Arrowhead Pharmaceuticals Reports Topline Results from Phase 3 SHASTA-3 and SHASTA-4 Studies of Plozasiran in Patients with Severe Hypertriglyceridemia

July 22, 2026

- Deep, durable, and consistent median triglyceride reductions of 79% and 81% from baseline in SHASTA-3 and SHASTA-4, respectively
- Statistically significant reduction in acute pancreatitis events versus placebo across the entire sHTG study population, with an unprecedented 100% event reduction in high-risk patients
- Continued and consistent safety and tolerability profile with no new safety signals
- Detailed results will be presented as a HOT LINE Late Breaker at the European Society of Cardiology (ESC) Congress on August 30, 2026

PASADENA, Calif.--(BUSINESS WIRE)--Jul. 22, 2026-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today announced topline results for the global Phase 3 SHASTA-3 and SHASTA-4 clinical studies of plozasiran in patients with severe hypertriglyceridemia (sHTG), a condition that significantly increases the risk of acute pancreatitis (AP), which is associated with repeated hospital admissions and can be fatal. SHASTA-3 and SHASTA-4 successfully met the primary endpoint of triglyceride reduction versus placebo and met all prespecified secondary endpoints in both studies, including a statistically significant reduction in the rate of acute pancreatitis compared to placebo.

“We continue to see plozasiran data as best in class with respect to safety, activity, efficacy, and convenience, with dosing only four times per year, and we are more confident than ever in its promise,” said Christopher Anzalone, Ph.D., President and CEO at Arrowhead. “These compelling Phase 3 data in a broad sHTG study population that closely resembles today’s diverse patient landscape demonstrate plozasiran’s potential to dramatically change the way people are treated. We now begin the process of seeking regulatory approval in multiple global geographies with the goal of bringing plozasiran to the millions of patients seeking new effective treatment options as quickly as possible. Our first planned filing is an sNDA in the U.S. before the end of the year, with additional planned submissions thereafter.”

In SHASTA-3 and SHASTA-4, 25 mg plozasiran administered as a subcutaneous injection once every three months led to median triglyceride reductions of 79% and 81%, respectively, at month 12, versus a placebo reduction of approximately 27%. In a pre-planned pooled analysis of AP events in SHASTA-3 and SHASTA-4, there was a statistically significant reduction in both the event rate (any individual patient with at least one AP event, $p<0.0221$), as well as the total incidence rate of AP events ($p<0.0077$) in plozasiran treated patients versus placebo. In the broad sHTG study population, defined as patients with triglycerides above 500 mg/dL with or without a prior history of AP, cumulative AP events were reduced by 78% in treated patients versus placebo. In a subset of patients with triglycerides above 880 mg/dL and a prior medical history of AP, widely considered to be at the highest risk for AP, plozasiran treatment demonstrated a 100% reduction in AP events versus placebo.

Plozasiran demonstrated a favorable safety and tolerability profile in SHASTA-3 and SHASTA-4, with overall treatment emergent adverse events (TEAE) and related TEAEs consistent with its established safety profile from prior studies. There were no clinically meaningful differences in routine clinical laboratory measurements, and no new safety signals. There were no statistically significant differences between plozasiran and placebo in mean liver fat content assessed by MRI-PDFF in a prespecified subgroup, and no clinically meaningful adverse changes in liver enzymes. There were no cases of hypersensitivity and no thrombocytopenia signal.

Full analysis of the safety and efficacy results from SHASTA-3 and SHASTA-4 studies is ongoing with detailed results anticipated for future presentations and publication.

James Hamilton, M.D., Chief Medical Officer and Head of R&D at Arrowhead, added, “These strong results from the Phase 3 SHASTA-3 and SHASTA-4 studies, evaluating plozasiran in patients with sHTG, build upon the promising results from prior Phase 2 and Phase 3 studies across various patient populations, including those with moderate hypertriglyceridemia, mixed hyperlipidemia, severe hypertriglyceridemia, and genetically confirmed and clinically diagnosed familial chylomicronemia syndrome. Plozasiran continues to demonstrate deep and durable pharmacodynamic effects with a consistently favorable safety and tolerability profile, including a highly encouraging liver safety profile. These findings highlight the potential of plozasiran as a promising therapy for patients across the spectrum of sHTG. We look forward to discussing detailed results from the SHASTA-3 and SHASTA-4 studies at the upcoming European Society of Cardiology Congress next month.”

Plozasiran has received regulatory approval, as REDEMPLO®, in the United States, the European Union, China, Australia, and Canada as an adjunct to diet to reduce triglycerides in adults with genetically confirmed or clinically diagnosed familial chylomicronemia syndrome (FCS), which is the most severe form of sHTG. Arrowhead intends to leverage the data from the Phase 3 SHASTA-3, SHASTA-4, and MUIR-3 studies to request marketing authorization for sHTG in multiple global geographies, beginning with a planned supplemental new drug application (sNDA) with the U.S. FDA before the end 2026.

Detailed results from SHASTA-3 and SHASTA-4 will be presented as a HOT LINE Late Breaker at the European Society of Cardiology (ESC) Congress in Munich on August 30, 2026, and the company plans to host a conference call and webcast to discuss the results on August 31, 2026.

ESC 2026 Presentation Details:
Session Title: HOT LINE 9 Late Breaker Session
Title: Plozasiran in patients with severe hypertriglyceridemia: the SHASTA-3 and SHASTA-4 pivotal trial 12-month results
Date & Time: Sunday, August 30, 2026, 17:30 CEST
Presenter: Gerald Watts, M.D.

The ESC 2026 presentation materials and a link to the conference call and webcast will be made available on the Events and Presentations page under the Investors section of the Arrowhead website.

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 SHASTA-3 and SHASTA-4 Phase 3 Studies

SHASTA-3 (NCT06347003) and SHASTA-4 (NCT06347016) are global double-blind, placebo-controlled, Phase 3 studies to evaluate the efficacy and safety of plozasiran in adults with severe hypertriglyceridemia. Between the two studies, approximately 750 participants were randomized to receive 4 doses (once every 3 months) of 25 mg plozasiran or placebo. The primary endpoint is percent change in fasting serum triglyceride levels from baseline to month 12 compared to placebo. After month 12, eligible participants are offered an opportunity to continue in an optional open-label extension.

About REDEMPLO® (plozasiran)

REDEMPLO (plozasiran) is currently approved by the U.S. Food and Drug Administration, Health Canada, China's National Medical Products Administration, the Australian Therapeutic Goods Administration, and by the European Commission as an adjunct to diet to reduce triglycerides for adults with FCS. REDEMPLO is the first and only siRNA treatment approved in these countries to be studied in both clinically diagnosed and genetically confirmed patients living with FCS.

REDEMPLO is designed to suppress the production of apolipoprotein C-III (APOC3), a protein produced in the liver that raises triglyceride levels by slowing their breakdown and clearance. By targeting APOC3 with sustained silencing, REDEMPLO delivers significant reductions in triglyceride levels. REDEMPLO is self-administered via subcutaneous injection once every three months.

REDEMPLO has been granted Orphan Medicinal Product Designation by the EMA for the treatment of patients with FCS, and Breakthrough Therapy Designation, Fast Track Designation, and Orphan Drug Designation by the U.S. FDA for the treatment of patients with FCS and was also granted Breakthrough Therapy designation by the U.S. FDA in severe hypertriglyceridemia.

Sanofi acquired the rights to develop and commercialize REDEMPLO in Greater China, with Arrowhead retaining rights to REDEMPLO in all geographies, outside of Greater China.

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.

Safe Harbor Statement under the Private Securities Litigation Reform Act:

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, products or product candidate or other characterizations of future events or circumstances are forward-looking statements. These forward-looking statements include, but are not limited to, statements about our beliefs and expectations regarding the long-term impacts of REDEMPLO® (plozasiran) on patient health and the health care system; our beliefs and expectations regarding the pricing, value, or expected timing for availability of our drugs and drug candidates; and our beliefs and expectations around the potential uses and value of the TRiM™ platform. These statements are based upon our current expectations and speak only as of the date hereof. Actual results or outcomes may differ materially and adversely from those expressed in any forward-looking statements as a result of numerous factors and uncertainties the safety and efficacy of our products and product candidates, pricing and reimbursement decisions related to our products, demand for our products, 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, 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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