ARROWHEAD PHARMACEUTICALS

Arrowhead Restructuring Call – Prepared Remarks

November 29, 2016

4:30 PM Pacific time

Operator

Ladies and gentlemen welcome to the Arrowhead Pharmaceuticals 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. We announced today that we are discontinuing development of product candidates that utilize the EX1 delivery vehicle, which includes ARC-520, ARC-521, and ARC-AAT. Arrowhead's president and CEO, Chris Anzalone, will talk about that decision and then we will open the call to questions. Also with us today for the Q&A are Bruce Given, our chief operating officer, Ken Myszkowski, our chief financial officer, and Patrick O'Brien, our general counsel.

Before we begin, I would like to remind you that comments made during today's call contains 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 statements regarding our expectations around the development, safety and efficacy of our IV drug candidates, projected cash runway, and expected future development activities. These statements represent management's current expectations and are inherently uncertain. Thus, actual results may differ materially. Arrowhead disclaims any intent and 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 subsequent quarterly reports on Form 10-Q for additional matters to be considered in this regard, including risks and other considerations that could cause actual results to vary from the presently expected results expressed in today's call.

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. We announced today that we are refocusing our development efforts on our subcutaneous and extra-hepatic delivery platforms for RNAi therapeutics and halting development of our intravenous-administered platform, called DPC_{iv} or EX1. As such, we are halting further development of our 3 clinical candidates: ARC-520, ARC-521, and ARC-AAT. Arrowhead is grateful to both the investigators and patients who have taken part in our clinical studies and

contributed to the significant increase in scientific understanding of hepatitis B infection as well as the potential for treating alpha-1 liver disease. We remain committed to finding therapeutic options for these patients and intend to continue to work to advance to the clinic our previously un-announced HBV and AAT programs using our subcutaneous delivery platform. As part of this transition, we are making the difficult decision to cut our clinical team and part of our R&D team. These changes will enable us to continue to move quickly with our subcutaneous and extra-hepatic programs and the partnerships that are based on them, while extending our cash runway into 2019. Let me now walk you through what led to these changes and what they mean for the company.

Let's start with the ARC-520, ARC-521, and ARC-AAT clinical programs. As we have previously reported, more than 300 patients and volunteers have received greater than 800 doses of EX1 across the 3 programs, at doses as high as 6 mg/kg. Three SAEs have been reported, only 2 of which were deemed drug-related, and we have seen good overall tolerability.

We have also seen good activity. For ARC-520, we previously reported reductions in surface antigen (or s-antigen) of almost 99%, or 2 logs, after a single dose. These remain exciting and unprecedented results for the HBV field. In subsequent multiple dose studies, for which data have not yet been reported, reductions of almost 3 logs were observed, with several patients appearing poised to possibly seroclear s-antigen, which would be a sign of functional cure. Needless to say, this would be a breakthrough for the field.

In addition, data presented earlier this month at The Liver Meeting® show that ARC-AAT achieved 90% knockdown of serum AAT in a Phase 1 clinical study,

which is believed to be near full suppression of liver production of the protein. ARC-521 was earlier in development, but activity levels were encouraging as well.

So what we had were clinical programs that were leading their fields, looked quite positive and we were working hard to move forward rapidly. Importantly, regulators had never expressed any concerns to us about our *clinical* data and to date that is still the case.

On November 8th, however, we received an oral notification from the FDA advising us that the Heparc-2004 study of ARC-520 was being placed on clinical hold in the United States. This was prompted not by observations from our clinical data of ARC-520, but rather by deaths at the highest dose of an ongoing non-human primate toxicology study that was being conducted to support long-term dosing using EX1. Because ARC-520, ARC-521, and ARC-AAT all use EX1, the findings in this toxicology study were reported to regulatory agencies globally with oversight for all of the programs. Across these three candidates, we had ongoing clinical sites and investigators in 17 countries.

We still have not received written notification from the FDA and do not yet have guidance about what might be required to remove its clinical hold. However, we have been in contact with regulators in all jurisdictions to address questions and provide information as needed.

As results have continued to emerge from the non-human primate toxicology study since the November 8th clinical hold and we've had the opportunity to consult experts regarding these results over the past several days, we have considered potential future mechanistic nonclinical studies that would need to be conducted to better understand the causality of the primate deaths. While a path forward has

been taking shape, it is becoming increasingly clear that the nonclinical studies required to test our hypotheses would be complicated, time-consuming, and expensive.

Why is that? We still do not know why some of the primates died at the highest dose, which, as we have said previously, is higher than human doses. Our hypothesis is that they were caused by dose related drug-induced toxicity exacerbated by extensive study-related handling procedures and infusion reactions for which the animals are not pre-treated, unlike patients and volunteers in our clinical studies who receive an oral antihistamine prior to treatment. Given time, we could test these hypotheses and possibly provide comfort to regulators, but risk to the company would still be high.

The primate study that prompted the FDA action had a 9-month in-life portion, so any study aimed at determining mortality causes would have to be at least this long. When adding time to plan the study, scheduling the study with an outside company, and analysis, we would not expect actionable results in less than 18 months. Even after this long delay, the possibility remains that the study could be inconclusive or fall short of satisfying the regulators in some way. This was our fear and, in fact, an expert toxicologist advised the company just yesterday that the standard of a new study would be high and that meeting it would be very difficult.

As such, the company believes it is prudent to discontinue development of ARC-520, ARC-521, and ARC-AAT. We will work together with investigators and clinical sites to ensure a smooth transition of study closure and patient medical care.

We will now focus entirely on our subcutaneous (or SubQ) and extra-hepatic programs. These include SubQ programs against HBV, AAT, Factor 12, ARC-Hif2, and several undisclosed subcutaneous and extra-hepatic programs. Of course, it also includes our programs partnered with Amgen, ARC-LPA and ARC-AMG1, which continue unaffected by our refocus of resources.

We sadly and reluctantly find ourselves turning away from a technology and set of products that we continue to see as ground-breaking and full of promise. However, sometimes it makes more sense to act quickly and move all resources behind a new platform rather than diluting human and financial capital by also supporting one with an unclear risk profile.

This is a pivot for us and we have the luxury of making this pivot because we are in advanced development with our SubQ and extra-hepatic platforms and because we have the capital to continue progress aggressively. We always recognized that our future was in addressing liver targets with subcutaneous formulations and going after extra-hepatic targets, so our exclusive focus on them represents a continuation of existing priorities. It is a natural transition now because our SubQ platform is capable of achieving similar results as the EX1-enabled iv system, with the added benefit of a more convenient mode of administration and expected improved safety margins.

In the past, we have discussed our SubQ platform primarily in the context of ARC-LPA and our partnership with Amgen. But most of our progress and initiatives on the platform have been undisclosed. For example, we recently presented encouraging ARC-LPA preclinical data at the American Heart Association conference but are now at least 2 generations beyond that and are seeing substantially more potency. These leaps forward are important because they

strengthen our partnership with Amgen and the resulting drug candidates; and they also strengthen the underlying SubQ platform which we use for internal programs as well as future partnered programs.

We are in advanced development in programs against Factor 12, HBV, and not far behind with AAT. We have talked about our Factor 12 program in the past but not specifically about the SubQ formulation. We had been developing that in parallel with the iv formulation and with the discontinuation of the EX1 program are close to declaring a SubQ lead.

We have had SubQ development programs for HBV for quite some time now and more recently for AAT. Internally, these were positioned as follow-on programs for the iv candidates that would leverage a more convenient mode of administration, and we should be close to declaring leads and moving toward IND-enabling studies. We have learned a lot during our prior HBV and AAT studies that will help us drive our SubQ programs efficiently.

Beyond our SubQ programs, we continue to be active in extra-hepatic delivery. We have discussed ARC-Hif2 and its hif 2 alpha target in the past and we continue to develop it and its underlying solid tumor targeting platform. We also have other non-oncology extra-hepatic programs that we have not yet announced. Progress has been rapid, so stay tuned for updates.

Until today, we were a company with 3 clinical programs and an R&D organization that was developing 3 broad platform classes. Unfortunately this is now changing. We will have a hiatus before returning to the clinic and require a smaller R&D force to drive our 2 remaining platforms. As such, we are reducing our workforce by approximately 30%. We will lose some great, loyal, and talented

people in this process, which is extremely difficult. This is, however, a necessary step to extend the runway of our current capital to a point where one or more of our pipeline products may be in the clinic. We have a plan in place to continue aggressive development of our SubQ and extra-hepatic platforms while stretching our current resources into 2019. Importantly, we will have undiminished bandwidth to effectively serve our current Amgen partnership, drive our internal programs, and work with potential new partners.

This is not a path we would have chosen, but one we can work with and through which we can create value. Of course giving up ARC-520, ARC-521 and ARC-AAT is painful because we see them as potentially break through products that have already established new standards in HBV and AAT. We are especially disappointed for the patients that we have worked so hard for over the last several years, and of course, those who have participated in our studies. We remain confident, however, that we will emerge from this as a stronger company on a more solid foundation and that we will ultimately be able to help HBV, AAT, and many other patients. The history of successful and ground-breaking biotech companies is seldom a straight line, so while we are disappointed about this regulatory set back, it does not diminish our drive to make Arrowhead a pioneer in the way many serious diseases are treated. This is our mission, and we have the technology, talent, experience, and capital to pursue it vigorously.

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

Operator

Operator opens the call to questions …