ARROWHEAD PHARMACEUTICALS

Fiscal 2019 Year End Conference Call – Prepared Remarks

November 25, 2019

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 year ended September 30, 2019. With us today from management are president and CEO Dr. Christopher Anzalone, who will provide an overview of the year; Dr. Bruce Given, our chief operating officer and head of R&D, who will discuss our clinical programs; and Ken Myszkowski, our chief financial officer, who will give a review of the financials. We will then open up 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 27(A) of the Securities Act of 1933 and Section 21(E) of the Securities Exchange Act of 1934. All statements other than statements of historical fact, including

without limitation those with respect to Arrowhead's goals, plans, and strategies are forward-looking statements. These include statements regarding our expectations around the development, safety and efficacy of our drug candidates, projected cash runway, and expected future development activities. These statements represent management's current expectations and are inherently uncertain. Thus, actual results may differ materially. Arrowhead disclaims any intent and undertakes no duty to update any of the forward-looking statements discussed on today's call.

You should refer to the discussions under risk factors in Arrowhead's annual report on Form 10-K and the Company's subsequent quarterly reports on Form 10-Q for additional matters to be considered in this regard, including risks and other considerations that could cause actual results to vary from the presently expected results expressed in today's call.

I want to quickly acknowledge a couple new analysts that recently began covering Arrowhead that will be on our call today for the first time. They are Madhu Kumar from Baird and Alethia Young from Cantor Fitzgerald. Both have covered Arrowhead at prior firms and I'm happy to welcome them back.

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.

I want to start by welcoming the newest members of the Arrowhead management team: Dr. Javier San Martin, who joins us in the role of Chief Medical Officer; and, Dr. Curt Bradshaw, who joins us as Chief Scientific Officer. We are very fortunate to have these talented and seasoned leaders on the team. I also want to say thank you to Dr. Bruce Given, who will be retiring on May 1, 2020. He will continue in his current role over the next six months as he transitions responsibilities to Javier and Curt. He has also agreed to remain in an advisory role to the company after May 1, as needed. Bruce has been an important asset to Arrowhead for almost a decade and to the biopharma industry for over 30 years. We wish him all the best during his retirement.

Now, turning to our business and the progress we've made over the last year. We have demonstrated, once again, that we can consistently achieve best-in-class speed and execution.

Arrowhead's TRiM™ platform is enormously flexible, and we have numerous and growing opportunities to develop innovative new medicines that address important medical conditions and potentially make a difference in a lot of people's lives. This is an enviable place to be for any biotech company. But technology and opportunity alone do not guarantee success. We think our unwavering commitment to innovation is what really sets us apart.

There are now 5 TRiM™-enabled candidates in the clinic, 3 of which are wholly-owned and 2 are partnered. Over the next month we plan to submit regulatory filings for 2 additional clinical candidates, and by the end of 2020, we intend to have 10 TRiM -enabled candidates in clinical studies targeting four different cell types. Further, we expect to be in 3 pivotal studies by the end of 2020. Let that all

sink in for a moment. We believe this is a strikingly unique position for a company our size.

We feel confident about our ability to achieve these aggressive targets, and we have good reason to believe in the ultimate success of these clinical programs for a number of reasons.

First, we have an increasingly validated technology in the TRiM™ platform. Keep in mind that over 250 people have been treated with over 450 doses of TRiM-enabled candidates. We continue to see very good activity and a benign safety profile in all programs.

Second, we focus on well-validated targets. We tend to select gene targets where there is a widely accepted belief in the scientific community that if you can knock the target down, there will be clinical benefits without known negative phenotypes. In other words, we leverage prior genetic studies to minimize our target and Biology risk. With the expanding body of knowledge on genetics and ever expanding published GWAS datasets, we believe new and interesting targets will continue to emerge.

Third, the RNAi field is just beginning what we believe to be a golden age. This modality is increasingly accepted as a reliable and powerful way to treat a variety of diseases after two decades of intensive study and development. While the potential and value of direct conjugation delivery in unlocking the potential of RNAi was clear to us by 2016, broader confidence took longer. Interestingly, the increasing validation of RNAi is growing amid a backdrop of scarcity related to companies capable of leveraging it therapeutically and near absolute scarcity of bringing RNAi outside the liver: we think we are probably years ahead of anyone else in this regard.

Lastly, and as we discussed at our R&D day last month, Arrowhead is constantly finding innovative ways to shave days, weeks, and even months off of

the traditional development cycle. We effectively try to take all of the wasted time out of the R&D process, without ever sacrificing quality or cutting regulatory corners, and we think we have demonstrated a level of speed and efficiency that has not been seen before.

So, at once we are expanding the potential uses and upside of our technology while squeezing more and more risk and development time out of the programs. This is a powerful idea, indeed.

During our R&D day last month, we went into some detail about several of our development programs. I will now give a quick review of the day.

At the event we discussed our two cardiometabolic candidates:

1. ARO-APOC3 targeting apolipoprotein C-III being developed as a potential treatment for patients with severe hypertriglyceridemia and familial chylomicronemia syndrome, or FCS
2. And, ARO-ANG3 targeting angiopoietin like protein 3 being developed for the treatment of dyslipidemias, such as homozygous familial hypercholesterolemia (HoFH), and metabolic diseases.

We believe that these are very powerful targets. There is strong genetic validation that loss of function mutations in ANGPTL3 or APOC3 result in improved cardiovascular outcomes relative to the population at large. Importantly, these loss of function mutations have not been associated with demonstrated adverse phenotypes, which means nobody has reported any symptoms or disease resulting from the loss of the protein. This has also been demonstrated in the clinic with other agents using other mechanisms, which gives us confidence that the targets likely have multiple points of validation. In addition, we believe that compounds

using other mechanisms to reduce these proteins have vulnerabilities, positioning RNAi as an important potential new option for patients. Bruce will discuss some specific clinical data from our Phase 1 studies that we recently presented at AHA on ARO-APOC3 and ARO-ANG3, but I will say that we were thrilled with the results and believe that they strongly support our plans to initiate Phase 3 studies in 2020. We've seen deep reductions in triglycerides after single doses of ARO-APOC3 and believe there are relatively clear regulatory pathways to treat patients with rare conditions, such as FCS, as well as those with more common conditions leading to elevated triglycerides and associated pancreatitis.

ARO-ANG3 has even greater optionality and opportunities. We expect it to lower triglycerides and LDL-cholesterol, and previous studies suggest that we could expect it to improve insulin sensitivity and decrease liver fat. Together, these are huge opportunities and we believe ARO-ANG3 has the potential to help a large variety of patients.

We also covered ARO-AAT, our second generation subcutaneously administered RNAi therapeutic being developed as a treatment for liver disease associated with alpha-1 antitrypsin deficiency, which is a rare genetic disorder. ARO-AAT is designed to reduce production of the mutant Z-AAT protein by silencing the AAT gene in hepatocytes in order to potentially prevent accumulation of Z-AAT in the liver, allow clearance of the accumulated protein, prevent repeated cycles of cellular damage, and possibly prevent or even reverse the progression of liver fibrosis. In preclinical studies in PiZ mice, RNAi treatment restored normal hepatocyte ultrastructure. In our Phase 1 clinical study, ARO-AAT led to significant reductions in serum AAT levels down to the lower limit of quantitation, with a long duration of effect that supports quarterly or less frequent dosing. We are currently conducting the SEQUOIA study, an adaptive design, potentially

pivotal Phase 2/3 clinical study, and AROAAT2002, which is an open-label Phase 2 clinical study to assess changes in a novel histological grading scale after 6 months, 12 months, 18 months, and 24 months of treatment.

During the R&D day we also discussed our three most advanced preclinical candidates:

1. ARO-HSD against the target HSD17B13 being developed as a treatment for alcohol and nonalcohol related liver diseases. Published human genetic data indicate that a loss of function mutation in HSD17b13 provides strong protection against nonalcoholic steatohepatitis (NASH) cirrhosis and alcoholic hepatitis and cirrhosis with approximately 30-50% risk reduction compared to non-carriers. We expect to file a CTA for ARO-HSD by the end of the year;
2. ARO-HIF2 against the target HIF2-alpha being developed as a potential treatment for clear cell renal cell carcinoma, or RCC. This will be the first TRiM™ enabled candidate targeting a tissue outside the liver to enter clinical trials. We expect to file an IND for ARO-HIF2 before the end of the year;
3. And, ARO-ENaC against the epithelial sodium channel, or ENaC, being developed to treat cystic fibrosis. In cystic fibrosis patients, increased ENaC activity contributes to airway dehydration and reduced mucociliary transport. Human genetic studies have validated ENaC as a CF target. This will be our first inhaled candidate targeting lung tissue using the TRiM™ system. IND-enabling studies are ongoing to support regulatory filings for first-in-human studies in 2020.

We also discussed, broadly, our product development strategy as we continue to expand our pipeline and detailed the guiding principles that make our R&D

organization best-in-class for execution and speed. In addition, we detailed advances to the TRiM™ system. We presented our second-generation muscle delivery platform that is highly active and amenable to subcutaneous administration, and we also discussed a new TRiM™ dimer structure that delivers multiple siRNA sequences together that can achieve high levels of knockdown of two different genes simultaneously.

These important advances dramatically increase the number of potential diseases that we may be able to address over the coming years. This gives us a distinct strategic and technical advantage over other RNAi companies. It can also drive a significant amount of value for us, and more importantly gives us the opportunity to potentially provide options for many patients without adequate treatments.

The R&D day had a very informative set of presentations, so I highly recommend that you listen to the replay on our website if you're looking to get a detailed overview about Arrowhead.

In addition to the R&D day, the period since our last conference call has been enormously productive. Included in our accomplishments were the following:

1. We began dosing patients in the SEQUOIA study of ARO-AAT, our first potentially pivotal study;
2. Our collaborator, Janssen, began dosing patients in the REEF-1 Phase 2b triple combination study in 450 patients with chronic hepatitis B infection. In connection with the start of this study, we earned a $25 million milestone payment from Janssen;
3. We presented additional preclinical data on ARO-ENaC at the North American Cystic Fibrosis Conference showing that ARO-ENaC can

accelerate mucociliary clearance in normal sheep and also preserve airway physiology in a sheep disease model of impaired mucociliary clearance;

4. With our collaborator, Janssen, we presented additional data on expanded cohorts of patients receiving the doublet of JNJ-3989 (formerly called ARO-HBV) and a NUC, and the first clinical data for triple HBV therapy, in this case the triplet of JNJ-3989, the capsid assembly modulator JNJ-6379, and a NUC.
5. We expanded our management team to include Javier San Martin as CMO and Curt Bradshaw as CSO, who I introduced at the outset of the call;
6. And, lastly and most recently, we presented new clinical data on ARO-APOC3 and ARO-ANG3 in back to back late breaker presentations, a very rare honor, at the American Heart Association Scientific Sessions.

We have made a lot of progress this year and we have great confidence that 2020 can be even more productive as we continue to expand our pipeline and begin to gain proof-of-concept in multiple extra-hepatic tissues.

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.

I want to talk about data recently presented in two late-breaking oral presentations at the American Heart Association Scientific Sessions on our two wholly owned cardiometabolic candidates, ARO-APOC3 and ARO-ANG3, and then I will give a status update on the clinical programs. As Chris mentioned earlier, we were thrilled with the data for both ARO-APOC3 and ARO-ANG3. The data were very

well received at the conference and have continued to generate a good amount of attention since then.

I will start with ARO-APOC3, Arrowhead's subcutaneously administered RNAi therapeutic targeting apolipoprotein C-III, being developed as a potential treatment for patients with hypertriglyceridemia.

The ARO-APOC3 first-in-human study, is called AROAPOC31001. It is a Phase 1 single and multiple dose study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamic effects of ARO-APOC3. The single-dose portion of the study is in adult healthy volunteers and the multiple-dose portion includes patients with severe hypertriglyceridemia and familial chylomicronemia syndrome.

The single dose portion of the study was presented at AHA. Consistent with our other clinical programs for liver targeted TRiM™ enabled candidates, the safety and tolerability appeared unremarkable for a first in human study. 40 subjects were enrolled to receive a single dose where 24 received active drug and 16 received placebo. There were no serious or severe adverse events reported. One adverse event, or AE, of moderate transient ALT elevation was reported with a peak of 210 U/L on Day 22 in a subject receiving ARO-APOC3. This subject had elevated ALT at baseline and returned to baseline by Day 85. There were 8 Local Injection Site Reactions - all rated mild.

Moving on to activity, we observed dose dependent reductions in serum APOC3, with mean maximum reductions ranging from 72% to 94%. Reductions were maintained through the end of study, which was 16 weeks after dosing, with mean reductions of 70% to 91%.

Reductions in triglycerides and VLDL-C were also observed with mean maximum reduction in triglycerides ranging from 53% to 64% and reductions in VLDL-C ranging from 53% to 68%. Reductions were maintained through the end of study, with week 16 mean reductions of 41% to 55% for TGs and 42-53% for VLDL-C

ARO-APOC also led to changes in LDL- and HDL- cholesterol. The mean maximum reduction from baseline in serum LDL-C was 12% to 25% and the mean maximum increase from baseline in serum HDL-C was 30% to 69%.

Now let's turn to ARO-ANG3, Arrowhead's subcutaneously administered RNAi therapeutic targeting angiopoietin like protein 3, or ANGPTL3, being developed as a potential treatment for patients with dyslipidemias and possibly metabolic diseases.

The ARO-ANG3 first-in-human study is called AROANG1001. It is a Phase 1 single and multiple dose study to evaluate safety, tolerability, pharmacokinetic, and pharmacodynamic effects. The single-dose portion of the study is in adult healthy volunteers and the multiple-dose portion includes patients with various types of dyslipidemia, including patients with non-alcoholic fatty liver disease, patients on a stable statin treatment regimen with persistently elevated LDL cholesterol, patients with heterozygous or homozygous familial hypercholesterolemia, and patients with hypertriglyceridemia.

Safety and tolerability for the single dose portion of AROANG1001 was as expected and also consistent with prior clinical safety readouts for TRiM hepatic-targeted drugs. 40 subjects were enrolled with 24 receiving active drug and 16 receiving placebo. No drug related severe or serious AEs were observed. Two AEs

of mild transient elevations in ALT were observed in one subject receiving ARO-ANG3 and one receiving placebo. The ALT elevation in one subject on ARO-ANG3 was confounded by concomitant ingestion of an herbal supplement with a known liver toxic profile. There was also 1 mild local injection site reaction.

ARO-ANG3 was active across measures and had good durability. Dose dependent reductions in serum ANGPTL3 were observe with mean maximum reductions ranging from 55% to 83%. Reductions were maintained through end of study, with week 16 mean reductions of 43% to 75%. Dose dependent reductions in TGs and VLDL-C were also observed, with mean maximum TG reductions of 31% to 66% and VLDL-C reductions of 30% to 65%. Reductions in TG and VLDL-C were maintained through end of study in the 200 mg and 300 mg cohorts, with week 16 mean reductions of 47% to 53% for TG, and 49% to 51% for VLDL-C

Changes in LDL- and HDL- cholesterol were also observed with mean maximum HDL-C reduced by 8% to 26% and LDL-C reduced by 9% to 30%. Mean maximum reduction in LDL-C with the 200 mg single dose was blunted by two subjects in this cohort with increasing LDL-C post-dose. The multiple dose healthy volunteer data at 200 mg dose demonstrates similar reductions to 100 mg and 300 mg doses of 33% to 46% reduction in LDL-C from baseline two weeks after a second dose, with the second dose given at week 4. Let me point out that both AHA presentations can be accessed from the Arrowhead website and are worth taking a look if you haven't already seen them.

We feel very good about the data for both candidates and we are currently enrolling and dosing the various multiple dose cohorts. The data from these multiple dose cohorts will inform our future development plans. We hope to have

those data in the first half of 2020 and intend to pursue abstract submissions to present at appropriate medical meetings.

I would now like to give an update on where we are with the other wholly owned candidates that are in or approaching the clinic.

I will start with ARO-AAT. We started dosing the SEQUOIA adaptive design Phase 2/3 study in August. SEQUOIA is designed to enroll 120 patients who will receive at least 9 doses, or approximately two years of treatment, with ARO-AAT or placebo. By protocol, efficacy will be assessed by the proportion of ARO-AAT treated patients relative to placebo achieving a 2-point improvement in a histologic grading scale of alpha-1 antitrypsin deficiency associated liver disease AND no worsening of liver fibrosis on end of study biopsy.
We intend to open around 40 sites in the US, Canada, and Europe. There are currently 7 sites open, and we are working diligently to bring more into the study as quickly as possible.

The second study we are running for ARO-AAT is AROAAT2002. It is a pilot open-label, multi-dose, Phase 2 study to assess changes in a novel histological activity scale in approximately 12 participants in two sequential cohorts. 2002 is now open for enrollment and will only be conducted in Europe. Patient screening has begun, and some patients are expected to receive their first dose before year end.

Moving on to our two candidates that are closest to submissions asking to start clinical trials.

ARO-HIF2 is our candidate being developed to treat clear cell renal cell carcinoma. We are in the process of preparing the IND filing, which we anticipate before the end of the year. Our plan is to launch a Phase 1 dose range finding study in the U.S. This will be conducted in clear cell RCC patients, that have been refractory to immuno-oncology treatment, with or without anti-VEGF agents or separately refractory to anti-VEGF monotherapy. The primary objectives of this study will be safety as well as determination of a Phase 2 dose. Secondary objectives will include pharmacokinetics and then efficacy based on RECIST criteria using either CT or MRI imaging. A key exploratory objective for ARO-HIF2 will be gene target knockdown in the tumors using tumor biopsy.

Lastly, I will talk about our plans for ARO-HSD. This is a somewhat new target in which genetic data indicates that loss-of-function mutations in the HSD17B13 enzyme provide the strongest known genetic protection against NASH cirrhosis, and alcoholic hepatitis and cirrhosis. One of the key challenges for the clinical program here is that there is no known serum biomarker for this target. But, the design of the first-in-human study is likely to resemble other Arrowhead Phase 1/2 studies. Our plan is to do a single dose study in normal volunteers, and a multiple dose study in patients with either suspected or documented NASH. We think we will have to do liver biopsies in this first trial to assess not only the depth of knockdown but also the duration of effect. The in-life portion of the GLP-toxicology studies is complete, and we are awaiting results in order to prepare the regulatory submissions. Our plan is to submit before the end of the year, so we are pretty close on this one as well.

With that brief review of our clinical programs, I'd like to turn the call over to Ken Myszkowski, Arrowhead's Chief Financial Officer. Ken?

Ken Myszkowski

Thank you, Bruce, and good afternoon everyone.

As we reported today, our net income for fiscal 2019 was $68.0 million, or $0.69 per share based on 98.6 million weighted average diluted shares outstanding. This compares with a net loss of $54.5 million, or $0.65 per share based on 83.6 million weighted average diluted shares outstanding, for fiscal 2018.

Revenue for fiscal 2019 was $168.8 million, compared to $16.1 million for fiscal 2018. Revenue in the current period relates to the recognition of a portion of the upfront payments and milestones from our license and collaboration agreements with Janssen, while revenue in the prior period related to the recognition of a portion of the upfront payments from our license and collaboration agreements with Amgen. Revenue from the Janssen agreement will be recognized based on our estimate of the proportion of effort expended toward fulfilling our performance obligations – primarily, overseeing the completion of the current phase 1/2 HBV clinical trial. In fiscal 2020, we anticipate recognizing approximately $80 million of the upfront payments and milestones already received that are currently reflected as Deferred Revenue in our Balance Sheet. Any additional milestones achieved with Janssen or Amgen would be additive to this projection.

Total operating expenses for the year ended September 30, 2019 were $107.6 million, compared to 72.1 million for the year ended September 30, 2018. This increase is primarily due to increased drug manufacturing, toxicology and clinical trial costs as our pipeline of clinical candidates has increased.

Net cash provided by operating activities in fiscal 2019 was $173.0 million, compared with net cash used by operating activities of $47.2 million in fiscal 2018. The operating cash generated in fiscal 2019 reflects the $175 million upfront payment and two $25 million milestone payments received from Janssen, offset by cash used for operations.

Turning to our balance sheet, our cash and investments of cash balances totaled $302.9 million at September 30, 2019, compared to $76.5 million at September 30, 2018. The increase in our cash and investments balance was driven by the payment received from Janssen. Next year, we anticipate a $25-30 million quarterly burn.

Our common shares outstanding at September 30, 2019, were 95.5 million.

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

Chris Anzalone

Thanks Ken.

These are exciting and important times at Arrowhead. We have always sought to follow the science and drive the RNAi field forward with new innovation and technologies. We will continue this with a series of firsts for the industry. I think that we'll see the first clinically relevant oncology RNAi drug candidate in ARO-HIF2. I think we'll have the first meaningful lung-targeted RNAi drug candidate in ARO-ENaC. I think we will be the first to develop a muscle-targeted RNAi drug candidate. And, I think we'll be the first to develop an RNAi drug candidate that

silences two genes simultaneously. Together, these significantly expand the universe of diseases and conditions we expect to treat.

The new cell types we are now able to target are key to our pipeline expansion model. My hope is that we will have early clinical validation for ARO-ENaC by the end of 2020. That could serve as a springboard for rapidly expanding our lung franchise as we go after various gene targets for diseases such as COPD, asthma, and pulmonary fibrosis. We could develop some of these by ourselves and some in collaboration with partners. Similarly, I expect that we could have early clinical validation for ARO-Hif2 by the end of 2020, and that could trigger a rapid push into new solid tumors and new gene targets. A bit further off, I expect to be filing to go into the clinic with our first muscle-targeting program by the end of 2020, with possible early clinical validation the following year. We could then look to rapidly expand our pipeline with new muscle targets. All of these are important in our push to continue Arrowhead's growth.

In 2018, ARO-AAT and ARO-HBV were sources of significant value creation at Arrowhead. In 2019, ARO-APOC3 and ARO-ANG3 have combined with ARO-AAT and ARO-HBV to drive tremendous value growth for us. Where do we go from here in 2020? We believe the next big value drivers will be highly distributed, and that is helpful from a risk mitigation standpoint as well as from the standpoint of maximizing our growth potential. I expect that you will see a company with the following attributes:

- A broad and deep pipeline;
- The ability to target 4 different cell types;
- A pipeline expansion model that is rapid and scalable; and

- Drug candidates with a good mix of early-, mid-, and late-stage clinical programs.

Most biopharma companies have historically sought to build value, sometimes substantial value as we saw today with Novartis's $9.7bn acquisition of the Medicines Company, by only developing 1 or a few drugs. We have a different approach. We have spent our time building out the TRiM platform with the hope that it could be the basis not for one or two drugs, but potentially for *dozens* of drugs across many disease areas. This is a truly exciting concept. We are now well down that road and, as I mentioned early in the call, we expect there to be 10 TRiM-enabled drug candidates in the clinic by the end of next year, three of which we expect to be in pivotal studies. I also believe that it is reasonable to expect that those 10 clinical candidates could double to 20 just 3 years later. We have always believed that this is where we have been headed, and it seems that the rest of the world is just now starting to appreciate this.

Thanks again for joining us today. I would now like to open the call to your questions. Operator?

Operator

Operator opens the call to questions …