ARROWHEAD PHARMACEUTICALS

Fiscal 2025 Year-End Conference Call – Prepared Remarks

November 25, 2025

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 2025 fiscal year ended September 30, 2025.

With us today from management are president and CEO Dr. Chris Anzalone, who will provide an overview; Bruce Given, outgoing chief medical scientist, who will provide an overview of the REDEMPLO FDA approval; 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.

Before we begin, I would like to announce that this will be Bruce Given's final earnings call. He has been a valuable member of the Arrowhead team for almost 15 years. He will continue to help Arrowhead as a trusted advisor but now that REDEMPLO has received its first FDA approval, he will be stepping back from day-to-day operational responsibilities and hopefully he can finally enjoy his time in retirement, or, in his re-retirement, which is probably more accurate. His contributions to Arrowhead's success, both current and future, have been critical and we owe him a heartfelt thank you. Later in the call you will hear from Bruce,

who will discuss the REDEMPLO FDA approval, which he came back to Arrowhead and out of retirement to help us get across the finish line.

Bruce leaves us in a strong position with very strong leaders across the organization. As you all know, James Hamilton has already assumed much of Bruce's prior responsibilities, as chief medical officer and head of R&D. So, thank you again Bruce for getting us to today, and thank you James for taking us into the next chapter for Arrowhead.

Let's turn to our business and what progress we've made during the recent period. This has been a very busy and enormously productive last few months.

The most impactful change is the FDA approval of REDEMPLO. On November 18, we announced that the FDA approved REDEMPLO - indicated 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 triglyceride 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 is Arrowhead's first FDA-approved medicine, marking a major milestone for the company as it transitions into commercial-stage. REDEMPLO is the first and only FDA-approved siRNA medicine for people living with FCS and can be self-administered at home with a simple subcutaneous injection once every three months. REDEMPLO is the first and only FDA-approved medicine to be backed by adequate and well controlled studies that include patients with genetically diagnosed and clinically diagnosed FCS.

After many months of preparation, our commercial team was able to hit the ground running, and I am happy to report that we have drug in channel a mere week after approval. We also launched Rely On REDEMPLO, a patient support program providing support services and resources for patients at each stage of the treatment journey with REDEMPLO, including financial assistance options for eligible patients.

In addition, we also announced 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. It also means that we will not ask different patients to pay different amounts for the same drug, based solely on what disease they've been diagnosed with. REDEMPLO is a pancreatitis drug, and when we think about pricing we look to those patient populations who are at greatest risk of acute TG-related pancreatitis.

The patients we are serving now are also those at the greatest pancreatitis risk: people with FCS. This includes those with a defined set of mutations as well as those who share the same level of chylomicronemia and symptoms, but with more heterogenous and often less well-characterized genetic backgrounds who we refer to as clinically-defined or phenotypic FCS.

The broader patient population with substantially-increased risk of acute pancreatitis are those with persistent chylomicronemia, meaning fasting triglycerides >880 mg/dL. We believe there are approximately 750,000 of these patients in the U.S., and while they often have less day-to-day symptoms than FCS patients, they are clearly at high risk for acute pancreatitis.

The One-REDEMPLO pricing model has these patients in mind, and the $60,000 annual WAC price is designed to provide real value to patients and healthcare systems in this population. Our SHASTA-3 and SHASTA-4 Phase 3 studies are designed to support an sNDA in this population, and while those studies are ongoing and we are actively serving FCS patients, we will have time to help payors properly appreciate REDEMPLO's value, and payors will have time to plan and budget for its possible eventual adoption, pending regulatory review and approval.

Outside of REDEMPLO, we have also made good progress with two other pipeline programs in the cardiometabolic space. Zodasiran and ARO-DIMER-PA.

Let's start with Zodasiran. During the recent period we dosed the first subject in the YOSEMITE Phase 3 clinical trial of zodasiran, our candidate being developed as a potential treatment for homozygous familial hypercholesterolemia, or HoFH. HoFH is a rare genetic condition that leads to severely elevated LDL-cholesterol and early onset cardiovascular disease. In YOSEMITE, approximately 60 subjects over the age of 12 will be randomized to receive 4 doses, once every 3 months, of 200 mg zodasiran or placebo. The primary endpoint is the percent change from baseline to month 12 in fasting LDL-C. The Phase 2 data in this patient population were encouraging and we hope to have this study fully enrolled in 2026, complete the study in 2027, and, if successful, enable an NDA filing by the end of 2027 and launch in 2028.

The next new pipeline program in cardiometabolic is ARO-DIMER-PA. During the last quarter we filed a request for regulatory clearance to initiate a Phase 1/2 clinical trial of ARO-DIMER-PA, being developed as a potential treatment for atherosclerotic cardiovascular disease, or ASCVD, due to mixed hyperlipidemia, in

which both LDL-cholesterol and triglycerides are elevated. This is a very large population without proper treatment options: we believe there are approximately 20 million people in the U.S. with mixed hyperlipidemia. ARO-DIMER-PA is a dual functional RNAi therapeutic designed to silence expression of the PCSK9 and APOC3 genes in the liver, 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.

Both of these programs fit well strategically with our growing commercial focus on the cardiometabolic space and on the physicians that treat these patients.

Also during the quarter, we expanded our clinical pipeline in CNS. We filed a CTA to initiate a Phase 1/2 clinical trial of ARO-MAPT as a potential treatment for tauopathies including Alzheimer's disease. ARO-MAPT is Arrowhead's first therapy to utilize a new proprietary delivery system which, in preclinical studies, has achieved blood-brain-barrier penetration and deep knockdown of target genes across the CNS, including deep brain regions, after subcutaneous injections.

Non-clinical evaluations in monkeys with subcutaneous administration of ARO-MAPT using clinically translatable doses have shown better than 75% knockdown of tissue level MAPT mRNA in the CNS. Importantly, monkey tissue level knockdown has translated into CSF tau protein reductions with duration of effect supportive of either monthly or quarterly subcutaneous dose regimens. This is an exciting program, and we look forward to initiating the study shortly.

We also continue to make good progress on our first two obesity programs, ARO-INHBE and ARO-ALK7. Together, we have randomized 192 patients, all with a BMI >30. Because we started ARO-INHBE earlier, it is about 2 quarters further into the Phase 1 study than ARO-ALK7. Our plan has been to share early data at the end of the year, but due to travel schedules and the holidays, this will push a couple weeks into the early part of January. We also expect to have more fulsome data toward the end of the 1st half of 2026.

We also made important progress in business development. First, as we announced yesterday, 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. This follows a $100 million milestone earned previously when Arrowhead reached the first of two pre-specified enrollment targets and subsequent authorization to dose escalate in a Phase 1/2 clinical study of ARO-DM1. This partnership continues to be productive, and we look forward to continued progress.

In addition to progress on the Sarepta partnership, we announced a new 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 from Novartis, 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.

As I mentioned before, the recent approval of REDEMPLO is clearly the most important recent development, but Arrowhead has been busy across the pipeline and in business development during the recent period. Business development and licensing is critical to our business model, so we are pleased to have these two significant deals close this year.

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

Bruce Given

Thanks Chris and Good Afternoon everyone.

I'm happy to give my final update to Arrowhead shareholders at such an important time and with Arrowhead in such a position of strength. We have built something truly unique and powerful at Arrowhead and with the first FDA-approval behind us it feels like the right time for me to step back into retirement.

So, let's review some of the key parts of the recent FDA approval that we announced last week. We'll start with the label and information 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. The most common adverse reactions include hyperglycemia, headache, nausea and injection site reactions.

The FDA submission was supported by clinical data from the Phase 3 PALISADE study in patients with both genetic FCS and those with the same clinical manifestations of disease, but without solely a genetic cause, referred to as clinically diagnosed FCS.

The blinded portion of the trial compared a year of therapy with plozasiran or placebo, dosed every 3 months and tested 2 doses of plozasiran vs placebo. The primary endpoint was change in median triglycerides at Month 10. There were also mulitiplicity controlled secondary endpoints, all of which were statistically significant, including notably, the occurrence of acute pancreatitis, for which the 25 and 50 mg doses were combined for comparison to placebo as called for in the analysis plan.

Plozasiran achieved deep and durable reductions in median triglycerides as early as 1 month, when the first measurement was taken. Overall, these reductions were around 80% from baseline and reductions largely maintained median TG levels below the guideline directed threshold of 500 mg/dL throughout the year of treatment. 500 mg/dL is the recognized threshold where the risk of pancreatitis increases relative to a normal population. 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.

Plozasiran also reduced the 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.

Let me close by saying that it's gratifying to have been a part of Arrowhead from the early days of our siRNA developments and part of the plozasiran program at its inception and again over the last several years, and more importantly it's exciting to hear the enthusiasm about this new medicine from patients, caregivers, and physicians. I'd also like to wish you all an enjoyable Thanksgiving holiday.

I will now turn the call over to Andy Davis.

Andy Davis

Thank you, Bruce.

It's been exactly one week since the Commercial launch of REDEMPLO and the early feedback we've received from healthcare professionals, patient societies, and payers has been very encouraging. We hear lots of enthusiasm about the differentiating attributes of REDEMPLO which generally fall into five value pillars – some of which the Team has touched on briefly already.

First, the reduction in triglycerides is both significant and sustained. In PALISADE, REDEMPLO reduced triglycerides by an unprecedented -80% from baseline as early as month one and maintained this marked reduction with minimal variation throughout the full 12-month treatment period. This compared to a -17% reduction in the pooled placebo group. With REDEMPLO, patients now have real hope – many for the first time – of achieving triglyceride levels below guideline-directed risk thresholds associated with acute pancreatitis, such as 500 mg/dL. In PALISADE, 50% of patients at the 25 mg dose achieved TG levels below 500 mg/dL, with approximately 75% achieving levels below 880 mg/dL at Month 10.

Second, the numerical incidence of acute pancreatitis in patients treated with REDEMPLO was lower compared with placebo. This is the outcome of most importance for healthcare professionals, patients, and payers.

Third, REDEMPLO demonstrated favorable safety and tolerability. Importantly, the US approved package insert contains NO contraindications, NO warnings, and NO precautions associated with the use of REDEMPLO.

Fourth, REDEMPLO can be self-administered at home with a simple subcutaneous injection once every three months – just four injections per year. Physicians tell us this infrequent dosing schedule is likely to reduce the treatment burden on physicians, patients, and caregivers.

And fifth, early feedback on the One-REDEMPLO pricing model has been positive. As Chris highlighted, this model creates one consistent price – $60,000 per patient per year – across current and potential future indications such as severe hypertriglyceridemia. Again, this means that we will not ask different patients to pay different amounts for the same drug based solely on what disease they have. We have been in important discussions with Payers and early signs for market access are encouraging.

As a reminder, we believe there are an estimated 6,500 people in the U.S. living with genetic and clinical FCS and the prescriber base comprises specialist physicians such as lipidologists, endocrinologists, preventive cardiologists, and internal medicine physicians with a focus on lipid disorders. These specialists often operate within multidisciplinary teams that may include gastroenterologists,

advanced practice providers, and specialized dietitians. At launch, we are targeting approximately 5,000 healthcare professionals through personal engagement.

And finally, our Rely on REDEMPLO Patient Support Program is operational and designed to make every step of the journey easier. The program is designed to assist patients and physicians with insurance verification, financial assistance options, a first-dose starter kit, and supplemental injection training.

We launched just one week ago, but our Care Coordinators are already actively processing REDEMPLO Start Forms, conducting patient welcome calls, and engaging payers to obtain approvals. And I'm happy to announce that we already have drug available in channel, ahead of schedule.

I will now turn the call over to James Hamilton to discuss the broader R&D portfolio.

James Hamilton

Thank you, Andy.

I want to give a quick review of the status of our late-stage Phase 3 studies and also describe the design of a couple of our early-stage programs.

Let's start with the suite of Phase 3 studies of plozasiran designed to potentially support supplemental NDA filing to expand the label beyond genetic and clinical FCS.

SHASTA-3 and SHASTA-4 are Phase 3 studies designed to compare reductions in in triglycerides with 25 mg plozasiran compared with placebo over 12 months of treatment. Between the two studies, we enrolled approximately 750 patients. In addition, the MUIR-3 study enrolled approximately 1400 patients. This study in patients with mixed hyperlipidemia is designed to supplement the safety database when we file the sNDA for plozasiran in severe hypertriglyceridemia. We are not planning to seek approval in this patient population.

We completed enrollment in the global SHASTA-3, SHASTA-4, and MUIR-3 Phase 3 clinical studies in June of 2025. We anticipate completing the primary portion of these studies in mid-2026 with topline data expected in the third quarter of 2026. If successful, we plan to make submissions before the end of 2026 for regulatory review and potential approval.

The SHTG program also features a study named 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 are currently enrolling patients in that study. Of note, we will also be assessing pancreatitis risk reduction in SHASTA-3 and SHASTA-4 as a key secondary endpoint, but SHASTA-5 is the first event driven study to assess acute pancreatitis as the primary endpoint.

I would also like to provide an update on our obesity programs, ARO-INHBE and ARO-ALK7. Both of these programs target the known Activin pathway that is involved with signaling to adipocytes to store fat. ARO-INHBE inhibits one of the ligands in the pathway and ARO-ALK7 inhibits the receptor on adipocytes that these ligands bind. So essentially, we are trying to reduce the message sent to store fat and the way the message is received.

ARO-INHBE started enrolling patients in December 2024 and ARO-ALK7 initiated in May 2025. Both programs are currently in Phase 1/2a first-in-human dose-escalating studies to evaluate safety, tolerability, pharmacokinetics, and pharmacodynamics. Both programs include Part 1 designed to assess single and multiple doses as monotherapy, and Part 2 designed to assess multiple doses in combination with tirzepatide.

As ARO-INHBE started about two quarters earlier, we have more mature data. The study is nearly fully enrolled, and we are on schedule and currently planning to share initial data from this program around the first week of 2026. This is a rather robust first-in-man study that is collecting multiple measures of drug activity and pathway activity and we are eager to share initial findings. We were originally planning on sharing the first data around the end of the year, but due to the holidays and travel the first week of January worked best for all schedules.

For ARO-ALK7, we intend to provide a brief snapshot of the early safety and target engagement results from that study. Both targets have strong genetic validation and both programs have yielded promising results in preclinical studies, so it will be interesting to see similarities and differences in patient response in the clinical 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 results.

As we reported today, our net loss for fiscal year 2025 was ($2) million dollars, or a loss of **one cent** per share, based on 133.8 million fully diluted weighted average shares outstanding. This "near break-even" result compares with a net loss of approximately $599 million…or a loss of ($5.00) per share based on 119.8 million fully diluted weighted average shares outstanding… in fiscal year 2024.

Revenue for fiscal year 2025 totaled $829 million dollars, and was driven entirely by our license and collaboration agreements with Sarepta, Sanofi and GSK. Of the $829 million, roughly $697 million dollars pertained to the Sarepta arrangement. Of that $697 million, $587 million relates to the on-going recognition of initial Sarepta consideration, $94 million relates to the achievement of the 1st DM1 milestone… and $16 million relates to reimbursement of incurred collaboration program costs. Additionally, the license to Sanofi for Greater China rights to Plozasiran contributed $130 million to our fiscal 2025 revenue, and… lastly…to round things out… we recorded $2.6 million earlier in the year related to a milestone payment under the GSK-HBV agreement.

Turning to expenses, total operating expenses for fiscal year 2025 were approximately $731 million dollars, compared to $605 million for fiscal 2024, an increase of $126 million dollars. The year-over-year increase was driven by $101 million dollars of higher R&D expenses, and $25 million of higher SG&A costs, both of which I will explain in brief.

The key drivers of research and development costs included costs to run our clinical trials, our clinical manufacturing costs, as well as costs related to active programs in the preclinical stage. 2025 R&D costs were heavily impacted by our phase 3 clinical

trials for plozasiran in sHTG. It's worth noting that, in fiscal year 2025, **nearly two thirds** of our clinical trial spend can be attributed to the late stage development of Plozasiran in sHTG. As we have mentioned, the sHTG registrational studies are now **fully** enrolled and we expect data to read out next year. Accordingly, the majority of remaining phase 3 registrational clinical trial costs will occur over the 12 months.

Our SG&A costs increased by $25 million year-over-year, driven primarily by our preparations for commercialization of REDEMPLO. All of us here at Arrowhead are enormously proud of the capabilities we have built to commercialize REDEMPLO…. Not only in our commercial functions, but also across regulatory, supply chain, and order-to-cash …and indeed across all our enabling support functions.

Turning now to cash, net cash provided by operating activities during fiscal year 2025 … was $180 million, compared with net cash used in operating activities of $463 million in the prior year, for a net positive change year over year of $643 million dollars. This increase in cash from operating activities was driven by cash received from licensing and collaboration agreements… partially offset by the aforementioned increase in R&D and SG&A costs.

Turning to the balance sheet, our cash and investments, including available for sale securities, totaled $919 million as of September 30, 2025 compared to $681 million as of September 30, 2024. The increase in our cash and investments was primarily related to our licensing and collaboration agreements with Sarepta, Sanofi and GSK, partially offset by our ongoing cash burn.

Our common shares outstanding as of the end of the quarter were 135.7 million, down 2.4 million from prior quarter due mainly to the repurchase of shares from Sarepta.

I'll use this opportunity to reiterate two developments subsequent to the fiscal year and leading up today, which were financially meaningful for Arrowhead. Firstly, as Chris mentioned earlier on the call, we announced a licensing and collaboration agreement with Novartis for ARO-SNCA, Arrowhead's preclinical stage siRNA program targeting alpha-synuclein for the treatment of synucleinopathies, such as Parkinson's Disease. Novartis will also be eligible to select a limited number of additional collaboration targets… outside of Arrowhead's current pipeline… to be developed using our proprietary (TRiM™) platform. The closing occurred last month… and we have already received $200 million as an upfront payment. As a reminder, we are also eligible to receive up to $2.0 billion in potential future milestone payments from Novartis… as well as royalties on commercial sales.

Secondly... just yesterday… we announced we earned our 2nd Development milestone under the Sarepta Collaboration Agreement for ARO-DM1. As Chris mentioned, this triggers a $200 million dollar obligation from Sarepta that will be recorded in first quarter fiscal 2026, and we expect to receive the cash in January 2026. This is of course additional to the $100 million earned for the first DM1 milestone in fiscal quarter four 2025.

Finally… we are not providing detailed financial guidance at this time for the coming fiscal year, beyond reiterating that … while we view the launch of REDEMPLO as a truly **transformational** event for the company…we do not anticipate commercial sales of REDEMPLO to have a material impact on our financial statements in fiscal

year 2026. We also believe our cash runway, even in the absence of ANY further capital from new deals or other sources… and all the while funding a broad, ambitious set of commercial and clinical programs… to be sufficient to extend into fiscal year 2028.

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

Chris Anzalone

Thanks Dan.

Arrowhead has been working to bring important new medicines to patients in need for over 15 years. As Bruce mentioned, it's very gratifying to see REDEMPLO approved by the FDA and the overwhelmingly encouraging feedback we've received from the FCS community.

But REDEMPLO is just one part of a large pipeline that we've created to help potentially millions of patients in a diverse set of disease areas. We've spent years building the TRiM platform to enable us to bring RNAi where it is needed. We are now able to address 7 different cell types and have current clinical programs in 5 of these. Further, we will meet our 20 in '25 goal whereby we will have 20 individual drug candidates in clinical trials by the end of this year.

Our partnering has been helpful but judicious, with approximately half of our clinical pipeline wholly-owned and half partnered. We have late-stage studies ongoing, again both independently and with partners, that may potentially lead to multiple new commercial launches over the next few years. In addition, we have a

strong financial position that enables us to properly invest in our growth today and in the future. We believe we now have everything we need to be in the next class of large and ultimately profitable biotech companies.

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

Operator