ARROWHEAD PHARMACEUTICALS

Fiscal 2022 First Quarter Conference Call – Prepared Remarks

February 2, 2022

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 Vincent Anzalone, Vice President of Investor Relations for Arrowhead. Please go-ahead Vince.

Vince Anzalone

Good afternoon everyone. Thank you for joining us today to discuss Arrowhead's results for its fiscal 2022 first quarter ended December 31, 2021.

With us today from management are president and CEO Dr. Christopher Anzalone, who will provide an overview of the quarter; Dr. Javier San Martin, our chief medical officer, will provide an update on our mid and later stage clinical pipeline; Dr. James Hamilton, our senior vice president of Discovery & Translational Medicine, will provide an update on our pulmonary platform; and Ken Myszkowski, our chief financial officer, will give a review of the financials. We will then open the call to your 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 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.

With that said, I'd 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.

The biotech market has been a difficult place of late. In 2021, the XBI Biotech Index was down 21% and during the first month of 2022, the index is down a further 18%. My goal today is not to fight market cycles, but rather to articulate where we are as a company to help you assess Arrowhead's true value. We are here to create innovative new medicines for the millions of patients who desperately need them, and if we stay focused on that important mission we will continue to create substantial value for our shareholders. That is the lens through which you should view our update today. As Javier, James, and I speak about our continued progress across our programs, think about what those programs will mean to patients and where those programs take us as a company. There is much that currently excites me about this great company.

We had another strong quarter executing on our strategy with respect to platform extension, pipeline expansion, and business development: we continue to make tangible progress across all our programs.

Early in the quarter we hosted a key opinion leader webinar on ARO-C3, our newest clinical stage investigational therapeutic designed to reduce production of complement component 3, or C3, as a potential therapy for various complement mediated diseases. We also filed a CTA to begin clinical studies and have been activating sites for first-in-human studies. As with all the other drug candidates currently in our pipeline, we expect ARO-C3 to be the first RNAi candidate against this target to reach the clinic. We see substantial unmet medical need we could address across a variety of indications including: PNH, autoimmune hemolytic anemia, C3 glomerulopathy, IgA nephropathy, and Lupus Nephritis. Our pre-clinical data have been encouraging, and given that this will be our 8th hepatocyte-directed TRiM^{TM} candidate in clinical studies, we have a high expectation of success.

This program is also a good example of our speed. We went from idea to initiating clinical studies in approximately 12 months. We expect to move at similar speed for future hepatocyte-directed candidates, and as the extra-hepatic platforms mature, we have the potential to move at a similar level of efficiency.

During the quarter we and our partners also presented encouraging clinical data on multiple programs, including ARO-HSD for NASH, ARO-AAT, also called TAK-999, for liver disease associated with alpha-1 antitrypsin deficiency, ARO-APOC3 for hypertriglyceridemia, and JNJ-3989 for hepatitis B virus infection. Without exception, all of those candidates appear to be doing what they are designed to do

and have been generally well tolerated. We look forward to continued clinical development and learning more about the potential disease-modifying capabilities of these agents.

We also signed a license agreement with GlaxoSmithKline for ARO-HSD, that just recently closed. We are happy to bring on a new partner and look forward to working closely with GSK as they prepare to start a Phase 2 study. Under the terms of the agreement, GSK received an exclusive license to develop and commercialize ARO-HSD in all territories except Greater China, which was retained by Arrowhead.

Arrowhead received an upfront payment of $120 million and is eligible for a $30 million milestone at the start of Phase 2, a $100 million milestone at the start of Phase 3, up to $190 million in milestones at launch in the US and major markets, and up to $590 million for key sales milestones. Arrowhead is further eligible to receive tiered royalties of mid double-digit to 20% on net product sales.

I expect GSK to be a great partner for this exciting, genetically validated candidate. They have a clear commitment to genetic medicine and to finding an effective treatment for NASH, which could include a staggering number of patients. Understanding the complicated biology of this disease and addressing a potentially very large global market are substantial challenges indeed, and we believe that GSK will be a powerful partner to complete clinical development and ultimately deliver a potentially important medicine to the tens of millions of patients who need it.

Moving to our cardiometabolic programs, we recently initiated Arrowhead's first Phase 3 study, which I see as a key milestone event and indicative of a maturing

company. The PALISADE study is a Phase 3 clinical study to evaluate the efficacy and safety of ARO-APOC3 in adults with familial chylomicronemia syndrome, or FCS. ARO-APOC3 is our investigational RNAi therapeutic designed to inhibit the production of apolipoprotein C3, or APOC3, a key regulator of triglyceride metabolism. Prior studies have been very encouraging, where we have seen greater than 90% triglyceride reduction in some patient populations. This type of dramatic effect could really move the needle for FCS patients, who have very little in the way of therapeutic options at present.

We also made good progress on patient enrollment for the two ARO-APOC3 Phase 2b studies in severe hyper triglyceridemic patients (the SHASTA-2 study) and those with mixed dyslipidemia (the MUIR study). These are populations that we believe have few therapeutic options, and data from our prior studies suggest that ARO-APOC3 could be highly meaningful by lowering triglycerides and raising HDL.

Progress on the ARO-ANG3 P2b study in mixed dyslipidemia (the ARCHES-2 study) has been rapid, and I expect enrollment to be complete in the coming months. We continue to see a big opportunity to help the millions of patients with elevated triglycerides and LDL-cholesterol, and we are optimistic that ARO-ANG3 could be an important future medicine given our prior data and exciting work done by others to validate the target. As has been our consistent practice at Arrowhead of bringing the first RNAi compound into the clinic against specific gene targets, ARO-ANG3 was the first RNAi compound in clinical studies that targets ANGPTL3. Further, the competitive landscape seems to have shifted even further in our favor with the recent announcement that Pfizer has discontinued its partnership with Ionis on its antisense approach to ANGPTL3. Of course we do not have deep knowledge of data coming out of that program and it is always

difficult to compare results across different studies, but given what we have seen publicly we continue to be confident in our candidate. For instance, data from our P1/2 study indicated the following:

- ARO-ANG3 has demonstrated very deep and durable activity, enabling quarterly or less frequent dosing;
- ANGPTL3 levels were reduced in a dose-dependent fashion from 78-90% after 100, 200, or 300mg of ARO-ANG3;
- We saw mean triglyceride reductions up to 73.5% and mean non-HDL cholesterol reductions up to 50%;
- Only 2 patients had elevated ALTs, and in both cases there were concomitant medications associated with increases in ALTs, and in both cases the elevation was transient and not associated with increase in bilirubin; and
- We have seen no indication that ARO-ANG3 led to an increase in liver fat

Let's now move to our pulmonary platform. James will give a full review during this call, but I wanted to highlight a few developments. First, we continue to make progress on the ENaC target, but will likely not continue with ARO-ENaC, the candidate that we were testing in a P1/2 study last year. We have 2-3 next generation compounds that appear to have favorable pharmacologic properties compared to ARO-ENaC. A step behind this, we are also exploring ways to deliver pulmonary-targeted drug candidates via subcutaneous administration, which we believe would be a true breakthrough, and are testing this for ENaC as well. So, we are likely changing horses in the ENaC program but we have not yet settled on *which* new horse.

We have also discussed our plans to file two new pulmonary CTAs this year but had not previously disclosed the targets or disease areas. I'm excited to announce these programs formally as ARO-RAGE and ARO-MUC5AC, each being developed for various muco-obstructive and inflammatory pulmonary conditions. We are on track to file CTAs for both of these over the next quarter. We will be presenting preclinical data at the American Thoracic Society meeting in May, and we also plan to host a KOL webinar or a pulmonary specific R&D day this year. At the latter event, we intend to go into detail on the biology of the targets, present preclinical data, introduce the commercial market opportunity, explain our plans for the clinical studies, and have an outside KOL describe the clinical presentation of the diseases and unmet medical need.

We are pleased that we expect to file 2 new pulmonary CTAs in the first half of 2022, and also are on track to file a third by the end of the year. That target and disease area remain undisclosed.

While still on the pulmonary platform, we continue to make progress in COVID and are currently testing compounds that are leading to substantially decreased lung inflammation and viral expression in animal models. This is exciting for what they may mean for the current SARS-CoV-2, but also potentially for other SARS-based corona viruses. As you may recall, we are working to develop antiviral agents by targeting regions that are well-conserved across known SARS corona viruses with the hope that we could treat current and future, novel infections. Our progress here has also opened doors for us in other respiratory viruses, where we now have active programs. We could see that becoming a substantial sub-franchise within our pulmonary platform. These are exciting opportunities for us and we look forward to updating you on our progress.

In addition to the 2 new pulmonary CTAs in the first half of this year, we are on track with ARO-DUX4, our first skeletal muscle-targeted candidate against FSHD. Consistent with our prior guidance, we expect to file that CTA by the end of the first half of the year. This represents a leap forward with the addition of another cell type we can target clinically and, more specifically, ARO-DUX4 may offer us the ability to help a group of patients with no real therapeutic options. Recent failures and setbacks in the field have underlined the unmet medical need that currently exists and we are moving as fast as we can for the FSHD patients who need us.

Our partnered programs have also made good progress. JnJ continues its P1 progress with JNJ-75220795, our partnered NASH therapeutic, and JNJ-3989, our partnered HBV therapeutic. The latter is in multiple large P2b studies that have started to read out, and I would expect regular data from them over the next few years. As we discussed on our last earnings call, JNJ-3989 is doing exactly what it was designed to do and we look forward to seeing how it performs over time and in combination with different agents.

Olpasiran, the candidate against cardiovascular disease that we licensed to Amgen, continues in a P2 study. Amgen has said publicly that they expect to complete the P2 in the first half of this year. Data from the P1 were impressive, and we look forward to seeing P2 data and the initiation of a P3.

ARO-AAT has an ongoing P2b study that is currently starting to read out PK data at 3 different dose levels and will readout biopsy data in the 3d or 4th quarter. We continue to work closely with Takeda and expect to continue discussions with regulators this year about our data and plans for a pivotal study.

Our work with Horizon continues to move rapidly in the area of chronic gout, and I will defer to them to provide guidance on future plans and timing.

Lastly, we completed a transaction to purchase 13 acres of land in the Verona Technology Park in Verona, WI, which is planned to be the site of a new GMP drug manufacturing facility and an associated laboratory and office facility. Construction is starting this quarter. Completion of the lab and office space is anticipated in early-to-mid 2023, and completion of the manufacturing facility is expected in late 2023. We will continue to operate additional research and development facilities in Madison, Wisconsin, and San Diego, California. We also signed a lease to what will allow us to substantially expand our research laboratories and administrative offices in San Diego in the first half of 2023.

We believe the new Arrowhead campuses will allow us to support our growing pipeline and we think positions us well to advance the manufacturing process, including at commercial scale, of our TRiM™-enabled drug candidates. We view this as a strong competitive advantage as we approach potential commercialization of our rapidly progressing clinical candidates.

So, in summary, our pipeline is expanding and maturing. Our platform is providing additional opportunities to discover and develop new investigational medicines in areas where Arrowhead has unique capabilities and expertise. We are using business development selectively to maximize the value or our technology and bring in non-dilutive capital to support our internal development programs. And, we are investing to expand our R&D footprint and take more control of the drug manufacturing process to support clinical and ultimately commercial supply needs. We believe all of this puts Arrowhead in a very strong competitive position.

With that overview, I'd now like to turn the call over to Dr. Javier San Martin. Javier?

Javier San Martin

Thank you, Chris, and good afternoon everyone.

I will provide status updates on three of our later stage clinical programs. ARO-APOC3 and ARO-ANG3, our investigational cardiometabolic medicines, and ARO-AAT, also called TAK-999, our investigational medicine designed to treat alpha-1 liver disease, which is being co-developed with Takeda.

First, ARO-APOC3 is our investigational medicine targeting apolipoprotein C-III being studied in patients with various lipid disorders. Collectively, the mid and late-stage clinical studies for ARO-APOC3 are called the SUMMIT program. We made good progress bringing on new sites for each of the studies and we are very pleased with the pace of patient enrollment. I will discuss each study individually.

SHASTA-2, is a double-blind, placebo-controlled Phase 2b study of ARO-APOC3 in adults with severe hypertriglyceridemia, or sHTG. This population is defined as having triglycerides greater than 500 mg/dL. The primary objective of the SHASTA-2 study is to evaluate the safety and efficacy of ARO-APOC3 and to select a dosing regimen for later stage clinical studies in this patient population. Approximately 216 patients will be enrolled in the study.

Moving on to the MUIR study, which is a double-blind, placebo-controlled Phase 2b study of ARO-APOC3 in adults with mixed dyslipidemia. This population is defined as having triglycerides between 150 and 500 mg/dL and non-HDL-cholesterol greater 100 mg/dL or LDL-cholesterol greater than 70 mg/dL. The primary objective of the MUIR study is to evaluate the safety and efficacy of ARO-APOC3 and to select a dose and dosing regimen for later stage clinical studies in patients with mixed dyslipidemia. A total of approximately 320 patients will be enrolled in the study.

The most recent study initiated in the SUMMIT program is PALISADE, a Phase 3 study to evaluate the efficacy and safety of ARO-APOC3 in adults with familial chylomicronemia syndrome, or FCS. These are patients with fasting triglycerides greater than 880 mg/dL that are refractory to standard lipid-lowering therapy and have a diagnosis of FCS. Because they tend to have extremely high triglycerides, patients with FCS have an elevated risk of recurrent and painful bouts of pancreatitis. These patients currently have very limited treatment options. The primary endpoint of PALISADE is the percent change from baseline at Month 10 in fasting triglycerides. Additional secondary and exploratory endpoints include the change in other lipid parameters, incidence of acute pancreatitis, and other measures. Approximately 60 patients will be enrolled in the study.

I will now move on to ARO-ANG3, our investigational medicine designed to reduce production of angiopoietin-like protein 3 ANGPTL3 as a potential treatment for patients with mixed dyslipidemia. The set of mid and late-stage studies for ARO-ANG3 is called the VISTA program. The VISTA program has one active study and one additional planned study that I will describe briefly in a moment.

The currently active study is ARCHES-2, a double-blind, placebo-controlled Phase 2b study of investigational ARO-ANG3 in adults with mixed dyslipidemia. This population is defined the same way as in the ARO-APOC3 MUIR study. These patients have triglycerides between 150 and 500 mg/dL and non-HDL-cholesterol greater 100 mg/dL or LDL-cholesterol greater than 70 mg/dL. The primary objective of the ARCHES-2 study is to evaluate the safety and efficacy of ARO-ANG3 in adults with mixed dyslipidemia and select a dosing regimen for later stage clinical studies in this patient population. A total of approximately 180 participants will be enrolled in the study.

The next study planned for the VISTA program is GATEWAY, a Phase 2 Study of ARO-ANG3 in patients with homozygous familial hypercholesterolemia, or HoFH. Statins and PCSK9 inhibitors can inhibit cholesterol synthesis and enhance hepatic clearance of LDL-Cholesterol through upregulation of the hepatocyte LDL receptor. Patients with HoFH can have dysfunctional or absent LDL receptors and thus can be resistant to statins and even resistant to alternatives such as PCSK9 inhibitors. Patients with HoFH are therefore a population with a particularly high need for additional therapy with a mechanism that works outside of the LDL receptor, such as ANGPTL3 inhibition.

GATEWAY is an open-label study that will be conducted in subjects with documented HoFH based on genotype or clinical criteria. Up to approximately 16 subjects who meet eligibility criteria will be randomized in a 1:1 ratio to receive 2 doses of 200 or 300 mg of ARO-ANG3 on Day 1 and Day 84 and will be evaluated over a 36-week period. We are gearing up to initiate this study in the first half of 2022 and will provide an update when the first patients have been enrolled.

Consistent with the other Phase 2 studies in both the VISTA and SUMMIT programs, we want to give Arrowhead maximum flexibility to initiate Phase 3 studies in multiple patient populations if the data warrant it. At the end of these Phase 2 studies, we hope to have a good understanding of the pharmacodynamic effects of both investigational medicines in various patient populations with different baseline lipid profiles. We believe this will inform our development strategy and also help shape our commercial strategy in both well-defined rare diseases as well as larger high prevalence diseases.

I also want to give a brief update on ARO-AAT, also called TAK-999. After receiving Breakthrough Therapy Designation, we began a productive dialogue with FDA about the program. We expect to have data on the reduction of circulating levels of AAT from SEQUOIA in the first half of this year, which will be used to select a dose for Phase 3. We should also be collecting the last 12-month biopsy from the last patient enrolled sometime in the summer of 2022. Together with Takeda, we look forward to continuing the dialogue with FDA after one or both of these data readouts.

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

James Hamilton

Thank you, Javier.

There are a lot of exciting new programs in discovery and early-stage clinical development. Our R&D organization is operating at an impressive pace and making important progress in multiple areas. Today, I would like to focus on the

pulmonary platform, the planned expansion of the pulmonary pipeline, and provide an update on where we are with ARO-ENaC.

As Chris mentioned, our newest pulmonary candidates are ARO-RAGE and ARO-MUC5AC. They are both on schedule to have CTA filings during the first half of this year. Additionally, we plan on filing a 3rd pulmonary CTA in Q4 of this year. The target for this third program will remain undisclosed at this time.

The first program, ARO-MUC5AC, targets expression of MUC5AC in bronchial epithelium. MUC5AC is a mucin protein with upregulated expression in the asthmatic airway. MUC5AC is not normally required for bacterial defense or mucociliary clearance in healthy individuals. However, in asthmatic patients its upregulation and enhanced secretion can lead to a muco-obstructive disease state which is not directly addressed by currently available therapies. The degree of mucus obstruction in the asthmatic airway is highly correlated with poor asthma control and increased disease severity. Additionally, multiple genome wide association studies have demonstrated a correlation between enhanced MUC5AC expression and the development of asthma. Similarly, mice with genetic deletion of MUC5AC are protected from airway hyperreactivity in the setting of allergic stimuli, again supporting the concept that MUC5AC driven mucus plugging plays a central role in allergen induced airflow obstruction. ARO-MUC5AC is an extremely exciting program, in part because it represents a fundamentally new way of treating asthma. By targeting the mucus, we have a unique and potentially very powerful tool.

An abstract summarizing pre-clinical data leading to the nomination of this clinical candidate will be presented at the American Thoracic Society meeting this spring.

The second program, ARO-RAGE, targets expression of the Receptor for Advanced Glycation End products, or RAGE, which is primarily expressed by alveolar and bronchial epithelium. RAGE is a transmembrane receptor that binds to numerous pathogen-associated and cell damage-associated ligands to activate various components of the innate immune system. RAGE represents an upstream mediator of the inflammatory cascade in asthma, as it is required for allergen-induced release of IL-33 into the airway and acts upstream of Type 2 cytokines including IL-4, IL-5, and IL-13. Importantly, a soluble component of RAGE known as sRAGE can be followed as a serum biomarker of gene target knockdown.

This is a very important point that I want to highlight. The availability of a circulating biomarker will teach us a lot about the candidate and, importantly, may inform on the pulmonary platform broadly. Our hepatocyte directed TRiM™ system has proven to translate very predictably from preclinical models to human results, and over the last few years that predictability has increased the speed of new programs and our expectation of success. We hope to get to the same point with the pulmonary directed TRiM™ system, and the availability of sRAGE circulating biomarker data informing on depth and duration of gene target knockdown using an inhaled route of administration, could get us closer to that point.

Animal data suggest that RAGE signaling plays a critical role in the pulmonary inflammatory responses to inhaled stimuli. RAGE knockout mice show a markedly attenuated response to allergen exposure. In animals, RAGE is necessary for activation of airway inflammatory pathways relevant to both Type 2 high and potentially Type 2 low asthma phenotypes. Further studies have indicated that RAGE knockout mice are protected from allergen provoked increases in IL-33 and

TSLP which represent key upstream drivers of asthmatic Type 2 inflammation. Thus, we believe RAGE inhibition offers the possibility of arresting the most proximal components of airway inflammation in asthma, with potentially broad effects on a wide range of downstream inflammatory mediators.

In rats using a tool trigger targeting RAGE mRNA, single inhaled doses of 0.5 mg/kg induce sRAGE reduction of over 90% lasting for approximately three months. Like our MUC5AC program, an abstract has been accepted for oral presentation at ATS this spring, which will summarize pre-clinical data for our RAGE program.

Inhibition of both the MUC5AC and RAGE targets may have clinical utility in severe asthma, COPD, cystic fibrosis, and other muco-obstructive or inflammatory pulmonary conditions. Additional target background, data, and clinical plans will be discussed in the future as we approach the start of the clinical studies.

We are also making good progress on two additional pulmonary programs that are being developed to address respiratory viruses. One is our COVID program that targets highly conserved sequences in essential viral mRNAs, which may address SARS-CoV-2 and potentially other future coronavirus outbreaks. In a hamster SARS-CoV-2 infection model, our current lead candidate reduced viral load in the lung by 80%, reduced histological indices of pulmonary inflammation by 50%, and prevented body weight loss. We are currently in the lead optimization stage and will provide additional updates when we can.

The other is a new program for an undisclosed viral infection. In a mouse model of infection the current lead compound reduced viral gene expression in the lung by

90%, and prevented body weight loss. This is an early program, but we are seeing what we believe are very promising results.

Moving to ARO-ENaC, as Chris mentioned we have decided to focus resources on next generation candidates. We previously announced that the clinical study was voluntarily paused after findings of local lung inflammation in a rat chronic GLP toxicology study. We have since seen some local inflammatory findings in chronic GLP monkey studies. It is certainly possible that we were overdosing the animals and by simply changing dose levels and/or dose intervals, we would see a cleaner tox profile. That could provide a faster path back to the clinic, but we decided that the better long-term path is to focus on next generation ENaC candidates. We are currently interrogating several next generation ENaC candidates that appear to be substantially more potent than ARO-ENaC.

It should be noted that the drug exposure levels used in CTA enabling GLP studies supporting the new pulmonary programs, including the MUC5AC and RAGE programs, are significantly lower than those used in support of our first generation ENaC program. Thus, we expect an ability to use less drug and less frequent dose administration with second generation programs compared to what was used in the ARO-ENaC chronic toxicology studies and anticipate overall enhanced toxicology species safety margins with second generation compounds.

The last update I'd like to provide on the pulmonary platform is about future opportunities and the potential to add additional flexibility with regard to route of administration. We have been working on addressing pulmonary tissues via subcutaneous administration. These are still early days, but we have recently generated some very promising preliminary data with the ARO-RAGE program using subcutaneous administration. Again this is early, but we view this as a

potential breakthrough if this line of discovery bears fruit. We intend to provide some data on these efforts when we go into more detail about the ARO-RAGE and ARO-MUC5AC candidates at the appropriate forum. This will likely take the form of a KOL webinar or an in-person and webcast pulmonary R&D day in the first half of this year. This is all very exciting progress and we look forward to discussing details publicly.

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, 2021 was $62.9 million or $0.60 per share based on 104.5 million fully-diluted weighted average shares outstanding. This compares with net loss of $20.7 million, or $0.20 per share based on 102.8 million fully-diluted weighted average shares outstanding, for the quarter ended December 31, 2020.

Revenue for the quarter ended December 31, 2021 was $27.4 million, compared to $21.3 million for the quarter ended December 31, 2020. Revenue in the current period primarily relates to the recognition of a portion of the $300 million upfront payment received under our collaboration agreement with Takeda and the $40 million upfront payment received under our collaboration agreement with Horizon. Revenue for each agreement will be recognized as we complete our performance obligations, which include managing the ongoing AAT phase 2 clinical trials for Takeda, and delivering a phase 1 ready candidate to Horizon. There remains $188 million of revenue to be recognized associated with the Takeda collaboration

which we anticipated will be recognized over approximately 2-3 years, and there remains $27 million of revenue for Horizon, which we anticipate will be recognized by the end of calendar 2022. Revenue in the prior period primarily related to the recognition of a portion of the milestones received from our license and collaboration agreements with Janssen. Finally, our licensing agreement with GSK for ARO-HSD resulted in a $120 million upfront payment to Arrowhead, which was collected in January 2022. We anticipate the majority of this to be recognized as revenue in fiscal second quarter 2022. Any additional milestones achieved from our collaboration agreements would be additive to these amounts.

Total operating expenses for the quarter ended December 31, 2021 were $90.8 million, compared to $45.4 million for the quarter ended December 31, 2020. This increase is primarily due to increased clinical candidate costs as our pipeline has expanded and advanced through clinical trial stages, as well as increased non-cash stock compensation.

Net cash used by operating activities during the quarter ended December 31, 2021 was $61.3 million, compared with net cash used by operating activities of $38.9 million during the quarter ended December 31, 2020. The key driver of this change was the increased candidate costs. We continue to estimate our operating cash burn to be $60 to $80 million per quarter in fiscal 2022, excluding any incoming milestone payments from our partners. In addition, we are planning to expand our manufacturing capabilities, and expand our R&D facilities. We continue to estimate that these capital projects, along with routine capital expenditures, will add an incremental cash outlay of $80 to $90 million for full year fiscal 2022.

Turning to our balance sheet, our cash and investments totaled $547.7 million at December 31, 2021, compared to $613.4 million at September 30, 2021. The decrease in our cash and investments was primarily due to cash used for operating activities. With the collection of the $120 million upfront payment in January 2022, our current cash and investments total approximately $650 million.

Our common shares outstanding at December 31, 2021, were 104.8 million.

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

Chris Anzalone

Thanks Ken. And thanks to all of you for joining us today.

As you've heard, our early pipeline is starting to grow rapidly, our mid and later stage pipeline is advancing on schedule, and we are working hard to continue to expand the reach of our TRiM™ platform to enable more growth in the future. These are all critical parts of building a sustainable business and growing shareholder value.

I want to take a moment to review what we see on the horizon as potential milestones for the business this year. There is a lot going on, so this list is certainly not exhaustive, but includes some of the key events that we will be tracking.

I will start with our partnered programs.

ARO-AAT, also called TAK-999, for alpha-1 liver disease with Takeda

- We expect data from the SEQUOIA study on reductions in circulating AAT levels and 12-month biopsy data, and we will continue discussions with the FDA

ARO-HSD for NASH with GSK

- We expect a Phase 2 study to begin this year

ARO-XDH for gout with Horizon

- We hope to complete preclinical studies this year

JNJ-3989 for HBV with Janssen

- We would expect additional clinical readouts from various ongoing studies

JNJ-75220795 for NASH with Janssen

- We expect progress on Phase 1 study

Olpasiran, formerly called AMG 890, for cardiovascular disease with Amgen

- Amgen has guided to a Phase 2 study readout this year

I will now talk about potential milestones for our wholly owned programs.

ARO-APOC3 for hypertriglyceridemia

- We expect to fully enroll SHASTA-2 and MUIR Phase 2 studies and make progress towards full enrollment on PALISADE Phase 3 study

ARO-ANG3 for mixed dyslipidemia

- We plan to fully enroll ARCHES-2 Phase 2 study and initiate GATEWAY Phase 2 study

ARO-C3 for complement mediated diseases

- We expect to initiate a Phase 1 study and potentially have initial data readout from single ascending dose portion of study in healthy volunteers and initiate multiple dose portion of study in various patient populations

Pulmonary programs

- We plan to file CTAs and initiate clinical studies for ARO-RAGE, ARO-MUC5AC, and file a CTA for one additional undisclosed pulmonary program. We could also have some early clinical data from the ARO-RAGE program.

ARO-HIF2 for renal cell carcinoma

- We intend to report additional Phase 1 data at ASCO GU in February

ARO-DUX4 for FSHD

- We plan to file a CTA and initiate clinical studies

This is a big year by any measure:

- we plan to push 4 new drug candidates into clinical studies, and possibly a 5th if ARO-XDH with Horizon makes it this year;
- we hope to have some data released from 6 different programs;
- and we hope to fully enroll 3 P2b studies.

Arrowhead has a lot going on and we look forward to numerous opportunities to show progress across the pipeline throughout the coming year.

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

Operator