ARROWHEAD PHARMACEUTICALS

Fiscal 2020 Third Quarter Conference Call – Prepared Remarks

August 5, 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 second quarter ended June 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. Curt Bradshaw, our chief scientific officer, will 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.

We've already made a lot of progress this year, notwithstanding the challenges that COVID-19 has presented to the world broadly and in particular to those of us developing new medicines. We took decisive action and placed a voluntary pause

on new patient screening and enrollment in some of our clinical studies in order to limit the risk to participants. We take very seriously our obligation to protect the health and safety of our employees, business partners, and patients that participate in our studies. That was the right thing to do.

The good news is that we don't believe any of our development programs were affected in a material way. That is a testament to the Arrowhead drive toward innovation, speed, and precision. We find a way forward, even when the way is not clear. This is a hallmark of the Arrowhead culture and something that I am very proud of.

Even though COVID still presents some uncertainty, we are confident that 2020 can continue to be highly productive as we work to:

1. Expand our pipeline;
2. Make progress and provide data readouts on multiple clinical programs; and,
3. Gain clinical proof-of-concept for our first extra-hepatic candidates;

So, what have we done and what are our plans in order to achieve these 3 important goals? Let's answer that by reviewing some key programs.

I will start by speaking broadly about our discovery stage programs. The partnership we signed with Janssen in 2018 included three potential new products against targets to be selected by Janssen. While we can't disclose the targets, the specific stage, or report data on these potential product candidates, we can say that we have made good progress on all three. We previously talked about ARO-JNJ1 because the first target was selected early on in the partnership and work began soon after. We are now at a sufficiently advanced stage for the other two potential

product candidates to add them to our pipeline and designate them ARO-JNJ2 and ARO-JNJ3. The partnership with Janssen has been very productive, including for ARO-HBV, now called JNJ-3989, which continues to progress rapidly in multiple Phase 2b studies being conducted by Janssen.

Staying with earlier stage development, let's move on to our preclinical programs that utilize our TRiM™ platform targeting the pulmonary space. Our second program after ARO-ENaC, is ARO-LUNG2 designed to treat COPD by inhibiting an undisclosed target in pulmonary epithelia. We previously announced that it had officially been nominated as a candidate and moved from preclinical into Pre-IND stage. We have continued to make good progress on the IND-enabling studies and are on track to potentially file a CTA for ARO-LUNG2 at the end of this year.

It has been our goal to gain clinical proof-of-concept and then move into a rapid pipeline expansion phase for the pulmonary platform. 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 the pulmonary space. We think the lung is a target rich environment with multiple opportunities for asthma, COPD, Idiopathic Pulmonary Fibrosis, and other diseases that are not adequately treated.

We have also made good progress on several potential candidates designed to treat the novel coronavirus that causes COVID-19. This is the first time we have disclosed that we are pursuing multiple different therapeutics at the same time, and I think it's important. This is a difficult virus and we believe the best way forward is to address multiple strategies. One is to try to close the front door, if you will, by knocking down a receptor that the virus uses to gain entry into cells; a second is a direct antiviral approach that targets the viral mRNA; and a third is to pursue anti-inflammatory pathways. We are pursuing all of these in parallel and believe

this broad, wholistic strategy gives us multiple shots on goal and a more complete approach to a poorly-understood virus. Given our experience in the lung and our work in HBV, I believe we are well-positioned to play a role in addressing COVID-19 and possibly future corona virus outbreaks.

With ARO-ENAC, ARO-LUNG2, our suite of COVID-19 programs, and the additional potential candidates that are progressing rapidly, we are confident in our belief that the emerging lung pipeline can be an engine that drives substantial value in the near to mid-term. What we have done, and continue to do, in the liver, we now seek to do in the lung.

Now moving on to our clinical pipeline, I will start with ARO-AAT, our Phase 2/3 candidate against a rare genetic liver disease associated with alpha-1 antitrypsin deficiency. We have fully enrolled, dosed, and collected 6-month repeat biopsies for the first cohort of the open-label 2002 study. Biopsies are now being analyzed and we plan to present data before the end of the year.

This is important progress and an important readout. It will be the first data for a therapeutic targeted at alpha-1 liver disease and it will be an important step in understanding what happens at the hepatocyte level after patients are treated. We will be looking at many measures of alpha-1 liver disease, but most focused on the change from baselines in Z-AAT monomer. That is a direct measure of the drug's ability to inhibit production of the faulty mutant protein. We have a high level of confidence in our ability to show improvement there. We will also be assessing other measures that will likely require longer drug exposure to show a treatment effect. That includes Z-AAT polymer content and inflammation. We don't believe that 6 months of therapy is enough time to see changes, but we are the first company to investigate this disease in humans, so we really don't know what to

expect. Remember that in the Phase 2/3 SEQUOIA study, patients will receive around 2 years of treatment. If we see signs of improvement at earlier time points than expected, that would be a very exciting result and could cause us to consider working with regulators to change the parameters of the study.

I will now talk about our cardiometabolic programs. Let's start with AMG 890, the candidate we licensed to Amgen targeting Lp(a) for the treatment of cardiovascular disease. We announced last week that Amgen started a Phase 2 study and that this triggered a $20m milestone payment. These represent important steps forward for the AMG 890 program, and support Arrowhead's strategy of utilizing our platform and expertise in RNAi therapeutics to build a valuable pipeline of both wholly-owned and partnered drug candidates. Amgen has extensive expertise in developing and commercializing innovative cardiovascular medicines and we are excited to see the program continue to advance.

Our two wholly-owned cardiometabolic candidates, ARO-APOC3 and ARO-ANG3, are both progressing rapidly towards value-inflection points, including multiple data readouts this year and advancement into the next stages of clinical development. The second half of 2020 is going to be an important time for both programs.

Both candidates are in Phase 1/2 studies, and together have enrolled nearly 200 healthy volunteers and patients. Both studies include single and multiple-dose assessments. And, both have various cohorts with specific patient populations. This accelerated first-in-human study design yields data on safety and tolerability, dose response, duration of effect, and how different types of patients respond to therapy. It allows us to give data readouts from both programs at two or three conferences over the next few months. It also gives us enough actionable information about

each candidate to engage regulators and discuss the next stages of clinical development, up to and including potential registrational studies.

We have already been communicating with the FDA on ARO-APOC3 and our plan is beginning to take shape. We will have similar discussions on ARO-ANG3 and also engage with European authorities to gain clarity on various study design characteristics, endpoints, and target patient populations. Importantly, both candidates provide a high-level of optionality on which patient populations and disease characteristics to focus on and how to stage the clinical studies to assess the candidates' utility. For example, for ARO-APOC3 there are potential patient populations that range from ultra-rare, genetically defined, such as FCS in which patients have triglycerides in the thousands of mg/dL, to extremely high prevalence diseases, such as patients with mildly elevated triglycerides above 150 mg/dL. There are also various levels in between these extremes, that each have their own characteristics and would require a different clinical design with respect to size of study, duration of treatment, and acceptable endpoints. Taken together, this represents a very large market opportunity. In the US alone, there are estimated to be approximately 1 million adults with triglycerides greater than 1,000 mg/dl; more than 3 million adults with triglycerides between 500 and 1,000; and more than 41 million with triglycerides between 200 and 500. Of course not all of these patients will be potential candidates for therapy, but thinking of ARO-APOC3 solely as an orphan indication drug candidate is missing the larger breadth of opportunities ahead.

This type of opportunity also exists for ARO-ANG3 and patients with mixed dyslipidemias – specifically, triglycerides, LDL-C, and other measures of cardiovascular and metabolic disease. I don't think investors fully appreciate the size of the potential commercial opportunities for both ARO-APOC3 and ARO-

ANG3. This is an exciting time for these programs as we are beginning to see potential paths to commercialization. We will be talking about these paths and timelines in the future, which should provide a level of detail for investors to properly assess how significant the opportunity is to help very large populations of patients that could benefit from new treatment options.

We have also made good progress on ARO-HSD, in development to treat alcohol and non-alcohol related liver disease. We began dosing in a Phase 1/2 study in March. We have since completed all healthy volunteer cohorts and have activated the cohorts that enroll patients with NASH or suspected NASH. The target, HSD17B13, is not a secreted protein so we will be collecting liver biopsies to measure target engagement. This program experienced a short pause in screening and enrollment due to COVID-19, but similar to other programs we don't think this had a material affect on our anticipated timelines. As long as patient screening and enrollment continue to move forward as planned, we should be generating data through the end of 2020 and be in position to present in the first half of 2021.

Lastly, I want to mention ARO-ENaC, our first inhaled RNAi candidate to target the pulmonary epithelium. We anticipate dosing to start this month in our Phase 1/2 study in healthy volunteers and in patients with Cystic Fibrosis. The candidate is designed to reduce expression of the epithelial sodium channel, or ENaC, in the lungs to help rehydrate CF-related dehydrated mucus and potentially help improve mucociliary clearance. As we discussed on our ENaC webinar last week, there has been great progress in new therapies to treat CF over the last decade, but significant unmet need still exists. We estimate that there are approximately 14,000 patients in the U.S. alone that are either not eligible for the most advanced therapies because of their specific genotype or have been shown in clinical trials to be non-responders or insufficient responders. This is a lot of patients who still

suffer from CF and are in need alternative treatments. We think ENaC may be that alternative and importantly, the mechanism of action should, theoretically, be genotype agnostic.

This is an exciting program and we hope to generate data through the rest of 2020 that may enable us to have a data readout in the first half of 2021. Our preclinical data has been highly promising, and we are eager to see the translation of animal data to humans in our new pulmonary TRiM™ platform.

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 a few of our clinical programs and some key progress we made since our last conference call. Just like all biotech companies, COVID had an effect on some of our programs, but I'm very pleased to say that it appears the effect has been generally minor. In fact, some programs experienced little to no delay in our anticipated timelines. We continue to monitor the situation closely to ensure that study participants are not being exposed to additional risk, while at the same time moving forward rapidly when it is safe to do so. Even in the challenging environment of the last several months, I'm proud that Arrowhead's clinical development team has executed at a very high level.

Let's start with ARO-AAT, our second-generation investigational RNAi therapeutic being developed as a treatment for the rare genetic liver disease associated with alpha-1 antitrypsin deficiency.

As we announced last quarter, we voluntarily put the SEQUOIA Phase 2/3 study and the 2002 open-label study on a temporary pause for new screening and enrollment due to concerns around COVID-19. Both studies are now back up and running and open to new patient screening and enrollment. The pause caused a delay of approximately 8 weeks for SEQUOIA and for the second cohort in 2002, after which, sites began to reopen and resume patient screening. The first cohort in 2002 was already fully enrolled and, importantly, we did not experience any concerning protocol deviations for those already on study.

Let's talk more about the 2002 open-label study, because we plan to have a data readout this year. To review, the study is designed to enroll approximately 12 participants in two sequential cohorts. Between the two cohorts, biopsy data will be assessed at baseline and after 6 months, 12 months, 18 months, and 24 months of treatment with ARO-AAT.

As I mentioned, the first cohort, which is 4 patients, was already fully enrolled prior to COVID-19 and patients have continued on study as planned. All doses were administered and the 6-month repeat biopsies have all been collected. Samples are being processed as we speak, and our plan is to have analysis completed in time to submit a late-breaker abstract to the AASLD Liver Meeting.

This is a potentially important readout for the program and for the field, because it is the first view of what happens inside the liver in alpha-1 patients after receiving therapy. We will be assessing reduction is the Z-AAT monomer, which we would expect based on plasma data from our Phase 1 healthy volunteer study. The Phase 1 data demonstrated that ARO-AAT treatment led to reductions in serum AAT levels down to below the level of quantitation with a multi-month duration of

effect. This suggests that we may be achieving near complete suppression of the liver production of the mutant Z-AAT protein. At this time, no other therapies have shown this type of result using any modality.

We will also be looking at whether the accumulated Z-AAT polymer can start to decrease after 6 months, which we are not expecting but would be pleasantly surprised to see. In addition, we will look at changes in inflammation and in various histologic parameters. Again, we wouldn't expect to see these measures change after only 6 months of treatment, but it would be a very exciting result if we were to see improvements this quickly.

Let's now move to our cardiometabolic pipeline.

I will start with AMG 890, an investigational siRNA therapeutic designed to lower lipoprotein (a), or Lp little a, for the treatment of cardiovascular disease, which is licensed to Amgen. As Chris mentioned, Amgen recently started a Phase 2 study, which we are very excited about. The study is a double-blind, randomized, placebo-controlled Phase 2 study to evaluate efficacy, safety, and tolerability of AMG 890 in approximately 240 subjects with elevated Lp(a). The primary endpoint is the percent change in Lp(a) from baseline to week 36. Key secondary endpoints include the percent change in Lp(a) from baseline to week 48, and percent change in LDL-C and Apolipoprotein (B) from baseline to weeks 36 and 48.

Moving on to our two wholly-owned cardiometabolic candidates, ARO-APOC3 and ARO-ANG3.

Let's begin with ARO-APOC3, our candidate targeting apolipoprotein C-III, being developed as a potential treatment for patients with hypertriglyceridemia. We continue to be very impressed and encouraged by results from the ongoing Phase 1/2 clinical study called AROAPOC31001. I will talk about the study design and progress and then discuss where and when we expect to present data.

AROAPOC31001 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. The study reached full planned enrollment of 80 subjects and we subsequently expanded the study to assess a total of up to 112 subjects. As of today, 100 subjects have been treated.

The first data from the single-dose healthy volunteer portion was presented at AHA in 2019. We have been accepted to present additional data at the European Society of Cardiology meeting, the National Lipid Association meeting, and we may potentially have additional data at AHA, pending abstract acceptance. Between these three meetings in the second half of 2020, we plan to have multiple dose and follow up data in both healthy volunteers and patient cohorts. Together these represent a rather full dataset and should be a good view on the safety and activity of ARO-APOC3.

Data from the ARO-APOC3 P1/2 study have indicated very potent triglyceride reduction, frankly more potent than anything I've seen before. Because of this, we are exploring potential designs for the next stages of clinical development to study the drug in multiple patient populations that may benefit from triglyceride reduction. We have been engaging with regulators on that topic and hope to

provide some clarity later this year. We are hopeful that during the first half of 2021 we will be able to initiate a Phase 3 study in smaller populations and a Phase 2b study in larger populations.

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 called AROANG1001. It is a Phase 1/2 single and multiple dose study to evaluate safety, tolerability, pharmacokinetic, and pharmacodynamic effects. Both the healthy volunteer and patient portions of this study have reached full planned enrollment of 93 subjects.

Similar to ARO-APOC3, we continue to be very encouraged by the clinical data and plan to present at ESC and NLA, and hope to also present at AHA, pending abstract acceptance. We are working on a clinical development plan and will be engaging with regulators shortly to discuss the plan. Our hope is to start a Phase 2b study in the first half of 2021 in an appropriate patient population that may benefit from a lowering of both triglycerides and LDL-C. This may affect multiple cardiovascular risk factors simultaneously, which is potentially very exciting.

I will now briefly touch on progress in our earlier stage pipeline.

ARO-HSD is our investigational candidate for the potential treatment of alcohol and/or nonalcohol related liver disease. The genetic validation is strong for inhibiting the target HSD17B13 in NASH cirrhosis, and alcoholic hepatitis and cirrhosis patients. This is an exciting program for us as it is the first candidate against this novel target using any modality to enter clinical studies.

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. Additional exploratory objectives include assessment of various measures of drug activity using liver biopsy.

We have completed enrollment and dosing of the healthy volunteer portion of the study and we have initiated the multiple-dose patient portion of the study. There was a short delay in this study due to COVID-19, but it did not materially affect our anticipated timelines. We anticipate that initial data should be available to present in 2021.

Our two other early stage programs, ARO-HIF2 and ARO-ENaC, are also our first candidates targeting tissues outside the liver. ARO-HIF2 is designed to treat renal cell carcinoma, and we are currently screening patients to begin a Phase 1b study.

ARO-ENaC, designed to treat cystic fibrosis, is scheduled to begin dosing in a Phase 1/2 study this month. We hosted a webinar last week to talk about the target, the preclinical data, and the plan for the candidate. The webinar also featured outside CF expert Dr. Marcus Mall. It was full of good information about the program and I highly recommend you watch a replay if you didn't see it live. It is still available on the Events and Presentations page on our website.

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

Ken Myszkowski

Thank you, Javier.

As we reported today, our net loss for the quarter ended June 30, 2020 was $13.6 million or $0.13 per share based on 101.8 million fully-diluted weighted average shares outstanding. This compares with net income of $20.3 million, or $0.21 per share based on 98.9 million fully-diluted weighted average shares outstanding, for the quarter ended June 30, 2019.

Revenue for the quarter ended June 30, 2020 was $27.4 million, compared to $42.7 million for the quarter ended June 30, 2019. Revenue in the current period relates to the recognition of a portion of the upfront payments and milestones received from our license and collaboration agreements with Janssen, as we continue to work toward completing our performance obligation of managing the current phase 1/2 HBV clinical trial. Revenue from the Janssen agreement is 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. We expect the remaining $26.3 million of deferred revenue to be recognized in this calendar year. In addition, current period revenue also included the $20 million milestone payment we accrued due to Amgen initiating their phase 2 clinical trial for AMG 890. Revenue in the prior period related to the recognition of a portion of the upfront payments and milestones received from our license and collaboration agreements with Janssen.

Total operating expenses for the quarter ended June 30, 2020 were $43.3 million, compared to $24.1 million for the quarter ended June 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 during the quarter ended June 30, 2020 was $33.4 million, compared with net cash provided by operating activities of $10.5 million during the quarter ended June 30, 2019. The increase in cash used by operating expenses during the quarter is consistent with the increase in our cash operating expenses. The cash provided by operating activities in the prior period was driven by the receipt of a $25 million milestone payment from Janssen due to the initiation of the triple combination cohort in the HBV phase 1 / 2 clinical study. We estimate our near-term cash burn to average $30-35 million per quarter.

Turning to our balance sheet, our cash and investments totaled $464.6 million at June 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 $250.5M in net cash proceeds for the Company.

Our common shares outstanding at June 30, 2020, were 102.3 million.

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

Chris Anzalone

Thanks Ken.

As we have discussed, Arrowhead has a lot going on in all of the following stages:

1. Platform development and expansion into new extra-hepatic tissues, such as lung, tumor, muscle, and other cell types;
2. Early discovery, as evidenced by several covid-related programs, ARO-JNJ1, 2, and 3, and other undisclosed programs;
3. Early development, such as ARO-LUNG2, ARO-HIF2, ARO-ENaC, and ARO-HSD; and,
4. Emerging mid-to-later stage development, such as ARO-AAT, ARO-APOC3, ARO-ANG3, and partnered programs JNJ-3989 and AMG 890

This is a very large pipeline with enormous opportunity for a company of only 200 people that currently only burns between $30-$35 million per quarter, and has a market cap less than $5bn. This again speaks to the Arrowhead culture of finding a way forward and not allowing bureaucracy or legacy processes block innovation. It is also a testament to our commitment to capital efficiency and being good, responsible stewards of the capital that we have been entrusted with.

Even as we continue to grow, these attributes will be important parts of the Arrowhead culture.

The rest of 2020 is going to be very busy. We anticipate multiple data readouts, important clarity on the future paths and timelines for some of our programs, and new announcements about previously undisclosed targets and candidates. Our

existing programs continue to advance, and the reach of our technology platform continues to expand. This is a very exciting place to be.

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 …