

ARROWHEAD PHARMACEUTICALS

Fiscal 2019 First Quarter Conference Call – Prepared Remarks

February 7, 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 2019 first quarter ended December 31, 2018. 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 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.

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.

2018 was a very productive year for us. A year ago we were preparing to start first-in-human clinical studies of the first two candidates built on the TRiM™ platform, and today there are five candidates either in or approaching the clinic:

- ARO-HBV against chronic Hepatitis B infection is in a Phase 1/2 study and is partnered with Janssen. ARO-HBV will now be referred to as JNJ-3989;

- The second candidate is ARO-AAT against a rare genetic liver disease associated with alpha-1 antitrypsin, or AAT, deficiency, which has completed a Phase 1 study. We are actively working with the FDA to get feedback on potential endpoints and design for our next study;
- The third candidate is AMG 890 against cardiovascular disease and is partnered with Amgen. Amgen is evaluating AMG 890 in a Phase 1 study to assess safety, tolerability, pharmacokinetics and pharmacodynamic effects;
- The fourth candidate is ARO-ANG3 against dyslipidemia in a Phase 1 study in adult healthy volunteers and dyslipidemic patients;
- And, the fifth candidate is ARO-APOC3 against hypertriglyceridemia. I'm pleased to announce that we have received ethics approval and now await regulatory feedback on our planned first-in-human Phase 1 study of ARO-APOC3. We are prepared to begin the trial rapidly once all necessary approvals have been received.

That is impressive progress to go from zero to five clinical programs, all built on the TRiM platform, in just twelve months. In fact, we have exceeded virtually all of the aggressive development goals that we set in 2018, and I believe that we are the fastest and most innovative company in the RNAi field. As productive as 2018 was, 2019 has the potential to be even more so.

Let's talk about some of our goals and expectations for calendar 2019. They are:

1. Complete dosing and report data from the Phase 1 study of ARO-ANG3
2. Complete dosing and report data from the Phase 1 study of ARO-APOC3
3. Present additional Phase 1/2 data on JNJ-3989 (formerly ARO-HBV). To that end, we already have accepted presentations at the Asian Pacific

Association for the Study of the Liver meeting in February and the EASL International Liver Congress in April, and we expect additional abstracts to be submitted throughout the year. Note that the abstracts use the new name of the compound, JNJ-3989, rather than ARO-HBV.

4. Begin a Phase 2 study or studies of ARO-AAT, and we hope to provide clarity on a potential path to commercialization
5. File a CTA for our first inhaled pulmonary program, ARO-ENaC, against cystic fibrosis
6. File a CTA for our first solid tumor program, ARO-HIF2, against renal cell carcinoma
7. Discuss additional programs we are developing using the TRiM™ platform
8. And, lastly, we also anticipate that Amgen may share initial clinical data on AMG 890 later this year or in early 2020.

This is a lot in a short amount of time, but Arrowhead has a proven track record of accomplishing what we set out to do. It also speaks to the growing maturity of the TRiM™ platform.

To review, the TRiM™ platform is built around structurally simple conjugates that utilize ligand-mediated delivery and stringent bioinformatics. The TRiM™ platform offers several potential competitive advantages including:

- A sophisticated RNAi trigger selection and screening process that identifies potent sequences rapidly in locations that RNAi competitors may miss
- Multiple routes of administration including subcutaneous, intravenous, and inhaled
- Potentially faster time to clinical candidates

- Optimized pharmacologic activity and long duration-of-effect allowing infrequent dosing
- Potentially wide safety margins
- Simplified manufacturing at reduced cost
- And, the promise of taking RNAi to tissues beyond the liver, which would represent a big leap forward for the field and a substantial competitive advantage for Arrowhead

The data that we presented at the AASLD Liver Meeting in November 2018 for our first two TRiM™ enabled candidates, ARO-AAT and ARO-HBV, have been very encouraging. They are both proving to be potent molecules with a long duration-of-effect.

For example, three monthly doses of 300 mg of ARO-AAT led to reductions in serum alpha-1 antitrypsin to below the level of quantitation in 100% of subjects. Deep reductions were sustained for greater than 14 weeks, indicating that quarterly or less frequent dosing appears feasible. ARO-HBV achieved a mean reduction in s-antigen of 1.9 Log₁₀, or 98.7%, with a range of 1.3 Log₁₀, or 95%, to 3.8 Log₁₀, or 99.98%. In addition, ARO-AAT and ARO-HBV appeared to be well-tolerated at all doses tested. This bodes well for these candidates and potentially for the rest of our TRiM™ enabled pipeline.

With that overview, I'd now like to turn the call over to Bruce Given. Bruce?

Bruce Given

Thank you, Chris and good afternoon, everyone.

Since we are just starting the clinical programs for ARO-ANG3 and ARO-APOC3, I want to spend some time describing these candidates and the current clinical studies.

Despite all of the progress with cardiovascular drugs over the past years and decades, atherosclerotic cardiovascular disease remains a major cause of death. While the current standard of care is effective at lowering LDL cholesterol in the vast majority of patients, large, well run trials continue to show substantial unmet medical need for risk modifying therapies with novel mechanisms of action.

Hypertriglyceridemia and elevations in triglyceride-rich lipoproteins have been shown to be important causal risks for atherosclerosis, *independent* of LDL cholesterol. Elevated triglycerides can lead to highly dangerous pancreatitis, may participate in hepatic steatosis and are seen in metabolic syndrome. Metabolic syndrome is a complex of interrelated risk factors for cardiovascular disease and type II diabetes mellitus.

Let's start with 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 metabolic diseases.

ANGPTL3 has emerged as an important regulator of plasma lipoprotein levels (including triglycerides, LDL cholesterol, high-density lipoprotein cholesterol, and very low-density lipoprotein cholesterol) by inhibition of enzymes including lipoprotein lipase and endothelial lipase. ANGPTL3 may also be involved in regulating apolipoprotein B particle containing synthesis and hepatocyte clearance of LDL cholesterol through mechanisms independent of the low-density

lipoprotein receptor (or LDLR). This feature of LDL receptor independence is potentially very important and makes ANGPTL3 inhibition potentially novel and interesting as a therapeutic for LDLR-deficient hypercholesterolemic patients.

Intrahepatic targeting of ANGPTL3 may also improve hepatic steatosis which can progress to nonalcoholic steatohepatitis, or NASH. Human genetic studies indicate that ANGPTL3-deficient homozygotes show lower serum insulin, lower serum glucose, and improved measures of insulin resistance compared to non-carriers. Given how often atherosclerotic cardiovascular disease and diabetes intersect, these effects if seen with ARO-ANG3 would be welcome.

Our first-in-human study, AROANG1001, is a Phase 1 single and multiple dose study to evaluate the safety, tolerability, pharmacokinetic, and pharmacodynamic effect of ARO-ANG3 in up to 70 adult healthy volunteers with elevated triglycerides and various types of dyslipidemic patients.

The single-ascending dose portion of the study is designed to include up to 4 cohorts of 10 adult healthy volunteers per cohort. Each SAD subject will receive a single-dose administration of either placebo or ARO-ANG3 at dose levels of 35, 100, 200, or 300 mg. The multiple-dose portion is designed to include up to 4 patient cohorts, including patients with non-alcoholic fatty liver disease (or NAFLD), patients on a stable statin treatment regimen with elevated LDL cholesterol and triglycerides, patients with heterozygous or homozygous familial hypercholesterolemia, and patients with severe hypertriglyceridemia. The MAD cohorts will receive two monthly doses of ARO-ANG3.

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

APOC3 has emerged as a therapeutic target for triglyceride reduction. APOC3 is a regulator of triglyceride-rich lipoproteins, or TRLs, and is present in TRLs. APOC3 is a known inhibitor of lipoprotein lipase, or LPL, activity and LPL-mediated lipolysis of TRLs. APOC3 also delays clearance of lipoprotein remnants by the liver by inhibiting hepatocyte receptor-mediated uptake. Insight gained from transgenic mice overexpressing APOC3 and APOC3 knockout mice has shown that APOC3 delays very low-density lipoprotein cholesterol hydrolysis in vivo and may delay the removal of TRL remnants. Human genetic studies indicate that APOC3-deficient heterozygotes show reductions in plasma triglycerides and LDL cholesterol levels. Risk for cardiovascular disease in these carriers was reduced as well. APOC3-deficient individuals do not demonstrate significant hepatic steatosis and appear to be phenotypically normal.

Familial Chylomicronemia Syndrome, or FCS, is a severe rare genetic disease, with a prevalence of 1 in 1,000,000, often caused by various monogenic mutations leading to extremely high triglyceride levels, typically over 900 mg/dL representing the top 0.1%. Such severe elevations lead to various serious signs and symptoms including acute pancreatitis, which can be fatal, chronic daily abdominal pain, type II diabetes mellitus, hepatic steatosis and cognitive issues. There is no currently available therapy that can adequately treat FCS.

Our first-in-human study of ARO-APOC3 is quite similar in design to that of ARO-ANG3. AROAPOC31001 is a Phase 1 single and multiple dose study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamic effects

of ARO-APOC3 in up to 63 adult healthy volunteers with elevated triglycerides and patients with severe hypertriglyceridemia and FCS.

The single-ascending dose portion of the study is designed to include up to 4 cohorts of 10 adult healthy volunteers per cohort. Each SAD subject will receive a single-dose administration of either placebo or ARO-APOC3 at dose levels of 25, 50, 100, or 200 mg. The multiple-dose portion is designed to include up to 3 cohorts of patients with severe hypertriglyceridemia and 1 cohort of patients with FCS. The MAD cohorts will receive two monthly doses of ARO-APOC3.

Consistent with our prior first-in-human studies, we have designed AROANG1001 and AROAPOC31001 to give us a readout on safety and tolerability as well as a robust look at the pharmacologic activity and duration of effect. We are planning to measure ANGPTL3 and APOC3 levels, as well as LDL cholesterol, total cholesterol, non-HDL cholesterol, HDL cholesterol, VLDL cholesterol, Triglycerides, liver fat content using Magnetic MRI-PDFF in one ARO-ANG3 cohort, and other measures of drug activity.

I also want to touch briefly on the status of ARO-AAT, Arrowhead's second generation subcutaneously administered RNAi therapeutic being developed as a treatment for a rare genetic liver disease associated with alpha-1 antitrypsin, or AAT, deficiency.

We are currently interacting with the FDA on that program. Keep in mind that, to our knowledge, there has never been a drug to treat AAT-related liver disease in front of the FDA, so they have never had the opportunity to consider an approval pathway.

We had a pre-IND meeting with them in October and our discussions since then have been helpful and productive. We have discussed ideas on potential study designs and endpoints, which they are considering. We have completed the required long-term toxicology studies and the study reports necessary for submission are now available as well, so our intention is to move forward with a Phase 2 clinical study or studies as soon as we have clarity on the FDA's thinking around endpoints. Our hope is that the next study or studies may be able to become pivotal and provide a path to potential commercialization, but we don't have clarity on that today.

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 the quarter ended December 31, 2018 was \$12.0 million or \$0.13 per share based on 95.6 million fully-diluted weighted average shares outstanding. This compares with a net loss of \$13.2 million, or \$0.18 per share based on 74.8 million weighted average shares outstanding, for the quarter ended December 31, 2017.

Revenue for the quarter ended December 31, 2018 was \$34.7 million, compared to \$3.5 million for the quarter ended December 31, 2017. Revenue in the current period relates to the recognition of a portion of the upfront payments received 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 received 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. We expect the majority of the revenue to be recognized in this fiscal year, but we also expect revenue in fiscal 2020 as we will continue to perform certain follow up activities through 2020.

Total operating expenses for the quarter ended December 31, 2018 were \$23.7 million, compared to \$17.3 million for the quarter ended December 31, 2017. This increase is primarily due to increased drug manufacturing and clinical trial costs as our pipeline of clinical candidates has increased.

Net cash provided by operating activities during the quarter ended December 31, 2018 was \$168.3 million, compared with net cash used in operating activities of \$14.7 million during the quarter ended December 31, 2017. The key driver of this change was the \$175 million upfront payment from Janssen during this quarter.

Excluding cash inflow, our cash burn in the quarter was higher than previous recent quarters as we paid off a note payable in the amount of \$2.3 million during the quarter. We estimate our near-term cash burn to average \$20 million per quarter.

Turning to our balance sheet, our cash and investments totaled \$303.3 million at December 31, 2018, compared to \$76.5 million at September 30, 2018. The increase in our cash and investments was primarily due to the cash received from Janssen.

Our common shares outstanding at December 31, 2018, were 92.6 million.

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

Chris Anzalone

Thanks Ken.

I mentioned at the beginning of the call that 2019 could be even more productive than 2018, and I view a few primary areas driving that.

First, we expect ARO-ANG3 and ARO-APOC3 to create a lot of value this year. These are attractive targets that could address a number of high value unmet medical needs and we are the first to use RNAi against them. Importantly, we expect to generate a substantial amount of data *across several patient groups* this year, and I believe that we will have a good idea if ARO-ANG3 and ARO-APOC3 can become drugs by the third or fourth quarter. I expect that this year the current studies will generate the type of data that people are used to seeing from small molecule candidates at the end of P2b studies. These will be important read-outs, and, as we did with ARO-AAT and ARO-HBV last year, we will look to report data at appropriate conferences. ARO-AAT and ARO-HBV were big value drivers for us in 2018, and I hope to see ARO-ANG3 and ARO-APOC3 producing similarly for us this year. Depending on what patient populations we choose to focus on, we could have a rapid path to pivotal studies.

Second, we are not finished generating and reporting data from the AROHBV1001 clinical study. Patients will continue to be monitored for one year post last dose. ARO-HBV was very active in all patients studied, and we look forward to seeing if

even short-term dosing can have longer-term beneficial effects. I expect that we will continue to report data throughout 2019.

Third, we expect to begin Phase 2 studies in ARO-AAT this quarter and are hopeful that these may become pivotal. As we discussed, we are in active discussions with regulators and beginning studies with agreed upon design and endpoints could be a substantial value driver.

Fourth, we expect to file CTAs for ARO-ENAC and ARO-Hif2 this year, representing what we believe to be the first commercially viable efforts to use RNAi outside the liver. This is a large leap forward for the field and an important strategic step for Arrowhead.

And finally, you can never discount Arrowhead's breakthrough potential. We have consistently shown breakthrough speed and innovation that we believe is best in the field, and I expect this to continue. We disclosed at our analyst day in the fall that we can now target muscle cells, and I believe that unexpected breakthroughs will continue to be our hallmark and continue to build value for our shareholders.

As I said, I expect 2019 to be a big year for us. We are well on our way towards achieving our long-term goals to: File 2-3 new CTAs every year; Target a new cell type with the TRiM™ platform every 18 months; and Have 10 TRiM™ enabled candidates in clinical studies by the end of 2020

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 ...