Regeneron and Ultragenyx Collaborate to Commercialize Evkeeza® (evinacumab) Outside the United States

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Evkeeza is a first-in-class medicine approved by the U.S. Food and Drug Administration (FDA) and European Commission (EC) to treat an ultra-rare inherited form of high cholesterol

TARRYTOWN, N.Y. and NOVATO, C.A., January 7, 2022 – Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) and Ultragenyx Pharmaceutical Inc. today announced a license and collaboration agreement for Ultragenyx to clinically develop, commercialize and distribute Evkeeza® (evinacumab) in countries outside of the U.S. This includes the European Economic Area, where Evkeeza was approved in June 2021 as a first-in-class therapy for use together with diet and other low-density lipoprotein-cholesterol (LDL-C) lowering therapies to treat adults and adolescents aged 12 years and older with homozygous familial hypercholesterolemia (HoFH). Regeneron discovered and developed Evkeeza, and launched the medicine in the U.S. in February 2021 when it was approved by the FDA.

“Evkeeza is a transformational medicine for those living with homozygous familial hypercholesterolemia, as previous therapies were insufficient for many patients who still faced extremely high LDL cholesterol levels and treatment-related tolerability issues,” said George D. Yancopoulos, M.D., Ph.D., Chief Scientific Officer and President of Regeneron. “With its focus on rare, debilitating genetic conditions, Ultragenyx is an ideal partner for us, and we look forward to working together to bring this much needed medicine to patients around the world.”

Under the terms of the agreement, Regeneron will receive a $30 million upfront payment and is eligible to receive up to $63 million in additional potential regulatory and sales milestones. Ultragenyx will receive the rights to develop, commercialize and distribute the medicine in countries outside of the U.S. and make payments to Regeneron based on net sales. Ultragenyx will share in certain costs for global trials led by Regeneron and also have the right to continue to clinically develop Evkeeza in countries outside of the U.S. for HoFH and other potential indications.

Regeneron has also granted Ultragenyx an exclusive option to negotiate a separate agreement to collaborate on the development and commercialization outside of the U.S. of Regeneron’s investigational antibody currently in Phase 2/3 development for the treatment of the ultra-rare disease, fibrodysplasia ossificans progressiva (FOP) under terms to be agreed upon by both companies.

“Evkeeza utilizes a novel, potent biological mechanism to significantly reduce LDL cholesterol levels beyond historical standard of care for people with HoFH. This is a highly complementary partnership that combines Regeneron’s bold science with our proficiency in rare disease,” said Emil D. Kakkis, M.D., Ph.D., Chief Executive Officer and President of Ultragenyx. “We have developed our commercial expertise to support patient identification and access across regions and we believe we can make a real difference for the HoFH community outside of the U.S.”

Regeneron will continue to solely commercialize Evkeeza in the U.S., where more patients with HoFH are now being treated with Evkeeza than the prior standard-of-care. In countries outside of the U.S., Ultragenyx will be responsible for commercialization efforts.

About Homozygous Familial Hypercholesterolemia (HoFH)

HoFH, also known as homozygous FH, is an ultra-rare inherited condition that affects 1 in 160,000 to 300,000 people worldwide. HoFH occurs when two copies of the familial hypercholesterolemia (FH)-causing genes are inherited, one from each parent, resulting in dangerously high levels (>400 mg/dL) of LDL-C, or bad cholesterol. Patients with HoFH are at risk for premature atherosclerotic disease and cardiac events as early as their teenage years.

About Evkeeza® (evinacumab)

Evkeeza is a fully human monoclonal antibody that binds to and blocks the function of angiopoietin-like 3 (ANGPTL3), a protein that plays a key role in lipid metabolism. Regeneron scientists discovered the angiopoietin gene family more than two decades ago. Human genetics research published in *New England Journal of Medicine* (*NEJM*) in 2017 by scientists from the Regeneron Genetics Center found that patients whose ANGPTL3 gene did not function properly (called a "loss-of function mutation") have significantly lower levels of key blood lipids, including LDL-C, and that this is associated with a significantly lower risk of coronary artery disease.

In the U.S., Evkeeza is indicated as an adjunct to other LDL-C lowering therapies for the treatment of adult and pediatric patients, aged 12 years and older with HoFH. The safety and effectiveness of Evkeeza have not been established in patients with other causes of hypercholesterolemia, including those with heterozygous familial hypercholesterolemia (HeFH). The effect of Evkeeza on cardiovascular morbidity and mortality has not been determined.

Evkeeza was invented using Regeneron's *VelocImmune*® technology and is the first ANGPTL3-targeted therapy approved by the European Commission and U.S. FDA. The approvals were based on results from the Phase 3 ELIPSE HoFH trial, which was published in the *NEJM* in August 2020.

The generic name for Evkeeza in its approved U.S. indications is evinacumab-dgnb, with dgnb the suffix designated in accordance with Nonproprietary Naming of Biological Products Guidance for Industry issued by the U.S. FDA.

About Regeneron's *VelocImmune* Technology

Regeneron's *VelocImmune* technology utilizes a proprietary genetically engineered mouse platform endowed with a genetically humanized immune system to produce optimized fully human antibodies. When Regeneron's President and Chief Scientific Officer George D. Yancopoulos was a graduate student with his mentor Frederick W. Alt in 1985, they were the first to envision making such a genetically humanized mouse, and Regeneron has spent decades inventing and developing *VelocImmune* and related *VelociSuite*® technologies. Dr. Yancopoulos and his team have used *VelocImmune* technology to create approximately a quarter of all original, FDA-approved fully human monoclonal antibodies currently available.

This includes Evkeeza® (evinacumab-dgnb), REGEN-COV® (casirivimab and imdevimab), Dupixent® (dupilumab), Libtayo® (cemiplimab-rwlc), Praluent® (alirocumab), Kevzara® (sarilumab) and Inmazeb™ (atoltivimab, maftivimab and odesivimab-ebgn).

IMPORTANT SAFETY INFORMATION FOR EVKEEZA® (evinacumab-dgnb) INJECTION

Who should not use EVKEEZA?

Do not use EVKEEZA if you are allergic to evinacumab-dgnb or to any of the ingredients in EVKEEZA.

Before receiving EVKEEZA, tell your healthcare provider about all of your medical conditions, including if you:

- Are pregnant or plan to become pregnant. EVKEEZA may harm your unborn baby. Tell your healthcare provider if you become pregnant while using EVKEEZA. **People who are able to become pregnant:**
  - Your healthcare provider may do a pregnancy test before you start treatment with EVKEEZA
  - You should use an effective method of birth control during treatment and for at least 5 months after the last dose of EVKEEZA. Talk with your healthcare provider about birth control methods that you can use during this time.
- Are breastfeeding or plan to breastfeed. It is not known if EVKEEZA passes into your breast milk. You and your healthcare provider should decide if you will receive EVKEEZA or breastfeed.

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

What are the possible side effects of EVKEEZA?

EVKEEZA can cause serious side effects, including:
Allergic reactions (hypersensitivity), including a severe reaction known as anaphylaxis. Tell your healthcare provider right away if you get any of the following symptoms: swelling (mainly of the lips, tongue or throat which makes it difficult to swallow or breathe), breathing problems or wheezing, feeling dizzy or fainting, rash, hives, and itching.

The most common side effects of EVKEEZA include symptoms of the common cold, flu-like symptoms, dizziness, pain in legs or arms, nausea, and decreased energy.

Tell your healthcare provider if you have any side effect that bothers you or does not go away. These are not all the possible side effects of EVKEEZA. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Please see full Prescribing Information, including Patient Information.

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, hematologic conditions, 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 Ultragenyx

Ultragenyx is a biopharmaceutical company committed to bringing novel products to patients for the treatment of serious rare and ultra-rare genetic diseases. The company has built a diverse portfolio of approved therapies and product candidates aimed at addressing diseases with high unmet medical need and clear biology for treatment, for which there are typically no approved therapies treating the underlying disease.

The company is led by a management team experienced in the development and commercialization of rare disease therapeutics. Ultragenyx's strategy is predicated upon time- and cost-efficient drug development, with the goal of delivering safe and effective therapies to patients with the utmost urgency.

For more information on Ultragenyx, please visit the company's website at: www.ultragenyx.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 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 or licensees (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 or licensees (collectively, "Regeneron's Product Candidates") and research and clinical programs now underway or planned, including without limitation Evkeeza® (evinacumab) and Regeneron's Product Candidate for the treatment of the fibrodysplasia ossificans progressiva (the "FOP Product Candidate"); 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), as well as Regeneron's collaboration with Ultragenyx Pharmaceutical Inc. discussed in this press release, to be cancelled or terminated; uncertainty of the utilization, 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) on any of the foregoing; 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 the FOP Product Candidate; the ability of Regeneron's collaborators, licensees, 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; the ability of Regeneron to manage supply chains for multiple products and product candidates; safety issues resulting from the administration of Regeneron's Products (such as Evkeeza) and Regeneron's Product Candidates (such as the FOP Product Candidate) 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, including without limitation Evkeeza and the FOP Product Candidate; 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 or licensees may be replicated in other studies and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; 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 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 and its Form 10-Q for the quarterly period ended September 30, 2021. 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).

Ultragenyx Forward-Looking Statements and Use of Digital Media

Except for the historical information contained herein, the matters set forth in this press release, including statements related to the expectations and projections of Ultragenyx Pharmaceutical Inc. ("Ultragenyx" or the "Company") regarding its business plans and objectives, the therapeutic potential and clinical benefits of its products and product candidates, expectations regarding the safety and tolerability of its products and product candidates, and future clinical developments or commercial success for its products or product candidates are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements involve substantial risks and uncertainties that could cause the Company's clinical development programs, commercial success of its products and product candidates, continued collaboration with third parties, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the ability of the Company and its third party partners to successfully develop product candidates, including Evkeeza® (evinacumab) in countries outside of the United States, the effects from the COVID-19 pandemic on the Company's clinical and commercial activities and business and operating results; risks related to reliance on third party partners to conduct certain activities on the Company's behalf; the potential for any license or collaboration agreement, including Ultragenyx's collaboration agreement with Regeneron as described in this press release, to be terminated; uncertainty and potential delays related to clinical drug development; uncertainties and unpredictability of obtaining regulatory approval for the Company's product candidates and the scope of such potential regulatory approval; smaller than anticipated market opportunities for the Company's products and product candidates; fluctuations in buying or distribution patterns by distributors and specialty pharmacies; competition to the Company's products and product candidates; potential undesirable or serious side effects from the Company's products or product candidates; the Company's ability to effectively manage the expansion of its commercial organization; market acceptance of the Company's current or future products; uncertainties related to insurance coverage and reimbursement status of newly approved products; manufacturing risks and supply chain disruptions; competition from other therapies or products; and other matters that could affect sufficiency of existing cash, cash equivalents and short-term investments to fund operations, the Company's future operating results and financial performance, the timing of clinical trial activities and reporting results from same, and the availability or commercial potential of Ultragenyx's products and product candidates. Ultragenyx undertakes no obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of Ultragenyx in general, see Ultragenyx's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 3, 2021 and its subsequent periodic reports filed with the Securities and Exchange Commission.

In addition to its SEC filings, press releases and public conference calls, Ultragenyx uses its investor relations website and social media outlets to publish important information about the Company, including information that may be deemed material to investors, and to comply with its disclosure obligations under Regulation FD. Financial and other information about Ultragenyx is routinely posted and is accessible on Ultragenyx's investor relations website (https://ir.ultragenyx.com/) and LinkedIn website (https://www.linkedin.com/company/ultragenyx-pharmaceutical-inc-/mycompany/).

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