ARROWHEAD RESEARCH

1Q Fiscal 2015 Conference Call – Prepared Remarks

February 9, 2015

1:30 PM Pacific time

Operator

Ladies and gentlemen welcome to the Arrowhead Research fiscal 2015, 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

Thank you. Good afternoon everyone and thank you for joining us today to discuss Arrowhead's results for its fiscal 2015 first quarter ended December 31, 2014. With us today from management are President and CEO Dr. Christopher Anzalone, Chief Operating Officer and Head of R&D Dr. Bruce Given, and Chief Financial Officer Ken Myszkowski. Management will provide a brief overview of the quarter and will then open up the call to your questions.

Before we begin, I would like to remind you that comments made during todays 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-AAT, and our other programs, as well as anticipated timing for study enrollment and completion. 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 break this call into 4 parts: first, we will talk about the accomplishments of the past quarter; second, we will discuss regulatory aspects and timing of the ARC-520 and ARC-AAT clinical programs; third, we will provide an overview of our financial results for the quarter; and fourth, we will discuss goals for calendar 2015.

Let us begin with our recent accomplishments. During the first fiscal quarter of 2015 and period since our last call, we achieved several key goals set in 2014. One of the broader goals was to build out our management team to give us deeper expertise internally and enable us to scale our operations and programs. We made great strides toward these ends during the quarter with the appointments of Susan Boynton as Vice President of Global Regulatory Affairs and Patrick O'Brien as General Counsel. The quality of these executives and the nature of the responsibilities they have assumed are representative of our maturation as a company. Our focus is increasingly geared toward clinical programs and the potential shareholder value they may drive.

As you know, our two clinical programs are ARC-520 and ARC-AAT for the treatment of chronic hepatitis B infection and liver disease associated with alpha-1 antitrypsin deficiency, respectively. We made important progress in both programs last quarter. We presented initial data from the ongoing Phase 2a study of ARC-520 in the late-breaking poster session at the 2014 American Association for the Study of Liver Diseases (or "AASLD") Meeting in Boston. ARC-520 showed clear reduction of HBV s-antigen after a single dose of 1 and 2mg/kg. Interestingly, the duration of s-antigen knockdown was substantially longer than we expected.

As we discussed on our last call, these are important data. We believe that ours is the first report demonstrating s-antigen reduction in humans after a single dose. This is something the field has been trying to accomplish for quite some time and the fact that we have done it is encouraging. This was only the beginning of our Phase 2a single dose escalation study, and we have since completed dosing both 3 & 4 mg/kg cohorts. We are still following the 4mg/kg cohort and both the 3 and 4 mg/kg groups remain blinded. The safety profile for ARC-520 appears to continue

to be very good. We have still not seen any signs of end organ toxicity and no reported AEs have been rated as severe or serious. We expect to have unblinded data that we can discuss next quarter.

We currently have no plans to escalate higher in the single dose Phase 2a study. We have always assumed that ARC-520 would be a multiple dose therapy and it is time to understand s-antigen reduction kinetics upon repeat dosing. Of course this is a far more clinically relevant endpoint than single dose. RNAi therapeutics rely on loading the RISC complex with RNAi triggers, and all the programs I am aware of require multiple doses to maximize the loading process. This is often done with several frequent initial doses, referred to as loading doses. Because of the long duration of activity we have seen in ARC-520 its possible that we may achieve this with fewer doses.

In December, we met our guidance and submitted an IND application to the FDA to begin Phase 2b multiple dose studies. Throughout the entire ARC-520 program, we have operated under very aggressive time schedules and, I believe, executed well on them. Keep in mind that we went from idea to starting a Phase 1 study of a novel molecule and delivery system in only approximately 18 months. Consistent with this desire to move quickly and increase our lead in the field, we proposed a parallel design for the Phase 2b whereby we would study multiple dose levels simultaneously. On a call in mid January, the FDA requested that we initiate a more traditional ascending dose protocol beginning at 1 mg/kg. Importantly, no additional studies were required to begin the 1mg/kg study. Since that time, we received an official letter from the FDA outlining its requests, and it was consistent with the discussions we had. We submitted the amended protocol to the FDA today.

This is a big step for the program and underlying platform. Phase 2a data suggest that 1mg/kg is an active dose, so we should generate important data during the first cohort. It is also an important step in building out our safety data set. More broadly, it represents another de-risking event for DPCs generally. As we build out our understanding of how DPCs work in humans, we will be able to better predict how future candidates, including ARC-AAT, will perform. This should enable the market to value follow-on candidates earlier in their development cycle. This is an important characteristic of RNAi therapeutics. Once we show that a delivery system is well tolerated and active in a given organ system, we believe it is a good assumption that new sequences against different gene targets may follow suit.

This is a good start to a program that is addressing a significant unmet medical need. We are approaching a post hepatitis C world and we see hepatitis B as the next great liver challenge. Because of the complexity of HBV, it is likely that multiple agents will be required to induce a functional cure in at least some populations of the disease. Reducing s-antigen levels is thought to be a critical backbone therapy, and we have a clear lead in this. We have learned a tremendous amount about the disease and how ARC-520 may fit into an effective therapy already, and as we see additional data I believe our lead actually increases. Of course nobody yet knows if we can achieve a functional cure with ARC-520, but I believe that if there is going to be a breakthrough in HBV over the next 2 years, it will come from Arrowhead given where we are in the clinic versus competitors.

As we think about potential combinations, we would like to be the anchor. Big pharma has clearly increased its focus on HBV and we know that virtually any way one can imagine disrupting the virus at different parts of its life cycle are in development. When you combine this with programs at large and small biotech

companies and the work being done with immune modulators, the market may begin to feel crowded. However, there is scarcity in potential strategies to reduce s-antigen, and where there is scarcity there is value. We do not know of any program targeting s-antigen reduction that is as far along as ours, we have demonstrated a very clean safety profile to date, we know that ARC-520 is active, and RNAi as a mechanism is known to be a reliable way of reducing target gene expression. In addition, remember that ARC-520 is designed to knock down the entire HBV genome, so while we often talk about s-antigen reduction, we actually hit the virus at multiple points of its life cycle. As such, we believe that ARC-520 will be a natural choice for companies to combine their new compounds with. This is good for us. Our strategy is to assess multiple combinations. Because of where we are in the clinic, we have the opportunity to find the best therapies in chronic HBV patients rather than relying on animal models that, with the exception of chimps, have questionable predictive value.

Lets now turn to ARC-AAT, our candidate for the treatment of liver disease associated with Alpha-1 antitrypsin deficiency. Last quarter we delivered a plenary presentation at AASLD with new preclinical efficacy data on ARC-AAT. This was a prestigious slot and the ARC-AAT abstract was highlighted in the AASLD President's Press Conference as a promising new treatment. Only 11 were chosen for this designation out of a total of 2106 abstracts. In the presentation, repeat dosing of ARC-AAT in primates showed reduction of approximately 90% of serum alpha 1 antitrypsin with long duration of effect, suggesting that monthly or less frequent dosing may be sufficient for sustained suppression of hepatic AAT production.

Late last year, we met our guidance and filed to begin a Phase 1 clinical trial of ARC-AAT. We are on track to begin dosing healthy volunteers in that study by

the end of this month. Remember that ARC-AAT uses the same DPC that is used in ARC-520. This gives us confidence in the ultimate safety profile of the candidate, and we are looking forward to understanding activity when targeting an endogenous gene. ARC-AAT addresses an important unmet medical need, as there are currently no treatments for liver disease associated with AAT deficiency. It also represents a relatively straightforward value proposition because liver disease associated with AAT deficiency is a storage disease that should be diminished, and possibly reversed, by reducing AAT production. The alpha-1 Foundation believes that there may be as many as 100,000 people in the US with the mutation that leads to AATD.

Looking deeper into our pipeline, we continued to make important progress on follow-on liver candidates. We expect to file an IND or equivalent for our next candidate by the end of calendar 2015. We have also made good progress on DPC formulations for subcutaneous administration against liver indications as well as iv formulations for extra-hepatic targets. We believe that we will nominate our first subcutaneous candidate or our first extra-hepatic candidate by the end of calendar 2015.

Turning to RNAi chemistry, we are always interested in new RNAi trigger technologies. More specifically, we are interested in structures and modifications that could increase gene silencing activity and/or provide additional freedom to operate across new targets and indications. Toward those ends, last quarter we acquired an exclusive option to purchase a basket of RNAi technologies and IP. We paid $7m for this exclusive option and it shows up in our financial statements as “other investing activities.” We continue to assess the potential value of these platforms and IP for Arrowhead.

With that overview, I would now like to turn the call over to our COO and Head of Development, Dr. Bruce Given. Bruce?

Bruce Given

Thank you Chris and good afternoon everyone.

It was another busy clinical quarter for us and we continue to move forward with our plans. Since our last call we completed enrolling the 3 and 4 mg/kg cohorts in Heparc-2001, our Phase IIa study in e negative Chronic HBV patients in Hong Kong. Those cohorts remain blinded while the 4 mg/kg cohort completes follow-up over the next few months. We submitted our IND for ARC-520 in December and announced in mid-January that we had been in communication with FDA and that they were uncomfortable with us progressing from single dose studies directly to a parallel design multi-dose study and had thus placed the program on partial clinical hold. We were informed of this during a call at which time FDA asked us to start the program with a rising multiple-dose study beginning at 1 mg/kg, the starting dose in our single-dose Heparc-2001 study. They had promised us a letter within 30 days fully detailing their thoughts.

We received the FDA letter and it did not contain any surprises relative to what had been communicated on the call regarding the partial hold. As such, we had already written a new protocol which had pretty faithfully captured the main themes. However, the letter also included some recommendations offered regarding non-hold ideas that FDA felt would be helpful to the program.

We saw these as quite constructive and recognized an opportunity to adjust the new protocol in a couple of aspects that took into account FDA's suggestions,

while being helpful and cost sparing to the program overall. This has caused us to make a few tweaks to the prospectively designed study. As such, the protocol has been finalized and is with our publishers for electronic submission to FDA either today or tomorrow. We are submitting the protocol to investigator site IRBs for review in parallel. Let me be clear that we do not intend to start this study until the FDA has blessed the new design.

We had previously guided that we expected to submit our global protocols to European and Asian authorities at the end of January. However, the additions of the new US protocol and the way it is being designed has given us the opportunity to reduce the planned size of the core international trials and also to simplify them in some ways that we expect should make them easier and faster to enroll. This has led to a minor delay in their planned submission. The protocol and accompanying documents should be finished this week or next and then will be provided to our CRO for final translation and submission.

Overall, we do not expect completion of the core global trials to be delayed relative to our original planning, as long as they meet with regulatory approval in those jurisdictions with normal review times. Once those submissions have been made, we will turn our attention to other studies included in our planned Phase II program. As we have discussed previously, it is unknown whether ARC-520 plus NUCS as a two drug combination therapy will produce a significant number of seroclearance events. Given how challenging this virus is, it would not be surprising if one or more additional drugs will be necessary to be included in a multi-drug cocktail for some, or even all, patients to reach our goal of producing a substantial number of functional cures.

As such, we have been planning to take an open collaboration approach regarding addition of other agents similar to what was done previously in Hepatitis C to the great benefit of the patient and treater communities. This will obviously include already approved agents, but we have also been in positive discussions with companies developing their own agents. Over the next 2 years there are a large number of agents that will be completing Phase I human testing, some known to the street, some not, that will be ready to participate. We believe, as do others we speak with, that testing their drugs in combination with NUCS and ARC-520 is a natural step to take in seeking the earliest path to demonstrating the functional cures that many or most in the field see as the next breakthrough step in HBV therapeutics development.

We believe that the next two years will be very exciting in Hepatitis B with the best shot in decades of getting to treatments that can actually convert chronic active disease HBV patients into functionally cured non-patients off therapy. Because of our leadership position, we think that if this occurs, it is most likely that it will occur in studies including ARC-520 as a core component of therapy.

Before I turn the call over to Ken Myszkowski, I'd like to say a few words about ARC-AAT. We submitted our application to initiate trials in Australia at the end of last year. I am happy to report that we have received all necessary approvals to proceed with the study and the screening process has begun. We expect to enroll our first subject in that trial this month. In this study, we will treat normal volunteers until we reach a dose that produces modest knockdown of circulating alpha 1 antitrypsin levels. At that time, we will switch to patients as we interrogate higher doses. As such, we expect to understand the depth and duration of

knockdown from a single dose in patients *from this trial* and we would hope to have that data this year.

With that, I'd like to turn the call over to Ken Myszkowski, Arrowhead's Chief Financial Officer.

Ken?

Ken Myszkowski

Thank you, Chris, and good afternoon everyone.

As we reported today, our net loss for the three months ended December 31, 2014 was $22.6 million, or $0.41 per share based on 54.7 million weighted average shares outstanding. This compares with a net loss of $10.7 million, or $0.28 per share based on 37.7 million weighted average shares outstanding, for the three months ended December 31, 2013.

Total operating expenses for the three months ended December 31, 2014 were $25.3 million, compared to $7.1 million for the three months ended December 31, 2013. The increase in operating expenses compared to the year ago period, are due to costs for research and development, primarily higher drug manufacturing costs which increased by $8.4 million during the period, mostly related to ARC-520, as well as higher clinical trial costs which increased $4.5 million. Clinical trial costs have increased as we incur start up costs from our CRO related to the planned ARC-520 phase 2b studies. We also incurred costs for our second clinical candidate ARC-AAT of about $2.4 million, while ARC-AAT clinical trial costs in the comparable period were minimal. Higher G&A costs, driven by higher

professional services, and higher compensation expense, primarily due to increased headcount, as compared to the prior year also contributed to higher operating costs.

Net cash used in operating activities for the first three months of fiscal 2015 were $24.2 million, compared with $7 million in the prior year period. The change in cash used in operating activities is consistent with the change in operating expenses.

Turning to our balance sheet, at December 31, 2014, including our investments in fixed income securities, our cash and investments balance was $145.3 million compared to $177.3 million at September 30, 2014.

Our common shares outstanding at December 31, 2014, were 54.7 million consistent with September 30, 2014. Also, at December 31, 2014, there were 18,300 shares of preferred stock outstanding. These preferred shares are convertible into 4 million shares of common stock. Common shares outstanding including the conversion of our preferred shares would be 58.7 million.

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

Chris Anzalone

Thanks Ken.

We made substantial progress last quarter. As we look at calendar 2015, there are several key goals we hope to meet. They are:

1. Complete the Phase 2a single dose study of ARC-520 and discuss the 3 and 4 mg/kg data. We believe that will happen next quarter.
2. Complete the initial cohort of the US Phase 2b study of ARC-520 and escalate to a higher dose as necessary.
3. Fully enroll the initial 3-month portion of the Phase 2b studies of ARC-520 in Europe and Asia.
4. Begin long-term extension Phase 2b studies of ARC-520 in Europe and Asia. These are designed to go out as long as 9 months immediately after the 3-month lead in studies.
5. Begin exploratory combination studies with ARC-520.
6. Begin exploratory studies with ARC-520 at different dosing schedules.
7. Begin dosing the ARC-AAT Phase 1 study this month.
8. Complete dosing of healthy volunteers and patients in the ARC-AAT Phase 1 study.
9. Present data from the ARC-AAT Phase 1 study.
10. Launch a multiple dose Phase 2 study of ARC-AAT.
11. File an IND or equivalent for a 3d clinical candidate.
12. Nominate our first subcutaneous administration candidate or first extra hepatic candidate.
13. Expand our RNAi chemistry toolbox to broaden the ways we can achieve freedom to operate in additional indications and targets.

This is indeed an aggressive set of goals for calendar 2015, but we believe it is achievable. Watch our progress and monitor how we do against these. We commit to do our best to create value by achieving these goals and to communicate our progress regularly.

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

Operator

Operator opens the call to questions …