NEWS RELEASE

# Arrowhead Pharmaceuticals to Advance RNAi-based Plozasiran into Phase 3 CAPITAN Cardiovascular Outcomes Trial

6/25/2024

– Based on promising results in the Phase 2 MUIR clinical study, the Phase 3 CAPITAN trial is designed to enroll patients with mixed hyperlipidemia and residual risk of atherosclerotic cardiovascular disease

– CAPITAN builds upon existing SUMMIT program of pivotal Phase 3 clinical studies of plozasiran including PALISADE in patients with familial chylomicronemia syndrome and the SHASTA studies in patients with severe hypertriglyceridemia

– Arrowhead allocating cardiometabolic development and commercial resources to plozasiran and will assess partnership options for future development of zodasiran

– Arrowhead hosting cardiometabolic R&D webinar detailing clinical data and plans to advance plozasiran today, June 25, 2024, at 11:00 am PDT as Part II of the 2024 Summer Series of R&D Webinars

PASADENA, Calif.--(BUSINESS WIRE)-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today announced plans to advance investigational plozasiran into a Phase 3 cardiovascular outcomes trial called CAPITAN. This comes after promising results were recently announced from multiple clinical trials in three distinct patient populations, including the pivotal Phase 3 PALISADE study in patients with genetically confirmed or clinically diagnosed familial chylomicronemia syndrome (FCS), the Phase 2 SHASTA-2 study in patients with severe hypertriglyceridemia (SHTG), which was published in **JAMA Cardiology** 1, and the Phase 2 MUIR study in patients with mixed hyperlipidemia, which was published in the **New England Journal of Medicine** 2.

“We recently announced successful topline results from the Phase 3 PALISADE study, which evaluated plozasiran in patients with FCS. The study met the primary endpoint of lowering triglycerides and met all key secondary endpoints, including reducing the incidence of acute pancreatitis, compared to placebo. Today, we are adding more context to those results and will show that plozasiran, administered once every three months, consistently maintained the median and mean triglyceride levels over the study period with low variability. These are exciting results, and we are eager to share more of these data at upcoming medical congresses,” said Bruce Given, M.D., chief medical scientist at Arrowhead. “We see plozasiran clinical data as strong and consistent across multiple studies in patients with FCS, SHTG, and mixed hyperlipidemia, and believe plozasiran has the potential to address significant unmet needs in all three patient populations. Based on this we are allocating substantial resources to the Phase 3 SHASTA studies in patients with SHTG and the newly announced Phase 3 CAPITAN study in patients with mixed hyperlipidemia and residual risk of ASCVD.

“Our second cardiometabolic program, zodasiran, achieved highly encouraging results, including decreases in triglyceride levels and robust and durable reductions in triglyceride-rich lipoproteins, remnants, and total atherogenic lipoproteins, which we believe supports further investigation in Phase 3 studies. However, based on our various assessments for both candidates, and resource allocation considerations, we have elected to broadly advance plozasiran ourselves and, at this time, will only conduct further development of zodasiran if we identify a suitable development and commercialization partner,” Dr. Given concluded.

Part II of Arrowhead’s 2024 Summer Series of R&D Webinars is being held today, June 25, 2024, at 11:00 AM PDT and will feature Arrowhead management and Christie M. Ballantyne, M.D., Baylor College of Medicine and Principal Investigator for the MUIR study of plozasiran. The live event and an archived webcast may be accessed on the **Events and Presentations** page in the Investors section of the Arrowhead website.

The agenda for today’s live event is listed below in Pacific Daylight Time.

| Time | Topic | Presenter |
|---|---|---|
| 11:00-11:10 | Introductions and Cardiometabolic Update | Vince Anzalone, CFA |
| 11:10-11:20 | Arrowhead’s Cardiometabolic Focus | Bruce Given, MD |
| 11:20-11:35 | The Unmet Need in Triglycerides | Christie Ballantyne, MD, FACP, FACC |
| 11:35-11:50 | Addressing the Triglyceride Spectrum of Diseases | Jennifer Hellawell, MD |
| 11:50-12:00 | Meeting the Triglyceride Challenge Beyond FCS | Bruce Given, MD |
| 12:00-12:05 | Arrowhead’s Future in Cardiometabolic Disease | Bruce Given, MD |
| 12:05-12:15 | Our Take on the Triglyceride Market | Vince Anzalone, CFA |
| 12:15-12:30 | Q&A | Panel |

## 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 reflect the comorbidities and underlying conditions of the study populations. Plozasiran is currently being investigated in the PALISADE Phase 3 clinical study in patients with FCS, which recently completed, SHASTA-3,4,5 Phase 3 studies in patients with SHTG, and an upcoming CAPITAN Phase 3 study 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.

## 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 received plozasiran.

PALISADE successfully met the primary endpoint of lowering triglycerides and met all key secondary endpoints, including reducing the incidence of acute pancreatitis compared to placebo. Plozasiran demonstrated a favorable safety profile in the PALISADE study. The number of subjects reporting treatment emergent adverse events (AEs) were similar in plozasiran and placebo groups. Severe and serious AEs were less common with plozasiran than with placebo. The most common AEs reported were abdominal pain, COVID-19, nasopharyngitis, headache and nausea.

## About Familial Chylomicronemia Syndrome

Familial chylomicronemia syndrome (FCS) is a severe and ultrarare 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 Severe Hypertriglyceridemia

Severe hypertriglyceridemia (SHTG) is characterized by triglyceride (TG) levels greater than 500 mg/dL3-5. Very severe forms (TG greater 880 mg/dl) include familial chylomicronemia syndrome (FCS) and multifactorial chylomicronemia syndrome (MCS)6-8. SHTG significantly increases the risk of atherosclerotic cardiovascular disease (ASCVD) and acute pancreatitis (AP), often with recurrent attacks requiring repeat hospital admissions and worsening outcomes3-5,8. AP risk is proportional to number, characteristics, and concentration of triglyceride rich lipoproteins (TRLs), particularly chylomicrons, and increases as TGs rise9. Limited treatment options exist to sustainably reduce TGs below the pancreatitis risk threshold3-5.

## About Mixed Hyperlipidemia

Mixed hyperlipidemia, also called mixed dyslipidemia, is a highly prevalent disorder characterized by elevated low-density lipoprotein cholesterol (LDL-C) and triglyceride levels. Despite the efficacy of LDL-C-lowering therapies in reducing atherosclerotic cardiovascular disease (ASCVD) risk in mixed hyperlipidemia, there remains substantial residual risk attributed to elevated non-HDL driven by remnant cholesterol in triglyceride-rich lipoproteins10-13. Genome-wide association and Mendelian randomization studies also support a causal role for triglyceride rich lipoproteins in ASCVD14-17.

## 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 early 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. Gaudet D, et al. JAMA Cardiol. Published online April 7, 2024. doi:10.1001/jamacardio.2024.0959
2. Ballantyne CM, et al. N Engl J Med. Published online May 28, 2024. doi:10.1056/NEJMoa2404143
3. Pejic RN, et al. J Am Board Fam Med. 2006; 19:310-6.
4. Grundy SM, et al. J Am Coll Cardiol. 2019; 73(24):e285-350
5. NCEP, ATPIII final report. NIH publication no.: 02–5215, 2002.
6. Christian JB, et al. Am J Cardiol. 2011;107(6):891-897.
7. Fan W, et al. Cardiol Ther. 2020;9(1):207-213.
8. Okazaki H. J Atheroscler Thromb. 2021; 28(9): 883–904.
9. Yang, A.L. et al., Pancreatology, 2020. 20(5): p. 795 800.
10. Gugliucci A. J Clin Med. 2023;12:4399.
11. Silverman MG, et al. JAMA. 2016;316(12):1289-1297.
12. Langsted A, et al. J Int Med. 2020;288:116–127.
13. Fu L, et al. Diabetes Care. 2022;45(9):2136-2143.
14. Bjornson E, et al. Eur Heart J. 2023;44:4186-4195.
15. Nordestgaard BG. Circ Res. 2016;118:547-563.
16. Virani SS, et al. J Am Coll Cardiol. 2021;78(9):960-993.
17. Hussain A, et al. Curr Atheroscler Rep. 2020;22:25.



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.