ARROWHEAD RESEARCH

Fiscal 2015 Year End Conference Call – Prepared Remarks

December 14, 2015

1:30 PM Pacific time

Operator

Ladies and gentlemen welcome to the Arrowhead Research Corporation fiscal 2015, year-end 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 today to discuss Arrowhead's results for its fiscal 2015 fourth quarter and year ended September 30, 2015. With us today from management are president and CEO Dr. Christopher Anzalone, who will provide an overview of the year; 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.

During fiscal 2015 and the recent period, Arrowhead made dramatic progress with our clinical stage drugs, our rapidly expanding pipeline, and on the underlying technology platform that enables us to develop what we think are best in class RNAi therapeutics. We accomplished some important multi-year goals and before discussing some of the specifics, I want to spend a moment to provide context about how you should view the company now versus a year ago.

We have always said that a key benefit of developing a suite of RNAi therapeutics is that data and experience from each program can be leveraged to inform the development of new drugs. Each of these new drugs can potentially have progressively lower risk and a faster path from discovery to human trials if they are built on an underlying delivery platform that is validated in humans. Once this validation is achieved in one candidate, it may provide better certainty in future candidates. We believe that recent data on the ARC-520 drug candidate against chronic hepatitis infection validate our DPC™ delivery system and show definitively that we can achieve robust, well-tolerated knockdown of target genes.

So, what did we show?

As you probably know, we have been very active over the last few months discussing new data on ARC-520 and our growing HBV program. We hosted an analyst and investor day in September, presented data in several presentations at the AASLD Liver Meeting last month, and presented additional data during 2 presentations at the HEP DART conference last week. These presentations included data from the ARC-520 clinical program as well as from a multi-dose study in chimpanzees. These studies were going on in parallel, which allowed us to learn a lot about ARC-520 and the HBV viral lifecycle. Some of these new concepts challenge long held beliefs about HBV and, we believe, pushed the field forward.

First, from our clinical studies we showed that Arrowhead's proprietary DPC™ platform can consistently and deeply silence target genes in humans. In HBV E-antigen positive patients who were not previously on antiviral treatment, a single 4 mg/kg dose of ARC-520 showed reductions in circulating E-antigen of up to 98%

and reductions in Surface-antigen, or s-antigen, of up to 99%. For those who were around last year, you will remember that there was a commonly held view on Wall Street that a 1 log, or 90%, reduction in s-antigen would be seen as a positive result. We far exceeded that level.

The clinical study, combined with insights from our work in HBV-infected chimpanzees, also helped us to identify subpopulations of HBV patients based on relative levels of viral cccDNA versus viral DNA integrated into the host genome. Specifically, we learned that E-antigen negative patients and patients that have been on chronic therapy with nucleoside analogs, or NUCs, tend to have lower levels of viral cccDNA. We also learned that DNA that integrates into the patient's genome becomes a significant source of S-antigen production. ARC-520 was specifically designed to target all mRNA transcripts, and thus all proteins, produced by HBV cccDNA but not necessarily those produced by integrated DNA. We believe this is why we were seeing less S-antigen reduction in E-negative and treatment experienced patients. This was a key finding that helped to inform the direction of the program.

So, where does this position ARC-520 as a potential therapy of chronic HBV? Our data suggest that we could be very potent in e-antigen positive patients who have not been on long-term NUC therapy. This is a very large patient population. It is thought that this population makes up approximately half of chronic infections in the US about 1/3 in Europe. It is believed that Asian populations will be similar to the US in this respect, so taken together this represents a huge global population. If this were the only patient type that we could address and ARC-520 could enable consistent functional cures, it would represent an extremely large market opportunity for a company of any size. But we think ARC-520 has potential even outside this population.

Based on our clinical and chimp data, we would expect to moderately reduce s-antigen production after a single dose of ARC-520 and deeply suppress all other viral proteins in other populations. We have good data indicating very deep reductions of e-antigen and core-related antigen production, and we would expect this to carry over to x-antigen and other proteins. These viral proteins are all immunosupressive and involved in various parts of the viral life cycle. Deeply suppressing these, particularly over time under multiple dosing, could have destabilizing effects on the virus and help achieve functional cures. It is not unreasonable to expect that the virus requires production of at least some of these proteins to enable chronic infection and evasion of immune control. Therefore blocking them, as we have shown with ARC-520, could have important therapeutic effects.

What if we're wrong about this and ARC-520 is only capable of addressing, the admittedly large, population of e-antigen positive patients who have not been treated with NUCS? What about the rest of the market? We have nominated ARC-521 to address these other populations as an insurance policy for ARC-520 and to better ensure we can address more of the HBV market. ARC-521 targets both cccDNA and integrated DNA. Our chimpanzee study showed that in E-negative animals, predicted to have higher relative levels of integrated DNA, administration of the new RNAi trigger in ARC-521 led to a further 2 logs of S-antigen reduction. This served as a powerful proof of concept that between ARC-520 and ARC-521, we can potentially address all of the HBV market. We expect to file an IND or equivalent for ARC-521 by the middle of 2016.

Turning to our chimpanzee study, we believe this was the longest and most comprehensive study of chronically HBV-infected chimpanzees ever conducted.

The wealth of data that continues to emerge from that study has been invaluable to us as we plan and execute our HBV development programs, some of which we have discussed publicly and some we have not.

We have made multiple presentations on this study recently, but I want to highlight a key finding that we just discussed last week at the HEP DART conference. We found that after treating chronically-infected chimpanzees with between 6 and 11 monthly doses of ARC-520 in combination with nucleoside analogs, 7 of 9 chimpanzees showed signs of immune reactivation during the ARC-520 treatment phase. To review, the hepatitis B virus causes infected cells to produce several proteins that suppress the host immune system, and, therefore, enable chronic viral infection by removing immune control. Our goal with ARC-520 is to reduce expression of all those proteins and thereby enable reconstitution of the immune system. Our chimp data demonstrated that we can do this, and it is a real breakthrough. We consistently enabled immune reconstitution not by directly stimulating the immune system, which is challenging and carries with it ancillary risks, but by essentially turning off the virus. As we said in the press release announcing these data, this is a big deal.

This finding represents a strong proof of principle that ARC-520 can begin the process of waking up the immune system, even in those chimps without deep reductions in s-antigen, which can potentially lead to immune control and functional cures. We have been asked the question for the last few years, what evidence do you have that ARC-520 can consistently lead to a therapeutic immune response? Our answer was that it was a theory that made sense and many experts subscribed to, but we had no direct evidence…until now.

Between our extensive chimp data and our ongoing clinical data, we believe we have clearly established ourselves as leaders in HBV. Small biotech companies, at their best, strive to lead a field in the translation of science from the lab to development of new therapeutic agents. We are clearly doing that, but we are also leading the scientific community in understanding many aspects of the viral lifecycle, and that is uncommon. We have changed the HBV textbooks and this is important for the entire field and, of course, gives us tremendous ammunition in developing therapeutics that may lead to consistent functional cures. As I mentioned, we have discussed some of these data and some we have not. We have a clear lead in developing a potentially powerful therapeutic aimed at inducing functional cures, and our deep understanding of the virus helps us increase that lead.

So we have clear time, data, and knowledge advantages over our competitors, but safety has to be the overriding priority in any drug development. We must ensure that our products have an appropriate safety profile. Where do we stand on this? ARC-520 has now been given to over 100 people and we continue to see no signs of end-organ toxicity, we have had no discontinuations due to the drug, and have seen no adverse events rated as serious or severe. ARC-520 has been very well tolerated. I would put our safety profile up against any of our competitors in the HBV and RNAi fields. This has important ramifications not only for ARC-520, but any candidate that we develop using the same DPC. These include ARC-521, ARC-AAT, and ARC-F12. We see this as an important risk mitigator and, therefore, a significant value driver.

With these exciting data behind us, we now focus on our ongoing multiple-dose and combination Phase 2b studies. During 2015 we initiated five multiple dose studies of ARC-520 in the US, Europe, Asia, Australia, and New Zealand. Those

studies are Heparc-2002, 2003, 2004, 2008 also called the MONARCH study, and an open label extension to 2001. Bruce will discuss these during his clinical update.

Beyond ARC-520, it has been a similarly productive year for us in terms of platform development and pipeline expansion. On the platform front, we acquired Novartis' entire RNAi business. We anticipate this acquisition will provide us with expanded freedom to operate, proprietary technology that appears to enhance the activity of RNAi triggers, and license to non-delivery Alnylam RNAi IP for 30 targets. We now have additional flexibility to optimize each new candidate using the most effective RNAi-trigger design and modifications.

In terms of pipeline expansion, during 2015 we added multiple internal programs. We initiated a Phase 1 study of ARC-AAT against alpha-1 antitrypsin deficiency, or AATD, which is a rare genetic disorder that can lead to lung damage and liver disease. During the Phase 1 study we met a predetermined level of knockdown in healthy volunteers and transitioned the study to enroll patients with AATD. ARC-AAT was also granted orphan drug designation by the FDA this year.

Beyond our two clinical stage programs, we added and presented data on the following preclinical programs:

- As discussed earlier, ARC-521 is a new therapeutic in Arrowhead's HBV portfolio that was developed to target both cccDNA derived mRNA transcripts, like ARC-520, as well as those from HBV DNA that has integrated into the host DNA

- ARC-F12 that is designed to reduce the production of factor 12 with the goal of providing a prophylactic treatment for hereditary angioedema (or HAE) and thromboembolic diseases
- ARC-HIF2 that is designed to reduce the production of hypoxia-inducible factor 2 alpha, or HIF-2 alpha, to treat clear cell renal cell carcinoma. It is the first drug candidate using a new DPC™ delivery vehicle designed to target tissues outside of the liver
- And, ARC-LPA that is designed to reduce production of apolipoprotein A, or apo(a), a key component of lipoprotein(a), or Lp little a, which has been genetically linked with increased risk of cardiovascular diseases. ARC-LPA employs Arrowhead's new hepatic delivery format being developed for subcutaneous administration

We have clearly been very busy this year. So what does this mean for the company and for our shareholder going forward?

Arrowhead is a substantially more mature company from a development standpoint as well from an investment standpoint. Our pipeline is more diverse with an additional clinical program and multiple candidates progressing towards the clinic. Our underlying technology, the DPC^{TM} delivery systems, has achieved clinical proof of concept with ARC-520. We have expanded beyond just IV administered, liver targeted therapeutics and now have a subcutaneous candidate **and** an extra-hepatic candidate. Our toolbox of RNAi chemistries has expanded, giving us additional capabilities and flexibility.

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.

As Chris mentioned, we presented data on ARC-520 at multiple venues over the last few months. Those presentations are available on the Events page of our website if you would like more information, but let me take a moment to highlight some of the findings.

In the Heparc-2001 clinical study, 58 patients with chronic HBV received doses of between 1mg/kg and 4 mg/kg of ARC-520 in 7 cohorts. The cohorts varied by ARC-520 dose, E-antigen status, and prior NUC treatment status. The primary objectives of the study were to determine tolerability and to measure the depth and duration of surface-antigen reduction in response to a single dose, or two doses in the case of cohort 6, of ARC-520 in combination with entecavir. Arrowhead also assessed additional secondary and exploratory endpoints.

On the safety side, ARC-520 was well tolerated with no serious adverse events, no dose limiting toxicities, no discontinuations due to the drug, and a modest occurrence rate of AEs that were all deemed unrelated to study drug by the principal investigator. No AE occurred more than once. There was a low occurrence rate of abnormal laboratory tests, with no observed relationship to timing or dose. There were no laboratory changes believed to indicate drug toxicity.

On the activity side, surface-antigen was reduced substantially with a maximum reduction of 1.9 logs, or 99%, and a mean maximum reduction of 1.5 logs, or 97%,

in treatment naïve e-antigen positive patients in cohort 7. In addition, ARC-520 in combination with entecavir achieved maximum reductions of HBV DNA, E-antigen, and core-related antigen of 4.3 logs, or 99.995%, 1.7 logs, or 98%, and 1.2 logs, or 94%, respectively. So clearly, the drug has shown very good single dose activity.

Consistent with findings from our chimpanzee study, also presented at AASLD, variations in viral antigen reduction indicated that patients previously treated with chronic entecavir and patients that were treatment-naive and negative for E-antigen likely had lower levels of cccDNA derived mRNA transcripts. As such, E-antigen positive treatment naïve patients experienced a greater relative reduction in HBsAg than patients that were HBeAg-negative or treatment experienced.

We are now focused on our global multiple-dose and combination Phase 2b studies, which are currently enrolling patients. These studies are as follows:

(1) The 2002 study is testing ARC-520 + NUCS in NUC-experienced e-negative patients;
(2) 2003 is testing ARC-520 + NUCS in NUC-experienced e-positive patients;
(3) 2004 is our US-only study testing NUCS + ARC-520 in NUC-experienced e-positive patients;
(4) A 2001-extension study is open to patients that were treated in our single dose 2001 study. We will be testing ARC-520 + NUCS in e-negative and e-positive patients who are both NUC-experienced and NUC-naïve. Unlike 2002/3/and 4, this is open label so we have flexibility as to when we disclose data.

(5) The final study in the series is 2008, or our MONARCH study. Let me say a few words about this study which, as with the others, is currently enrolling patients.

We view this study as a test kitchen, of sorts, in which we intend to assess various dosing regimens of ARC-520 in combination with different agents. It has a flexible iterative design so we can ask specific questions about ARC-520 in small open-label cohorts and quickly initiate additional cohorts based on the answers that we get or the availability of new agents to be tested in combination. The goal of MONARCH is to identify the "recipes", if you will, that enable functional cures in patients.

Today, the test kitchen only has a few ingredients to work with: ARC-520, NUCs, and interferon. So the initial 6 cohorts that are enrolling now are looking at ARC-520 as monotherapy and in combination with NUCs and interferon. These cohorts are currently recruiting both E-antigen negative and positive treatment-naïve patients and are stratified by HBV genotype. Based on data recently presented at HEP DART, ARC-520 in combination with NUCs led to immune reactivation after multiple doses in 7 of 9 chimpanzees chronically infected with HBV. So, we are very eager to see results as they emerge from MONARCH and our other multiple dose studies. As mentioned, MONARCH is open label so we have flexibility as to when we disclose data.

As far as additional ingredients for the test kitchen, there are definitely some other interesting agents and mechanisms that, when ready, we would like to add to a MONARCH cohort. Stay tuned during 2016 on this front.

Lets now turn to ARC-521, the second drug in our HBV portfolio. As we've discussed, this drug takes the best RNAi trigger from ARC-520 that targets all transcripts produced by cccDNA and adds a second trigger that targets the s-antigen transcript produced by integrated DNA. We are currently conducting GLP toxicology studies and manufacturing the drug supply to support clinical studies that we plan to begin in 2016. While the study protocols are still being developed, I do want to mention that our intent is to have an accelerated Phase 1/2 development path that can hopefully get us to multiple dose data in patients rather quickly. Remember that we are using the exact same DPC™ delivery system as ARC-520 and our experience and that of the investigators who conducted ARC-520 studies suggest that the safety profile should support an accelerated path.

Let's now move to ARC-AAT, our drug candidate for the treatment of liver disease associated with a rare genetic disorder alpha-1 antitrypsin deficiency. We are conducting a Phase 1 single dose-escalation, first-in-human study to evaluate the safety, tolerability and pharmacokinetics of ARC-AAT and the effect on circulating AAT levels. The study has been enrolling in dose cohorts of six participants each, with participants randomized at a ratio of 2 active to 1 placebo to receive a single intravenous injection of either ARC-AAT or placebo. The study consists of two parts; Part A in healthy volunteers and Part B in patients with the PiZZ genotype of AATD. Part B is currently enrolling patients in Australia, Germany, U.K., and Netherlands. We will continue to dose escalate in patients until we believe that ARC-AAT is approaching maximal suppression of the AAT produced in the liver.

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 year ended September 30, 2015 was $91.9 million, or $1.60 per share based on 57.4 million weighted average shares outstanding. This compares with a net loss of $58.7 million, or $1.25 per share based on 46.9 million weighted average shares outstanding, for the year ended September 30, 2014.

Total operating expenses for the year ended September 30, 2015 were $96.4 million, compared to 53.5 million for the year ended September 30, 2014.

Net cash used in operating activities in fiscal 2015 was $65.7 million, compared with $35.4 million in fiscal 2014, an increase of $30.3 million, primarily due to higher R&D expenses of $24.1 million, reflecting higher drug manufacturing costs and higher clinical trial costs, on progress of ARC-520 and ARC-AAT. Additionally, our salary and compensation-related costs increased on higher headcount, and general and administrative costs increased as a result of higher outside professional services costs.

The change in operating expenses were additionally influenced by a charge of $10.1 million for acquired in-process research and development costs, a component of the accounting related to the Novartis acquisition.

Turning to our balance sheet, our cash and investments of cash were $98.8 million at September 30, 2015, compared to $177.3 million at September 30, 2014. The decrease in our cash and investments balance reflects the $65.7 million cash used in operating activities, as well as a $10 million cash payment related to the Novartis acquisition, and $2 million in capital expenditures.

For the quarter ended September 30, 2015, our cash used in operations was $12 million compared to $13.1 million during the quarter ended June 30, 2015, and cash used in operations of $16.4 million in the quarter ended March 31, 2015.

Our common shares outstanding at September 30, 2015, were 59.5 million, and would be 62.2 million, assuming conversion of preferred shares outstanding at September 30, 2015.

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

Chris Anzalone

Thanks Ken.

We feel very good about where we are today and we expect considerable progress over the next several quarters. We have been asked about capital needs, so I wanted to address that briefly here today. We are not prepared to give forward guidance on our cash burn since it will depend largely on the number, size, and speed of enrollment of clinical trials we have open at any given time. I would, however, like to go through a list of goals that we believe we will hit during

calendar 2016 and, based on our internal forecasting, can all be accomplished with the cash we currently have on hand.

These goals are:

1. Fully enroll the currently planned 6 MONARCH cohorts
2. Add new MONARCH cohorts
3. Enter into one corporate collaboration in MONARCH with a new compound for combination therapy
4. Complete enrollment of Heparc-2002
5. Complete enrollment of Heparc-2003
6. Complete enrollment of Heparc-2004
7. Complete enrollment of Heparc-2001 open label extension
8. File IND or equivalent for ARC-521
9. File IND or equivalent for ARC-F12
10. Complete Phase 1 study of ARC-AAT in healthy volunteers and patients
11. Initiate longer-term multi-dose study of ARC-AAT
12. Report additional preclinical data for ARC-LPA and ARC-HIF2

As you can see, we have many events over the coming year and beyond that are opportunities to drive substantial value creation for our shareholders.

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

Operator

Operator opens the call to questions …