ARROWHEAD PHARMACEUTICALS

Fiscal 2026 First Quarter Conference Call – Prepared Remarks

February 5, 2026

1:30 PM Pacific time

Operator

Ladies and gentlemen, welcome to the Arrowhead Pharmaceuticals conference call. Throughout today's recorded presentation all participants will be in a listen-only mode. After the presentation, there will be an opportunity to ask questions. I will now hand the conference call over to Vince Anzalone, Vice President of Investor Relations for Arrowhead. Please go-ahead Vince.

Vince Anzalone

Good afternoon and thank you for joining us today to discuss Arrowhead's results for its fiscal 2026 first quarter ended December 31, 2025.

With us today from management are president and CEO Dr. Chris Anzalone, who will provide an overview; Andy Davis, senior vice president and head of the global cardiometabolic franchise, who will provide an update on commercialization activities; Dr. James Hamilton, chief medical officer and head of R&D, who will discuss our development programs; and Dan Apel, chief financial officer, who will give a review of the financials.

Following management’s prepared remarks, we will open the call to questions.

Before we begin, I would like to remind you that comments made during today's call contain certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. All statements other than statements of historical fact are forward-looking statements and are subject to numerous risks and uncertainties that could cause actual results to differ materially from those expressed in any forward-looking statements. For further details concerning these risks and uncertainties, please refer to our SEC filings, including our most recent annual report on Form 10-K and our quarterly reports on Form 10-Q.

I'd now like to turn the call over to Chris Anzalone, President and CEO of the Company. Chris?

Chris Anzalone

Thanks Vince. Good afternoon everyone and thank you for joining us today.

We had another quarter of strong execution across all areas of our business and we are well-positioned to build on this progress throughout 2026 and beyond. In fact, the recent months have included some of the more significant achievements in Arrowhead's history. Let's talk about some of these.

First, on November 18, 2025, Arrowhead received its first regulatory approval and began the next phase of growth as a commercial company marketing its own medicines. The FDA approved REDEMPLO as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome, or FCS. FCS is a severe, rare disease, with an estimated 6,500 people in the U.S. living with genetic

or clinical FCS, characterized by TG levels that can be 10 to 100 times higher than normal, leading to a substantially higher risk of developing acute, recurrent, and potentially fatal pancreatitis.

This approval was supported by clinical data from the Phase 3 PALISADE study in adults with either clinically diagnosed or genetically confirmed FCS. The PALISADE study demonstrated deep and durable reductions in TGs, with a median reduction of 80% from baseline and a lower numerical incidence of acute pancreatitis compared with placebo.

Arrowhead launched REDEMPLO independently in the U.S. with the One-REDEMPLO pricing model that creates one consistent price across current and potential future indications. This is important. We are committed to sustainable innovation, and this requires rational drug pricing according to the value a medicine offers to patients and healthcare systems. REDEMPLO is a pancreatitis drug, and when we think about pricing we look to those patient populations at greatest risk of acute TG-related pancreatitis.

We've only had drug in channel for about 10 weeks, which included Thanksgiving, Christmas, and New Year's holidays, so it is difficult to infer too much about launch. However, initial trends in prescriptions, payor interactions, and shipments have been encouraging. To date, over 100 prescriptions for REDEMPLO have been received from a diverse prescriber base, with geographically balanced uptake across the U.S. Early patient starts fall into three categories: patients transitioning from our Expanded Access Program, patients naïve to the APOC3 class, and patients switching from olezarsen. In addition, REDEMPLO shipments are being made for patients with clinically diagnosed and genetically confirmed FCS.

In addition to FDA approval, we announced in January 2026 that REDEMPLO also received approval for the treatment of FCS from Health Canada and from the Chinese National Medical Products Administration.

REDEMPLO will be available later this year in Canada and we anticipate it will be marketed independently by Arrowhead. Pending regulatory review and approval, we expect to potentially launch REDEMPLO later this year in select EU countries and in the UK. In Greater China, REDEMPLO will be marketed by Sanofi.

Our cardiometabolic pipeline is off to a good start with REDEMPLO and the ongoing Phase 3 study of zodasiran in homozygous familial hypercholesterolemia, or HoFH. We are actively expanding this pipeline with a number of discovery programs and, importantly, 3 clinical programs. ARO-INHBE and ARO-ALK7, being developed as potential treatments for obesity, are in Phase 1/2 studies. We also recently initiated a Phase 1/2 study of ARO-DIMER-PA in patients with mixed hyperlipidemia.

For our initial obesity candidates, we recently announced some early interim clinical data. ARO-INHBE enhanced weight loss and fat reduction versus tirzepatide alone in obese patients with type 2 diabetes. More specifically, two administrations of ARO-INHBE at the 400 mg dose in combination with tirzepatide achieved approximately two-fold better weight loss at week 16 than with tirzepatide alone. This appears to be high quality weight loss, as we saw an approximately three-fold reduction in each of: total fat, visceral fat, and liver fat measures based on the week 12 MRI, versus tirzepatide alone in these patients.

The ARO-ALK7 Phase 1/2 study is approximately 2 quarters behind the ARO-INHBE study, but early data are encouraging. We believe this is the first RNAi-

therapeutic to show adipocyte gene target silencing in a clinical trial, and we've seen dose dependent reductions in adipose ALK7 mRNA with a mean reduction of -88% at the 200 mg dose at week 8 with a maximum reduction of -94%.

While these are very intriguing data, they are early and incomplete, so we have substantial work ahead of us before we get too excited about how these candidates could eventually be used. We will continue to run both Phase 1/2 studies, we are expanding existing cohorts to increase power, and we are adding new cohorts to better understand these candidates and underlying biology. We intend to report additional results later in 2026.

ARO-DIMER-PA is being developed as a potential treatment for atherosclerotic cardiovascular disease, or ASCVD, due to mixed hyperlipidemia, where both LDL-cholesterol and triglycerides are elevated. We believe there are approximately 20 million people in the U.S. with mixed hyperlipidemia, and this is a patient population without adequate treatment options.

We recently announced that we dosed the first patients in a Phase 1/2 clinical trial of ARO-DIMER-PA, which is a dual functional RNAi therapeutic designed to silence expression of the PCSK9 and APOC3 genes, thus designed to reduce both LDL-c and TGs. This represents an important step forward for the RNAi field as we believe it is the first clinical candidate to target two genes simultaneously in one molecule, and an important step forward for preventive cardiology as both LDL and TGs have epidemiologic support as being important drivers of ASCVD risk.

We expect to have interim data for ARO-DIMER-PA in the second half of 2026. If we see good LDL and TG reduction in a well-tolerated manner, we may have

something truly special for a very large and currently underserved patient population.

Outside of cardiometabolic, we made important advances in our CNS portfolio; specifically in programs that utilize a new proprietary delivery system designed to achieve blood-brain-barrier, or BBB, penetration utilizing sub-cutaneous administration. In non-clinical studies across multiple animal models, we saw deep target gene knockdown across the CNS, including deep brain regions. This underscores Arrowhead's leadership in the delivery of siRNA to multiple tissues and cell types throughout the body utilizing the proprietary TRiM^{TM} platform.

Our first wholly owned program using the BBB platform is ARO-MAPT being developed as a potential treatment for tauopathies including Alzheimer's disease. During the last quarter we announced that we dosed the first subjects in a Phase 1/2 clinical trial that will include healthy volunteers and Alzheimer patients. ARO-MAPT targets the tau protein in the brain, which has good biological validation as a potential driver of pathology and has emerged as a promising target for Alzheimer's disease and additional tauopathies. We anticipate interim clinical data from the healthy volunteer portion of the study should be available in 2026 with data from Alzheimer's patients to follow in 2027. This is a very exciting program for us.

The second program to use our BBB delivery system is SRP-1005, formerly called ARO-HTT, for the treatment of Huntington's disease. This program is partnered with Sarepta, which recently announced the submission of its CTA for Study SRP-1005-101, also known as INSIGHTT in approximately 24 participants.

While our cardiometabolic and CNS work by no means encompass everything we are doing, they are areas of substantial focus and potential value drivers in the near-, mid-, and long-term. Within these areas we are addressing 3 of the greatest public health challenges of our time: obesity, cardiovascular disease, and neurodegenerative conditions.

Now, I'd like to move on to some key events during the recent period that have dramatically strengthened our balance sheet and give us the necessary resources to push multiple programs toward commercialization. We anticipate being funded through multiple potential independent commercial launches and potential partner launches. These meaningfully increase potential revenue opportunities for the company and push us toward becoming cash flow positive and self-sustaining from commercial sales.

Since our last reporting period we have completed transactions with gross proceeds of $1.33 billion dollars. Let's break that down.

First, we completed a global licensing and collaboration agreement with Novartis for ARO-SNCA, Arrowhead's preclinical-stage siRNA therapy against alpha-synuclein for the treatment of synucleinopathies, such as Parkinson's Disease. The collaboration includes a limited number of additional targets outside our pipeline that will utilize Arrowhead's proprietary TRiM™ platform. Arrowhead received a $200 million upfront payment and is also eligible to receive development, regulatory, and sales milestone payments of up to $2 billion. Arrowhead is further eligible to receive tiered royalties on commercial sales up to the low double digits.

Second, we earned a $200 million milestone payment from Sarepta following a drug safety committee review and subsequent authorization to dose escalate, and achievement of the second pre-specified patient enrollment target for ARO-DM1.

And third, we closed concurrent public offerings of $700 million aggregate principal amount of 0% coupon convertible senior notes and $230 million of common stock. Both offerings were several times oversubscribed and priced at company-friendly terms.

As I mentioned at the beginning of the call, we demonstrated strong execution across all areas of our business.

- We received regulatory approval in 3 different countries
- We launched our first commercial product
- We continued to grow our cardiometabolic portfolio
- We had encouraging early results from our obesity programs
- We advanced our TRiM platform and CNS pipeline, and
- We meaningfully improved our financial position to push these and other programs forward.

It has really been a productive last few months at Arrowhead with so much potential to continue this strong progress in 2026 and beyond.

With that overview, I'd now like to turn the call over to Andy Davis. Andy?

Andy Davis

Thank you, Chris, and good afternoon everyone.

It has been just over two months since the approval of REDEMPLO on November 18, 2025, and we are very pleased with the progress we are seeing. I'd like to share some early insights across healthcare provider engagement, patient dynamics, and payer developments.

I'll start with healthcare provider engagement. As a reminder, we are targeting approximately 5,000 healthcare professionals through personal promotion, complemented by a much broader omnichannel effort. Early prescribing has been led by preventive cardiologists and endocrinologists, who together account for approximately 70% of total prescriptions, with the remainder coming from internal medicine physicians focused on lipid disorders. In addition, advanced practice providers — including nurse practitioners and physician associates — working within multidisciplinary care teams are playing a meaningful role in patient identification and treatment decisions.

Turning to patient dynamics, as Chris mentioned, over 100 prescriptions for REDEMPLO have been received to date. We see this as a very strong start that exceeded our expectations for the early months of the launch. We are also seeing geographically balanced uptake across the U.S. Early patient starts fall into three categories: patients transitioning from our Expanded Access Program, patients naïve to the APOC3 class, and patients switching from olezarsen. Class-naïve patients represent the overwhelming majority of starts, with Expanded Access and switch patients contributing evenly to the remainder. Patients receiving REDEMPLO include both clinically diagnosed and genetically confirmed FCS, with the majority not required to submit genetic testing to gain access. Importantly, a high proportion of patients are enrolling in the *Rely on REDEMPLO* Patient Support Program, and

in the fiscal first quarter, patients eligible for co-pay assistance paid zero dollars out of pocket.

Next, I'll touch on payer developments. While it is still early, we remain encouraged by positive payer feedback on both the clinical profile of REDEMPLO and our unified "One REDEMPLO" pricing approach. We are actively engaged with the largest payers, and discussions to date reflect a willingness to cover REDEMPLO to label, including access based on either genetic or clinical diagnosis of FCS.

I'd like to conclude with a brief comment on execution. Within days of FDA approval, we had product available in the channel for FCS patients. Our REDEMPLO Care Coordinators, Rare Disease Specialists, and Field Reimbursement Navigators were deployed on day one to support prescribers and patients, and our payer account team continues to work closely with customers to minimize access barriers. The teams are off to a great start.

And our teams are highly encouraged by early stakeholder feedback; this feedback reinforces the key differentiating attributes of REDEMPLO. As a reminder, in the PALISADE study, REDEMPLO reduced triglycerides by 80% from baseline as early as month one and maintained this reduction with minimal variability through 12 months of treatment. In addition, the numerical incidence of acute pancreatitis was lower in REDEMPLO-treated patients than in placebo. The U.S. approved prescribing information includes no contraindications, no warnings, and no precautions, and REDEMPLO can be self-administered at home once every three months — just four injections per year.

With that, I'll turn the call over to James Hamilton to discuss the R&D portfolio.

James Hamilton

Thank you, Andy.

I want to start with a review of the REDEMPLO FDA approval and information in the label and contained in the package insert.

REDEMPLO is approved as an adjunct to diet to reduce triglycerides in adults with FCS. The recommended dose of REDEMPLO is 25 mg and it can be self-administered at home by subcutaneous injection once every three months.

REDEMPLO has no contraindications, warnings, or precautions in the U.S. FDA approved label. The most common adverse reactions include hyperglycemia, headache, nausea and injection site reactions.

REDEMPLO was studied in patients with both genetic FCS and clinically diagnosed FCS in the Phase 3 PALISADE study.

Patients achieved deep and durable reductions in median triglycerides of around 80% from baseline, with reductions largely maintained below the guideline directed threshold of 500 mg/dL throughout the year of treatment. Importantly, patients with genetic FCS versus clinical FCS showed similar reductions from baseline. We see the clinical FCS population as having the same high unmet need as the genetic FCS group and as such, we think it is crucial to have shown that both patient populations showed similar, large reductions from baseline in triglycerides.

In PALISADE, treated patients also had a reduced rate of adjudicated pancreatitis events, a very welcome finding for FCS patients and their caregivers and an important validation that reductions in triglycerides can, in fact, lead to reductions in pancreatitis.

In addition to FCS, we are also investigating plozasiran in patients with severe hypertriglyceridemia, or SHTG. We announced last quarter that the FDA granted Breakthrough Therapy designation to investigational plozasiran as an adjunct to diet to reduce triglyceride levels in adults 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. This is another important step for the program.

The global Phase 3 studies of plozasiran designed to support supplemental NDA filing to expand the label beyond genetic and clinical FCS are SHASTA-3 and SHASTA-4, which enrolled approximately 750 patients, and MUIR-3, which enrolled approximately 1400 patients. We are also enrolling patients in SHASTA-5 to directly assess the ability of plozasiran to reduce the risk of acute pancreatitis as the primary endpoint in SHTG patients at high risk of acute pancreatitis.

We remain on schedule to complete the blinded portion of the SHASTA-3, SHASTA-4, and MUIR-3 Phase 3 clinical studies in mid-2026. We expect topline data to be available in the third quarter of 2026, with planned sNDA submission for SHTG before the end of 2026.

We presented the study design and baseline characteristics of the SHASTA-3 and SHASTA-4 studies at the 23rd World Congress Insulin Resistance, Diabetes, and Cardiovascular Disease in December 2025. I want to spend a moment to go over a few key parts of that poster.

The primary endpoint of the studies and the accepted regulatory endpoint is TG lowering versus placebo. Plozasiran has been highly active in all patient populations studied, so these studies are over-powered to show TG lowering. One of the additional objectives and a key secondary endpoint of the SHASTA-3 and SHASTA-4 studies included the assessment of acute pancreatitis rates in patients with sHTG.

To be clear, the study was not designed or prospectively powered to demonstrate AP rate reduction after just a year of treatment. However, there are a meaningful number of SHTG patients enrolled that would be considered at high risk for AP. Specifically, among the two studies, which will be pooled for AP event assessment, 37% of enrolled patients reported TGs greater than 880 mg/dL, an accepted high-risk threshold for AP. In addition, 20% of enrolled patients had a prior medical history of pancreatitis.

Lastly, we are seeing AP events in the studies. We are of course still blinded and have about another 4 months before the last patient reaches the end of the blinded period, but overall the studies are progressing as planned.

Chris mentioned the interim obesity results from our ARO-INHBE and ARO-ALK7 programs earlier, but I want to add a little more color and talk about what we are adding to the programs. First, these early results were very encouraging. The next steps would be to investigate whether and where there is a therapeutic

benefit and in the patient segments and treatment settings where it may be applicable.

To review, the interim clinical trial results represent the first demonstration in humans that the Activin E/ALK7 pathway, a genetically validated pathway that regulates adipose fat storage, may potentially be harnessed therapeutically to improve body composition and enhance weight loss versus tirzepatide treatment alone in obese patients with type 2 diabetes mellitus. This patient population typically experiences less weight loss with incretin therapy, are less likely to reach weight loss targets, and need more effective treatment options. Importantly, ARO-INHBE in combination with tirzepatide achieved approximately two-fold weight loss and an approximately three-fold reduction in visceral fat, total fat, and liver fat versus tirzepatide alone in these patients.

We saw signals that the pathway was active in non-diabetics as well, but based on early data, the diabetic signal, particularly in combination with tirzepatide, appeared to be the clearest signal.

So, what are we doing with the studies now? We are already in the planning and execution stage of many of the following next steps:

- Increasing the numbers of patients in the Phase 1 diabetic cohorts
- Including longer follow up to better understand drug durability and activity out to 1 year
- Initiating monotherapy cohorts in obese diabetic patients

We expect to have more data later in 2026 from these programs as we see data from the new expanded scope of the Phase 1/2 studies.

I will now turn the call over to Dan Apel.

Dan Apel

Thank you, James, and good afternoon everyone. I'll provide a brief outline of our financial picture.

As we reported today, net income for the quarter ended December 31, 2025 was $30.8 million, or $0.22 per share, based on 140.7 million fully diluted weighted-average shares outstanding. This compares to a net loss of $173.1 million, or a loss of $1.39 per share, for the quarter ended December 31, 2024, based on 124.8 million fully diluted weighted-average shares outstanding.

Revenue for the quarter totaled $264 million, driven primarily by our license and collaboration agreements with Sarepta and Novartis. Of this amount, approximately $229 million related to the Sarepta collaboration. This included $181 million from the achievement of the second DM1 milestone, $32 million from ongoing recognition of the initial Sarepta consideration, and $17 million related to reimbursement of incurred collaboration program costs. In addition, we recognized $34 million of the $200 million upfront payment received from Novartis under our global licensing and collaboration agreement. The remainder will be deferred over time as we fulfill our preclinical collaboration obligations.

Finally on revenue, we also recorded our first commercial sale of Plozasiran in FCS. As both Chris and Andy have mentioned, we are very encouraged with the feedback and uptake we are seeing with patients and providers. For now, we are

not disclosing specific sales numbers until such time as they become a meaningful driver to our financials.

Turning to expenses, total operating expenses for the quarter were approximately $223 million, compared to $164 million in the prior-year quarter, representing an increase of $59 million year over year. This increase was driven by $40 million of higher R&D expenses and $19 million of higher SG&A expenses.

The increase in R&D expense was primarily attributable to… as planned… higher clinical costs associated with our Phase 3 registrational studies for plozasiran in sHTG, as well as increased clinical supply chain costs. Nearly half of our clinical trial spend in the quarter was associated with our three registrational sHTG studies… Shasta 3, Shasta 4 and MUIR…which again should readout in the summer.

SG&A expenses increased year over year compared to the prior year's first fiscal quarter, primarily driven by investments to support the commercialization of REDEMPLO. As previously discussed, in advance of the U.S. launch, we built robust commercial capabilities to fully support FCS, and…. importantly… capabilities that were intentionally designed to be highly leverageable downstream should we obtain approval for plozasiran in sHTG… and zodasiran in HoFH.

Turning to the balance sheet, cash and investments totaled over $916 million as of December 31, 2025. Common shares outstanding at quarter end were 137.4 million. The reported cash balance does not include the $200 million that we earned for the DM1 2nd Milestone, which was received in January. Nor does it

include the $50 million anniversary payment that we expect to receive from Sarepta on or before February 10th.

Finally, and importantly, the cash balance of $916 million does not include the financing transaction announced in early January consisting of a concurrent offering of convertible senior notes and common stock, along with associated capped call transactions. As Chris mentioned, these were on "company friendly terms" in the sense that the convertible was 0% coupon and the initial conversion premium was 35%. Said another way… the 0% coupon means the notes will not bear regular interest, and the principal amount of the notes will not accrete. The initial conversion price represents a significant premium of approximately 35.0% over the public offering price per share of common stock in the common stock offering. Moreover, the private capped calls will prevent dilution to existing shareholders up to 85% premium over the offering price, or roughly $119. We estimate the total cost of capital … at any share price below that $119 … to be below 1.5%.

All that is to say that we have very significantly and efficiently strengthened our balance sheet … which provides additional flexibility to support ongoing clinical development, current and future commercialization activities, and other long-term strategic priorities.

With that brief overview, I will now turn the call back to Chris.

Chris Anzalone

Thanks Dan.

This is, indeed, an exciting time to be at Arrowhead or an Arrowhead shareholder. We're coming off an historic period for the company where we executed extremely well and all the hard work of the last several years is starting to pay off. While 2025 was productive, we look to the remainder of 2026 and the years ahead to be even more transformational.

Let's look at some key 2026 events that we anticipate could be important value creating events for the company and our shareholders:

- Commercial sales progress for REDEMPLO
- Q3 2026 readout for the Phase 3 SHASTA-3 and SHASTA-4 studies of plozasiran in patients with SHTG, which we believe has the potential to be a $3-4 billion commercial opportunity
- 2nd half 2026 readout for ARO-DIMER-PA targeting PCSK9 and APOC3 for LDL and TG lowering, which may address mixed hyperlipidemia; a population with potentially 20 million patients in the U.S.
- Additional ARO-INHBE and ARO-ALK7 data presented in 2026 that may build on the already encouraging early data for this novel non-incretin strategy
- Early ARO-MAPT data in 2026, potentially providing validation for this drug candidate and our emerging CNS pipeline with systemic delivery via subcutaneous administration

These are just a few potentially important events in 2026 alone. If you fast forward 1-3 years, we expect many more opportunities in our pipeline to build value and multiple potential commercial launches, both independently and with partners.

Thank you for joining us today and I would now like to open the call to your questions.

Operator