upfront payment and an equity investment in exchange for an option to an exclusive, global license for ISA101. If Regeneron exercises its option to commercialize ISA101, there is potential for various milestone payments and tiered royalty payments to ISA contingent on regulatory approvals, sales and additional indications. Further financial details were not disclosed.

"Regeneron continues to expand and advance our immuno-oncology program by studying multiple combination therapies in order to fully explore the scientific possibilities in this relatively new field," said Israel Lowy, M.D., Ph.D., Vice President Clinical Sciences, Head of Translational Science and Oncology at Regeneron. "Early clinical results with ISA101 in HPV16-positive indications have been promising, and we're eager to investigate the impact of adding cemiplimab with the goal of further enabling the body's immune system to attack the cancer."

"This collaboration with Regeneron is a strong validation of our proprietary SLP® (Synthetic Long Peptides) platform and know-how," added Ronald Loggers, Chief Executive Officer of ISA Pharmaceuticals. "We are proud to work with Regeneron, a science- and technology-driven biotechnology company, and aim to further strengthen our pioneering role in the development of innovative treatment options for oncology indications with a high unmet medical need."

Cemiplimab is being jointly developed by Regeneron and Sanofi under a global collaboration agreement for immuno-oncology therapeutics, and was developed using Regeneron's proprietary *VelocImmune*® technology that yields optimized fully-human antibodies. Cemiplimab is currently being studied as a monotherapy in multiple cancers - including cutaneous squamous cell carcinoma (CSCC), basal cell carcinoma (BCC), non-small cell lung cancer (NSCLC) and cervical cancer - and in various therapeutic combinations. Cemiplimab is currently under clinical development, and its safety and efficacy have not been fully evaluated by any regulatory authority.

ISA101 is an SLP® immunotherapy based on the delivery of oncogenic antigens in the form of synthetic long peptides and targets HPV-induced diseases. This innovative concept was discovered by emeritus professor Cornelis J. M. Melief and his team at the Leiden University Medical Center and has been the subject of multiple studies and peer-reviewed publications. It is ISA´s most advanced clinical-stage immunotherapeutic and is in clinical development in advanced and recurrent cervical cancer and incurable HPV16-positive solid tumors (such as squamous cell carcinoma of the head and neck). The first proof-of-concept data on ISA101 as a monotherapy treatment were published in the *New England Journal of Medicine*[2] and initial results from the recently completed ISA101 combination trials in advanced cervical cancer and head-and-neck cancer were presented at ASCO-SITC and ESMO, respectively, in 2017.[3]

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 nearly 30 years by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to six FDA-approved treatments and over a dozen product candidates in development, all of which were homegrown in our laboratories. Our medicines and pipeline are designed to help patients with eye disease, heart disease, allergic and inflammatory diseases, pain, cancer, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary *VelociSuite*® technologies and ambitious initiatives such as the Regeneron Genetics Center, 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 ISA Pharmaceuticals

ISA Pharmaceuticals B.V. is an immunotherapy company developing rationally designed, fully synthetic immunotherapeutics against cancer and persistent viral infections. The company has built a proprietary immunotherapy platform based on the Synthetic Long Peptide (SLP®) concept and AMPLIVANT® technology. SLP® immunotherapies are designed to fully harness and direct the body's own defenses towards fighting the disease. In addition, ISA develops MyISA®, a personalized SLP® immunotherapy, targeting tumor-specific, mutation-derived neo-antigens. For more information, please visit www.isa-pharma.com

SLP®, AMPLIVANT® and MyISA® are registered trademarks in Europe.

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 Regeneron's immuno-oncology program, cemiplimab (REGN2810), and the clinical collaboration to advance ISA101, an immunotherapy targeting human papillomavirus type 16 (HPV16)-induced diseases, in combination with cemiplimab in patients with cervical cancer or head-and-neck cancer (the "Cemiplimab/ISA101 Combination Therapy"); the extent to which the results from the research and development programs conducted by Regeneron or its collaborators (such as ISA Pharmaceuticals B.V.) may be replicated in later studies and lead to therapeutic applications; 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 and its collaborators' product candidates in clinical trials, such as the Cemiplimab/ISA101 Combination Therapy; determinations by regulatory and administrative governmental authorities which may delay or restrict Regeneron's or its collaborators' ability to continue to develop or commercialize their respective products and product candidates, including without limitation the Cemiplimab/ISA101 Combination Therapy; 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 cemiplimab in patients with cutaneous squamous cell carcinoma, basal cell carcinoma, non-small cell lung cancer, cervical cancer, and other potential indications; ongoing regulatory obligations and oversight impacting Regeneron's marketed products, research and clinical programs, and business, including those relating to patient privacy; competing drugs and product candidates that may be superior to Regeneron's and its collaborators' respective products and product candidates; uncertainty of market acceptance and commercial success of Regeneron's and 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 such products and product candidates; the ability of Regeneron's collaborators, suppliers, or other third parties to perform filling, finishing, packaging, labelling, distribution, and other steps related to Regeneron's products and product candidates; coverage and reimbursement determinations by third-party payers, including Medicare and Medicaid; the ability of Regeneron to manufacture and manage supply chains for multiple products and product candidates; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its sales or other 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 HealthCare LLC, and Teva Pharmaceutical Industries Ltd. (or their respective affiliated companies, as applicable), as well as Regeneron's collaboration with ISA Pharmaceuticals B.V. discussed in this news release, to be cancelled or terminated without any 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 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 United States Securities and Exchange Commission, including its Form 10-K for the year ended December 31, 2016 and its Form 10-Q for the quarterly period ended September 30, 2017. 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).

Regeneron Investor Relations
Manisha Narasimhan, Ph.D.
Tel: +1 (914) 847-5126
Manisha.narasimhan@regeneron.com

Regeneron Media Relations
Alexandra Bowie
Tel: +1 (914) 847-3407
alexandra.bowie@regeneron.com

ISA Contact & Media Inquiries:
akampion
Dr. Ludger Wess, Ines-Regina Buth
Managing Partners
Tel. +49 40 88 16 59 64, Tel. +49 30 23 63 27 68
info(at)akampion.com

[1] www.hpvcentre.net; Chaturvedi *et al*., 2011 J. Clin. Oncol. 29(32).

[2] Kenter et al. 2009 N Engl J Med 361. Available at http://www.nejm.org/doi/full/10.1056/NEJMoa0810097#t=article.

[3] Melief et al 2017 ASCO-SITC abstract #140; Glisson et al. 2017 ESMO abstract #11360

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