



FDA Approves First-in-class Evkeeza™ (evinacumab-dgnb) for Patients with Ultra-rare Inherited Form of High Cholesterol

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Homozygous familial hypercholesterolemia (HoFH) is an ultra-rare inherited condition that affects approximately 1,300 patients in the U.S. and is characterized by extremely high low-density lipoprotein cholesterol (LDL-C)

In pivotal Phase 3 HoFH trial, adding Evkeeza to standard lipid-lowering therapies reduced LDL-C by nearly half at 24 weeks, compared to placebo

Regeneron Pharmaceuticals, Inc. (NASDAQ: REGN) today announced that the U.S. Food and Drug Administration (FDA) approved Evkeeza™ (evinacumab-dgnb) as an adjunct to other low-density lipoprotein cholesterol (LDL-C) lowering therapies to treat adult and pediatric patients aged 12 years and older with homozygous familial hypercholesterolemia (HoFH). Evkeeza is the first FDA-approved treatment that binds to and blocks the function of angiopoietin-like 3 (ANGPTL3), a protein that plays a key role in lipid metabolism.

"The FDA's approval of Evkeeza is a watershed moment for individuals born with HoFH, a severe form of familial hypercholesterolemia," said Katherine A. Wilemon, Founder and CEO of the FH Foundation. "Those living with HoFH have faced devastatingly high LDL-C levels and an uncertain future. Evkeeza significantly lowered LDL-C levels in clinical trials and this new treatment offers an important new option for people living with HoFH."

HoFH, also known as homozygous FH, is an ultra-rare inherited condition that affects approximately 1,300 patients in the U.S. 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 (bad cholesterol). Patients with HoFH are at risk for premature atherosclerotic disease and cardiac events as early as their teenage years.

"Evkeeza is a potentially transformational new treatment for people with HoFH," said Daniel J. Rader, M.D., Professor and Chair of the Department of Genetics in the Perelman School of Medicine of the University of Pennsylvania, a leading HoFH expert who was involved with Evkeeza clinical trials. "Existing therapies for HoFH are insufficient for the majority of patients. Evkeeza, through its unique mechanism of action, was shown to reduce LDL-C levels in patients with all forms of HoFH, even those with nearly no LDL receptor activity, and represents a highly meaningful improvement in our ability to control LDL-C levels in patients with HoFH."

"Evkeeza is the first FDA-approved ANGPTL3 inhibitor and the latest example of the promise of Regeneron's development approach that harnesses genetic insights and pioneering technology to deliver new treatment options for patients who need them," said George D. Yancopoulos, M.D., Ph.D., President and Chief Scientific Officer at Regeneron. "We are proud to bring Evkeeza to patients with HoFH, and Regeneron is grateful to the patients and doctors who participated in our trials to make this a reality."

The FDA approval is based on results from the Phase 3 ELIPSE HoFH trial, [published](#) in the *New England Journal of Medicine (NEJM)* in August 2020. In the trial, 65 patients were randomized to receive either Evkeeza 15 mg/kg intravenously every four weeks (n=43) plus other lipid-lowering therapies, compared to lipid-lowering therapies alone (placebo, n=22). The mean baseline LDL-C level of patients in both groups was 255 mg/dL.

The trial met its primary endpoint, with Evkeeza-treated patients reducing their LDL-C from baseline by 49% on average compared to placebo at week 24 (47% reduction Evkeeza, 2% increase placebo, $p < 0.0001$). At the same time point, compared to baseline, Evkeeza-treated patients also experienced:

- 132 mg/dL average reduction in LDL-C compared to placebo (135 mg/dL reduction Evkeeza, 3 mg/dL reduction placebo, $p < 0.0001$).
- Significant reductions were also observed in other key secondary endpoints including levels of apolipoprotein B (ApoB), non-high-density lipoprotein cholesterol (non-HDL-C) and total cholesterol, compared to placebo ($p < 0.0001$ for all).
- Similar levels of LDL-C lowering were also observed in the most difficult-to-treat patients who often don't respond to certain other therapies because of limited LDL receptor function, described as "null/null" (<15% LDL receptor function by in vitro assays) or "negative/negative" (genetic variants likely to result in minimal to no LDL receptor function by mutation analysis) patients.

Reductions in LDL-C seen with Evkeeza were observed as early as week 2 and maintained throughout the double-blind treatment period (week 24) and open label trial period (through week 48).

The most common adverse reactions (>3% of patients) reported from the combined safety analysis of placebo-controlled trials after 24 weeks that occurred more frequently in Evkeeza patients (n=81) than placebo (n=54) were nasopharyngitis (16% Evkeeza, 13% placebo), influenza-like illness (7% Evkeeza, 6% placebo), dizziness (6% Evkeeza, 0% placebo), rhinorrhea (5% Evkeeza, 0% placebo), nausea (5% Evkeeza, 2% placebo), pain in extremity (4% Evkeeza, 0% placebo) and asthenia (4% Evkeeza, 0% placebo). In clinical trials, adverse reactions led to discontinuation of treatment in 2% of patients treated with Evkeeza, including 1 case of anaphylaxis that resolved with treatment, and 2% of patients who received placebo.

Evkeeza is administered based on weight (15 mg/kg) once a month via intravenous infusion. The average Wholesale Acquisition Cost (WAC) per patient in the U.S. will vary based on weight, and is expected to be approximately \$450,000 per year on average. Regeneron is committed to helping patients who have been prescribed Evkeeza access their medication. Regeneron's myRARE™ patient support program offers financial assistance to eligible patients who need help with the out-of-pocket cost of Evkeeza. Under the program, eligible patients with commercial insurance may pay as little as \$0 in out-of-pocket costs for Evkeeza. In addition, myRARE™ offers resources to help patients and healthcare providers get started with Evkeeza including product information, insurance benefit verification, community resources and appointment reminders. For more information, call 1-833-EVKEEZA (833-385-3392) or visit www.EVKEEZA.com.

The FDA evaluated Evkeeza under Priority Review, following the decision in 2017 to grant Evkeeza Breakthrough Therapy designation for the treatment of hypercholesterolemia in patients with HoFH. The FDA reserves its Priority Review for medicines that represent significant improvements in safety or efficacy in treating serious conditions, and its Breakthrough Therapy designation is designed to expedite the development and U.S. review of drugs that target serious or life-threatening conditions.

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.

About Evkeeza™ (evinacumab-dgnb)

Evkeeza is a fully-human monoclonal antibody that binds to and blocks the function of ANGPTL3. Regeneron scientists discovered the angiopoietin gene family more than two decades ago. Human genetics research [published](#) in *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 this is associated with a significantly lower risk of coronary artery disease.

Evkeeza was invented using Regeneron's *VelocImmune*® technology that utilizes a proprietary genetically-engineered mouse platform endowed with a genetically-humanized immune system to produce optimized fully-human antibodies. *VelocImmune* technology has also been used to create multiple antibodies including Dupixent® (dupilumab), Libtayo® (cemiplimab-rwlc), Praluent® (alirocumab), Kevzara® (sarilumab), Inmazeb™ (atoltivimab, maftivimab, and odesivimab-ebgn) and Regeneron's antibody cocktail for COVID-19, which was recently granted Emergency Use Authorization (EUA) in the U.S.

Regulatory review for Evkeeza is ongoing in the European Union. In June 2020, the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) recommended an accelerated assessment for Evkeeza based on the high unmet medical need and therapeutic innovation demonstrated by the product.

Important disclosures:

- *The FH Foundation is a 501(c)-3 public charity and receives funding support from federal grants, pharmaceutical companies including Regeneron, laboratory and medical device companies, as well as donations from individuals and families impacted by familial hypercholesterolemia and lipoprotein(a).*
- *Dr. Rader has received research support and consulting fees from Regeneron, including for service on an evinacumab advisory board, and Regeneron has provided in-kind support for work conducted in the Penn Medicine Biobank.*

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, 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.

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 (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 Evkeeza[™] (evinacumab-dgnb) as an adjunct to other low-density lipoprotein cholesterol (LDL C) lowering therapies to treat adult and pediatric patients aged 12 years and older with homozygous familial hypercholesterolemia (HoFH); uncertainty of market acceptance and commercial success of Regeneron's Products (such as Evkeeza) and Regeneron's 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 Products and Regeneron's Product Candidates; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's Product Candidates (including possible regulatory approval of Evkeeza in the European Union) and new indications for Regeneron's Products; safety issues resulting from the administration of Regeneron's Products (such as Evkeeza) 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 (such as Evkeeza) 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® (afibercept) 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>).

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