ARROWHEAD RESEARCH

Fiscal 2016 First Quarter Conference Call – Prepared Remarks

February 9, 2016

1:30 PM Pacific time

Operator

Ladies and gentlemen welcome to the Arrowhead Research Corporation fiscal 2016, first quarter financial results 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 to discuss Arrowhead's results for its fiscal 2016 first quarter ended December 31, 2015. 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 may 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, but are not limited to, statements regarding the anticipated safety and/or efficacy of ARC-520, ARC-521, ARC-AAT, ARC-F12 and our other programs, as well as anticipated timing for study enrollment and completion and the potential for regulatory and commercial success. They represent management's current expectations and are inherently uncertain. Thus, actual results may differ materially. Arrowhead 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 quarterly reports on Form 10-Q for additional matters to be considered in this regard.

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.

I would like to start the call by addressing the weakness we have seen in the broader markets and, in particular, within the biotech sector. It has been a difficult start to the year for the overwhelming majority of biotech companies and we at Arrowhead have been frustrated that our stock price does not properly reflect what we see as our true value. That is unfortunate, and currently uncomfortable, but this is a cyclical issue, not a structural problem in our view. There have always been

cycles in the biotech capital markets and while the field is in a difficult cycle now, this will pass. This is a normal part of working in this sector and as long as we plan for such disruptions, have a flexible cost structure, and are going after important diseases in novel ways, we can build value during these times. I have always thought that we could get through anything as long as we could say 4 things. They are:

1. Our technology works;
2. We are working to solve real medical problems;
3. We have capital now; and
4. We have access to additional growth capital.

We believe that all of these are true today. Let us look at the past quarter and period since our last call through that lens.

This was a pivotal period for Arrowhead in terms of providing further validation of our technology and setting up the rest of the year with multiple milestones and, therefore, value inflection points. We presented important data with ARC-520, our drug candidate against chronic hepatitis B infection, showing that it does what it is designed to do and, more broadly, that our proprietary DPC™ delivery platform can effectively and consistently silence target genes in humans. This was a critical step for us and allows us to enter the next stage of growth for Arrowhead.

The next step for ARC-520 is multiple dose Phase 2 studies. We have begun 5 separate Phase 2 studies at 25 sites and counting, spanning 4 continents. During 2016 we expect to have over 200 patients on various multiple-dose regimens and we also intend to add cohorts, including at least one clinical collaboration with an additional novel agent. This is a large number of patients, so if ARC-520 is

ultimately helpful in enabling functional cures I believe we have a good chance of seeing evidence this year.

Now, what are the chances that we see something exciting? I believe quite good. Based on human and animal data that we presented over the last few months at our analyst day, at AASLD, and HepDART, ARC-520 is highly active against cccDNA derived mRNA transcripts and thus can dramatically reduce the production of all HBV proteins. In fact, I believe we set a new single dose knock down record for RNAi. In addition, our long-term study in chimpanzees showed that after repeat dosing, 7 of 9 animals treated with ARC-520 exhibited signs of immune reactivation. Interestingly, it took as few as 3 doses of ARC-520 to begin to see these signs. Further, given ARC-520's mode of action, it makes intuitive sense that it could be part of a therapy that leads to functional cures. Evolution drives toward efficiency so we think that expression of all HBV proteins is likely important for normal function of the virus and maintenance of chronicity. Put another way, we would expect that silencing all viral proteins would make it increasingly difficult for the virus to continue to evade immune control, particularly with an otherwise healthy immune system or one that is stimulated by another agent. Taken together, these and other evidence give us confidence that ARC-520 will play a role in enabling functional cures.

If we do see encouraging data in 2016 and beyond, when can investors hope to see it? This, of course, is a difficult question because if we do see functional cures we don't know how long patients will need to be on therapy to experience them. However, the 2001 extension study, which is open to most of the patients in the 2001 single and 2-dose study, and the Monarch study are both open label. We see unblinded data in nearly real-time and have flexibility as to how and when we communicate them. We intend to present data at relevant medical meetings, but

upstream of that we will look for opportunities to give updates on what we are seeing which may happen at any time. So stay tuned.

Remember that there are no available therapies that lead to a reasonable number of functional cures, and consequently even relatively infrequent functional cures during the early exploratory phases of our studies would be very exciting for Arrowhead and for the approximately 350-400 million patients worldwide who are chronically infected with HBV.

What about competitors? As with any clear unmet medical need, there is now meaningful competition in this space and big pharma has recently focused on the opportunity. However, we are substantially ahead of our competitors, we have the strong advantage of data from the long term chimp study and dozens of patients, our safety profile has looked good, and we do not require steroid pretreatment that brings its own AEs and immunosuppresses a patient at the exact time that a therapy is trying to enable the immune system to reconstitute itself. Given where we are in multiple Phase 2 studies now, we believe that if a breakthrough in HBV is going to occur in the next 12 months it should come from us.

Turning to ARC-521, the second drug in our HBV portfolio, we intend to accomplish some important steps during 2016. We previously reported that our clinical studies and our chimpanzee study showed that E-antigen negative patients and those on chronic antiviral therapy tend to have lower levels of viral cccDNA. We also learned that DNA that integrates into the patient's genome can become a significant source of S-antigen production. ARC-521 is designed to hit mRNA transcripts derived from both HBV cccDNA and integrated HBV DNA. This means that ARC-520 may be optimal in patient populations with higher levels of cccDNA, such as E-antigen positive NUC naïve patients, and ARC-521 may be

optimal in patients with lower levels of cccDNA. We will have to see what the various clinical studies show, but we think having both drugs should allow us to address all of the HBV market in a powerful way.

ARC-521 uses the same DPC™ delivery vehicle as ARC-520 and ARC-AAT, so we have a good amount of experience with it clinically. To date it has been well tolerated at all dose levels studied, which gives us great confidence as we prepare to initiate clinical studies of ARC-521 during 2016. We have an aggressive plan for the development of ARC-521 that includes an accelerated first-in-man Phase 1/2 design intended to get us into a multiple dose study in patients rapidly. We will talk more about this design as we get closer to initiating the study, which has planned regulatory submissions toward the end of second quarter 2016.

In addition to ARC-520 and ARC-521, we have an equally eventful year planned for ARC-AAT, our drug against the liver disease associated with a rare genetic disorder that causes alpha-1 antitrypsin deficiency, or AATD. We recently announced that ARC-AAT was granted Orphan Drug Designation in Europe and previously was granted the same designation in the U.S. in 2015.

We are currently conducting a Phase 1 single-ascending-dose study that consists of Part A in healthy volunteers and Part B in patients with AATD. During 2015 we achieved a predetermined level of AAT knockdown in healthy volunteers, which triggered the study to transition into patients. We have since been enrolling patients at several sites in Australia and Europe. We decided that it would be useful to compare AAT knockdown in healthy volunteers at the same therapeutic dose levels that patients are or will be receiving. Because of this, we have added additional cohorts in Part A of the Phase 1 in parallel with Part B and we have continued to dose escalate in healthy volunteers alongside patients. We intend to

complete enrollment and release top-line results from both the expanded Part A and Part B this year and then report full data at a relevant medical meeting.

We think that AATD is a great target for an RNAi-based intervention and one that has relatively low target risk. AATD is caused by a genetic mutation that leads to the production of mis-folded AAT, produced primarily in the liver. This mis-folded protein in not efficiently secreted and accumulates in hepatocytes, which is thought to be the cause of progressive liver disease. Patients with mutations that make no AAT have normal livers. It seems like a very clear straight line between knocking down production of this protein in the liver and an ultimate clinical benefit for patients.

We are preparing to begin a pilot Phase 2a multiple dose study that we expect to initiate and hopefully fully enroll this year. The biology of the disease is clear, so we believe the ARC-AAT Phase 2a study combined with results from the Phase 1 study may represent clinical proof-of-concept. Once that is achieved, we can discuss with regulators the potential endpoints of a pivotal study. Having Orphan Drug Designation in the U.S. and Europe allows us to have expanded interaction with regulators, which we intend to leverage to identify the best path to marketing authorization and ultimately to patients with AATD.

As you've heard, there are a lot of potentially impactful events for our lead clinical programs planned for 2016 and many more beyond that. It is our greatest priority to ensure that these are properly resourced because they are our key near-term value drivers. We have clear leadership positions in HBV and liver disease associated with AATD, and we have the potential to be both first- *and* best-in-class. We are building on this success through a pipeline that includes ARC-F12, ARC-HIF2, and ARC-LPA that address other high impact diseases.

In order to support the development of these drugs and continued improvements to our underlying platforms, which now includes subcutaneous and extra-hepatic delivery constructs, we have expanded the company and our capabilities over the last few years in terms of headcount, facilities, and equipment. We have taken these steps because we are confident that our DPC™ and oligonucleotide platforms will give us numerous opportunities to create drugs that change the way important diseases are treated and at the same time create lasting value for our shareholders.

We have not only had our foot on the gas over the past few years, we've had it on the floor. Our lead programs, ARC-520, -AAT, and -521, are now at important points in their development when substantial value inflections are possible. Pushing through those points is critical to us as a company and we want to ensure that we have the capital for this, particularly during this time of uncertainty in the broader markets. In order to keep our foot on the gas with these more mature programs, we are easing up a bit on some of our earliest-stage programs. We created a flexible cost structure that enabled us to move quickly but also to dial down spending on a program-by-program basis, and we are taking advantage of that now in order to fully resource HBV and AAT. All earlier programs continue to move forward, but some will just move at a slower pace for now. This is a good strategy and we are quite confident that there will be ample opportunities to fully fund these and other programs through various shareholder friendly methods.

So what do we have now and where does it get us? Today we reported total cash resources of $76.6 million at the end of the fiscal 2016 first quarter. We expect this gives us sufficient liquidity to fund our programs as described above through at least 12 months from now. This is important because we have many important milestones we expect to reach within this window.

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.

On our last call in December, I highlighted some of the data that we presented on ARC-520 last quarter at our analyst day, AASLD, and HepDART. There was a good amount of data that described some new concepts and underappreciated biology that we discovered through our clinical studies and through a long-term study conducted in chimpanzees with chronic HBV. Specifically, patients that become e-antigen negative and patients that receive chronic antiviral treatment with NUCs appear to have reduced cccDNA and consequently HBV DNA that has integrated into the host genome can become an important source of production for HBV surface-antigen, or s-antigen, in these patient populations. We presented data showing that because of this, there was a differential response to ARC-520 with respect to s-antigen in these various patient populations. Importantly, we demonstrated that log reductions with e antigen and core related antigen were similar across these different patient populations. We would anticipate that the same would be true for polymerase and the viral x antigen, as well.

In an unexpected but gratifying surprise, we also presented data showing that in chimpanzees, 7 of 9 animals that received multiple-dose treatment with ARC-520 showed signs indicative of immune reactivation. This occurred in all of the e-antigen positive animals and half of the e-antigen negative animals. One of the chimps had a viral flare and had large, persistent reductions in s-antigen and viral

DNA as far out as 6 months following discontinuation of all therapy. Six months was the last time point measured.

I'm not going to go through all the data, but I wanted to review some key findings so I can provide some context on how you should view the studies we have going on now and those that are planned in the future. Before I do that, let's quickly review the intended mechanism of ARC-520 treatment.

ARC-520 is designed to silence the production of all proteins produced by HBV. The virus produces multiple proteins in excess of what is needed to produce fully formed viral particles, some of which are secreted into the blood stream and some remain in hepatocytes. It is believed that many, if not all, of these proteins play a critical role in the viral lifecycle and allow the virus to evade immune control and clearance. The idea behind ARC-520 is that if you reduce the production of these proteins you may tip the scales, if you will, so that the immune system has a chance to control the virus and potentially get to a functional cure for patients. As I mentioned, in our chimpanzee study we saw signs that the immune system was reawakening in all e-antigen positive animals and half of the e-antigen negative animals. This suggests that ARC-520 may be doing exactly what it is designed to do.

So, what does that mean for the design of our clinical program? We see patients as being in one of four main groups based on their e-antigen status and whether they have received chronic therapy with NUCs. These are:

1. NUC naïve, e-antigen positive;
2. NUC naïve, e-antigen negative;
3. NUC experienced, e-antigen positive; and,
4. NUC experienced, e-antigen negative.

Our clinical program is enrolling patients from all of these quadrants. Based solely on s-antigen reduction, the first quadrant may be predicted to see the highest level of activity. However, our chimpanzee study suggests that ARC-520 is hitting the virus at multiple points beyond just s-antigen production, which may be important to reawaken the immune system.

We intend to enroll over 200 patients this year across the various global multiple-dose and combination Phase 2b studies. These are the 2001 open label extension, 2002, 2003, 2004, and 2008, also called MONARCH. These are enrolling and dosing as we speak and we are pleased with the pace of patient accrual so far.

Including the Phase 1 studies, ARC-520 has now been administered to well over 100 people to date. It continues to be well tolerated across all studies. The most common reported AEs in all subjects completing treatment to date were upper respiratory infection and headache.

For ARC-521, the second drug in our HBV portfolio, we are working on completing GLP toxicology studies to support a regulatory submission to begin the first-in-man study. Our goal is to have an accelerated Phase 1/2 development path that can get us to multiple dose data in patients rather quickly. We have some ideas about a trial design that would accomplish this, which we will share more about when the study gets started. We continue to plan for a late 2nd quarter 2016 regulatory submission timing.

ARC-AAT is our drug candidate for the treatment of liver disease associated with a rare genetic disorder called alpha-1 antitrypsin deficiency. As Chris mentioned earlier, we are conducting a Phase 1 single-ascending-dose study in both healthy

volunteers and patients in parallel. Part A of the study in healthy volunteers has dosed up to 5 mg/kg and we are not precluded from going higher. It is likely that Part A in healthy volunteers will complete before Part B in patients, so we may report top-line data from Part A later in the year and prior to Part B. The timing of this release will depend on the number of dose levels that we decide to study.

While the Phase 1 continues, we are also preparing to begin a pilot Phase 2a multiple dose study. This study will look at the effect on circulating levels of AAT after multiple doses of ARC-AAT. We also intend to take biopsies to determine the effect at the hepatocyte level. This study should also get underway this year.

So with all these studies going on, our clinical team is very busy. As you can see, we have several studies that can potentially yield interesting data throughout 2016 and beyond. We are looking to transform the treatment of both HBV and the liver disease associated with AATD, thus making a critical difference in patients' lives, which is when being a drug developer is most rewarding.

With that, 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 loss for the three months ended December 31, 2015 was $19.3 million, or $0.32 per share based on 59.5 million weighted average

shares outstanding. This compares with a net loss of $22.6 million, or $0.41 per share based on 54.7 million weighted average shares outstanding, for the three months ended December 31, 2014.

Total operating expenses for the three months ended December 31, 2015 were $19.4 million, compared to $25.3 million for the three months ended December 31, 2014.

Net cash used in operating activities during the three months ended December 31, 2015 was $21.2 million, compared with $24.2 million during the three months ended December 31, 2014, a change of $3.1 million, primarily due to reduced expenses associated with the drug manufacturing campaign to support our Phase 2b studies for ARC-520. The manufacturing campaign for this clinical trial for ARC-520 is largely complete, however, as other clinical candidates are nominated, and as other clinical trials advance, further expenditures will be incurred.

Turning to our balance sheet, our cash and investments of cash were $76.6 million at December 31, 2015, compared to $98.6 million at September 30, 2015. The decrease in our cash and investments balance is primarily related to the $21.1 million cash used in operating activities.

Our common shares outstanding at December 31, 2015, were 59.6 million, and would be 62.3 million, assuming conversion of preferred shares outstanding at December 31, 2015.

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

Chris Anzalone

Thanks Ken.

These are challenging times in the financial markets. While it's easy to say and somewhat more difficult to do, we try not to use the day-to-day movements in the stock price as an indication of the true fundamental value we are creating. We focus on how far we've come in the last year, and how far we will go in 2016. And when we look beyond the next twelve months to the next few years, we see dramatic potential for Arrowhead as our mid-stage pipeline matures and our early and preclinical stage pipeline start to show clinical proof-of-concept across multiple disease areas. Just like every market cycle before, this cycle too will pass. Innovative drugs like the ones we're developing at Arrowhead will always have great value.

At the beginning of the call I mentioned 4 things that we believe are true and that will enable us to build value through a difficult market. Lets take another look at them now.

Does our technology work? Yes. Data in chimps indicate that ARC-520 and -521 are capable of deep target knockdown. Substantial clinical data with ARC-520 and ARC-AAT indicate that deep knockdown translates well from non-human primates to humans. Between ARC-520 and ARC-AAT, we have seen DPC exposure in well over 150 people and the safety profile has been promising. In fact, from what has been shared publicly, I do not believe there is an RNAi delivery platform with a cleaner safety profile in humans than ours.

Are we working to solve real medical problems? Yes. Between 350 and 400 million people world-wide, or approximately 1 in 20 people on the planet, have chronic HBV infection and there is no cure. Approximately 100,000 people in the US and a similar proportion in Europe suffer from AATD and there is no treatment for liver disease associated with this.

Do we have capital? Yes, we have enough to run at least through the next 12 months while pushing our lead programs as fast as possible and continuing work on our pipeline.

Do we have access to additional capital? Yes, through a number of sources. We have clearly demonstrated that ARC-520 and ARC-AAT are active and well tolerated in humans, and 2016 is full of value inflection points. These include: treating over 200 patients in multiple phase 2 studies of ARC-520, some of which are open label; the introduction of ARC-521 into the clinic and expected quick progression of Phase 1/2 studies; release of ARC-AAT healthy volunteer and patient data and progression into Phase 2 studies. These are important for rapid value creation and, therefore, important to investors. We are also at a point in development and platform validation that we are an increasingly attractive partner to larger companies. Many companies looking for exposure to the areas we are addressing with current candidates would be interested in our ongoing programs. Similarly, companies looking to address areas in which we do not have active programs will find Arrowhead an attractive discovery and development partner. We have broad IP coverage through internal development, the Novartis transaction, and the Roche transaction; we have a delivery platform that has demonstrated extremely deep target knock down in humans and arguably the best safety profile in the field; we are capable of addressing both hepatic and extra-

hepatic targets; we are capable of both iv and subcutaneous administration; and we have demonstrated very rapid development times.

As we have mentioned, 2016 is set up to be an exciting year for us across multiple fronts. I think we will start to see answers to questions that have vexed medicine for some time now, and we look forward to regular communication with the Street. I think 2016 is a big year for us and I also think we will surprise some people.

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

Operator

Operator opens the call to questions …