ARROWHEAD RESEARCH

2Q Fiscal 2015 Conference Call – Prepared Remarks

May 11, 2015

1:30 PM Pacific time

Operator

Ladies and gentlemen welcome to the Arrowhead Research fiscal 2015, second 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 second quarter ended March 31, 2015. 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 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-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.

In review of the previous quarter and period since our last call, we are very pleased with the progress we've made on several fronts. I will cover a few of the highlights now and then turn the call over to Bruce Given, our chief operating officer and head of R&D, to discuss our clinical programs in more detail.

During the quarter we acquired Novartis' entire RNAi business. This portfolio of assets represents almost a decade of work by Novartis, and gives us some

important new capabilities. The portfolio includes multiple patent families covering RNAi-trigger design rules and modifications that we believe fall outside of key patents controlled by competitors. Combined with the chemistry portfolio constructed by Roche, we feel that we can work on any target and indication. In addition, Novartis discovered novel intracellular targeting ligands that can enhance the activity of some RNAi-triggers by targeting the RNA-induced silencing complex (or RISC) more effectively and improving stability once RISC is loaded. Think of these as sophisticated RNAi activity enhancers. Also included was an assignment of Novartis' license from Alnylam Pharmaceuticals granting Arrowhead access to Alnylam intellectual property, excluding delivery IP, for 30 gene targets already chosen by Novartis. And lastly, a pipeline of three candidates that were in active development and went through the rigorous Novartis vetting process.

View this acquisition, then, as the addition of new tools to our already substantial RNAi toolbox, and this feeds into our broad two-pronged philosophy. First, we want to have the freedom to address any target and indication from an IP standpoint. Second, we want to have access to as many RNAi trigger structures and modifications as possible in order to tune each candidate and employ the optimum chemistries on a candidate-by-candidate basis. When these two frameworks are substantially in place, a company shifts from developing the candidate it **can** make to developing the best possible drug for patients. That is where I believe we are and the Novartis acquisition contributes to this. We have already been working to integrate these assets into our development operation and, in fact, we are currently testing the Novartis chemistries to determine if they should be used in our most advanced pre-clinical programs.

Our research and early development groups have also made some important advancements in DPC technology and in some of our preclinical programs. We published a paper describing our next generation DPC constructs that use proprietary masking chemistries with increased stability and longer circulation times. These constructs have the added benefit of allowing conjugation of the RNAi trigger directly to the DPC. All of these changes are designed to enable both subcutaneous administration and extra-hepatic delivery, which would dramatically expand the universe of diseases that may be addressed by DPC-enabled RNAi therapeutics.

Last week we also presented preclinical data at the TIDES conference on ARC-F12, our potential new drug candidate targeting factor 12 mediated diseases such as hereditary angioedema and thrombosis. The studies we presented demonstrated that ARC-F12 achieved deep, dose dependent, and durable knockdown of the target gene in rodent and primate studies. In multiple-dose primate studies with IV administration once every four weeks, approximately 90% knockdown was achieved after the first dose and even greater knockdown following subsequent doses. In a relevant mouse model of thromboembolism, ARC-F12 showed a dramatic increase in occlusion times and appeared to protect against thrombus formation, or clotting. ARC-F12 appeared to be generally well-tolerated and no drug-related changes in toxicity markers were observed in these animal studies. We are in the process of conducting studies in additional models for hereditary angioedema, or HAE, to provide further data to decide if we will advance ARC-F12 as a clinical candidate and initiate IND enabling studies.

Patients with the rare genetic disorder HAE can experience recurrent and dangerous acute inflammatory attacks in multiple tissues, with attacks of laryngeal edema being particularly serious and potentially fatal. Currently approved

prophylactic treatments targeted toward HAE involve frequent intravenous dosing of 1-3 times weekly and many patients do not respond adequately, so we believe there is a great opportunity to develop an improved therapeutic that may only require dosing every 4 or 6 weeks.

Turning to our clinical programs, in February of this year we began dosing ARC-AAT, our clinical candidate for the treatment of liver disease associated with alpha-1 antitrypsin deficiency (or AATD). We announced last week that we had completed the healthy volunteer portion, or part A of the study, and that we had been cleared by the Data Safety Committee to transition the study into part B, which will be conducted in patients with AATD. This transition was triggered when a pre-defined knockdown target was achieved in cohort 3 of the study.

AAT is an endogenous gene, so healthy volunteers without AATD produce functional AAT that can be easily measured with a simple blood draw. These early results suggest that in humans we can knock down endogenous genes that are expressed in the liver. We have always been confident that this would be the case, but now we have clinical data to support it. This is very exciting and I believe another important validation for our underlying technology platform that may have far reaching implications as we continue to expand our pipeline. The planning and execution of this study by our clinical development team has been outstanding to date, and they are now working to get the patient portion of the study moving forward.

We also made good progress on the clinical program for ARC-520, our candidate against chronic hepatitis B infection. We had productive discussions with the FDA on our plans for a multi-dose study and received some valuable feedback about the program that has been incorporated in our plans for the U.S. as well as Europe and

Asia. In April, we gained clearance from the FDA to proceed with the Heparc-2004 clinical study with an initial dose of 1 mg/kg. We are pleased to be moving forward with that study here in the U.S., and expect that it will generate valuable data about ARC-520's activity in a multi-dose setting.

Thus, our multiple dose Phase 2b studies remain on track and we expect to begin dosing patients in the US this quarter. We also believe that we may begin receiving approvals to start international studies this quarter, with dosing likely beginning in the summer.

As we have said in the past, we are true pioneers in HBV. Everything we learn in clinical and non-clinical studies helps shape our strategy for the indication, and much of what we are doing represents firsts for the field. Of course this is extremely helpful to us, but it also introduces real questions relating to communication strategy in light of competitive considerations. We have been fairly quiet about the program since presenting early data at AASLD, which, I might add, was notable because only a single initial dose of ARC-520 elicited what we believe to be the first reliable report of significant s-antigen reduction in humans. This relatively quiet period does not mean that we were idle. To the contrary, we have been very busy and have learned a tremendous amount about ARC-520 and the hepatitis B virus. Here is what we are prepared to disclose at this time.

For the first time we can report that we have been conducting a long-term study of ARC-520 in 9 chimpanzees chronically infected with hepatitis B. It has been going on for about a year and is nearing completion. We believe this to be the largest and longest study ever conducted in chronically infected chimpanzees and certainly the most exhaustive study to date with ARC-520. We have generated a

large amount of very exciting data, and we are not yet finished. I believe this study will advance the entire field of HBV and it has been very important in advancing our understanding of how ARC-520 may fit into a treatment strategy.

The wealth of data the chimp study and single dose Phase 2a study have provided very important insights into the drug and disease, some of which challenge current dogma. To date we have not spoken publically about any of this chimp data. These studies have led to new hypotheses, and we have decided to test some of these new hypotheses in humans by adding 3 cohorts to the Phase 2a study in Hong Kong, which remains blinded. None of these employ doses greater than 4 mgs per kg, and two are open label while the third is a double blind placebo controlled cohort. These are important groups and we are very excited about completing them. We have said repeatedly in the past that this program would be iterative in nature and that we would follow the data. This is an example of that flexible stance. Unfortunately, because one of the new cohorts is placebo-controlled, this will mean pushing back unblinding of the entire study to next quarter rather than this quarter.

I appreciate that some will be disappointed that we are changing guidance for release of the 3 and 4 mg/kg results from 2nd to 3d quarter, but we did not anticipate expanding the Hong Kong study when we set that guidance. Our regulatory team and advisors agree that unblinding the study once all of the blinded cohorts have run their course is the prudent course of action under these circumstances to maintain the integrity of the studies in the eyes of the scientific community and international regulatory authorities. It is simply unwise, and frankly uncommon in the pharmaceutical industry, to unblind cohort-by-cohort without a compelling reason to do so, such as our decision to unblind the first two cohorts in preparation for an FDA filing. I strongly believe that our long term

chimp study will be considered seminal HBV work, and it has enabled us to build a more complete Phase 2a study in humans. This is all great news for the field and the Company, so a 1-quarter delay in data release is a small price to pay when we are focused on creating durable long-term value.

We will have a tremendous amount of data to report between the 7 cohorts of patients in the enlarged Phase 2a and the greater than 1-year study of 9 chronically infected chimps. Because of the quantity and importance of these data, we will have an analyst day next quarter to present the findings in detail. We plan on having not only our scientists participate, but also internationally recognized experts in the field. It will be an important event for us and I also believe it will be an important event for the entire HBV field.

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.

As you heard from Chris, our clinical development and regulatory teams have been very busy recently and are doing great work designing and managing our clinical studies. Chris touched on this, but I would like to talk for a moment about the Heparc-2001 study of ARC-520. As you recall, this was originally a single-dose Phase 2a study in e-antigen negative chronic HBV patients at two sites in Hong Kong. We previously reported initial results from the first two dose cohorts at 1 and 2 mg/kg, and as of our last quarterly conference call we had enrolled an additional two dose cohorts at 3 and 4 mg/kg. Observation periods are complete

for these, and the cohorts remain blinded. We have since made protocol amendments to add three additional cohorts, two of which have already received IRB approval to proceed, and we expect the third to be approved as early as this month. We have already enrolled and dosed 7 of 8 patients in the first new cohort and hope to dose the last patient shortly. The second additional cohort is recruiting patients now. Similarly, we expect the third new cohort to enroll at a good pace once IRB approval is achieved.

As you know, we unblinded the 1 and 2 mgs per kg cohorts early in order to support an IND and other regulatory filings for multiple dose Phase 2b studies. We expect to unblind the entire Phase 2a study, which will include the 3 and 4 mgs per kg cohorts as well as the additional blinded cohort, next quarter. We understand that many would like us to disclose data from the 3 and 4 mgs per kg cohorts now, and we would also like to be able to discuss those. However, unblinding cohorts for the sake of eager curiosity is not the right way to run a development program. This is a marathon not a sprint, and we need to ensure the long-term integrity of the program and studies that may ultimately support regulatory approval. We are committed to following GCP standards and regulatory norms in order to ensure as smooth a regulatory process as possible.

As Chris mentioned, we have already generated a great deal of information in the long-term chimp study and the now expanded Phase 2a that we believe will prove important for the HBV field. Once we are able to unblind the entire Phase 2a next quarter, we will have an in depth analyst day to discuss these data along side of the long-term chimp data. We expect to host internationally recognized KOLS as part of this event. Given the scope of the data, we believe that several important presentations and peer-reviewed articles will emerge from these studies, in addition

to what is reported at the analyst day. This will be an exciting time for us. Stay tuned.

Turning to the multiple-dose Phase 2b studies of ARC-520, we received clearance from the FDA to proceed with the Heparc-2004 study in the US. This is a multicenter, randomized, double-blind, placebo-controlled, multi-dose study of ARC-520 administered intravenously to patients with chronic immune active HBV infection maintained on entecavir or tenofovir therapy. The study is planned to enroll up to 12 patients who will be randomized at a ratio of 2:1 with 8 patients receiving 1 mg/kg of ARC-520 and 4 patients receiving placebo. Each patient will receive 3 total doses, once every 4 weeks. Patients will be followed through Day 147.

The primary objective of Heparc-2004 is to evaluate the depth of hepatitis B surface antigen decline in response to multiple doses of ARC-520 compared to placebo.

We intend to open three sites for enrollment. One site was opened for enrollment last week and patient screening has begun. Site initiation for the other two is scheduled for the coming weeks and then they may begin recruiting and screening patients.

As we have mentioned before, we still intend to proceed with additional core international multi-dose trials. We have incorporated the FDA recommendations, which were constructive and cost sparing to the program overall, into our international regulatory filings which have been submitted during the last couple of months. We are working diligently with regulators in select European and Asian

countries now, and we intend to provide an update publicly after we have been cleared to proceed.

We have also made great progress in a very short amount of time on our second clinical candidate, ARC-AAT against liver disease associated with alpha-1 antitrypsin deficiency (or AATD). In just over two months, we initiated a phase 1 study, completed enrollment and dosing of three ascending dose cohorts in healthy volunteers, collected follow up data, surpassed predefined knockdown targets, and have received Data Safety Committee approval to transition into patients with AATD. I want to applaud our clinical operations team for great execution and a successful start to this ground-breaking study.

We plan to conduct Part B of the study, which will recruit patients with PiZZ genotype AATD, in Australia and potentially other geographies. The site in Australia is on schedule to gain ethics approval to begin recruiting of alpha 1 patients in the next week or so and we hope to add 3-5 additional sites going forward. The protocol for part B is essentially the same as part A. It is a placebo-controlled, double-blind, single dose-escalation study to evaluate the safety, tolerability and pharmacokinetics of ARC-AAT and the effect on circulating alpha-1 antitrypsin levels in patients with alpha -1 antitrypsin deficiency. The study plans to enroll in dose cohorts of six participants each, with participants randomized at a ratio of 2:1 (active:placebo) to receive a single intravenous injection of either ARC-AAT or placebo. Dosing in patients with AATD will begin at 2.0 mg/kg of UNA and 1.0 mg/kg DPC, which was the highest dose level used in Part A, and then dose escalation will proceed according to the protocol. The study evaluates participants for 28 days following dosing, with additional follow-up if needed every 2 weeks until AAT levels return to baseline. We hope to complete the Phase 1 study by the end of 2015.

While I have presented a healthy amount of work for our clinical team, we are also starting to design the Phase 2, multiple-dose study of ARC-AAT and some of the Phase 2b combination studies of ARC-520, so stay tuned for more details about our plans later 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 Bruce, and good afternoon everyone.

As we reported today, our net loss for the three months ended March 31, 2015 was $28.7 million, or $0.51 per share based on 55.7 million weighted average shares outstanding. This compares with a net loss of $14.0 million, or $0.31 per share based on 44.3 million weighted average shares outstanding, for the three months ended March 31, 2014.

Net cash used in operating activities during the second fiscal quarter were $16.4 million, compared with $7.7 million in the prior year period and $24.2 million in the first fiscal quarter. Cash used in operating activities during the quarter of $16.4 million were primarily composed of research and development costs, mostly program costs for ARC-520 and program costs for ARC-AAT, as well as R&D salary and wages, and related discovery research costs.

Total operating expenses for the three months ended March 31, 2015 were $29.7 million, compared to $11.3 million for the three months ended March 31, 2014. The increase in operating expenses compared to the year ago period, are heavily influenced by a non-cash charge of $10.1 million for acquired in-process research and development costs, a component of the accounting related to the Novartis acquisition. Additionally, there were higher research and development expenses, primarily drug manufacturing costs which increased by $3.2 million during the period, mostly related to ARC-520, as well as higher clinical trial costs which increased $1.2 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 $2.9 million, while ARC-AAT clinical trial costs in the comparable period were minimal.

The primary drivers of the change in cash used in operating activities as compared to fiscal 2014 is consistent with the drivers of the change in operating expenses, aside from the $10.1 million acquired in-process research and development expense. The consideration provided for the acquisition of the Novartis assets was cash and stock. $25 million of stock was issued during the fiscal period, and $7 million in cash was paid during the fiscal period. $3 million was paid in April 2015.

Turning to our balance sheet, at March 31, 2015, including our investments in fixed income securities, our cash and investments balance was $128.4 million, a decrease of $16.9 million from December 31, 2014. Our cash and investments at September 30, 2014 were $177.3 million.

Our common shares outstanding at March 31, 2015, were 59.4 million, which increased from 54.7 million at September 30, 2014 primarily due to the issuance of

3.3 million shares for the Novartis asset acquisition. Also, at March 31, 2015, there were 15,652 shares of preferred stock outstanding. These preferred shares are convertible into 2.7 million shares of common stock. Common shares outstanding including the conversion of our preferred shares would be 62.1 million.

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

Chris Anzalone

Thanks Ken.

During our last conference call we set out a list of goals for calendar 2015. We are measuring our execution versus those goals, and our investors should too. We have already achieved three of the goals and are on schedule to reach several more. We still have a lot of work to do, but we believe the achievement of these goals, among others, will help to build long-term value for our shareholders.

There is a lot of exciting work going on at Arrowhead and the next several months are shaping up to be quite active indeed. We look forward to keeping you up to date on our progress and presenting data from the long-term chimp study and ARC-520 clinical program at a special analyst day next quarter.

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

Operator

Operator opens the call to questions …