Arrowhead Pharmaceuticals Receives FDA Breakthrough Therapy Designation for Plozasiran

September 10, 2024

PALISADE Phase 3 results demonstrate plozasiran reduced triglycerides by 80% from baseline and reduced the risk of developing acute pancreatitis by 83% in patients with genetically confirmed and clinically diagnosed FCS[1]

PASADENA, Calif.--(BUSINESS WIRE)--Sep. 10, 2024-- 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 triglycerides in adults with familial chylomicronemia syndrome (FCS), a severe and rare genetic disease characterized by extremely high triglyceride levels which can cause acute and potentially fatal pancreatitis. There are currently no approved treatments in the U.S. for FCS.

“There are currently no FDA-approved therapies to specifically treat FCS, leaving physicians with very few options to help their patients,” said Chris Anzalone, Ph.D., President and CEO of Arrowhead. “Results from clinical studies of investigational plozasiran have been highly encouraging and strongly supportive of further development and commercialization in multiple patient populations. Receiving FDA Breakthrough Therapy designation for plozasiran provides important benefits and the potential to expedite the process of getting plozasiran to the patients who need it.”

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[2]. Plozasiran has also previously been granted Orphan Drug Designation and Fast Track Designation by the FDA and Orphan Drug Designation by the European Medicines Agency.

Arrowhead intends to submit a New Drug Application to the FDA by year-end 2024 and plans to seek regulatory approval with additional global regulatory authorities thereafter.

About Familial Chylomicronemia Syndrome

Familial chylomicronemia syndrome (FCS) is a severe and rare genetic disease often caused by various monogenic mutations. FCS leads 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, the therapeutic options that can adequately treat FCS are limited.

About Plozasiran

Plozasiran, previously called ARO-APOC3, is a first-in-class investigational RNA interference (RNAi) therapeutic designed to reduce production of apolipoprotein C-III (APOC3) which is a component of triglyceride rich lipoproteins (TRLs) and a key regulator of triglyceride metabolism. APOC3 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 APOC3, thereby reducing triglycerides and restoring lipids to more normal levels.

In multiple clinical studies, investigational plozasiran demonstrated reductions in triglycerides and multiple atherogenic lipoproteins in patients with familial chylomicronemia syndrome (FCS), severe hypertriglyceridemia (SHTG), and mixed hyperlipidemia. Plozasiran has demonstrated a favorable safety profile to date with treatment emergent adverse events reported that generally reflect the comorbidities and underlying conditions of the study populations.

Plozasiran is being investigated in the SUMMIT program of clinical studies, including the PALISADE Phase 3 study in patients with FCS, which recently completed, the SHASTA studies in patients with SHTG, and the MUIR and CAPITAN studies in patients with mixed hyperlipidemia.

Plozasiran has been granted Orphan Drug Designation and Fast Track Designation by the U.S. Food and Drug Administration and Orphan Drug Designation by the European Medicines Agency. Arrowhead intends to file a New Drug Application with the FDA in 2024 and plans to seek regulatory approval with additional global regulatory authorities. Investigational plozasiran has not been reviewed or approved to treat any disease.

About PALISADE Phase 3 Study

The PALISADE study (NCT05089084) is a Phase 3 placebo controlled study to evaluate the efficacy and safety of plozasiran in adults with genetically confirmed or clinically diagnosed FCS. The primary endpoint of the study is percent change from baseline in fasting TG versus placebo at Month 10. A total of 75 subjects distributed across 39 different sites in 18 countries were randomized to receive 25 mg plozasiran, 50 mg plozasiran, or matching placebo once every three months. Participants who completed the randomized period were eligible to continue in a 2-part extension period, where all participants receive plozasiran.

About Plozasiran EAP

Arrowhead is committed to bringing new investigational medicines to patients with serious diseases as quickly and efficiently as possible. The company has established an expanded access program (EAP) for some individuals living with FCS. As with any investigational medicine that has not been approved by regulatory authorities, investigational plozasiran may or may not be effective in treating your diagnosis or condition, and there may be risks associated with its use. If you are a patient or caregiver wishing to know more about this plozasiran EAP for FCS, please discuss this EAP and all treatment options with your treating physician. If you are a treating physician and are seeking information about the plozasiran EAP or would like to request access for a patient, please contact EAP@arrowheadpharma.com.

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 or on LinkedIn. 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 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 impact of the ongoing COVID-19 pandemic on our business, 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.

---

1. European Society of Cardiology Congress 2024
2. https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/breakthrough-therapy (accessed 9/9/24)

View source version on businesswire.com: https://www.businesswire.com/news/home/20240910509591/en/

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:
LifeSci Communications, LLC
Kendy Guarinoni, Ph.D.
724-910-9389
kguarinoni@lifescicomms.com

Source: Arrowhead Pharmaceuticals, Inc