ARROWHEAD PHARMACEUTICALS

Fiscal 2024 Year-End Conference Call – Prepared Remarks

November 26, 2024

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 2024 fiscal year ended September 30, 2024.

With us today from management are president and CEO Dr. Chris Anzalone, who will provide an overview of the quarter; Dr. Bruce Given, interim chief medical scientist, who will provide an update on our cardiometabolic pipeline; Andy Davis, senior vice president and head of global cardiometabolic franchise, who will provide an update on commercialization activities; Dr. James Hamilton, chief of discovery & translational medicine, who will discuss our earlier stage development programs; and Ken Myszkowski, chief financial officer, who will give a review of the financials. We will then 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 Christopher Anzalone, President and CEO of the Company. Chris?

Chris Anzalone

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

Over the years, we've built platforms capable of addressing liver, lung, adipose, CNS, skeletal muscle, cardiomyocyte, and soon other cell types to bring RNAi therapeutics where a multitude of diseases are. Any one of these would represent an important advance in human health, but together we believe they have revolutionary potential. I don't think it's hyperbole to say that we've created a machine that spits out high quality drug candidates if you just feed it money and gene targets. Importantly, those drug candidates can be produced quickly relative to other methodologies and given the modality and increasingly validated nature of the platforms, we have an expectation that most will do what they are designed to do.

We've always had conviction that building and constantly expanding this machine is critical to our dual mission of serving as many patients as possible and creating long-term durable value. In the early- to mid-stages of building a company around such a machine, we require partnerships to develop and commercialize non-core assets and provide capital for us to develop and commercialize our wholly-owned assets while also reinvesting in the machine to expand its reach and capacity. When this is done well and in a timely fashion, it creates balance for us. Of late we had become out of balance. The partnership we announced today with Sarepta is transformational because it:

- Returns balance to our business model
- Helps to focus our investment thesis without constricting upside potential, and
- Puts us on a fairly straight path to profitability.

Let's take a closer look at this deal. Arrowhead and Sarepta entered into a licensing and collaboration agreement that includes select programs utilizing multiple TRiM™ delivery systems targeting various tissue and cell types. Under the agreement, Arrowhead will advance each program to an agreed upon milestone and then Sarepta will assume responsibility for further development and commercialization. These include select programs from three distinct buckets:

1. Certain Arrowhead clinical candidates
2. Certain Arrowhead non-clinical programs; and,
3. Discovery programs to be pursued jointly between Sarepta and Arrowhead

In the clinical candidate bucket, Arrowhead is granting Sarepta an exclusive license to the following 4 programs:

1. ARO-DUX4, as a potential treatment for patients with facioscapulohumeral muscular dystrophy type 1, or FSHD1. ARO-DUX4 is currently dosing patients in a Phase 1/2 clinical study.
2. ARO-DM1, as a potential treatment for patients with type 1 myotonic dystrophy, or DM1. ARO-DM1 is currently dosing patients in a Phase 1/2 clinical study.
3. ARO-MMP7, as a potential treatment for idiopathic pulmonary fibrosis. ARO-MMP7 has completed dosing healthy volunteers in a Phase 1/2 clinical study and is currently dosing IPF patients to assess target engagement. And,
4. ARO-ATXN2, as a potential treatment for spinocerebellar ataxia 2, or SCA2. ARO-ATXN2 is in a Phase 1/2 study that is currently open for enrollment.

In the non-clinical bucket, Arrowhead is granting Sarepta an exclusive license to 3 programs that utilize Arrowhead's next generation TRiM™ platform for subcutaneous administration to the central nervous system. The programs are ARO-HTT for Huntington's disease, and ARO-ATXN1 and ARO-ATXN3, both for spinocerebellar ataxia.

Lastly, in the discovery programs bucket, Sarepta can propose up to 6 new skeletal muscle, cardiomyocyte, or CNS targets on which Arrowhead will perform discovery and preclinical development. Sarepta would then receive an exclusive license to those programs and be responsible for clinical development and commercialization.

During the 5-year term of the agreement, Arrowhead will be excluded from working on a large list of skeletal muscle targets for its internal use or in partnership with other companies. Arrowhead will also be providing contract manufacturing services to Sarepta for clinical, and eventually commercial, drug supply for programs arising out of the collaboration.

At close of the agreement, Arrowhead would receive the following:

1. A $500 million upfront cash payment
2. $325 million through the purchase by Sarepta of Arrowhead equity priced at $27.25, representing a 35% premium to the 30-day volume weighted average price of Arrowhead stock
3. $250 million to be paid in annual installments of $50 million over 5 years, and
4. Up to $300 million in near-term payments, broken up into two separate payments of $100 and $200 million, associated with the continued enrollment of certain cohorts in the Phase 1 study of ARO-DM1, which Arrowhead may achieve during the next 12 months.

Arrowhead is eligible to receive development milestone payments between $110 and $410 million per program and sales milestone payments between $500 and $700 million per program. Arrowhead is also eligible to receive tiered royalties on commercial sales up to the low double digits. The total potential value of this deal exceeds $11bn plus royalties.

This is an important deal for both of our companies. In one transaction it gives Sarepta multiple new promising pipeline opportunities, all with the potential to be best-in-class, in areas where Sarepta has extensive development, regulatory, and

commercial expertise and where clear synergies exist with their existing organization. The folks at Sarepta are specialists in these areas, and we see them as having a high potential to maximize the value of the programs and be a dominant competitor. They are an ideal partner for us.

For Arrowhead, the deal answers two primary questions the market had about us.

First, we've seen general acceptance that our technology works and that current and future drug candidates have a good chance of becoming important medicines, but there was a lack of clarity about how we would pay for them. This deal provides us with substantial capital immediately and potential access to very large amounts of additional funding throughout the life of the collaboration and beyond. This cannot be overstated. According to our long-term plan and budget, we are now funded toward the end of 2028 and potentially through multiple commercial launches, by Arrowhead and our partners.

Second, we've built a massive clinical and pre-clinical pipeline across different therapeutic areas that has the potential to create substantial value, but (a) it is difficult for the market to properly value everything there, particularly when it has been unclear what would remain wholly-owned versus partnered; and (b) it is difficult for us to build out clinical and regulatory expertise as well as commercial infrastructure across diverse therapeutic areas. This deal goes a long way toward providing a more manageable wholly owned pipeline, focused on areas we intend to commercialize ourselves, namely in the cardiometabolic space.

This more focused pipeline allows us to take advantage of the expertise we have built in clinical development and regulatory in the cardiometabolic area and our growing medical affairs and commercial presence in the space as well.

Now, in the cardiometabolic area we are focusing resources on the following:

- Plozasiran, which is rapidly progressing toward commercial stage;
- Zodasiran, which is Phase 3 ready;
- The APOC3-PCSK9 dimer program, that we expect to file a CTA on in 2025;
- ARO-INHBE, which should begin enrolling a P1/2 study in the next couple months;
- ARO-ALK7, for which we expect to file a CTA shortly and begin enrollment by mid-2025;
- Additional undisclosed adipose-targeted programs;
- Undisclosed CNS programs that leverage our systemic sub cutaneous delivery; and
- Possible cardiomyocyte-targeted programs.

These provide us with near- mid- and long-term value growth and leverage common resources and expertise, making us progressively more efficient for each subsequent program. This is a solid and scalable model.

A focused pipeline also allows us to manage the growth of our R&D expenses. Four clinical candidates and 3 pre-clinical programs come off our books immediately while still moving rapidly toward the patients who need them. On the discovery side, we believe we have an engine that is second to none and has the potential to create substantial value, so we will not slow it down. We now have a partner that will take advantage of our significant discovery capacity and take as many as 6 new candidates that we are not yet working on into clinical studies. This is a great use of our discovery engine, represents scalable value creation, and

leaves us with plenty of capacity for our own future wholly-owned programs ***and*** additional partnerships.

Another important piece of the Sarepta partnership that may be overlooked is the manufacturing component. Providing clinical and commercial material to Sarepta for programs included in this deal soaks up current excess manufacturing capacity in our new Verona manufacturing plant and defrays our operating costs. It also provides Sarepta with a high quality, cost effective partner for important RNAi medicines it will develop and ultimately commercialize.

Our cardiometabolic focus and the Sarepta license agreement together do not capture all of our promising programs. Rather, we believe there are additional programs we have that could be partnered at some point to capture additional value and ensure that they reach the patients who need them.

The programs that sit within this category are:

- ARO-RAGE for asthma and COPD, which is Phase 2 ready and we are assessing various options and designs before moving forward
- ARO-PNPLA3 for MASH, which is also Phase 2 ready and for which we are also considering options
- ARO-C3 and ARO-CFB in the complement space, which should both have clinical readouts by mid-2025
- ARO-MAPT for Alzheimer's and other tauopathies, as well as ARO-SCNA for Parkinson's, which both use what we believe is our very promising subcutaneous TRiM™ system for CNS delivery and are on schedule for CTAs in 2025

We are excited about each of these programs and while we do not require partners immediately, our current strategy is to eventually find the right companies to develop and commercialize each one. In the meantime, we are assessing timing and possible additional development that could maximize risk-adjusted value to us.

As part of this pipeline focus, we have decided not to pursue further development of ARO-MUC5AC. To be clear, this decision was not due to any emerging safety issue but rather the inability to reliably assess target engagement with the available biomarkers. While we still believe that MUC5AC is an intriguing target for muco-obstructive diseases, we believe that we have programs without this biomarker limitation where we can better allocate capital.

We have also made great progress with our lead program and potential first commercial product, plozasiran, from a clinical, regulatory, and commercial perspective, which Bruce and Andy will discuss in a moment. We now feel like all the pieces are in place to accelerate growth.

Let's review what we see as the key steps that enable that growth.

We have generated important Phase 3 data in the PALISADE study of plozasiran in patients with genetically defined or clinically diagnosed FCS, forming the basis of submission of our first NDA. This is a big step for any biotech company and we were excited to make that submission earlier this month.

We now have field and home office medical affairs organizations in place within clinical development. We have also built out the key headquarters commercial infrastructure and are in the process of building out a commercial field team, right-sized for this rare disease. We are confident that we will be ready for our potential

first commercial launch in 2025, provided we receive positive FDA review and approval. We have also begun leveraging outsourced resources for a European commercial launch, provided we receive positive EMA review and approval, which we intend to seek in 2025.

We also have a comprehensive plozasiran Phase 3 program for the large patient population with severe hypertriglyceridemia, or SHTG. We believe there are 3-4 million people in the US making up this population and there are very limited treatment options at present. We expect the studies needed for regulatory approval to be fully-enrolled by mid-year 2025, leading to final patient visits in the middle of 2026 and potential sNDA filing at the end of 2026 or early 2027. We see this as a large patient population with inadequate treatment options that alone could make plozasiran a $2-3bn per year drug.

Further, we continue to see a big opportunity in the larger mixed hyperlipidemia market. Plozasiran has always looked like a potentially powerful medicine for secondary prevention of ASCVD as well as primary prevention for high-risk patients by the KOL community we've been working with. Addressing this patient population approximately doubles our revenue forecasts for plozasiran but would require a cardiovascular outcomes trial, or CVOT, for approval. As such, we are waiting until we have better visibility on additional capital before launching this trial.

Arrowhead now has a combination of traits that puts it in the strongest position ever in the history of the company. These include:

- Substantial immediate capital

- The expectation of large amounts of additional non-dilutive capital in coming years via existing partnerships
- A lead program that is gearing up for commercial launch
- A lead program that could see substantial label expansions in coming years
- A focused cardiometabolic pipeline that spans early discovery to P3-ready
- A discovery engine capable of creating new candidates rapidly
- Strong partners in place for non-core assets
- Several non-core programs that could be partnered in the future for additional non-dilutive near- and long-term capital, and
- A state-of-the-art high-capacity manufacturing facility that is qualified for clinical material now and could be qualified for commercial material soon

With that overview, I'd now like to turn the call over to Bruce Given who will discuss what we've accomplished with plozasiran and the status of the Phase 3 program. Bruce?

Bruce Given

Thank you, Chris, and Good Afternoon everyone.

It has been a remarkable year for plozasiran. We've had a series of high impact presentations at major international academic meetings accompanied by 4 simultaneous publications in highly selective, high impact medical journals, initiated our Phase 3 program in Severe Hypertriglyceridemia or SHTG this

summer and culminating with our New Drug Application, or NDA, submission to the US FDA earlier this month. I'll review some of those highlights over the next few minutes.

First, it was a great pleasure to submit our NDA for plozasiran in the orphan condition of Familial Chylomicronemia Syndrome, or FCS, to the FDA. That started the clock for their validation process, which is expected to take up to 60 days. If the FDA determines that the filing is complete and accepts it for review, they will inform us at that time of the PDUFA date by which a decision on approval may be made. Because the FDA has granted plozasiran Breakthrough Therapy Designation, we are hopeful for a priority review, but that determination will be made solely at the discretion of the FDA. Our database for the pivotal PALISADE study in subjects with genetically confirmed or clinically diagnosed FCS was only locked on May 16 of this year, so this was an excellent performance by the Arrowhead team, especially given that this was the organization's first NDA. We look forward to hearing the FDA's filing decision.

If we take a step back to assess the results that have been generated with plozasiran over the last year at medical meetings and in publications, a clear picture emerges. As data from the Phase 2 trials were presented and published in JAMA Cardiology and The New England Journal of Medicine in the first half of the year, we saw in the Muir study of patients with mild to moderate hypertriglyceridemia in the context of mixed hyperlipidemia and in patients with severe hypertriglyceridemia in SHASTA-2 that plozasiran produced deep and durable reductions in Apolipoprotein C-3, or apo C3, with quarterly subcutaneous dosing and that these reductions led to deep and durable reductions in triglycerides, remnant cholesterol, apolipoprotein B, or apo B and non-HDL-cholesterol, while substantially increasing HDL cholesterol as we had anticipated based on human genetic data and

our Phase 1 study results. While Phase 2 data require replication and expansion in Phase 3 studies, which I'll describe in a moment, we learned a number of important things from these results.

First, we evaluated doses from 10 to 50 mg and determined in both of these studies that we could confidently select 25 mg as being at the top of the dose response curve for efficacy, while also having safety and tolerability that appeared favorable. On this basis we chose the 25 mg dose, administered every 3 months, for future Phase 3 development in both mixed hyperlipidemia and severe hypertriglyceridemia. Second, the reductions in our lipid targets were substantial and consistent with the human genetic data from individuals who had inherited genetic variants with low or no activity for apoC3, who display favorable lipid profiles and appear to have reduced risk for cardiovascular disease. Finally, these individuals inheriting loss of function apoC3 genes have been thought to have no negative safety or tolerability issues and our Phase 2 data suggests that this therapy may be well tolerated in Phase 3 studies. In fact, subjects from the Phase 2 MUIR and SHASTA-2 studies were offered the opportunity to enter a long-term extension study called ARO-APOC3-2003, which was reported out at the American Heart Association Scientific Sessions on November 18. Those data in 418 patients suggested that lipid changes remained essentially unchanged out 15-18 months while receiving plozasiran 25 mg quarterly, with no new safety signals detected. HbA1c was essentially unchanged over that period.

Most of you will be familiar with our Phase 3 PALISADE study that reported at the European Society of Cardiology, with another simultaneous publication in the New England Journal of Medicine. We observed an 80% reduction from baseline in median triglycerides at Month 10 with the 25 mg dose, while placebo subjects showed a reduction of 17%. The reduction in triglycerides at Month 10 was highly

statistically significant with a p value <0.0001. This study also included a 50 mg quarterly dosed group with plozasiran with similar, significant results, which together with the results from Muir and SHASTA-2 have convinced us that we have achieved the maximum efficacy possible for the apoC3 mechanism with the 25 mg dose, regardless of indication.

Because both 25 and 50 mg achieved significant reductions on the primary triglyceride endpoint, we were allowed to assess the significance of our alpha-controlled secondary endpoints. In this regard, apoC3 reductions at 10 and 12 months and average triglyceride reductions at 10 and 12 months combined were also highly significant. Our final alpha-controlled secondary was a comparison of incidence of expert adjudicated cases of acute pancreatitis for the placebo group compared to a combined group of the 25 and 50 mg plozasiran dose cohorts. This important endpoint showed a statistically significant 83% reduction in incidence of acute pancreatitis with plozasiran with a p value of 0.029. Not surprisingly given the reduction in pancreatitis, percentages of patients reaching recognized risk reduction thresholds for triglycerides with the clinical dose of 25 mg quarterly showed that 75% of patients reached levels below 880 mg/dL and 50% were able to reach triglyceride levels less than 500 mg/dL.

There were a number of exploratory endpoints in this study which were reported on at AHA and simultaneously published in the high impact AHA journal Circulation. Meaningful reductions in remnant cholesterol, apoB and non-HDL-cholesterol were shown as well as increases in HDL cholesterol. The expected increases in mean LDL-cholesterol were seen but remained below guideline levels for cardiovascular risk reduction. Finally, longitudinal data was shown from Month 1 through 12 for the clinical 25 mg dose indicating that the reductions in triglycerides from baseline of approximately 80% were similar whether patients

had genetically confirmed or clinically diagnosed FCS, a finding that we believe is important.

Tolerability has been good across all 3 study populations. The most common treatment emergent adverse events for the PALISADE FCS study were abdominal pain, COVID-19, nasopharyngitis and nausea. For the Phase 2 MUIR and SHASTA-2 studies, the most frequent adverse events were COVID-19, upper respiratory tract infection, headache, Type 2 diabetes mellitus, and abdominal pain.

While all of this was going on, we were also busy obtaining regulatory input and initiating our Phase 3 program for plozasiran in SHTG. Our twin pivotal, Phase 3 studies in patients with SHTG, called SHASTA-3 and -4 were initiated in the middle of the year. We now have centers open in the US, Europe, and China with new centers opening weekly and we have patient screening and enrollment ongoing in all 3 territories. We are also conducting a Phase 3 study in patients with mixed hyperlipidemia, named MUIR-3 which is there to provide safety numbers needed for the expected SHTG supplement to our plozasiran NDA. All 3 of these studies are largely patterned after their Phase 2 counterparts except that patients will receive 4 quarterly doses of 25 mg or placebo for a full year of treatment and follow-up before entering into an extension if they so choose.

We are also getting ready to start SHASTA-5, a first of its kind study where the primary outcome will be reduction in acute pancreatitis in patients with severe hypertriglyceridemia and a history of pancreatitis. This study has not been requested by regulatory authorities and is not critical path for the SHTG submissions. Rather this is a study that we are conducting for payers and to support the market.

Finally, regarding CAPITAN, our planned outcomes study with plozasiran for prevention of cardiovascular events in patients with elevated triglycerides and a history of atherosclerotic cardiovascular disease, or ASCVD, or at high risk for ASCVD, we continue to receive feedback from global regulatory authorities and our executive committee and expect to have our design finalized in the first half of 2025.

So, in summary, an amazing 2024 for plozasiran is setting up a busy and exciting 2025.

I will now turn the call over to Andy Davis.

Andy Davis

Thank you, Bruce.

Just over one week ago, our team was at the American Heart Association Scientific Sessions 2024, or AHA, where we announced new results from the Phase 3 PALISADE study and the open-label extension from the Phase 2 MUIR and SHASTA-2 studies of investigational Plozasiran. The feedback we collected onsite from both physicians and patient societies continues to be very encouraging. We hear lots of enthusiasm about the differentiating attributes of Plozasiran which generally fall into five value pillars you've heard me speak about before.

First, the reduction in triglycerides has been both deep and durable. In PALISADE, Plozasiran reduced triglycerides by around 80% from baseline as early as month one and maintained this reduction with limited variation throughout the full 12-month treatment period.

Second, – for the first time – patients and their doctors see real hope of achieving triglyceride levels below guideline-directed risk thresholds associated with acute pancreatitis, such as 880 and even 500 mg/dL. Around half of the patients at the 25 mg dose in PALISADE maintained TGs below 500 mg/dL, with approximately 75% achieving levels below 880 mg/dL. To support physician education on guideline-directed risk thresholds, we announced on FCS Awareness Day earlier this month the launch of a new disease awareness campaign, called *'We'll Get There Soon'*. A key focus of our messaging is to educate the physician community, about expert guidelines from several professional medical societies, which recommend maintaining triglyceride levels below 500 mg/dL to reduce the risk of acute pancreatitis.

Third, the triglyceride reductions in PALISADE were generally consistent in patients with genetically confirmed and clinically diagnosed FCS. As I mentioned at the outset, new results from PALISADE were presented in an oral presentation at AHA and simultaneously published in the journal *Circulation*. Plozasiran, at the 25 mg dose, induced rapid, deep, and sustained reductions in APOC3, of greater than -90%, and in triglycerides, of approximately -80%, independent of gene variants causing FCS. As Bruce mentioned, we believe this supports the potential value of Plozasiran in patients with clinically diagnosed disease, regardless of genetic status.

Fourth, Plozasiran is the first and only investigational medicine to report a statistically significant reduction in the risk of developing acute pancreatitis in patients with genetically confirmed and clinically diagnosed FCS. This important endpoint showed a statistically significant 83% reduction in incidence of acute pancreatitis with plozasiran. This is the outcome of most importance for physicians, patients, and payers.

And lastly, Plozasiran demonstrated favorable safety and tolerability, largely similar to placebo and is conveniently dosed every three months, reducing the treatment burden on both physicians and patients with only 4 injections per year.

To support this value proposition, we have built best-in-class Medical, Market Access, and Marketing organizations. Our teams are solidly in place. The Medical Affairs group is fielding Medical Science Liaisons to conduct scientific exchange. And on the Sales and Marketing side, we've recently hired our National Sales Director who will be executing our field force hiring plans over the next several months. We are on track and we're incredibly excited about 2025 and the possibility of bringing investigational Plozasiran to those FCS patients and their families who are burdened by this condition.

I will now turn the call over to James Hamilton.

James Hamilton

Thank you, Andy.

With our sharpened focus on the cardiometabolic therapeutic area, I'd like to discuss our two new programs for obesity and metabolic disease. Clearly, there have been advancements in the obesity space of late. This has created excitement in the field and we believe our programs, ARO-INHBE and ARO-ALK7, have attractive profiles and may fill gaps in the current standard of care.

We held a webinar in August on the obesity and metabolic space as part of our Summer Series of R&D Webinars. We covered the biology of these targets, our

preclinical data, and our clinical plans. That presentation is still available as an archive on the website.

As a high-level refresher, activation of the INHBE / ALK7 pathway instructs adipocytes to store fat. In an environment of nutrient excess, this pathway can become dysfunctional and overactive. Both targets are supported by human genetics, where loss-of-function carriers have favorable body composition and metabolic characteristics compared to non-carriers.

ARO-INHBE is a GalNAc siRNA conjugate intended to silence hepatic INHBE expression. INHBE mRNA codes for activin E protein which is one of the ligands binding to ALK7 on the adipocyte surface. It is the expression of ALK7 mRNA that is targeted with ARO-ALK7, which uses Arrowhead's novel adipocyte siRNA delivery platform.

ARO-INHBE and ARO-ALK7 achieved 22% and 50% reduction in fat mass respectively, versus saline controls in a mouse diet induced obesity model. Importantly, this is achieved with the preservation of lean mass. In the same mouse model, when studied in conjunction with incretin therapy, inhibition of the INHBE/ALK7 pathway can potentiate weight loss with lower doses of incretin therapy, while simultaneously preserving lean mass.

Again, for those interested, I refer you to our August Obesity and Metabolic R&D Webinar for more preclinical data details.

Turning to the clinical studies planned for these molecules, both Phase 1 studies will evaluate single and multiple ascending doses as a monotherapy in obese

patients as well as multiple doses in obese patients with or without type 2 diabetes in combination with incretin therapy.

ARO-INHBE dosing should initiate very soon and dosing with ARO-ALK7 should initiate in 2025. We look forward to providing updates on these studies throughout 2025.

I will now turn the call over to Ken Myszkowski.

Ken Myszkowski

Thank you, James, and good afternoon everyone.

As we reported today, our net loss for fiscal 2024 was $599.5 million or $5.00 per share based on 119.8 million fully diluted weighted average shares outstanding. This compares with net loss of $205.3 million or $1.92 per share based on 106.8 million fully-diluted weighted average shares outstanding for 2023.

Revenue in 2024 was $3.6 million as there were no new partnership or license agreements executed during the year, and no major milestones from previous license agreements were triggered during 2024. Revenue in 2023 was $240.7 million. Revenue in the 2023 primarily relates to our collaboration agreements with Takeda, GSK & Amgen.

Total operating expenses for fiscal 2024 were $604.6 million, compared to $445.7 million for 2023, an increase of $158.9 million. In 2024, operating expenses excluding noncash stock compensation charges and depreciation and amortization, a better indicator of cash spend, were $512.1 million compared to $355.1 million in 2023, and increase of 157.0 million.

The key drivers of this change were increased research and development costs, primarily candidate costs which is driven by clinical costs, manufacturing costs and toxicology costs. In particular, during the third fiscal quarter, we kicked off certain large phase 3 clinical trials for our drug candidate plozasarin to address further indications beyond FCS, namely Severe Hypertriglyceridemia or SHTG.

Net cash used in operating activities during fiscal 2024 was $462.9 million, compared with net cash used in operating activities of $153.9 million during 2023. The increase in cash used in operating activities is driven primarily by higher research and development expenses, as well as lower revenue versus the prior year.

Our footprint expansion is complete with only minor final payments to be made over the next few months totaling about $8 million. We expect very little in capital expenditures in fiscal 2025.

Turning to our balance sheet, our cash and investments totaled $681 million at September 30, 2024, compared to $403.6 million at September 30, 2023. The increase in our cash and investments was primarily related to the $450 million equity issuance, as well as the $400 million debt facility, partially offset by our ongoing cash burn.

We expect our largest cash expenditure in 2025 to be related to the phase 3 studies for plozasiran. We expect that costs for the ongoing studies will start to decrease in 2026 and 2027. Thus, a large portion of those study costs were incurred in 2024 as start-up costs, and in 2025 as ramp up costs which then start to decrease in 2026. Our other clinical studies are earlier phase studies which require much less capital.

The collaboration agreement with Sarepta brings in $500 million in upfront cash, $325 million as an equity investment priced at $27.25 per share (representing a 35% premium to the 30-day volume weighted average price), and additional near-term cash of $350 million. Proforma cash resources at September 30, 2024, including just the upfront cash and equity investment would be $1.5 billion. We estimate that this partnership agreement extends our cash runway into 2028 during which time we expect plozasiran may be approved for the additional indication of SHTG. This capital significantly enhances our balance sheet and puts us on very solid financial footing for several years.

Turning to financial guidance, we expect total cash burn in fiscal 2025 to be $500 to $550 million, of which about $62 to $65 million is related to G&A costs. We expect similar cash burn in 2026, with G&A comprising about $65 million of spend.

Incorporating debt repayments and cash inflows, we expect our cash balance at the end of 2025 to be about $1 billion, and we expect our cash balance at the end of 2026 to be between $600 million and $650 million. We believe our cash runway extends into 2028. These estimates include modest revenue for FCS, but do not include potential revenue from future business development deals. So, if these assumptions prove overly conservative, our cash balances may be higher.

Our common shares outstanding at September 30, 2024, were 124.4 million.

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

Chris Anzalone

Thanks Ken.

As I mentioned, Arrowhead is now extraordinarily well positioned to build value in the short, medium, and long-term. We think all the necessary pieces are in place to execute effectively and efficiently.

We are funded into 2028, with additional non-dilutive funding expected when existing and potentially new partnerships advance through clinical studies and generate commercial products.

We are building out commercial to be ready on day one for our first commercial launch of plozasiran in patients with genetically confirmed or clinically diagnosed FCS. We are eager to receive our PDUFA date from FDA, but our expectation for commercial planning purposes is to be ready to launch in the middle of 2025.

Plozasiran, our lead program, is also in Phase 3 studies to potentially expand into the large and significantly underserved SHTG population a couple years after we launch in FCS. If successful, that would provide a potentially large revenue stream.

Outside of plozasiran, we have focused our pipeline around a cluster of cardiometabolic programs, providing some mid-term opportunities for commercial launches and multiple long-term opportunities.

We also retain select key early-stage programs providing opportunities to build pipeline value while still managing to limit growth in R&D expense.

Lastly, we have a new collaboration partner with extensive clinical, regulatory, and commercial expertise to advance and commercialize multiple promising candidates outside of our cardiometabolic commercial focus.

So, we end fiscal 2024 in a strong position across the board and are now well positioned to execute on our long-term strategy and bring several important new medicines to patients over the coming years.

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

Operator