ARROWHEAD PHARMACEUTICALS

Fiscal 2024 First Quarter Conference Call – Prepared Remarks

February 6, 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 fiscal 2024 first quarter ended December 31, 2023.

With us today from management are president and CEO Dr. Chris Anzalone, who will provide an overview of the quarter; We also welcome back Dr. Bruce Given who previously served as Arrowhead's Chief Operating Officer and Head of R&D and who has rejoined the company on an interim basis as chief medical scientist, Bruce will provide an update on our cardiometabolic pipeline; Dr. James Hamilton, our Chief of Discovery & Translational Medicine, who will provide an update on our earlier stage programs; and Ken Myszkowski, our chief financial officer, who will give a review of the financials. In addition, Patrick O'Brien, our chief

operating officer and general counsel, will be available during the Q&A portion of the call.

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.

Arrowhead has made a name for itself as a company capable of rapid innovation and development that is building a broad-based, diverse business. This is exemplified by our "20 in '25" initiative, where we expect to grow our pipeline of RNAi therapeutics to at least 20 clinical stage or marketed products by the year 2025. This commitment to creating a very large number of new medicines as quickly as we can speaks to our dual mandate:

- To maximize the number of patients we can help, and

- To maximize our ability to create durable value for our shareholders.

These mandates can be entirely aligned during early development. We decrease biology risk by focusing on well-validated targets and delivery platforms. At this stage, the cost of discovery and early development are relatively low, particularly when considering the potential value we can create with novel medicines. In short, we can do many things at this stage without spending too much money and without building large teams with deep therapeutic area expertise. However, as our pipeline grows and we enter later-stage expensive and complex clinical studies requiring significant capital, deeper domain expertise, and ultimately commercial infrastructure, we need to prioritize what we do internally. That is where we are now, and we are currently building out late-stage development and commercial infrastructure to serve the cardiometabolic vertical. This is the primary engine of our near-term value proposition. We expect to follow that up and add a pulmonary vertical as our lung-targeted platform and candidates mature and we have the data we need to make a commitment to build out specialized commercial infrastructure.

Does this mean we will slow down or stop early development outside our focus areas? It does not. We will continue to develop new candidates outside these verticals because (a) we have confidence in our ability to find appropriate partners to continue development and commercialize programs that are non-core for us, and (b) we anticipate adding new verticals in the future. Think of this part of our business as generating capital to support our internal programs and as a farm system to create additional focus areas that could create long-term value as platforms and candidates mature.

Let's start with our cardiometabolic vertical. Our lead program is plozasiran, which targets Apolipoprotein C-III, or APOC3. This is potentially a big year for plozasiran and for the cardiometabolic vertical broadly.

The PALISADE phase 3 study of plozasiran in patients with genetically or clinically confirmed familial chylomicronemia syndrome, or FCS, is on schedule for the last patient to have their last study visit in the second quarter of this year. This would be the first complete phase 3 dataset for Arrowhead that potentially would allow us to file our first NDA and launch our first commercial product. FCS is a severe disease in which patients have extraordinarily high triglyceride levels, often in the thousands of milligrams per deciliter. Many of these patients experience painful and recurrent bouts of severe abdominal pain, pancreatitis, and hospitalization. These patients have inadequate treatment options, and we believe that plozasiran could represent a significant leap forward. We see the data from the P2 studies as compelling. Plozasiran has been generally well-tolerated and consistently did what it was designed to do. We have a high degree of confidence that this will be a powerful drug for this patient population with very high unmet medical needs.

We believe plozasiran could also help a broader population of patients. Therefore, we plan to initiate Phase 3 studies in patients with severe hypertriglyceridemia, or SHTG. These studies will likely begin next quarter and are aimed at addressing a larger patient population that we believe totals 3-4m in the US alone. As with the FCS population, our Shasta 2 study gives us confidence that plozasiran will do exactly what it is designed to do. We believe it will be a powerful and welcomed leap forward for patients. Bruce will discuss study designs for SHTG in a moment.

We are still considering whether we also want to study plozasiran in the broader atherosclerotic cardiovascular disease, or ASCVD, population, but have not yet made a final decision on that. We will be completing our analysis this quarter and will communicate our plans after they are finalized and we have had some regulatory interactions.

If our cardiometabolic vertical represents the foundation of our value proposition, plozasiran is the bedrock for that foundation for the following reasons:

- The target, APOC3, is well-validated across a variety of genetic studies;
- Our data across hundreds of human subjects indicates consistent target engagement with deep and durable APOC3 silencing;
- Triglyceride levels were deeply reduced in patients and healthy volunteers treated with plozasiran;
- We know that elevated triglyceride levels in certain patient populations can lead to severe abdominal pain, acute pancreatitis, hospitalizations, and other difficult downstream effects and even, in rare cases, death;
- There is currently no FDA-approved therapy that lowers triglycerides by more than 20-30%;
- And plozasiran has been generally well-tolerated in prior studies.

Together, these set up an attractive opportunity: we just need to get to market. We expect to launch plozasiran as early as next year in FCS. We would hope to follow that relatively quickly by launching into the larger sHTG market, and we will see if we follow that with the even larger ASCVD market.

This brings me next to zodasiran, which targets angiopoietin-like protein 3, or ANGPTL3. As we have discussed, we are assessing both zodasiran and plozasiran to determine which may be better suited for investment in a cardiovascular outcomes study in patients with ASCVD. The data we presented at AHA in November on zodasiran's ability to reduce remnant cholesterol, which is believed to be a major contributor to the residual risk of ASCVD after LDL-cholesterol is well controlled, was very encouraging. In fact, we have not seen any other therapy capable of the type of reductions seen after zodasiran treatment in the Phase 2 study. Just as available drugs have shown modest lowering of triglycerides, available therapies have similarly produced only modest reductions in remnant cholesterol.

Zodasiran has also shown promising results in a Phase 2 study in patients with homozygous familial hypercholesterolemia, or HoFH. We are currently preparing materials for an end of Phase 2 meeting with the FDA and intend to begin a Phase 3 study in HoFH after we have regulatory feedback on our plans. We could also expand into the much larger heterozygous, or HeFH, population.

If we decide to conduct a Phase 3 study of zodasiran in ASCVD, the commercial plan will likely follow a similar path as plozasiran. That plan is to launch in a rare population and continue to build out commercial infrastructure and capabilities to support larger patient populations while the additional Phase 3 studies are being conducted. For zodasiran this could mean addressing the small HoFH population relatively quickly, then expanding into HeFH, and, ultimately, the very large ASCVD market as we get each approval. This path makes a lot of sense for us as an emerging commercial company and would allow us to grow in a measured step-wise fashion.

We believe that plozasiran and zodasiran clearly warrant investment into cardiometabolic commercial infrastructure. Those outlays become increasingly cost efficient as we increase the number of drugs that infrastructure manages. Therefore it makes sense to expand the cardiometabolic vertical to include additional complementary medicines in the portfolio, and we have several in mind. One is based on our adipose-targeting TRiM™ platform, which has shown impressive preclinical data. We have seen target gene silencing with this platform in excess of 90% after a single dose in animal models, with activity that lasted over six months. Adipose tissue is the largest endocrine organ in the body and there are multiple attractive metabolic targets that may be amenable to an RNAi based knockdown strategy. We are not prepared to disclose the first gene target we are addressing, but it is in the metabolic space.

Another program we are adding to the cardiometabolic vertical is ARO-INHBE. This utilizes the liver targeted TRiM™ platform and targets the INHBE gene, which encodes inhibin subunit βE. James will talk about the target in a moment, but the intention is to study this in an obesity and metabolic disease population.

Both programs fit well in our cardiometabolic vertical and are on schedule for CTA filings as early as the end of this year.

It is difficult to overstate the importance of our cardiometabolic vertical in driving our value proposition. We have near-term commercial opportunities in plozasiran and zodasiran, a high expectation of success surrounding the programs, and longer-term opportunities with future drug candidates.

The next vertical we expect to invest in late-stage clinical studies and commercialization is pulmonary. There are only about 16,000 pulmonologists in the United States, and we believe it's an attractive prospect to build a specialized commercial sales organization to support a growing pipeline of medicines that addresses various respiratory diseases. We currently have three programs in clinical studies that collectively address three major components of chronic lung disease: inflammation, muco-obstruction, and interstitial lung disease.

We also see the pulmonary space as a target rich environment where we believe we can advance and ultimately bring to market a number of different drugs for various diseases treated by a relatively small number of physicians. We like the leverage this creates.

The current programs in clinical studies are ARO-RAGE, ARO-MUC5AC, and ARO-MMP7. We expect to have multiple clinical readouts for these programs this year and intend to start at least one Phase 2 study in 2024. We also expect additional targets, potentially this year.

Cardiometabolic and pulmonary are where we are focusing a lot of our attention and will represent quite a bit of our spend moving forward. What does that mean for the rest of the existing and future pipeline?

As I mentioned, we are not slowing down our discovery organization and will not limit growth in our early-stage pipeline. For example, in calendar 2023 we nominated 9 new clinical candidates and filed 4 new CTAs.

These are promising programs, so the question is where do they fit strategically and what role do they each play in our business? I think of 3 primary categories that new programs can slot into:

1. New candidates that fit into existing verticals. ARO-INHBE is a good example of this: it fits neatly into the cardiometabolic vertical.
2. New candidates that, pending clinical proof of concept, could warrant an expansion into a new vertical. Our work in CNS is very early but given the vast unmet medical needs and the broad target-rich environment, this could be an area we build out should clinical data support it.
3. New candidates that are interesting from a medical and commercial standpoint, but may not fit into one of our verticals. This is an important category for us and can serve as a substantial source of capital to fund the other 2 categories. We've brought in close to a billion dollars in partnering capital over the past 7 years and we anticipate this will be an increasingly important piece of our financing plan going forward as existing partnerships mature and we continue to do new deals.

Our partnership with Amgen on olpasiran, formerly ARO-LPA, is a good example of what we can do after even a modest investment in discovery. In late 2016 when we partnered with Amgen, ARO-LPA was still an early pre-clinical program. Since then, we have received around $362 million in cash and are still eligible to receive another $535 million in potential payments as certain clinical and commercial milestones are achieved. In fact, we are eligible to receive $50 million when the olpasiran Phase 3 study is fully enrolled, which Amgen recently publicly guided could be in the first half of this year.

Business development is an important source of capital but, of course, not the only source we will rely on. Last month we announced a $450 million equity financing: the first such deal we have done in approximately 4 years. That transaction was confidentially marketed to just a handful of funds, and we were pleased with the result. It was substantially oversubscribed and saw terrific participation from high quality investors. We viewed that as the first step in substantially increasing our balance sheet.

We expect the second step to be a structured finance transaction that could be based around taking in capital in return for royalties on one of our future products that is capped at some return. This could also have a debt component to it. We anticipate executing such a transaction in the coming months.

We expect the third step to be one or more partnership transactions, and while we cannot control the exact timing of these, our goal is to do one or more economically meaningful deals this year. Together, we expect these multiple steps to provide a strong financial base on which we may continue to invest in our core programs and new innovations.

There is also a cost management side to creating a strong financial base. As I discussed, we have reached the point where we need to be more strategic about the particular drug candidates we take into late stage studies and, ultimately, to commercialization. It is simply not economically feasible to do everything on our own past a certain stage of development. That means looking more vigorously for partners and potentially pausing or even culling some programs that are outside our chosen verticals. To that end, we've recently conducted a portfolio review.

We are moving forward with clinical studies for our complement programs, ARO-C3 and ARO-CFB and our muscle targeted programs, ARO-DUX4 and ARO-DM1. We are continuing to assess a clinical path and designing Phase 1b/2a studies for our NASH candidate, ARO-PNPLA3. The gout candidate, HZN-457, which was returned to us by Amgen after its Horizon acquisition, is being terminated and will not move forward. In addition, ARO-SOD1, our CNS candidate against SOD1 ALS, will not move forward. We are continuing work on additional CNS programs and expect a new candidate against a different target to begin clinical studies later this year. It is more commercially attractive than ARO-SOD1 while still serving as a good proof of concept for the CNS platform.

Our portfolio review also affected some undisclosed preclinical programs. We have revised our budget to reflect an anticipated reduction in growth of our spend over this fiscal year and beyond. Ken will talk about the specifics in a moment, but we are reducing our guidance on fiscal year operating burn by approximately $100 million. We are achieving these estimates while, importantly, continuing to fully fund our core pulmonary and cardiometabolic verticals and innovative new technologies and programs. Continuously assessing our anticipated uses and sources of capital and ensuring that they align with the overall goals of the business is, of course, a critical exercise. I think our revised budget puts us in a stronger position strategically and financially.

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

Bruce Given

Thank you, Chris, and Good Afternoon everyone.

It’s great to be back helping Arrowhead move forward in the most effective and efficient way possible. I have been doing a good amount of work getting up to speed with the cardiometabolic clinical development teams, which are operating at a very high level. We are doing important design and analysis work to ensure our studies are world class. Shortly, we will be getting centers initiated so additional Phase 3 studies can get up and running rapidly.

Chris mentioned that we are in the middle of a process to assess which program, plozasiran or zodasiran, we want to take forward into an ASCVD population, and we have nothing new to update on that front today.

So, I will focus my time today on where we are with plozasiran and the progress we’ve made. To review, plozasiran is designed to reduce production of Apolipoprotein C-III, or APOC3, a component of triglyceride rich lipoproteins (or TRLs) and a key regulator of triglyceride metabolism. APOC3 increases plasma TG levels by inhibiting breakdown of TRLs by lipoprotein lipase and uptake of TRL remnants by hepatic receptors in the liver.

We’ve studied plozasiran in multiple clinical studies in different patient populations with several hundred subjects having been dosed. We have been consistently encouraged by safety and tolerability results with treatment emergent adverse events reported to date that generally reflect the comorbidities and underlying conditions of each study population. This is encouraging and consistent with our expectations of a properly designed RNAi therapeutic that leverages our proprietary TRiM^{TM} platform.

In addition, plozasiran has demonstrated a high level of pharmacodynamic activity with a mean maximum reduction in APOC3 of around 90% give or take, regardless

of the patient population studied. This is also consistent with our expectations and speaks to the consistency of the RNAi mechanism. This was a hallmark of Arrowhead candidates in our earlier days in the HBV and AAT space and continues to be the case as we have developed new candidates targeting diverse genes.

So, where is plozasiran going and what has changed over the last couple months. First, and most critically in the short-term, we are making some changes to the proposed design of the suite of Phase 3 SHASTA studies for patients with SHTG. Our goal with these changes, which I will discuss in a moment is twofold:

1. We want to accelerate enrollment and enable regulatory filings in the U.S. and other key markets as quickly as possible; and,
2. We want to maximize the probability to show an effect on severe abdominal pain and acute pancreatitis, which could be a significant differentiator from other TG lowering therapies and could aid in value and access discussions with payors.

So what are we doing towards those ends? Our plan was to conduct two similar Phase 3 studies: SHASTA-3 and SHASTA-4 in approximately 700 patients with TGs greater than 500 mg/dl across the two studies combined, and a primary endpoint of lowering TGs after 1 year of treatment. This general design remains largely unchanged but we have streamlined several features of the study to potentially speed up time to NDA submission in Europe and the US.

We also intended to include a predefined number of patients at higher risk of severe abdominal pain and acute pancreatitis events, with the goal of potentially characterizing the risk of these events in SHTG patients treated with plozasiran. This remains an important goal, but we believe the best way to assure ourselves of

adequate power to show this effect is to run a separate study designed specifically for that purpose. This separate study will be called SHASTA-5 and we will provide more details on the design, sizing, and inclusion criteria when we initiate the study. This separate study strategy could potentially do two things: It gives us the best chance of showing a reduction in events versus placebo; and, second, removing the predefined number of high risk patients in SHASTA-3 and SHASTA-4 is expected to further speed enrollment for these studies.

Between these changes and a handful of others, we estimate that we can get to full enrollment for SHASTA-3 and SHASTA-4 more rapidly, and potentially get to NDA 6-10 months faster. This is a significant advance if our predictions are correct.

We are actively working on getting these studies ready to go. We estimate SHASTA-3 and SHASTA-4 will begin next quarter and SHASTA-5 shortly thereafter. Plozasiran has demonstrated best-in-class data at each prior step of the clinical development process and we are eager to move rapidly through these Phase 3 studies.

The next important event for plozasiran is the completion and readout of the Phase 3 PALISADE study. This is in patients with genetically confirmed or clinically diagnosed familial chylomicronemia syndrome, or FCS. This is a severe disease of extremely high TG levels that puts patients at high risk of episodes of severe abdominal pain, acute pancreatitis, and hospitalization and can be fatal. There are no adequate treatment options for these patients.

PALISADE a one-year study with a primary endpoint of TG lowering versus placebo. We enrolled 75 patients globally and the last patient in is scheduled to

have their last study visit in May. After that visit, we will work quickly to complete sample analysis and data collection, preparation, and analysis. We intend to report topline results from the study in the third quarter and begin work toward filing Arrowhead's first NDA. That will likely be at the end of the year or into the first quarter of 2025.

This is an exciting time and I'm thrilled to be back to be a part of this next big milestone for Arrowhead.

I will now turn the call over to Dr. James Hamilton. James?

James Hamilton

Thank you, Bruce.

As you know, we have a very robust pipeline of early clinical stage programs and an even more robust pipeline of discovery stage programs, most of which we haven't disclosed yet. I want to talk about a few of the newer programs and give an update on where we are with some of clinical programs that are approaching readouts.

First, Chris mentioned two programs that we added to our cardiometabolic pipeline. One utilizes our new adipose delivery platform and the other utilizes our liver targeted platform. We intend to talk more about the adipose platform program later in the year, so I will focus on the liver-targeted program.

This new liver targeted program is called ARO-INHBE. INHBE is a gene that codes for a serum measurable protein, Activin E, which is primarily synthesized by

hepatocytes. Increased circulating Activin E levels signal adipose tissue to store excess nutrients as fat. INHBE expression is increased in obesity and INHBE loss-of-function variants identified in human genetic databases are protective of type-2 diabetes and are associated with reduced visceral fat and a reduced waste to hip ratio.

We have conducted studies in mouse obesity models, where INHBE silencing with siRNA reduced weight gain by over 20% compared to controls. Importantly, the difference in weight gain was primarily due to changes in fat mass with no difference seen in lean mass. We hope that INHBE therapeutic silencing could be an interesting adjunct to GLP1 agonists. We think the potential benefits of combination therapy could include the ability to use a lower dose of the GLP1 agonists which might result in reduced lean mass loss, reduced gastrointestinal side effects, and prevention or slowing of weight regain post cessation of GLP1 agonist therapy. We have selected a clinical lead and are on schedule to file a CTA by the end of 2024.

Moving on to our two muscle targeted programs, ARO-DUX4 for patients with facioscapulohumeral muscular dystrophy, or FSHD, and ARO-DM1 for patients with type 1 myotonic dystrophy, or DM1. Both of these programs are in Phase 1/2a dose-escalating studies to evaluate the safety, tolerability, and PK/PD profiles of single and multiple ascending doses. Both studies have ethics and regulatory clearance to initiate and we expect first-patient-in for both in Q1 or Q2 of this year.

To review, ARO-DUX4 is designed to target the gene that encodes human double homeobox 4, or DUX4, protein as a potential treatment for patients with FSHD. FSHD is an autosomal dominant disease associated with the failure to maintain complete epigenetic suppression of DUX4 expression in differentiated skeletal

muscle. Overexpression of DUX4 is myotoxic and can lead to muscle degeneration.

ARO-DM1 is designed to reduce expression of the dystrophia myotonica protein kinase, or DMPK, gene. DM1 is the most common adult-onset muscular dystrophy and there is currently no approved disease-modifying therapy.

I also want to give a status update on our two complement programs. At the end of last year, we filed a CTA to begin a Phase 1/2 study of ARO-CFB for the treatment of various complement mediated diseases and possibly Geographic Atrophy, or GA. ARO-CFB is designed to reduce hepatic expression of complement factor B, which has been identified as a promising therapeutic target.

Our preclinical studies have demonstrated that ARO-CFB can achieve deep and durable reductions in liver production of complement factor B, which plays a key role in the activation of the alternative complement pathway involved in the pathogenesis of renal diseases such as IgAN as well as other conditions like GA. We anticipate that first-patient-in for the Phase 1/2 study will occur in Q2 of this year.

Our more advanced complement program is ARO-C3. As you may recall, ARO-C3 is designed to reduce production of complement component 3, or C3, as a potential therapy for various complement mediated diseases. We previously presented data from Part 1 in healthy volunteers of an ongoing Phase 1/2 study that demonstrated the following promising results:

- A dose-dependent reduction in serum C3, with 88% mean reduction at the highest dose tested;

- A dose-dependent reduction in AH50, a marker of alternative complement pathway hemolytic activity, with 91% mean reduction at the highest dose tested; and,
- Duration of pharmacologic effect supportive of quarterly or less frequent subcutaneous dose administration.

These results made us confident to move on to Part 2 in patients with IgAN and C3 glomerulopathy. We are currently enrolling that part of the study and intend to present patient data around year end 2024.

Lastly, the three clinical stage pulmonary programs continue to progress efficiently and are all on schedule for clinical readouts this year. These pulmonary programs are as follows:

ARO-RAGE, which is designed to reduce expression of the receptor for advanced glycation end products, or RAGE, as a potential treatment for inflammatory pulmonary diseases. For the Phase 1/2 study, we have fully enrolled and dosed all healthy volunteer cohorts and the mild-to-moderate asthma patient cohorts. We should have additional PD data by the end of the first quarter for both of these. We are also in the process of enrolling three cohorts of asthma patients with high baseline levels of fractional exhaled nitric oxide, or FeNO, which is a biomarker for IL-13 driven type 2 inflammation in the lung. We believe we will have initial results from these high FeNO cohorts in the third quarter of this year. The biology of RAGE and where it sits in the inflammatory cascade as well as our own preclinical studies have suggested that RAGE inhibition may provide potent anti-inflammatory effects with impacts on an array of cytokines, including IL-13, IL-5, TSLP, IL-18, IL-33, IL-1B, IL-6. In addition to FeNO, we are assessing other

potential biomarkers of anti-inflammatory effect, including sputum and blood cytokines, in the asthma patient cohorts.

The next two programs are ARO-MUC5AC, which is designed to reduce production of mucin 5AC, or MUC5AC, as a potential treatment for muco-obstructive pulmonary diseases, and ARO-MMP7, which is designed to the reduce expression of matrix metalloproteinase 7, or MMP7, as a potential treatment for idiopathic pulmonary fibrosis, or IPF. In both programs, we are conducting Phase 1/2 studies in healthy volunteers and then in patients. Both programs require patient data to assess PD, unlike ARO-RAGE which has the benefit of a readily available and measurable PD marker in healthy volunteers. Both ARO-MUC5AC and ARO-MMP7 have already enrolled and dosed healthy volunteers and we anticipate the patient cohorts will be enrolled and dosed in time to enable initial clinical readouts in the second half of the year.

I will now turn the call over to Ken Myszkowski. Ken?

Ken Myszkowski

Thank you, James, and good afternoon everyone.

As we reported today, our net loss for the quarter ended December 31, 2023 was $132.9 million or $1.24 per share based on 107.4 million fully-diluted weighted average shares outstanding. This compares with net loss of $41.3 million or $0.39 per share based on 106.0 million fully-diluted weighted average shares outstanding for the quarter ended December 31, 2022.

Revenue for the quarter ended December 31, 2023 was $3.6 million, compared to $62.5 million for the quarter ended December 31, 2022. Revenue in the current period primarily relates to our collaboration agreements with GSK. Revenue in the prior period primarily related to the recognition of revenue from our license and collaboration agreements with Takeda & Amgen. All upfront payments from existing agreements have now been fully recognized.

Total operating expenses for the quarter ended December 31, 2023 were $140.1 million, compared to $104.7 million for the quarter ended December 31, 2022. The key drivers of this change were increased candidate costs and salaries as the Company's pipeline of clinical candidates has both increased and advanced into later stages of development.

Net cash used by operating activities during the quarter ended December 31, 2023 was $117.8 million, compared with $75.5 million for the quarter ended December 31, 2022. The increase in cash used by operating activities is driven primarily by higher research and development expenses, and lower cash revenue in the period.

We have reviewed our cash forecast and would like to provide additional guidance on our expected cash burn. For the next several quarters we expect operating burn to be $80 to $100 million per quarter. Our footprint expansion is mostly complete with final payments to be made over the next several months totaling about $70 million, after which we expect capital expenditures to be nominal.

Breaking down the operating burn a bit further, our cash burn related to G&A has been about 10% of costs so think of that as about $10 million of G&A each quarter which is expected to grow slowly going forward as we continue to advance

commercialization efforts. We expect quarterly R&D expenditures be about $80 million this year, increasing modestly next year as our registrational studies advance.

Turning to our balance sheet, our cash and investments totaled $220.3 million at December 31, 2023. Proforma cash and investments accounting for the recent capital raise would be approximately $649 million.

Our common shares outstanding at December 31, 2023, were 107.5 million, and proforma shares outstanding accounting for the capital raise would be 123.8 million.

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

Chris Anzalone

Thanks Ken. This is an important year for Arrowhead in 5 primary areas.

First, we expect a lot of activity within our cardiometabolic vertical. We will have our first P3 readout for plozasiran and plan to file our first NDA. We plan to initiate several additional P3 studies in patient populations including HoFH, HeFH, SHTG, and potentially ASCVD across 2 different drug candidates: plozasiran and zodasiran. We also intend to expand the cardiometabolic vertical to include 2 additional candidates: ARO-INHBE and an undisclosed adipose-targeted candidate.

Second, we plan to have multiple clinical readouts in our pulmonary vertical across 3 different drug candidates and initiate at least 1 P2 study.

Third, we intend to continue to strengthen our balance sheet with a structured finance transaction and 1 or more business development transactions.

Fourth, our other clinical programs continue to move forward. These include:

- Continuing enrollment of the fazirsiran P3 study with Takeda;
- Amgen potentially completing enrollment of its P3 study of olpasiran;
- Progress in P2 studies in HBV with GSK;
- Progress in P2 studies of GSK-4532990 in NASH;
- Planning for P2 studies of PNPLA3;
- Progress in P1 studies of our neuromuscular candidates, ARO-DUX4 and ARO-DM1; and
- Progress in P1 studies of our complement-based candidates, ARO-C3 and ARO-CFB;

And fifth, we are not done innovating. As I mentioned, we expect to bring our first adipose-targeted candidate to the clinic and initiate clinical studies for an undisclosed CNS candidate this year.

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

Operator