Akcea and Pfizer Inc. Announce Licensing Agreement for investigative antisense therapy AKCEA-ANGPTL3-L_{Rx}

Akcea and Ionis to earn $250 million license fee

BOSTON, Mass. and NEW YORK, NY, October 7, 2019 – Akcea Therapeutics, Inc. (NASDAQ: AKCA), a majority-owned affiliate of Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) and Pfizer Inc. (NYSE:PFE), today announced that the companies have entered into a worldwide exclusive licensing agreement for AKCEA-ANGPTL3-L_{Rx}, an investigational antisense therapy being developed to treat patients with certain cardiovascular and metabolic diseases.

AKCEA-ANGPTL3-L_{Rx} is designed to reduce the production of angiopoietin-like 3 (ANGPTL3) protein in the liver, a key regulator of triglycerides, cholesterol, glucose and energy metabolism. AKCEA-ANGPTL3-L_{Rx} is currently being evaluated in a Phase 2 study in patients with Type 2 diabetes, hypertriglyceridemia and non-alcoholic fatty liver disease (NAFLD).

"AKCEA-ANGPTL3-L_{Rx} has the potential to treat people suffering from certain cardiovascular and metabolic diseases. Given the unmet medical need for this patient population and the broad market potential, we believe Pfizer's expertise and breadth of experience in cardiovascular and metabolic diseases makes it well suited to accelerate clinical development of AKCEA-ANGPTL3-L_{Rx}, and to deliver it to patients in need of additional therapies for these life threatening diseases," said Damien McDevitt, Ph.D., interim chief executive officer at Akcea.

"Pfizer is committed to delivering breakthrough medicines to patients with unmet medical needs," said Mikael Dolsten, Chief Scientific Officer and President, Worldwide Research & Development and Medical, Pfizer. "AKCEA-ANGPTL3-L_{Rx} is a novel therapy that will complement our clinical mid-stage internal medicine pipeline, and we believe that our deep expertise in cardiovascular and metabolic diseases will help allow this program to reach its maximum potential for patients."

Under terms of the agreement, Akcea and Ionis will receive a $250 million upfront license fee, which will be split equally between the two companies. Akcea will settle its $125 million obligation to Ionis in Akcea common stock. The companies are also eligible to receive development, regulatory and sales milestone payments of up to $1.3 billion and tiered, double-digit royalties on annual worldwide net sales following marketing

approval of AKCEA-ANGPTL3-L_{Rx}. Future milestone payments and royalties will be split equally between Akcea and Ionis. Pfizer is responsible for all development and regulatory activities and costs beyond those associated with the ongoing Phase 2 study. Prior to regulatory filing for marketing approval, Akcea has the right, at its option to participate in certain commercialization activities with Pfizer in the U.S. and certain additional markets on pre-defined terms and based on meeting pre-defined criteria.

This transaction is subject to clearance under the Hart-Scott Rodino Antitrust Improvements Act and other customary closing conditions.

ABOUT AKCEA-ANGPTL3-L_{Rx}

AKCEA-ANGPTL3-L_{Rx} is an investigational antisense therapy being developed to treat patients with certain cardiovascular and metabolic diseases. This antisense medicine is designed to reduce the production of angiopoietin-like 3 (ANGPTL3) protein in the liver, a key regulator of triglycerides, cholesterol, glucose and energy metabolism. AKCEA-ANGPTL3-L_{Rx} was developed using Ionis' advanced **LI**gand **C**onjugated **A**ntisense (LICA) technology platform. The potential therapeutic benefits of ANGPTL3 reduction are supported by the discovery that people with a genetic deficiency in ANGPTL3 have reduced levels of low-density lipoprotein cholesterol (LDL-C) and triglycerides, and a decreased risk of diabetes and cardiovascular disease[1]. In a Phase 1/2 study, patients treated with AKCEA-ANGPTL3-L_{Rx} achieved robust, dose-dependent reductions of ANGPTL3, triglycerides, LDL-cholesterol and total cholesterol with a positive safety and tolerability profile[2]. AKCEA-ANGPTL3-L_{Rx} is currently being evaluated in a Phase 2 study in patients with Type 2 diabetes, hypertriglyceridemia and non-alcoholic fatty liver disease (NAFLD). AKCEA-ANGPTL3-L_{Rx} was discovered by Ionis and has been co-developed by Akcea and Ionis.

ABOUT AKCEA THERAPEUTICS, INC.

Akcea Therapeutics, Inc., an affiliate of Ionis Pharmaceuticals, Inc., is a biopharmaceutical company focused on developing and commercializing drugs to treat patients with serious and rare diseases. Akcea is commercializing TEGSEDI® (inotersen) and WAYLIVRA® (volanesorsen) as well as advancing a mature pipeline of novel drugs, including AKCEA-APO(a)-L_{Rx}, AKCEA-ANGPTL3-L_{Rx}, AKCEA-APOCIII-L_{Rx}, and AKCEA-TTR-L_{Rx}, with the potential to treat multiple diseases. All six drugs were discovered by Ionis, a leader in antisense therapeutics, and are based on Ionis' proprietary antisense technology. TEGSEDI is approved in the U.S., E.U. and Canada. WAYLIVRA is approved in the E.U. and is currently in Phase 3 clinical development for the treatment of people with familial partial lipodystrophy, or FPL. Akcea is building the infrastructure to commercialize its drugs globally. Akcea is a global company headquartered in Boston, Massachusetts. Additional information about Akcea is available at www.akceatx.com and you can follow us on twitter at @akceatx.

Pfizer Inc.: Breakthroughs that Change Patients' Lives

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care

products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

AKCEA FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding the business of Akcea Therapeutics, Inc. and the therapeutic and commercial potential of AKCEA-ANGPTL3-L_{Rx} and other products in development. Any statement describing Akcea's goals, expectations, financial or other projections, intentions or beliefs, including the commercial potential of AKCEA-ANGPTL3-L_{Rx} or other of Akcea's drugs in development is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. Akcea's forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Akcea's forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Akcea. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Akcea's programs are described in additional detail in Akcea's quarterly report on Form 10-Q and annual report on Form 10-K, which are on file with the SEC. Copies of these and other documents are available from the company.

In this press release, unless the context requires otherwise, "Pfizer", "Akcea," "Company," "Companies," "we," "our," and "us" refers to Pfizer and/or Akcea Therapeutics.

Ionis Pharmaceuticals™ is a trademark of Ionis Pharmaceuticals, Inc. Akcea Therapeutics®, TEGSEDI® and WAYLIVRA® are trademarks of Akcea Therapeutics, Inc.

PFIZER DISCLOSURE NOTICE: *The information contained in this release is as of October 7, 2019. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.*

This release contains forward-looking information about a worldwide exclusive licensing agreement among Pfizer, Akcea Therapeutics, Inc. and Ionis Pharmaceuticals, Inc., and

AKCEA-ANGPTL3-L$_{Rx}$, an investigational antisense therapy being developed to treat patients with certain cardiovascular and metabolic diseases, including its potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when drug applications may be filed in any jurisdictions for AKCEA-ANGPTL3-L$_{Rx}$; whether and when any such applications may be approved by regulatory authorities, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether AKCEA-ANGPTL3-L$_{Rx}$ will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of AKCEA-ANGPTL3-L$_{Rx}$; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2018 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

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References

1. JAMA Cardiol. 2018 Oct 1;3(10):957-966.
2. N Engl J Med. 2017 Jul 20;377(3):222-232.