ARROWHEAD RESEARCH

3Q Fiscal 2014 Conference Call – Prepared Remarks

August 12, 2014

1:30 PM Pacific time

Operator

Ladies and gentlemen welcome to the Arrowhead Research fiscal 2014, third 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 2014 third quarter ended June 30, 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. 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.

The fiscal third quarter and recent period have been exciting and productive times for Arrowhead. We continue to push forward rapidly with our product development and pipeline expansion goals and now have two drug candidates in or approaching the clinic and a handful of other undisclosed programs that are progressing nicely.

Let's begin with our lead candidate ARC-520 for the treatment of chronic HBV infection. I'll provide some highlights and later in the call Bruce will provide more detailed information.

As you know, earlier this year we initiated a dose-finding Phase 2a study designed to inform a multi-dose Phase 2b study. Our two primary goals were to identify a dose that:

(a) induces a 90% reduction of circulating s-antigen after a single administration; and

(b) provides durable enough knockdown to enable once per month dosing.

Given our studies in multiple animal models, we were quite confident that we could achieve these but just did not know what that dose would be in humans.

Our interim results have been extremely exciting. We completed dosing of 1 and 2 mg/kg in June and though the study is still blinded, several exciting conclusions may already be drawn. We are seeing clear knockdown in both groups and duration of that knockdown has been substantially longer than we expected. We currently have data from the 2mg/kg cohort as far out as 2 months after dosing, and in the patients we perceive as having received ARC-520 we still see substantial knockdown at this timepoint. Interestingly, some of those patients may have s-antigen levels that are still declining. Safety profiles in both groups were also at least as good as those seen in the Phase 1 study.

Because of the favorable safety profiles in volunteers and patients and because we thought we could demonstrate even deeper knockdown, we decided to explore 3mg/kg in patients. We have begun dosing that cohort. We see substantial opportunity to demonstrate deep knockdown because of the steep dose-response curve observed in non-human primates. We also see limited downside risk at this dose because we completed 3mg/kg in healthy volunteers and that safety profile was quite positive, consistent with all other groups tested.

We view these emerging data from the Phase 2a study as very important for the HBV field, where, to my knowledge, clear and consistent reduction of s-antigen in humans have never been demonstrated. These preliminary data are also important in the broader RNAi field because they suggest a uniquely long duration of activity in humans. This not only speaks to the potential power of ARC-520, but also to that of future candidates built on the DPC platform. To this point, during the quarter we nominated our second clinical candidate using DPC delivery, ARC-AAT, and hosted an analyst day to present preclinical data.

ARC-AAT is designed to treat liver disease associated with a genetic disorder called alpha-1 antitrypsin deficiency, or AATD. This disease is characterized by the production of a mutant form of the enzyme alpha-1 antitrypsin that cannot be properly exported from hepatocytes. The non-mutant form, or native, alpha-1 antitrypsin protects lungs from inflammation, so AATD causes lung damage due to a lack of the native enzyme in circulation. It may also cause clinical liver disease because accumulation of mutant alpha-1 antitrypsin in hepatocytes can lead to cirrhosis and hepatocellular carcinoma. It is thought that there are approximately 100,000 people in the U.S. with the most severe form of AATD and while there are well-established therapies to treat the pulmonary sequelae, there are no approved therapies for liver disease associated with AATD. It is believed that stopping the production of mutant, un-exported enzyme will halt the progression of AATD-associated liver disease and reverse prior fibrosis associated with it. For these reasons, we believe this is a substantial unmet medical need that we can address effectively.

We have generated impressive data sets in animal models and are moving quickly toward the clinic. We are on track to file to commence clinical studies for ARC-AAT by the end of calendar 2014.

During the quarter we also announced that we signed an agreement with The Alpha-1 Project (or TAP), the venture philanthropy subsidiary of the Alpha-1 Foundation. Under the terms of the agreement, TAP will provide funding for the development of ARC-AAT, make its scientific advisors available to Arrowhead, assist with patient recruitment for clinical trials, and engage in other collaborative efforts that support the development of ARC-AAT. The Alpha-1 Foundation is an extraordinarily well-organized and sophisticated patient advocacy group, so we view TAP funding as validation for our program and gateway to an effective partner to our clinical program and ultimate product roll-out.

Overall, we continue to demonstrate rapid and effective execution of our product development programs and we have clearly made great strides in the recent period. Our clinical data are tracking our field-leading non-clinical data, and I believe we are increasing our first mover advantage in HBV. Similarly, we are well positioned as leaders in liver disease associated with AATD and I expect that advantage to continue.

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

Thanks Chris and good afternoon everyone. For those of us developing new platforms, there is nothing more exciting than taking them into humans for the first

time. ARC-520 is that product for us. As you know, that process started in normal volunteers last year. That study was designed to assess doses up to 2 mg/kg and was reported at the end of last year to show no premature discontinuations, no serious adverse events, similar rate and severity of mild or moderate adverse events for placebo and ARC-520 subjects and no laboratory or other safety parameters looking to us or the investigator like end-organ toxicity. We did note a flushing reaction at 0.6 mg/kg and an urticarial rash at 2 mg/kg, both in ARC-520 treated patients. Those seemed like histamine related events to us so we repeated the 2 mg/kg dose, but with pre-treatment with an over the counter oral anti-histamine. This dose cohort also went smoothly and no skin-related AEs were observed.

With this data in hand, we designed a first in patient study with chronic HBV patients in Hong Kong, where disease prevalence is high. The protocol doses were 1 and 2 mg/kg and this was our first opportunity to not only assess safety and tolerability in patients, but also to assess gene knockdown in patients. We wanted to isolate HBsAg as the parameter of interest, so we conducted this trial in patients negative for e antigen and on chronic entecavir therapy with undetectable circulating viral DNA. This is the first report of those results. As Chris mentioned, the trial is ongoing and still blinded.

As in the normal volunteers, the treatment has been well tolerated. There have been no dropouts, and no serious adverse events. The overall rate of AEs has been even lower than in the normal volunteers and nothing out of the ordinary has occurred. Safety labs continue to lack indication of end organ toxicity. These patients also received oral over the counter anti-histamine and no skin reactions have occurred.

While the trial is still blinded, we have been able to review anonymized profiles for individual surface antigen levels. The 1mg/kg dose showed clear activity at a modest level. We have surface antigen data for all patients in the 2 mg/kg dose group through 6 weeks and for 5 patients we have data through 8 weeks. Again with the caveat that the data are still blinded, we believe that knockdown is clearly deeper in this group versus 1mg/kg and at 8 weeks the patients we perceive as having received active drug show surprisingly large reductions in surface antigen. Overall, duration of knockdown appears to be substantially more sustained in humans compared to non-human primates we have studied at the same doses. However, depth of knockdown appears to be similar in magnitude with what we see in non-human primates at the same doses, including the HBV infected chimpanzee presented at AASLD last year. We think that we are right around the middle of the ascending part of the dose response curve at the 2 mg/kg dose.

When the surface antigen data started to emerge, we saw the potential to expand the dose-finding study and explore doses higher than 2 mg/kg in patients. In preparation for that, we enrolled a 3 mg/kg cohort in our still open normal volunteer study. This dose also performed well, without detected differences from safety and tolerability results at the other doses. Overall AEs do not appear to be increasing in frequency or severity with dose.

With this safety data in hand, as well as that from the Hong Kong patients, we amended the Hong Kong study to include a new 3 mg/kg cohort. This amendment has been approved by both Hong Kong site IRBs, and the study DSMB also recommended going forward. This cohort is now dosing.

So how should we think about these results? The dose range for knockdown in humans appears to be similar to that seen in non-human primates, including the

previously reported HBV-infected chimpanzee. In all of our animal species studied so far, the dose response curve for DPC assisted RNAi triggers has been steep. Assuming this holds for humans, and we think it will, the 3 mg/kg dose is likely to give deep knockdown. Given what we've already seen at 1 and 2 mg/kg, we would expect that knockdown to be prolonged well beyond 30 days and likely even longer than predicted by non-human primate models. This suggests that we will be able to explore dosing less frequent than once per month in the phase 2b.

We think these data bode well for our upcoming Phase 2b studies, which I want to talk about briefly. Our current plan is to initiate a study in the fourth quarter that will test two dose levels in e-antigen negative and e-antigen positive patients on entecavir or tenofovir. It will be multi-dose, placebo controlled study conducted in the United States, Western Europe, and Asia with a long-term extension. Our primary endpoint in the extension will be achieving a functional cure in patients, characterized by s-antigen clearance with or without seroconversion. We consider these our core or anchor Phase 2b studies. We also plan to initiate a number of smaller exploratory studies in 2015 including various dosing regimens and studies of ARC-520 in combination with immune stimulatory agents. The core Phase 2b and additional exploratory studies aim to provide us with a comprehensive understanding of ARC-520's activity in a broad range of settings, and we believe will allow us to expand our leadership position in HBV.

Let's now turn to ARC-AAT. As Chris mentioned, we have generated impressive non-clinical data. In animal models, ARC-AAT has been highly effective at knocking down the Alpha-1 antitrypsin gene transcript and reducing the hepatic production of the mutant AAT protein. In PiZ mice, which are genetically modified to produce the mutant human AAT, ARC-AAT induced a greater than 95 percent reduction in circulating AAT after a single dose. After eight weeks of

treatment in multi-dose studies, soluble (monomeric) and insoluble (polymeric) forms of Z-AAT were greatly reduced in the livers of PiZ mice treated with ARC-AAT. In addition, liver globule burden was substantially reduced from baseline levels and in comparison to treatment with saline, which showed progressive globule formation. In primate studies, which as discussed earlier appear to be predictive of the response in humans, knockdown of AAT in serum persisted for over ten weeks with greater than 80 percent knockdown still observed at the six-week time point. Keep in mind that AAT is produced extra-hepatically as well and ARC-AAT only targets that produced in hepatocytes, so what we observed likely translates into multi-log knockdown in the target hepatic cells.

We have initiated the final steps required to file for initiation of human dosing, including necessary toxicology studies.

With that update, I would now like to turn the call over to our CFO Ken Myszkowski to review our financials for the period. Ken?

Ken Myszkowski

Thank you, Bruce, and good afternoon everyone.

As we reported today, our net loss attributable to Arrowhead for the three months ended June 30, 2014 was $11.6 million, or $0.22 per share based on 51.9 million weighted average shares outstanding. This compares with a net loss attributable to Arrowhead of $6.1 million, or $0.23 per share based on 26.1 million weighted average shares outstanding, for the three months ended June 30, 2013.

Total operating expenses for the three months ended June 30, 2014 were $12.7 million, compared to $6.4 million for the three months ended June 30, 2013. Research and development related expenses were $6.4 million, while G&A costs were $1.6 million. The increase in operating expenses, compared to the prior year period, are due to the ARC-520 clinical trial, related on-going toxicology studies, and drug manufacturing costs in preparation for phase 2 clinical trials. Additionally, last quarter, we nominated ARC-AAT as a clinical candidate, and have incurred costs related to preclinical toxicology and manufacturing as we prepare to enter the clinic. We expect these expenses to continue to increase as ARC-520 enters phase 2b, a much larger clinical trial, and as ARC-AAT enters the clinic. In addition to outside costs related to clinical trials, operating expenses increased due to higher headcount, primarily research and development personnel, as compared to the prior year.

Net cash used in operating activities for the first nine months of fiscal 2014 were $24.5 million, compared with $13.6 million in the prior year period. The increase in cash used in operating activities is consistent with the change in operating expenses.

Turning to our balance sheet, our cash balance at June 30, 2014 was $138.3 million. Including short and long-term investments in fixed income securities, our cash and investments balance was $188.5 million at June 30, 2014, compared to $29.8 million at September 30, 2013. The increase reflects the financings completed in October 2013 and February 2014. Additionally, the Company received cash inflow of $12.4 million from the exercise of warrants and stock options.

Our common shares outstanding at June 30, 2014, were 52.9 million, and there were also 21 thousand shares of preferred stock outstanding. These preferred shares are convertible into 5.6 million shares of common stock. Common shares outstanding including the conversion of our preferred shares would be 58.5 million.

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

Chris Anzalone

Thanks Ken.

We have begun a very exciting phase, characterized by the transition from a science-based company that is full of promise to a drug company providing real benefits to patients. Until now, we have demonstrated exciting data in animal models – some of the most dramatic in the field – and a good safety profile in healthy human volunteers. We are now taking the next leap forward with ARC-520 by expanding the emerging positive safety profile in more patients and at higher doses, and generating knockdown data in patients. We are seeing unexpectedly durable knockdown in humans, reinforcing our belief that DPCs are best-in-class delivery for RNAi and suggesting that ARC-520 may ultimately be dosed less frequently than monthly. We are also seeing depth of knockdown that is similar to that predicted in animal models. This suggests that primates, and indeed mice, are good models for predicting dose and effect in patients for our technology. This is a critical insight that we expected, but could only confirm by observing knockdown directly in human subjects. This allows us to move forward with our entire R&D program with greater confidence and speed.

Our newly disclosed ARC-AAT program continues to move forward as expected, and the ARC-520 human data validate and de-risk it. We have executed on our goals during the quarter and are committed to continuing that in the periods ahead.

Some of our upcoming goals include the following:

- We will present additional clinical data on the Phase 2a study of ARC-520 around AASLD and additional nonclinical data on ARC-AAT through press release and at key scientific and medical meetings in the fourth quarter
- File in the fourth quarter to initiate first-in-man studies for ARC-AAT
- Also in the fourth quarter we plan to initiate the core Phase 2b studies of ARC-520
- Throughout 2015 we plan to initiate multiple pilot or exploratory clinical studies of ARC-520 to look at dosing schedules and combinations that may improve cure rates
- Also in 2015 we intend to nominate one or more additional clinical candidates, which we will talk more about in the future

So, as you can see, we're working on a lot of projects that we believe will add substantial value in the long-term as well as near-term.

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

Operator

Operator opens the call to questions …