ARROWHEAD PHARMACEUTICALS

Fiscal 2020 Year End Conference Call – Prepared Remarks

November 23, 2020

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, 2020.

With us today from management are president and CEO Dr. Christopher Anzalone, who will provide an overview of the quarter; Dr. Javier San Martin, chief medical officer, who will discuss our clinical programs; and Ken Myszkowski, our chief financial officer, who will give a review of the financials. In addition, James Hassard, our chief commercial officer, and Dr. James Hamilton, who was recently promoted to senior vice president and head of Discovery & Translational Medicine, will both be available during the Q&A session of today’s 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 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 and commercialization 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.

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.

This is our final earnings call of 2020, so in addition to discussing our progress for the quarter and plans for 2021, I would also like to speak a bit more broadly about our philosophy and model.

We're building a different kind of biotech company. We are not focused on a single therapeutic area, but rather on *any* disease with unmet medical need that is addressable with our technology. We are not focused solely on rare diseases, but rather address large and small populations. We do not rely solely on partners for late-stage clinical development and commercialization, but rather we use partnering strategically and judiciously to enable us to build substantial value by commercializing our own drugs. We are fast, probably the fastest in the business from idea to the clinic, and we intend to remain fast as we grow. That devotion to speed also applies to pipeline expansion. I believe we have the fastest growing pipeline in our field, and we do not intend to slow that input just because we are entering later-stage clinical studies. We are not in the me-too product business where we only provide incremental benefit to patients. Rather, we seek to be pioneers. We believe that everything in our clinical pipeline represents the first RNAi approach to each target in humans. We don't operate like a normal pharmaceutical company. We are not burdened by endless gating committees, but rather empower our people to make decisions. Operationally, think of us as a start-up in $7bn market cap clothing, and we intend to continue in this nimble and creative fashion even as we become a substantially larger and more valuable company. We see this as the most effective way to build a business and, most importantly, to serve patients. Every day that we can shave off the development process puts our patients one day closer to a new treatment they need. This is a powerful motivator for us because the value of our work depends on the number of lives we touch.

I mention all of this now because we are at a moment of transition for our company. We have created a lot value to this point by building what we believe will soon be the largest RNAi-based clinical pipeline in biopharma. As we move into later-stage clinical studies, our focus needs to expand to include commercial planning. Ultimately, this is the reason we're in this business and we need to do that well. However, we also need to continue to do the things in discovery and early development that have made us successful while we build our commercial presence. On average, we expect to continue to introduce 3 new drug candidates into clinical studies *every* year, and we expect to be able to address a new cell type every 18 to 24 months. Think of the potential value embedded in those statements. I expect that we will have 10 clinical programs by summer, spanning 4 different cell types. That could grow to 20 clinical programs spanning 5 or 6 cell types just 4 years from now. We expect this to drive substantial value because we expect some of those to become products we will commercialize ourselves and some can be partnered to fund development and commercial endeavors.

Our ability to rapidly grow our pipeline enables this hybrid model of establishing a limited number of partnerships in order to fund wholly-owned programs. We see this as a powerful model because it allows for the rapid value creation associated with commercializing wholly-owned drugs while financing this expensive endeavor largely through non-dilutive capital from partnered programs.

So even as we approach and ultimately expand our commercial presence, our pipeline strategy should continue to be an important part of our value proposition. This is not only due to the brute force of the large numbers of potential drugs in clinical studies, but should also reflect our expectations of success. There are two components to this. First, we seek to choose only well-validated targets. These are gene targets where a consensus of experts agree that reducing expression will

likely have positive therapeutic benefits. By focusing on this, we believe we enter clinical studies with reduced Biology and target risk relative to other drug candidates. Second, the RNAi mechanism and experience with the TRiM platform can provide additional wind at our back. As we continue to treat more patients with drug candidates built on the TRiM platform and see consistent activity and positive safety profile, our confidence increases that other candidates targeting different genes will also be successful. RNAi doesn't care what gene is being silenced. Once we validate our ability to reduce expression of a given gene in a given cell type, we have confidence that we can replicate that in other gene targets. We believe this is a powerful and scalable concept that gives us confidence that a larger percentage of our candidates entering the clinic will ultimately become drugs compared to traditional small molecules.

We hope that as we approach and become a commercial company, the market will properly value our growing pipeline. As I mentioned, it will continue to be an important part of our value proposition and we expect it to remain a substantial differentiator versus our competitors. With that, let's move into an overview of the last quarter.

During the last few months our accomplishments included the following:

1. We hosted a KOL webinar on ARO-ENaC, our first lung targeted candidate to treat cystic fibrosis, and we initiated dosing in a Phase 1/2 clinical study
2. We earned a $20 million milestone payment from Amgen following the start of a Phase 2 study of AMG 890, now called olpasiran, which is a partnered program targeting Lp(a) to treat cardiovascular disease
3. We initiated a Phase 1b study of ARO-HIF2, our first tumor targeted candidate to treat renal cell carcinoma

4. We presented new data on Phase 1/2 studies of both of our wholly-owned cardiometabolic candidates, ARO-APOC3 and ARO-ANG3, at multiple medical meetings, including the European Society of Cardiology and the American Heart Association meetings, and subsequently hosted KOL webinars to discuss the data and our plans for their future development
5. We presented Phase 2 data at AASLD on ARO-AAT, our candidate against liver disease associated with alpha-1 antitrypsin deficiency, showing that ARO-AAT strongly reduced the production of the mutant Z-AAT protein and led to improvements in multiple biomarkers of alpha-1 liver disease; and,
6. We signed an agreement with Takeda to co-develop and co-commercialize ARO-AAT, which includes $300 million upfront, $740 million in milestone payments, a 50/50 profit sharing agreement in the U.S., and 20-25% royalty on sales outside the U.S.

This is a lot of progress in a short period of time, and even more impressive with the backdrop of disruptions caused by COVID-19.

Let's take a look at the Takeda deal.

It's a good example of our selective partnering strategy. We expect ARO-AAT to benefit from Takeda's global footprint, existing infrastructure, expertise, and 18-year history in the AAT market to enable a rapid launch. If approved, ARO-AAT will join Takeda's global commercially available products, including Glassia® Aralast® and Entyvio® and their growing GI pipeline. Takeda is clearly invested and committed to these areas and has a proven track record of success.

The deal is also important in terms of capital. In addition to the $300m upfront, we have potential access to substantial capital in the near-, mid-, and long-term with a possible stream of milestone payments, profit sharing, and royalties. When this is added to the potential milestone payments and royalties down the line from our partnerships with Amgen and Janssen, we feel our balance sheet is in a very strong position. This allows us to confidently move our wholly-owned programs into later stage development and ultimately commercialization.

This deal is also a step in an ongoing process toward rationalizing our growing pipeline, where we look to build commercial infrastructure in areas where we expect multiple drugs, such as cardiometabolic and pulmonary. We will look for synergy and leverage when deciding where to focus commercial buildout.

So let's take a look at the cardiometabolic pipeline. We presented data recently at AHA and also held two KOL webinars to discuss these programs. Javier will discuss these specifically in a moment, but I want to talk about where we are with those programs at a high level. The data across single and multiple doses and in healthy volunteers as well as various patient populations has been very strong and highly consistent.

In addition, ARO-APOC3 and ARO-ANG3 are each showing unique profiles. What I mean by that is that we believe each drug may ultimately give cardiologists more tools to tailor their treatments to the specific lipid profiles of their patients. We also think they each fill holes in the current treatment paradigm and may potentially address lipid targets that have not been adequately addressed. For instance, there are more than 4 million patients in the U.S. with severe hypertriglyceridemia, and given published data, we would expect the overwhelming majority of them would not reach reach normal triglyceride levels

with currently available treatments. There are also approximately 30-40 million addressable patients in the U.S. with mixed dyslipidemia, which is elevated triglycerides and elevated LDL cholesterol. We have become increasing confident in these programs and in our ability to move them to commercialization.

We have also been able to move forward in our other clinical programs. ARO-HSD, our drug candidate against NASH and alcoholic hepatitis, is now in the patient portion of the Phase1/2 study. ARO-Hif2, our candidate against renal cell carcinoma, and ARO-ENAC, our candidate against cystic fibrosis, are both being dosed in patients as well.

Progress in ARO-Hif2 and ARO-ENAC is particularly important because it has been our goal to gain clinical proof-of-concept and then move into a rapid pipeline expansion phase for tumor and pulmonary tissue types. We think we are just on the cusp of that phase now. To that end, we continue to work in parallel on multiple additional targets in tumor and pulmonary and also to expand our reach into new tissue types beyond these.

Before I move on to 2021, I'd like to say a few words about the novel corona virus. As with the rest of the world, we were excited to see the interim results from some of the COVID-19 vaccine studies. Multiple safe and effective vaccines will be a humanitarian triumph and we applaud the impressive work done by several companies. From an Arrowhead standpoint, some may ask if progress on the vaccines affects our internal program. The answer is: not really. We continue to make progress on an anti-viral approach that is designed to work across different corona viruses. The history of SARS, MERS, and now the current corona virus suggests that the world should expect some type of corona virus outbreak approximately every 7 years. As such we are studying conserved regions in known

corona viruses with the goal of creating an inhalable anti-viral that could be applied to future outbreaks, as well as the current virus, should there be blind spots with the vaccines. We are still in early animal studies, but I hope we will have an idea about the feasibility of this approach in 2021.

Moving to the future, there is a lot you should expect from us during the final month of the year into early 2021. Our expectations include the following:

1. We are on track to file a CTA for ARO-LUNG2 at the end of this year. This second program in our pulmonary franchise is designed to treat COPD by inhibiting an undisclosed target in pulmonary epithelia.
2. We are on pace to potentially have preliminary data readouts by the middle of 2021 for ARO-HSD, ARO-HIF2, and ARO-ENaC.
3. During the first half of the 2021 we also intend to engage with the FDA and other regulators to discuss pivotal trial study design and endpoints for ARO-AAT. Based on the impressive data that came out of our 2002 open-label study, it appeared that patients had large reductions in Z-AAT monomer, which we expected, but also had improvements in other downstream markers, such as polymer, globules, LFTs, and others. These discussions may allow us to find a more streamlined and accelerated path to a potential approval. There also may be additional open label data in 2021 for patients with 12 month and 18 month repeat biopsies.
4. We also intend to initiate multiple studies in the first half of 2021 for both of our cardiometabolic programs. For ARO-ANG3 in mixed dyslipidemia patients, we are working on a Phase 2b dose finding study. For ARO-APOC3, we are working to start three studies:
    a. A Phase 2b dose finding study in patients with triglycerides ranging from 150 to 499

   b. A Phase 2b dose finding study in patients with triglycerides over 500
   c. And, a Phase 3 study in patients with familial chylomicronemia syndrome, or FCS
5. In the second half of 2021, we intend to file a CTA for our first muscle targeted RNAi therapeutic. That program has moved forward very nicely and we are eager to talk more about what it is and what the data look like.
6. For our partnered programs with Amgen and Janssen, we can't provide specific guidance on timing, but we continue to be pleased with their progress and look forward to additional future progress
7. Lastly, we are working on several other undisclosed programs and will likely have another CTA filed for a new program in 2021

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 to everybody on the call.

I want to highlight data from the ARO-AAT, ARO-APOC3, and ARO-ANG3 programs since we had important readouts for each during the last quarter. Before I do that, I will give a very quick review of the status of the earlier stage clinical programs.

ARO-HSD is our investigational candidate for the potential treatment of alcohol and nonalcohol related liver disease. The genetic validation is strong for inhibiting the target HSD17B13 in NASH cirrhosis, and alcoholic hepatitis and cirrhosis patients.

We are conducting a Phase 1/2 single and multiple dose-escalating study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamic effects of ARO-HSD in normal healthy volunteers as well as in patients with NASH or suspected NASH. We have complete single dose escalation in healthy volunteers and are currently enrolling the multiple-dose patient portion of the study in NASH or suspected NASH patients. This study includes liver biopsies to assess drug activity.

ARO-HIF2 is designed to treat clear cell renal cell carcinoma, and we are currently dosing patients in a Phase 1b dose-finding clinical study in up to 18 patients with advanced ccRCC. The study is designed to evaluate the safety of ARO-HIF2 and to determine the recommended Phase 2 dose. We are also assessing pharmacokinetics and preliminary efficacy, based on RECIST, and post-dose tumoral expression of HIF2-alpha and HIF associated genes.

Our last early-stage clinical program is ARO-ENaC, designed to treat cystic fibrosis. ARO-ENaC is in a Phase 1/2 dose-escalating study to evaluate the safety, tolerability, and pharmacokinetic effects of ARO-ENaC in up to 24 normal healthy volunteers and to evaluate the safety, tolerability, and efficacy in up to 30 patients with CF. We have dose-escalated multiple times, as planned, in healthy volunteers and so far we are pleased with the safety and tolerability results. This is always an important finding for a new investigational drug and even more so for a new platform. We are now enrolling CF patients in the multiple dose portion of the study.

Now I will move onto the recent data readouts.

For ARO-AAT, our investigational RNAi therapeutic being developed as a treatment for the rare genetic liver disease associated with alpha-1 antitrypsin deficiency, we presented data at AASLD on our 2002 open label study. To review, the study is fully enrolled with 16 participants in three cohorts. 4 patients in Cohort 1 receive 200 mg of ARO-AAT and will have repeat biopsies after 6 and 18 months of treatment. Cohort 1b is the same, but patients receive the 100 mg dose. 8 patients in Cohort 2 receive 200 mg of ARO-AAT and will have repeat biopsies after 12 and 24 months of treatment.

At AASLD, we reported on 6-month results from Cohort 1. We think the data strongly suggest that ARO-AAT is doing what it's designed to do, which is reduce the production of the misfolded mutant Z-AAT protein. The results also indicate that the liver may have the ability to clear out accumulated Z-AAT and begin to heal itself faster than anticipated.

Importantly, we saw the following:

- 86-93% reduction in serum Z-AAT
- All patients demonstrated greater than 80% reduction in liver Z-AAT monomer
- 3 of 4 patients had a decrease in liver globule involvement
- 3 of 4 patients demonstrated reductions in Z-AAT polymer with a range of 68-97%
- All patients showed ALT reductions ranging from 36-66%

We think these are all positive indications of a strong pharmacodynamic response and improvement in liver health, following just three doses of ARO-AAT.

As Chris mentioned, we are currently preparing to engage with FDA and other regulatory agencies in the first half of 2021 to discuss areas where the ARO-AAT program may potentially be streamlined and accelerated.

Let's now move to our cardiometabolic programs, ARO-APOC3 and ARO-ANG3.

We held two KOL webinars last week to discuss the data and these programs in some depth. We were fortunate to have Dr. Christie Ballantyne from the Baylor College of Medicine and Dr. Ira Goldberg from the NYU School of Medicine join us and provide their perspective and valuable insights. Replays of these events are available on the Investors section of our website for those who missed the live presentations.

Let's start with ARO-APOC3, our candidate targeting apolipoprotein C-III, being developed as a potential treatment for patients with hypertriglyceridemia. The current clinical study is a Phase 1/2 single and multiple dose study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamic effects of ARO-APOC3. There is a single-dose and multiple-dose portion of the study in adult healthy volunteers and a multiple-dose portion of the study in patients with hypertriglyceridemia, including a cohort enrolling up to 20 chylomicronemia patients. At AHA we reported data from the multiple dose patient portion of the study. The results were very impressive and highly encouraging to us as we prepare to begin the next stage of development for the program in the first half of next year.

In patients with hypertriglyceridemia, ARO-APOC3 treatment resulted in robust and sustained reductions in triglycerides and Non-HDL cholesterol, with increases in HDL-C.

Specifically, we observed:

- Maximal mean reduction of -80% to -99% in APOC3
- Maximal mean reduction of -74% to -92% in TG and -39% to -62% in non-HDL-C
- And, maximal mean increase of +95% to +116% in HDL-C

In patients with chylomicronemia, 50 mg ARO-APOC3 achieved similar levels of reduction of APOC3 and changes in key lipid parameters. We observed:

- Maximal mean reduction of -98% in APOC3
- Maximal mean reduction of -88% in TG, -59% in non-HDL-C
- Maximal mean increase of +120% in HDL-C

Importantly, the effects of ARO-APOC3 were maintained for greater than 12 weeks post second dose regardless of patient population. We think this indicates that once quarterly or less frequent dosing may be possible.

Our other wholly-owned cardiometabolic candidate is ARO-ANG3, targeting angiopoietin like protein 3, or ANGPTL3, and is being developed as a potential treatment for patients with mixed dyslipidemia. The current clinical study is a Phase 1/2 single and multiple dose study to evaluate safety, tolerability, pharmacokinetic, and pharmacodynamic effects. At AHA and the recent webinar, we also presented data on the multiple dose patient portion of the ARO-ANG3 study. As with ARO-APOC3, we were thrilled with the clinical results and move forward with that program with a lot of confidence in its potential to help patients with mixed dyslipidemia.

The data showed that in heterozygous familial hypercholesterolemia patients and Non-FH patients, ARO-ANG3 resulted in mean reductions of:

- -78% to -90% for ANGPTL3
- -29% to -47% for TG
- -29% to -35% for LDL-C
- -31% to -35% for non-HDL-C

In high triglyceride patients, ARO-ANG3 resulted in mean reductions of:

- -83% for ANGPTL3
- -75% for TG
- -56% for non-HDL-C

As with ARO-APOC3, the effect of ARO-ANG3 was maintained for greater than 12 weeks post second dose regardless of patient population. We believe this indicates that once quarterly or less frequent dosing may be possible.

These results provide further support that the RNAi mechanism in general and more specifically therapeutics developed using our TRiM platform, tend to perform very consistently regardless of the gene target. So far, we have experienced very good translation of preclinical data to human clinical data with respect to safety, tolerability, and activity. This gives us great confidence in each new program we develop, even at very early stages. The next steps are to study in larger and longer clinical trials whether inhibition of the respective gene targets leads to the desired clinical benefit in specific patient populations. As Chris mentioned earlier, we try to select targets at the discovery stage with generally well understood biology and strong support from human genetic studies. This provides

us with even more confidence that we are reducing risk to the extent possible and maximizing our probability of success.

I will now turn the call over to Ken Myszkowski, Arrowhead's Chief Financial Officer. Ken?

Ken Myszkowski

Thank you, Javier, and good afternoon everyone.

As we reported today, our net loss for fiscal 2020 was $84.6 million, or $0.84 per share based on 100.7 million weighted average diluted shares outstanding. This compares with net income of $68.0 million, or $0.69 per share based on 98.6 million weighted average diluted shares outstanding, for fiscal 2019.

Revenue for fiscal 2020 was $88.0 million, compared to $168.8 million for fiscal 2019. Revenue in both periods primarily relates to the recognition of a portion of the upfront payments and milestones from our license and collaboration agreements with Janssen. Revenue from the Janssen agreement is being recognized based on our estimate of the proportion of effort expended toward fulfilling our performance obligations – primarily, overseeing the completion of the phase 1/2 HBV clinical trial. We expect the remaining $19 million of deferred revenue to be recognized in the first half of fiscal 2021. Any additional milestones achieved with Janssen or Amgen would be additive to this projection. In addition, current period revenue also included the $20 million milestone payment we received Amgen upon the initiation of their phase 2 clinical trial for AMG 890, which is now referred to as Olpasiran.

Total operating expenses for the year ended September 30, 2020 were $181.1 million, compared to 107.6 million for the year ended September 30, 2019. This increase is primarily due to increased non-cash stock compensation expense. Stock compensation expense has increased because the valuation of new stock option and restricted stock awards granted has increased with the growth in our stock price. Additionally, stock compensation expense increased due to the timing of the achievement of certain performance-based awards in each period. The increase in total operating expenses was also driven by increased clinical trial costs as our pipeline of clinical candidates has increased, and increased personnel costs in both R&D and G&A as our headcount continues to grow.

Net cash used by operating activities in fiscal 2020 was $95.4 million, compared with net cash provided by operating activities of $173.0 million in fiscal 2019. 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 $453.0 million at September 30, 2020, compared to $302.9 million at September 30, 2019. The increase in our cash and investments was primarily due to the December 2019 equity financing we completed, which generated $250.5 million in net cash proceeds for the Company.

In addition to the cash and investments assets discussed as of September 30, 2020, we also anticipate receiving the $300 million upfront payment from Takeda by the end of this calendar year or shortly thereafter. Similar to our deal with Janssen, we anticipate recognizing this upfront payment as revenue over the course of completing our performance obligation within the deal, which primarily consists of

managing the ongoing ARO-AAT clinical studies and providing certain manufacturing services.

Looking ahead to fiscal 2021, we expect our full year cash burn to be $200 - $250 million. This increase is due to growth throughout the Company. Our program costs are expected to increase as ARO-ANG3 and ARO-APOC3 begin larger phase 2 clinical trials, and our newer programs continue to advance. Our headcount increased significantly in 2020 and we expect continued increases in 2021 which drives increases in payroll, related facility costs, discovery R&D costs and G&A expenses.

Our common shares outstanding at September 30, 2020, were 102.4 million.

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

Chris Anzalone

Thanks Ken.

There's no question we have had a productive recent period. The more clinical experience we gain with the TRiM system, the more confident we become that we are on the path to providing physicians with potentially transformational therapies that may make a big difference in the lives of millions of patients. That's important and gratifying.

We also feel confident that we have the right strategy. We believe the combination of:

- focusing on well-validated targets,
- our speed from idea to the clinic,
- our expected ability to address a new cell type every 18-24 months,
- the rapid nature of our pipeline expansion,
- and our selective partnering model

together provide our shareholders with the potential for rapid value creation.

So, what's next for us? We think our initial commercial focus on cardiometabolic and pulmonary will allow us to build out the necessary infrastructure over the coming years in a focused and effective manner, but also in a way that is ever conscious of capital efficiency. That has been an Arrowhead hallmark and we intend for that to continue.

And, lastly, we are eager to gain clinical validation of our TRiM platform's ability to target tissues outside the liver. This includes lung, tumor, muscle, and other tissue types that we have not yet disclosed. RNAi works well in hepatocytes: we know that. But our goal has never been simply to address liver-based disease. Rather, we have always worked to bring RNAi wherever it is needed, and we are on the brink of demonstrating that right now.

We are, indeed, building a different kind of biotech company, and we look forward to continuing to share our progress.

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

Operator