Arrowhead Pharmaceuticals Presents New Long-Term Efficacy and Safety Data for Plozasiran Across a Spectrum of Hypertriglyceridemia at the American College of Cardiology's 75th Annual Scientific Session and Expo

March 28, 2026

– Patients with severe hypertriglyceridemia (sHTG) achieved an 83% median reduction in triglycerides (TG), with 96% of patients achieving TG levels below 500 mg/dL, a threshold associated with increased risk of acute pancreatitis

– No adjudicated acute pancreatitis events occurred in any patient receiving plozasiran during the 2-year Phase 2b Open-Label Expansion (OLE) Study

– Favorable and durable improvements in atherogenic lipoproteins, including remnant cholesterol, non-HDL cholesterol, and ApoB, were observed, with a safety profile consistent with earlier trials

PASADENA, Calif.--(BUSINESS WIRE)--Mar. 28, 2026-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today announced long-term efficacy and safety data from a two-year long open-label extension (OLE) study of investigational plozasiran supporting its potential as therapeutic solution for a diverse spectrum of patients with hypertriglyceridemia (HTG).

The data were presented by Dr. Christie M. Ballantyne, MD, professor at Baylor College of Medicine, member of the Texas Heart Institute at Baylor, and Principal Investigator of the 2-year OLE study, during an oral presentation at the American College of Cardiology 75th Annual Scientific Session & Expo (ACC.26) in New Orleans and published in the American Journal of Preventive Cardiology.

"With a new therapy, it is always important to see longer term data to better understand both efficacy and safety. In a long-term open-label extension study, plozasiran treatment was associated with dramatic and meaningful reductions in TGs. In addition, the lack of any acute pancreatitis events during two years of treatment in a patient population that includes those at high risk was particularly reassuring," said Dr. Ballantyne. "These data reinforce the importance of APOC3 silencing as a central mechanism in promoting triglyceride clearance. The study provides promising evidence that plozasiran treatment may lead to durable, sustained reductions in triglycerides and atherogenic lipoproteins across the hypertriglyceridemia spectrum."

Plozasiran is designed to reduce the hepatic production of apolipoprotein C-III (APOC3) through targeted RNA interference. APOC3 is a key regulator of triglyceride metabolism that inhibits both lipoprotein lipase (LPL)-dependent and LPL-independent pathways involved in triglyceride catabolism and clearance, leading to elevated triglyceride levels. Individuals with genetic loss-of-function variants in APOC3 typically have markedly lower triglyceride levels and a reduced risk of atherosclerotic cardiovascular disease.

The ACC.26 presentation builds on positive findings from two Phase 2b double-blind, placebo-controlled studies of plozasiran: SHASTA-2, conducted in adults with severe hypertriglyceridemia (sHTG), and MUIR, which enrolled patients with hypertriglyceridemia, both of which demonstrated short-term efficacy and safety. With the same patient populations, the company initiated an extension phase in which both groups received plozasiran 25 mg quarterly via subcutaneous injections.

During the two-year OLE, patients saw median reductions in their triglycerides by -83% in sHTG patients from SHASTA-2 and -67% in HTG patients from MUIR with favorable reductions in remnant cholesterol and non-HDL-cholesterol.

In both studies, the majority of patients achieved TG levels below thresholds for acute pancreatitis (AP) risk or below normal thresholds. 96% of sHTG patients achieved TGs below 500 mg/dL and 63% achieved TGs below 150 mg/dL, a threshold associated with increased risk of ASCVD. 93% of HTG patients achieved TGs below 150 mg/dL. These findings support the potential of plozasiran as a promising approach for managing patients with moderate to severe HTG phenotypes who are at risk of AP and potentially other cardiometabolic comorbidities.

Plozasiran demonstrated a consistent long-term safety and tolerability profile across both sHTG and HTG patient populations, with stable glycemic parameters, no clinically meaningful differences in routine clinical laboratory measurements, and no new safety signals. Common treatment-emergent adverse events included diabetes, COVID-19, upper respiratory tract infection, and back pain, consistent with prior studies; HbA1c levels remained stable. In SHASTA-2, mean placebo-adjusted liver fat content, as assessed by MRI-PDFF, did not change significantly over time with 25 mg plozasiran treatment.

"We're pleased with the consistent, positive clinical results we're seeing with plozasiran across the spectrum of hypertriglyceridemias and we're excited about what this could mean for patients," said Christopher Anzalone, Ph.D., President and CEO at Arrowhead. "In the four months since its FDA approval for treating FCS, plozasiran is already making a meaningful difference for the FCS community, and we believe it has the potential to become an important therapy for people living with severe hypertriglyceridemia as well. These advances, enabled by our innovative TRiM™ platform, reflect our commitment to developing targeted RNAi therapeutics to silence genes associated with cardiometabolic disorders as well as serious diseases in numerous tissue types throughout the body."

Arrowhead is on schedule to complete the SHASTA-3, SHASTA-4, and MUIR-3 Phase 3 clinical studies, the company's global Phase 3 clinical studies designed to support regulatory submissions for marketing approval of plozasiran for the treatment of severe hypertriglyceridemia, in mid-2026 and intends to submit a supplemental New Drug Application (sNDA) to the U.S. FDA by year-end 2026. Arrowhead also plans to seek regulatory approval with additional global regulatory authorities thereafter.

The ACC.26 presentation can be accessed on the Events and Presentations page under the Investors section of the Arrowhead website and the data have also been published in the American Journal of Preventive Cardiology.

About Severe Hypertriglyceridemia

Severe hypertriglyceridemia (SHTG) is characterized by triglyceride (TG) levels greater than 500 mg/dL, with the most severe form being familial chylomicronemia syndrome (FCS) where TGs typically exceed 880 mg/dL. SHTG significantly increases the risk of acute pancreatitis (AP), which can

often include recurrent attacks requiring repeat hospital admissions and worsening outcomes. AP risk is proportional to the number, characteristics, and concentration of triglyceride rich lipoproteins (TRLs), particularly chylomicrons, and increases as TGs rise. Elevated TGs can also increase the risk of atherosclerotic cardiovascular disease (ASCVD). Limited treatment options exist to sustainably reduce TGs below guideline directed risk thresholds.

About FCS

Familial chylomicronemia syndrome (FCS) is a severe and rare disease leading to extremely high triglyceride (TG) levels, typically over 880 mg/dL. Such severe elevations can lead to various serious signs and symptoms including acute and potentially fatal pancreatitis, chronic abdominal pain, diabetes, hepatic steatosis, and cognitive issues. Currently, there are limited therapeutic options to adequately treat FCS.

About Plozasiran

Plozasiran is a first-in-class investigational RNA interference (RNAi) therapeutic designed to reduce production of apolipoprotein C-III (apoC-III) which is a component of triglyceride rich lipoproteins (TRLs) and a key regulator of triglyceride metabolism. ApoC-III increases triglyceride levels in the blood by inhibiting breakdown of TRLs by lipoprotein lipase and uptake of TRL remnants by hepatic receptors in the liver. The goal of treatment with plozasiran is to reduce the level of apoC-III, thereby reducing triglycerides and restoring lipids to more normal levels.

Plozasiran is being investigated in the SHASTA-3, SHASTA-4, and SHASTA-5 Phase 3 studies in patients with severe hypertriglyceridemia and the MUIR Phase 3 study in patients with mixed hyperlipidemia.

About REDEMPLO® (plozasiran)

REDEMPLO (plozasiran) is approved by the U.S. Food and Drug Administration, Health Canada, and the Chinese National Medical Products Administration as an adjunct to diet to reduce triglycerides for adults with Familial Chylomicronemia Syndrome (FCS). REDEMPLO is an siRNA therapeutic designed to suppress the production of apoC-III, a protein produced in the liver that raises triglyceride levels by slowing their breakdown and clearance. By targeting apoC-III with sustained silencing, REDEMPLO delivers significant reductions in triglyceride levels. REDEMPLO is the first and only siRNA FDA-approved treatment studied in both genetically confirmed and clinically diagnosed patients living with FCS.

For more information about REDEMPLO, visit Our Medicines.

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 www.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 http://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.

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Arrowhead Pharmaceuticals, Inc.
Vince Anzalone, CFA
626-304-3400
ir@arrowheadpharma.com

Investors:
LifeSci Advisors, LLC
Brian Ritchie
212-915-2578
britchie@lifesciadvisors.com

Media:
Jacqueline Wickwire
617-901-2854
Jacqueline.wickwire@havasred.com

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