Arrowhead Pharmaceuticals Completes Enrollment in Global Phase 3 YOSEMITE Study of Zodasiran for the Treatment of Homozygous Familial Hypercholesterolemia

July 27, 2026

- Study completion anticipated in mid-2027

PASADENA, Calif.--(BUSINESS WIRE)--Jul. 27, 2026-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today announced that it has completed enrollment in the global Phase 3 YOSEMITE clinical trial of zodasiran, the company's investigational RNA interference (RNAi) therapeutic being developed as a potential treatment for homozygous familial hypercholesterolemia (HoFH), a rare genetic condition that leads to severely elevated low density lipoprotein-cholesterol (LDL-C) and early onset cardiovascular disease. Arrowhead anticipates that YOSEMITE will be completed in mid-2027 and, pending successful clinical results, intends to seek regulatory approval in multiple geographies thereafter.

"Completing enrollment in the global YOSEMITE Phase 3 study represents an important milestone in the development of zodasiran for people living with HoFH, a rare disease with limited effective treatment options which carries a very high risk of developing atherosclerotic cardiovascular disease. By harnessing RNA interference to reduce ANGPTL3 expression, zodasiran is designed to lower atherogenic lipoproteins through a mechanism distinct from conventional LDL-C–lowering therapies," said James Hamilton, M.D., Chief Medical Officer and head of R&D at Arrowhead. "The YOSEMITE Phase 3 study was initially designed to enroll 60 participants; however, strong global HoFH patient and physician interest led to an increased total of 70 patients enrolled. We believe this speaks to the remaining global unmet need in this population of patients with exceptionally high cardiovascular risk."

About Homozygous Familial Hypercholesterolemia

Homozygous Familial Hypercholesterolemia is an ultra-rare treatment-resistant genetic condition characterized by elevated LDL-C and early-onset cardiovascular disease. Most cases of HoFH are due to mutations in the gene that encodes the LDL receptor (LDLR). Thus, HoFH represents a unique disease where LDL-C lowering therapies not requiring functional LDL receptors may have benefit.

If left untreated, individuals with HoFH can have median LDL-C levels above 400 mg/dL (over 10 mmol/L), leading to early clinical manifestations of coronary artery disease[1]. Patients with HoFH may also have cholesterol deposits under the skin (xanthomas), around the eyes (xanthelasmas), or around the cornea (corneal arcus), but physical signs are not always present, particularly in children. HoFH remains challenging to treat and currently only patients with the more severe HoFH phenotypes get diagnosed and treated early. The estimated prevalence of HoFH globally is between 1:360,000 and 1:250,000[1].

About YOSEMITE Phase 3 Study

YOSEMITE (NCT07037771) is a global Phase 3 multicenter, randomized, double blind, placebo-controlled study to evaluate the efficacy and safety of zodasiran in adolescent and adult patients with genetically or clinically diagnosed homozygous familial hypercholesterolemia (HoFH) on maximally tolerated lipid lowering therapy. 70 subjects over the age of 12 were randomized (2:1) to receive 4 doses (once every 3 months) of 200 mg zodasiran or placebo. The primary endpoint is the percent change from baseline to month 12 in fasting LDL-C. After month 12, eligible participants will be offered an opportunity to continue in an optional open-label extension.

About Zodasiran

Zodasiran, previously called ARO-ANG3, is a first-in-class investigational RNA interference (RNAi) therapeutic designed to reduce production of angiopoietin-like protein (ANGPTL3), which is a hepatocyte expressed regulator of lipid and lipoprotein metabolism with multiple potential modes of action, including inhibition of lipoprotein lipase (LPL) and endothelial lipase (EL)[2,3]. ANGPTL3 is an emerging therapeutic target with relevance to hypercholesterolemia, hypertriglyceridemia, and mixed hyperlipidemia. Genetic studies suggest that individuals with ANGPTL3 loss-of-function variants have enhanced lipoprotein lipase and endothelial lipase activity, resulting in lower levels of atherogenic lipoproteins and a reduced risk of ASCVD[4-6]. Zodasiran has received Orphan Drug Designation for the treatment of HoFH from the US Food and Drug Administration.

In prior clinical studies, investigational zodasiran was associated with dose-dependent reductions in triglycerides, triglyceride rich lipoprotein remnants, and total atherogenic lipoproteins, including LDL-C, in patients with homozygous (HoFH) and heterozygous (HeFH) familial hypercholesterolemia and mixed hyperlipidemia. Zodasiran also showed a favorable safety profile. In the Phase 2 GATEWAY study in patients with HoFH, there were no drug discontinuations, drug-related serious adverse events, or deaths. The most frequent adverse events were COVID-19, nasopharyngitis, upper respiratory tract infection, and dizziness.

About Arrowhead Pharmaceuticals

Arrowhead Pharmaceuticals (NASDAQ: ARWR) is a commercial-stage pharmaceutical company developing medicines that treat intractable diseases by silencing the genes that cause them, harnessing the natural RNA interference (RNAi) mechanism. The company has built a broad portfolio of clinical and commercial RNAi therapeutics through its industry-leading targeted RNAi molecule (TRiM™) platform, which can precisely silence genes in a wide range of cell types, including liver, lung, muscle, adipose, and central nervous system tissue. At Arrowhead, we rapidly advance potential best- and first-in-class RNAi treatments for diseases with significant unmet medical need, because every day matters to the patients we serve.

For more information, please visit arrowheadpharma.com, or follow us on X (formerly Twitter) at @ArrowheadPharma, LinkedIn, Facebook, and Instagram. To be added to the Company's email list and receive news directly, please visit ir.arrowheadpharma.com/email-alerts.

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This news release contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Any statements contained in this release except for historical information may be deemed to be forward-looking statements. Without limiting the generality of the foregoing, words such as "may," "will," "expect," "believe," "anticipate," "hope," "intend," "plan," "project," "could," "estimate," "continue," "target," "forecast" or "continue" or the negative of these words or other variations thereof or comparable terminology are

intended to identify such forward-looking statements. In addition, any statements that refer to projections of our future financial performance, trends in our business, expectations for our product pipeline or product candidates, including anticipated regulatory submissions and clinical program results, prospects or benefits of our collaborations with other companies, or other characterizations of future events or circumstances are forward-looking statements. These forward-looking statements include, but are not limited to, statements about the initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs; our expectations regarding the potential benefits of the partnership, licensing and/or collaboration arrangements and other strategic arrangements and transactions we have entered into or may enter into in the future; our beliefs and expectations regarding milestone, royalty or other payments that could be due to or from third parties under existing agreements; and our estimates regarding future revenues, research and development expenses, capital requirements and payments to third parties. These statements are based upon our current expectations and speak only as of the date hereof. Our actual results may differ materially and adversely from those expressed in any forward-looking statements as a result of numerous factors and uncertainties, including the safety and efficacy of our product candidates, decisions of regulatory authorities and the timing thereof, the duration and impact of regulatory delays in our clinical programs, our ability to finance our operations, the likelihood and timing of the receipt of future milestone and licensing fees, the future success of our scientific studies, our ability to successfully develop and commercialize drug candidates, the timing for starting and completing clinical trials, rapid technological change in our markets, the enforcement of our intellectual property rights, and the other risks and uncertainties described in our most recent Annual Report on Form 10-K, subsequent Quarterly Reports on Form 10-Q and other documents filed with the Securities and Exchange Commission from time to time. We assume no obligation to update or revise forward-looking statements to reflect new events or circumstances.

Source: Arrowhead Pharmaceuticals, Inc.

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1 Cuchel, et al. Eur Heart J. 2023;44(25):2277-91

2 Adam, et al. J Lipid Res. 2020;61(9): 1271-86.

3 Rosenson. J Lipid Res. 2021:62:100060.

4 Dewey, et al. *N Engl J Med.* 2017;377 (3):211-21.

5 Minicocci, et al. *J Lipid Res.* 2013;54(12): 3481-90

6 Musunuru, et al. *N Engl J Med.* 2010; 363(23):2220-7

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