Arrowhead Pharmaceuticals Receives FDA Breakthrough Therapy Designation for Plozasiran in Severe Hypertriglyceridemia

December 2, 2025

PASADENA, Calif.--(BUSINESS WIRE)--Dec. 2, 2025-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today announced that the United States Food and Drug Administration (FDA) has granted Breakthrough Therapy designation to investigational plozasiran as an adjunct to diet to reduce triglyceride (TG) levels in adults with severe hypertriglyceridemia (SHTG) (TG levels greater than or equal to 500 mg/dL). There are currently limited and inadequate treatment options for the millions of people globally living with SHTG.

Breakthrough Therapy designation is a process designed to expedite the development and review of drugs that are intended to treat a serious condition and where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapies on clinically significant endpoints[1].

Arrowhead is on schedule to complete the SHASTA-3, SHASTA-4, and MUIR-3 Phase 3 clinical studies of plozasiran in mid-2026 and intends to submit a supplemental New Drug Application (sNDA) to the FDA by year-end 2026. Arrowhead also plans to seek regulatory approval with additional global regulatory authorities thereafter.

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. 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 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 will be offered an opportunity to continue in an optional open-label extension.

About MUIR-3 Phase 3 Study

MUIR-3 (NCT06347133) is a double-blind, placebo-controlled, Phase 3 study to evaluate the efficacy and safety of plozasiran in adults with hypertriglyceridemia (TGs greater than 150 mg/dL and less than 500 mg/dL). Approximately 1450 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.

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. Plozasiran is approved in the U.S. as REDEMPLO as an adjunct to diet to reduce triglycerides in adults with Familial Chylomicronemia Syndrome, with additional global regulatory submissions and reviews in process.

About REDEMPLO® (plozasiran)

REDEMPLO (plozasiran) is approved by the U.S. Food and Drug Administration as an adjunct to diet to reduce triglycerides in 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 FDA-approved treatment studied in both genetically confirmed and clinically diagnosed patients living with FCS.

For more information about REDEMPLO, visit Our Medicines.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

None.

ADVERSE REACTIONS

Most common adverse reactions in REDEMPLO treated patients (incidence ≥10% of patients treated with REDEMPLO and >5% more frequently than with placebo) are hyperglycemia, headache, nausea, and injection site reaction.

Please see full Prescribing Information for REDEMPLO®.

About Arrowhead Pharmaceuticals

Arrowhead Pharmaceuticals develops medicines that treat intractable diseases by silencing the genes that cause them. Using a broad portfolio of RNA chemistries and efficient modes of delivery, Arrowhead therapies trigger the RNA interference mechanism to induce rapid, deep, and durable knockdown of target genes. RNA interference, or RNAi, is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. Arrowhead's RNAi-based therapeutics leverage this natural pathway of gene silencing.

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 believes 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.

1. https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/breakthrough-therapy (accessed 12/1/25)

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