ARROWHEAD PHARMACEUTICALS

Fiscal 2017 Year End Conference Call – Prepared Remarks

December 12, 2017

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 2017 fourth quarter and year ended September 30, 2017. With us today from management are president and CEO Dr. Christopher Anzalone, who will provide an overview of the quarter; Dr. Bruce Given, our chief operating officer and head of R&D, who will discuss our near term clinical candidates; 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.

With that said, I'd like to turn the call over to Dr. Christopher Anzalone, President and CEO of the Company. Chris?

Chris Anzalone

Thanks Vince. Good afternoon everyone and thank you for joining us today.

2017 has been an enormously productive year for Arrowhead, as we moved forward from the very difficult decision in 2016 to discontinue development of prior generation drugs, ARC-520, ARC-521, and ARC-AAT, that utilized the EX1 delivery vehicle. That decision moved us from a clinical-stage company with two Phase 2 candidates and one Phase 1 candidate, to a preclinical-stage company overnight. In addition, at that time we had not disclosed much about our new

platform and had not given guidance on timelines for getting back into the clinic. Understandably, there was a lot of uncertainty for investors about where Arrowhead was going.

We were clearly on our heels, but the real meddle of a company only makes itself known in the face of adversity. As we look back on what we accomplished and forward to what is to come, I am extraordinarily proud of this company.

We are on pace to file two CTAs to begin clinical trials during the next two quarters. These are for ARO-AAT to treat alpha-1 liver disease with a CTA planned in Q1 2018, and ARO-HBV as a potentially curative therapy for chronic hepatitis B infection with a CTA planned in Q2 2018. We think the insights gleaned from our prior programs in HBV and alpha-1 liver disease represent real competitive and strategic advantages, and should enable us to move with speed and precision once the clinical programs begin.

We are also on schedule to file three additional CTAs in the next twelve months. These are for ARO-APOC3 and ARO-ANG3 to treat hypertriglyceridemia and ARO-Lung1 against an undisclosed lung disease target, all three are planned for CTA filings around the end of 2018.

In addition, our two cardiovascular collaborations with Amgen are moving forward rapidly. One, which was previously called ARO-LPA against the target lipoprotein(a), or Lp little a, has been formally nominated as a clinical candidate and which is now referred to as AMG-890 by Amgen. We anticipate that this may enter the clinic some time in 2018. The Amgen deal was announced in September of 2016 and Arrowhead received 56.5 million dollars in upfront payments and

initial equity investment and we are eligible to receive an additional $617 million in potential milestone and equity payments.

So we plan to go from zero clinical programs to 5 or possibly 6 over the next 12 months. I don't believe I have ever seen any biotech company do this. The table is now set for a potential breakout 2018 and 2019 as the makeup of this company changes dramatically and we see how these drug candidates perform in patients. Lets now unpack this a bit and take a look at these programs.

First, they are all built on a new platform. In September we hosted an R&D day to unveil the new Targeted RNAi Molecule, or TRiM™ platform, that builds on more than a decade of research at Arrowhead on actively targeted drug delivery vehicles. We view TRiM™ as an evolutionary step for the field of RNAi delivery. The TRiM™ platform retains the maximal activity of prior generation technologies but moves towards structural simplicity that offers several advantages. These include:

1. Simplified manufacturing and, therefore, reduced costs;
2. Multiple routes of administration, including subcutaneous injection and inhaled administration; and,
3. Potential for improved safety, because smaller molecules with reduced metabolites may reduce the risk of intracellular accumulation. Also, the TRiM platform does not rely on DPC's so we expect substantially wider safety margins than we had in previous generations.

ARO-AAT is a good example of what we believe TRiM can do. It appears to be more potent than ARC-AAT and provides a longer duration of activity, but we expect a significantly better safety profile. In addition, much of what we learned from the ARC-AAT program gives us confidence in ARO-AAT.

First, potency of ARC-AAT, our previous generation compound, in non-human primates was predictive of potency in humans. Should this hold for ARO-AAT, we would expect monthly or even less frequent dosing should provide near complete suppression of hepatic sources of AAT. Second, knock down in healthy volunteers was very similar to knockdown in patients. If this holds for ARO-AAT, we could predict proof of concept, at least as it relates to activity, early in Phase 1.

Similarly, our experiences with prior HBV programs have guided many of our plans and expectations for ARO-HBV. We have always believed that a sufficiently potent and well-tolerated RNAi-based therapy could enable s-antigen seroclearance and functional cure of chronic hepatitis B infection, which has been elusive for other drugs and mechanisms. Our case for the potential importance of ARO-HBV toward this goal was strengthened last week when we presented new data at the HEP DART conference from the ARC-520 open label extension study. Specifically, we showed that 50% of patients in the follow-up study, or 2 of 3 e-antigen positive and 2 of 5 e-antigen negative patients, have achieved a sustained host response after receiving ARC-520 treatment in combination with entecavir, characterized by continued reduction of multiple HBV viral markers, including s-antigen, and coinciding with an increase in ALT, indicative of host response.

What does this mean and why should you care? Our goal has been to silence everything the hepatitis B virus makes and, thereby, enable the body to overcome immunosuppressive forces and control the virus on its own. ARC-520 appears to have done something that enabled the host to fight the virus on its own even *after* ARC-520 was withdrawn, and this is a big deal. It is the first clinical evidence that an RNAi-based approach can lead to the type of favorable sustained host response that we have always believed is possible and, in fact, critical if a functional cure is

to be reached. If this was in fact a marker of the immune system being re-awakened, then it bodes well for ARO-HBV.

When considering these results in the context of ARO-HBV, keep in mind that ARC-520 was a sub-optimal therapy in part because it could only silence gene expression from cccDNA. This leaves continued production from viral DNA that integrated into host DNA unchecked, and we have demonstrated that integrated DNA can be a major source of s-antigen production. Therefore, ARC-520 was fighting the virus with one arm tied behind its back: it was only targeting one source of immunosuppressing s-antigen. Importantly, ARO-HBV may be substantially more active against s-antigen than ARC-520 since it was designed specifically to hit all viral mRNA transcripts from both cccDNA and integrated DNA.

We also have reason to be optimistic about our newly announced hypertriglyceridemia programs, ARO-ANG3 and ARO-APOC3. Angiopoietin-3 and Apolipoprotein C3 are validated targets that are independent risk factors for cardiovascular disease and they are not effectively addressed by traditional therapies. In addition to large cardiovascular market opportunities, these targets are associated with smaller, orphan indications as well, providing multiple regulatory pathways and market approaches. This flexibility is important in part because it offers strategies that could involve partnering or keeping candidates in house for internal development.

Finally, we believe that our new lung programs represent a fundamental leap forward for RNAi generally and for Arrowhead specifically. In multiple animal models, we have been able to deeply silence lung targets via inhaled administration. This capability is a good example of the flexibility of the TRiM

platform, and addressing lung targets will open a host of new opportunities. Once we validate the first program, whose target remains undisclosed, we view the lung targeting TRiM technology as a franchise unto itself. We will provide additional details on the initial program as well as more data in 2018.

With that overview, I would now like to turn the call over to Dr. Bruce Given, our COO and head of R&D. Bruce?

Bruce Given

Thank you, Chris, and good afternoon everyone.

Chris mentioned that ARO-AAT and ARO-HBV are on pace for CTA filings during the next two quarters and then we anticipate having up to three additional CTAs before the end of 2018. These are all very exciting programs for us.

Today I want to focus just on ARO-AAT and ARO-HBV, since they are our current lead programs and are on pace to get into the clinic shortly. I will go over two areas for each candidate:

1. The therapeutic rationale for the target; and,
2. Select data that provides us with confidence in the candidate's potential.

Let's start with ARO-AAT. Alpha-1 antitrypsin, or AAT, deficiency involves a genetic mutation that causes the AAT protein to be misfolded and thus not properly exported from hepatocytes. This causes two downstream issues for patients with this disorder. First, AAT protects tissues from inflammation and damage. Patients that have the misfolded protein have low levels of AAT in the circulation which

can lead to early onset lung disease. Second, since the protein is not properly exported from the liver, it accumulates and then aggregates into polymers and globules inside the cell. So, the lung disease is due to a deficiency in functional AAT and in the liver it is a storage disease. There are approved protein replacement therapies for the lung disease, but at this time the only option for treating the liver disease is transplant.

There are estimated to be around 100,000 potential patients in the U.S. and possibly more in Europe with alpha-1 anti-trypsin deficiency. Based on those numbers it qualifies for orphan disease designation, but it is one of the more common rare diseases.

RNAi as a mechanism is very good at halting the production of an individual protein, so we think alpha-1 liver disease, which is clearly caused by the accumulation of the misfolded mutant AAT protein, is a very attractive therapeutic target.

We have done extensive work with the transgenic mouse model that produces the human Z mutant protein, which is the one we care about. And fortunately, this model recapitulates several aspects of the human disease well. The mice have problems secreting the Z protein, but they do get some out into circulation just like humans. The Z protein in hepatocytes forms polymers and globules, their livers get inflamed and they develop hepato-cellular carcinoma as a result.

We completed separate studies in which we intervened early in disease progression, mid-stage, and then also in older mice that had started to develop hepatocellular carcinoma. We really wanted to confirm that RNAi was the right approach here.

In young mice, we demonstrated that we could virtually eliminate their monomer production, and they had less polymer and globules just 8 weeks later than they had at baseline and substantially less than mice that had gone untreated over the 8 weeks. So, the liver is doing what we would hope. In older mice that already had a lot of globules in their liver at baseline, when treated for 32 weeks, their livers moved a long way back towards normal. They had minimal to moderate globules, but much less. They also no longer had compressed nuclei, which were present at baseline and which were seen in mice treated with placebo. Treated mice also had no inflammatory cells. When we studied older mice, we also saw significant benefit from treatment. The liver architecture of treated animals improved and they had a clear reduction in hepatocellular carcinoma. These results provide us with confidence that an RNAi-based therapy like ARO-AAT has a lot of promise against alpha-1 liver disease.

In addition to the work we've done in mice, we have also looked at knockdown of circulating AAT in primates, and we also have clinical experience with our prior generation compound ARC-AAT. In primates, ARO-AAT led to a reduction of circulating AAT of over 90%. Keep in mind that around 10% of AAT is produced outside the liver, so we believe 90% represents near full suppression of the liver produced protein. The duration of effect in primates was long, which may enable a monthly, bi-monthly, or even longer dosing interval.

As Chris mentioned, we intend to file a CTA for ARO-AAT in Q1 2018. We are excited to get back into the clinic and we have designed an innovative first-in-human study that is intended to generate single dose and multiple dose data rapidly in one study. We will discuss this design in further detail when the study is initiated.

Now, I will turn to HBV. There are estimated to be between 200 and 350 million people chronically infected with HBV, and it is a difficult to treat virus for which curative therapies have been elusive. HBV is clearly a global health problem that needs to be addressed. The current standard of care involves nucleotide and nucleoside analogs, or NUCs, that inhibit reverse transcriptase. This class of drugs is very good at reducing circulating virus, but does almost nothing to improve functional cure rates over patients that receive no treatment at all.

Many experts believe that HBV infection remains chronic, because in addition to fully formed viral particles, the virus produces a large excess of viral proteins that silence the immune system and prevent the body from exerting immune control. At Arrowhead, we sought to develop a therapy that reduces the production of all HBV gene products, including pre-genomic RNA, polymerase, the core protein that forms the capsid, surface antigen, e-antigen, and the x-protein. We believe deeply reducing everything that HBV produces, may allow the body's immune system to re-constitute leading to a sustained host response, and ultimately a functional cure of HBV. In fact, we recently presented some follow up data on ARC-520 that we think represents the first clinical evidence that an RNAi-based approach may lead to the type of favorable sustained host response that we have always believed is possible.

Just like other difficult to treat viruses, HBV will likely require a combination approach. So why do we see a central role for an RNAi-therapy like ARO-HBV? Because we attack the entire transcriptome. And what's most important is, I think, any other direct-acting HBV drugs are going to be enhanced by RNAi because we reduce the inputs. We reduce the stress on those drugs and we have already seen synergistic effects with NUCs. Also, RNAi has been the only way, to date, to

address s-antigen coming off of integrated DNA. So, from my perspective, anybody who wants to have the best possible chance of achieving a functional cure, better have an RNAi in their combination regimen.

I recently had the opportunity to present some select preclinical data on ARO-HBV. Notably, 3 doses of ARO-HBV monotherapy in wild type plasmid HBV mice led to reductions in HBV DNA of 3.44 logs and both s-antigen and e-antigen dropped below the lower limit of quantitation. This represents reductions of greater than 3.0 logs and greater than 2.2 logs, respectively.

In addition, Arrowhead created a mutated plasmid HBV mouse model that eliminates the HBx trigger site to simulate HBV patients with high levels of integrated HBV DNA relative to cccDNA. In this model, a single dose of ARO-HBV led to a reduction in s-antigen of 2.95 logs. The duration of effect was long and s-antigen was still reduced by approximately 2.0 logs at 8 weeks following the dose.

This is highly encouraging and ARO-HBV was clearly very active in these models. We plan to file a CTA by Q2 2018 and, like ARO-AAT, we intend to generate as much single and multiple dose data as we can in our first-in-human study. Importantly, we intend to include HBV patients during Phase 1 in the multiple ascending dose portion of the study. As with ARO-AAT, we will provide further detail when the study is initiated.

I'd now like to turn the call over to Ken Myszkowski, Arrowhead's CFO, who will review our financials?

Ken?

Ken Myszkowski

Thank you, Bruce, and good afternoon everyone.

As we reported today, our net loss for fiscal 2017 was $34.4 million, or $0.47 per share based on 73.9 million weighted average shares outstanding. This compares with a net loss of $81.7 million, or $1.34 per share based on 61.1 million weighted average shares outstanding, for fiscal 2016.

Revenue for fiscal 2017 was $31.4 million, compared to $158 thousand for fiscal 2016. This increase is driven by the upfront payments received from our collaboration agreements with Amgen. During fiscal 2017, we have recognized revenue for all but $5.3 million related to the Amgen agreements, and we expect to recognize the balance in fiscal 2018.

Total operating expenses for the year ended September 30, 2017 were $68.4 million, compared to 81.9 million for the year ended September 30, 2016.

Net cash used in operating activities in fiscal 2017 was $23.9 million, compared with $64.4 million in fiscal 2016. Our R&D expenses declined from $41.5 million to $31.7 million primarily due to discontinuation of our previous clinical candidates in November of last year, although close-down expenses continued into the second fiscal quarter. Salary and payroll expenses also declined due to the workforce reduction we put in place after the discontinuation of our previous clinical candidates. General and administrative expenses also declined primarily due to reduced professional services expenses.

Turning to our balance sheet, our cash and investments of cash balances totaled $65.6 million at September 30, 2017, compared to our cash balance of $85.4 million at September 30, 2016. The decrease in our cash and investments balance reflects cash used in operations of $53.9 million and $7.8 million of capital expenditures primarily related to the build out of our new research facility in Madison, offset by $42.5 million in cash received from Amgen, consisting of a $30 million upfront payment for ARO-LPa, and $12.5 million in additional equity investment.

Our common shares outstanding at September 30, 2017, were 74.8 million.

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

Chris Anzalone

Thanks Ken.

As you can see, we have made an incredible amount of progress throughout 2017, and we believe that 2018 is set up to be transformational. Transition onto the TRiM platform has been rapid and we expect to file CTAs for 5 drug candidates in calendar 2018 where we believe we have strong competitive advantages.

- We are clear leaders in alpha-1 liver disease and expect to be the only company with a clinical candidate against this manifestation of Alpha-1 antitrypsin deficiency in the first quarter of 2018.

- We are clear intellectual leaders in chronic HBV and expect to be, once again, development leaders in RNAi treatment of HBV. We believe that RNAi will become a backbone therapy for HBV, and we plan on being back in the clinic in the second quarter with what we see as the first RNAi therapeutic with a real chance of enabling functional cures.
- We are leaders in RNAi for cardiovascular disease and believe that Amgen, with the candidate we developed, will be the first company to use RNAi against LP(a) in humans. Similarly, we expect to file CTAs for ARO-ANG3 and ARO-APOC3 by the end of 2018 and that we will be the first company to use RNAi against Angiopoeitin-3 and Apolipoprotein C3 in humans.
- We are also now leaders in RNAi for lung targets. This opens a new chapter for us and enables us to go after diseases in ways no other company is currently capable of. We expect to file a CTA for our first lung candidate by the end of 2018 and believe we will be the only company currently with a viable approach to using RNAi against lung diseases with inhaled administration.

This is certainly a lot, but given our non-clinical data and experience in AAT and HBV, we feel comfortable with these aggressive plans. It is also safe to assume that we will continue to build our pipeline in 2018 and that we will go after additional high value disease targets where new therapies are badly needed by patients.

Our ability to create new potential medicines outstrips our ability to develop them all into marketed products, at least for now. Therefore, it makes sense to do more collaborations, like we did with Amgen last year, for some of our programs. The world has seen how fast we are able to move over the past 12 months and that the

TRiM technology may be optimized to address a variety of target tissues, so we believe we are well positioned to attract high quality partners to maximize the number of products we can ultimately get to patients.

It has been a productive 2017 and we look forward to an exciting 2018.

I would now like to open the call to your questions. Operator?

Operator

Operator opens the call to questions …