

ARROWHEAD PHARMACEUTICALS

Arrowhead/Takeda Collaboration Conference Call – Prepared Remarks

October 8, 2020

8:30 AM Eastern 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, I will give instructions on how to ask a question. 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 morning everyone. We are happy to announce today that Arrowhead and Takeda have signed an agreement whereby the two companies will co-develop and co-commercialize Arrowhead's investigational ARO-AAT candidate against alpha-1 liver disease. Our president and CEO, Dr. Christopher Anzalone, will provide an overview of the deal. James Hassard, our chief commercial officer, will discuss why we think Takeda is the ideal partner for ARO-AAT. And, Dr. Asit Parikh, head of Takeda's gastroenterology therapeutic area unit, will talk about why they are excited about ARO-AAT. We will then open up the call to your questions. Also with us today for the Q&A portion of the call are Ken Myszkowski, our chief financial officer, Javier San Martin, our chief medical officer, and Patrick O'Brien, our general counsel.

Before we begin, I would like to remind you that comments made during today's call 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 statements regarding our expectations around the development, safety and efficacy of our drug candidates, projected cash runway, and expected future development activities by Arrowhead or our partners. 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 Christopher Anzalone, President and CEO of the Company. Chris?

Chris Anzalone

Thanks Vince. Good morning everyone and thank you for joining us today.

Earlier today we announced that Arrowhead and Takeda signed an agreement to co-develop and co-commercialize ARO-AAT, our second generation investigational RNAi therapeutic being developed as a treatment for the rare genetic liver disease associated with alpha-1 antitrypsin deficiency.

Under the terms of the agreement, Takeda and Arrowhead will co-develop ARO-AAT which, if approved, will be co-commercialized in the United States under a 50/50 profit-sharing structure. Outside the U.S., Takeda will lead the global commercialization strategy and receive an exclusive license to commercialize ARO-AAT with Arrowhead eligible to receive tiered royalties of 20-25% on net ex-U.S. sales. Arrowhead will receive an upfront payment of \$300 million and is eligible to receive potential development, regulatory and, commercial milestones up to \$740 million.

We are thrilled to have Takeda as a partner for this program and believe that this structure provides the best opportunity for patients around the world to gain access to what we believe could be a first in class potentially important new medicine, while maximizing the probability of success for both companies. I want to talk briefly about the ARO-AAT program before discussing what the deal means to Arrowhead.

We have always been confident in the potential of the ARO-AAT program to help patients with alpha-1 liver disease, who currently have no approved therapies. Our preclinical data in the transgenic PiZ mouse, which recapitulates many aspects of human AATD-associated liver disease, showed that our RNAi-based intervention could achieve good target engagement and dramatically reduce the hepatic production of the mutant Z-AAT monomer. Sustained treatment in this model reduced hepatic Z-AAT polymer, restored endoplasmic reticulum and

mitochondrial health, normalized expression of disease-associated genes, reduced inflammation, and prevented tumor formation. Further, we found that young, middle age, and older mice all benefited from treatment, suggesting that there may be a broad range of patients for whom ARO-AAT may be helpful.

In addition to our preclinical work, the clinical program for ARO-AAT has given us increased confidence in its potential to help patients. Our Phase 1 study in healthy volunteers showed that ARO-AAT treatment led to a rapid reduction in circulating AAT levels with a duration of effect that should enable quarterly or less frequent dosing. In fact, most dose levels reduced circulating AAT to below the lower limit of quantitation, suggesting that it may have achieved near complete suppression of the liver production of the mutant protein. We think this is an important differentiator against other approaches that will likely not see the same level of activity. Our belief is that the closer you can get to full suppression of Z-AAT production, the higher the chance that the liver will be able to breakdown and clear the high levels of accumulated Z-AAT, which is the cause of progressive liver disease, and ultimately allow the liver to heal itself.

To that point, we recently announced interim 24-week liver biopsy results in four patients from the Phase 2 AROAAT2002 open-label clinical study. The results demonstrate what we believe to be important pharmacodynamic effects by ARO-AAT, leading to improvements in relevant biomarkers, including:

1. Substantial reductions in intra-hepatic mutant Z-AAT protein, both Z-AAT monomer and Z-AAT polymer;
2. Improvements in liver stiffness based on FibroScan; and,
3. A decrease in ALT and GGT, both serum biomarkers of liver injury.

These were extremely exciting results to us at Arrowhead as well as to Takeda, the investigators whose patients are participating in the study, and members of the Alpha-1 community. Based on these important data, we are actively assessing our clinical and regulatory path forward, including engaging with the U.S. FDA and other regulatory agencies to identify areas where the program could potentially be streamlined and accelerated. Our late-breaker abstract has been accepted, so we intend to present more details at the AASLD Liver Meeting in November.

So, even though our confidence in ARO-AAT has been high all along, our confidence level took a big leap forward when we saw the results I just mentioned. As such, it is clearly time to move forward with commercial planning.

Our broader strategic plan has always included a substantial commercial presence, and early this year, Jim Hassard joined Arrowhead as Chief Commercial Officer. As he has built out his team, we have been focused on determining markets where we want to commercialize drugs ourselves and where we want to co-commercialize with the right partners. Given the depth and breadth of our pipeline, this is at once an important and complicated set of decisions.

As we considered ARO-AAT, a few things became immediately clear. A global company that is in the AAT enzyme replacement business *and* has existing infrastructure, relationships, and deep experience in GI and other rare-diseases could be a powerful partner. Such a company could help maximize the value of ARO-AAT by helping to accelerate time to approval, enabling a faster and smoother launch, decreasing commercial costs by leveraging existing sales channels, and expanding the population of addressable patients. We think there is no partner in the world better suited than Takeda to help move ARO-AAT forward and bring it to the patients who need it. We also believe the deal structure reflects

the substantial amount of value we have created, and it gives Arrowhead and our shareholders an attractive share of the future economic opportunity.

Jim will discuss the strengths of Takeda as a partner in a moment, but I want to talk a bit more about the deal, why it's important for Arrowhead, and how it supports our strategic commercial focus areas moving forward.

First, I want to provide a little more color on the potential milestone payments associated with the deal. In addition to receiving \$300 million upfront, this deal potentially provides Arrowhead with a substantial amount of non-dilutive capital upstream of a potential approval and launch, and then, potentially an ongoing stream of revenue with the 50/50 profit sharing structure in the U.S. and 20-25% tiered royalties on sales outside the U.S. Approximately 40% of the \$740 million in potential milestones are for development and regulatory events that may be achievable in the near- to mid-term. That's an important point for Arrowhead, our balance sheet, and our need for outside capital in the future.

This makes our already strong financial position even stronger and further decreases our reliance on the capital markets to fund development of our platform and growing pipeline. Remember that we have partnerships with Amgen and Janssen that may also be sources of capital as products progress in clinical trials, and, similarly, may also be ongoing streams of revenue if the candidates are ultimately approved.

One of the big advantages of RNAi, and our TRiM™ platform specifically, is that it enables us to discover and develop a broad range of therapeutics against many different disease areas. We are RNAi specialists and clear leaders at bringing RNAi to diverse cell types, enabling us to address an increasing number of unmet

medical needs. Consequently, we are faced with a very good but challenging problem: how do we handle the sheer number of drug candidates we are generating from a clinical development and commercial standpoint? We expect there to be 10 TRiM™-enabled drug candidates in clinical trials by the middle of next year. We also expect to introduce 2 – 4 new candidates into clinical studies every year, so we could double that to 20 in 3 - 4 years. We have built a lot of value this way: I don't believe there is any company remotely our size that is building a pipeline even half as large and as potentially valuable as ours. Going forward, we will either have to slow down our pipeline growth or find good partners to help develop and commercialize some of our drug candidates. We obviously have no intention of doing the former.

This deal with Takeda is a good example of our limited partnering strategy. We expect ARO-AAT to be a substantially more valuable drug that helps more patients with Takeda as a partner. It is also a step in an ongoing process toward rationalizing our growing pipeline. We intend to find good partners for a limited number of TRiM™-enabled drugs and build a commercial organization that addresses multiple disease areas efficiently by focusing on synergy and leverage. As we look at our current and expected pipeline over the next couple years, we see attractive opportunities to build deep commercial expertise in cardiometabolic and pulmonary therapeutic areas.

That doesn't mean that all products in those areas will be developed commercially ourselves, and also that products not in those areas will be partnered. Rather, it should be viewed as our focus areas and what we will be building infrastructure to support in the near term. Given the broad potential of the TRiM™ platform and the fact that we expect to be able to address a new cell type every 18-24 months, we certainly expect this to expand in the future.

So, strategically, this deal with Takeda could not have come at a better time.

- The ARO-AAT program is moving toward commercialization rapidly
- Our cardiometabolic candidates, ARO-APOC3 and ARO-ANG3, are progressing towards Phase 2b studies and we are approaching clarity on what the pivotal studies may look like and when they may begin
- Our first pulmonary program, ARO-ENaC, is moving towards a potential data readout in the first half of 2021, with additional new pulmonary candidates behind it that are approaching clinical studies, and
- Our large and growing pipeline outside of those areas continue to provide additional opportunities to create value.

With that overview, I'd now like to turn the call over to James Hassard, our Chief Commercial Officer. Jim?

James Hassard

Thanks Chris. Good morning everyone and thank you for joining us today.

As Chris mentioned, Arrowhead is now at a point where we would need to move forward with commercial planning and buildout to support a future launch of ARO-AAT. We would need to do this in a way that is:

1. Cost effective;
2. Comprehensive; and,
3. Ensures the broadest patient access to this important new medicine.

We had already begun the analysis process and were developing a plan to accomplish these three priorities. However, the opportunity for Arrowhead and Takeda to co-develop and co-commercialize ARO-AAT in the U.S. provided an alternative to building and going alone. The opportunity for Arrowhead to profit-share 50/50 in the US and receive a healthy 20-25% royalty outside of the U.S., made this decision an easy one. Being able to leverage Takeda's resources allow us to accomplish all three priorities to a greater degree than we would have independently.

We are excited to collaborate with Takeda and leverage the deep expertise they have built within the clinical development, regulatory, and commercialization landscape in both Alpha-1 Antitrypsin Deficiency and Gastrointestinal diseases. We anticipate Takeda's global clinical development and regulatory expertise may also help facilitate expedited registration for ARO-AAT in the US and abroad.

Takeda's global medical affairs organization is well-positioned to provide critical disease state education around the severe unmet need of AATD-associated liver disease. As with other rare diseases without approved therapies, Alpha-1 liver disease is often undiagnosed or misdiagnosed. Takeda's proven ability to educate physicians and its long-standing relationships make them very effective at this critical function.

Due to their robust rare disease portfolio and years supporting the Alpha-1 community, Takeda also brings significant experience working with payers and stakeholders in order to navigate the orphan drug pricing landscape, drive product differentiation, and pursue label expansion, ensuring optimal patient access globally.

Arrowhead will be able to leverage Takeda's global footprint, strong relationships, and promotional reach in the US and outside of the US to support rapid and competitive commercialization. If approved, ARO-AAT will join Takeda's global commercially available products, including Glassia® Aralast® and Entyvio® and their growing GI pipeline. So clearly Takeda is invested and committed to these areas and has a proven track record of success.

With that overview, I'd now like to turn the call over to Dr. Asit Parikh, Takeda's head of gastroenterology therapeutic area unit. Dr. Parikh?

Asit Parikh

Thank you Jim and the Arrowhead team for having me on the call to represent Takeda.

We are very excited about the ARO-AAT program, and we are thrilled to sign this agreement to co-develop and co-commercialize ARO-AAT with Arrowhead. What drew us to Arrowhead and the ARO-AAT program were primarily three things:

1. Patients suffering from Alpha-1 antitrypsin deficiency-associated liver disease (AATLD), a devastating genetic condition, have no approved therapies for their progressive liver disease.
2. Our deep expertise developing and launching GI therapies which includes the chronic liver disease space. Moreover we also have world class expertise in AAT related plasma-derived therapies ; and,

3. The impressive data generated for ARO-AAT clearly demonstrate that it reduces the production of mutant Z-AAT protein in the liver, which strongly supports its potential to treat the underlying cause of AATLD.

To expand a bit on my three points: This collaboration reinforces Takeda's commitment to the Alpha-1 community as it complements our expertise discovering and developing groundbreaking therapies like Glassia® and Aralast®, which are indicated for chronic augmentation therapy in adults with clinically evident emphysema due to alpha-1 antitrypsin deficiency.

Liver disease is a rising area of strategic importance for Takeda. We are currently focused on the development of therapeutics for late-stage liver fibrosis including cell transplantation, complications of end-stage liver diseases, and select monogenic liver diseases. Arrowhead's platform is a powerful way to achieve gene knockdown in the liver. This collaboration is a very good fit for us at Takeda as it takes us into a new therapeutic modality to achieve a strategic aim.

We will work swiftly and with great purpose to build on Arrowhead's progress toward our shared goal of one day bringing ARO-AAT to patients. We greatly look forward to working with Arrowhead as a partner.

I will now turn the call back to Chris.

Chris Anzalone

Thanks Asit. We appreciate you being here today.

To recap what we have all said today, we are very excited about this partnership. It fits with our strategic priorities, it provides significant capital immediately and potentially in the near- to mid-term, it allows us to retain substantial long-term economics for a product that we believe shows great promise to address a serious disease, and we believe it brings a partner to the table that is better-positioned than any other company to support a global launch and ensure broad patient access. This is truly a win-win-win deal, where both companies and the patients we serve all benefit.

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

Operator

Operator opens the call to questions ...