Zacks Small-Cap Research

February 11, 2016
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Arrowhead Research (ARWR-NASDAQ)

ARWR: New data presented for ARC-520, multiple Phase IIb studies initiated, new candidate nominated--- maintaining Buy

Current Recommendation	**Buy**
Prior Recommendation	N/A
Date of Last Change	06/11/2013
Current Price (02/10/16)	$3.21
Twelve- Month Target Price	**$10.00**

OUTLOOK

ARWR is a clinical stage biotech company focused on RNAi targeted therapy using DPC platform technology. We are optimistic about the Company's lead program ARC-520 for HBV.

ARC-520 is in five Phase II trials and a new HBV candidate ARC-521 added to the HBV program. The Company also initiated Phase I trial of its second clinical candidate ARC-AAT for liver disease and expanded its pipeline. The acquisition of Novartis' RNAi assets expands and complements its current RNAi estate.

We maintain our Buy rating on its shares.

SUMMARY DATA

52-Week High	**$8.00**
52-Week Low	**$3.18**
One-Year Return (%)	**-49.68**
Beta	**2.15**
Average Daily Volume (sh)	**951,820**
Shares Outstanding (mil)	**60**
Market Capitalization ($mil)	**$190**
Short Interest Ratio (days)	**15.11**
Institutional Ownership (%)	**N/A**
Insider Ownership (%)	**N/A**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2013 Estimate	**N/A**
P/E using 2014 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**High,**
Type of Stock	**Small-Growth**
Industry	**Biotechnology**
Zacks Rank in Industry	**N/A**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2015	0.17 A	0.04 A	0.12 A	0.04 A	0.38 A
2016	0.04 A	0.04 E	0.04 E	0.04 E	0.16 E
2017					0.50 E
2018					5.00 E

Earnings per Share
(EPS is operating earnings before non recurring items)

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2015	-$0.37 A	-$0.50 A	-$0.27 A	-$0.51 A	-$1.64 A
2016	-$0.32 A	-$0.35 E	-$0.37 E	-$0.40 E	-$1.45 E
2017					-$1.51 E
2018					-$1.23 E

Zacks Projected EPS Growth Rate - Next 5 Years % **N/A**

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WHAT'S NEW

Arrowhead Exited Fiscal 1Q16 with A Strong Balance Sheet

The company reported total revenue of $43,750 for the three months ended December 31, 2015, compared to total revenue of $170,750 for the same period of 2014. Revenue is primarily related to licensed technology in both periods.

R&D expenses were $10.3 million for the fiscal 1Q16 ended December 31, 2015, as compared to $17.7 million for the same period of 2014. The decrease was primarily due to reduced drug manufacturing and clinical trial costs.

SG&A expenses were $5.9 million for the fiscal 1Q16 ended December 31, 2015, as compared to $5.2 million for the same period of 2014.

Adjusted net loss for fiscal 1Q16 was $19.3 million ($0.32 per share), as compared to net loss of $20.0 million ($0.37 per share).

As of December 31, 2015, Arrowhead has $76.6 million in cash and investment, which can support the company's operations into fiscal 2017.

In addition to the balance sheet, our focus is also on the progress the company has made to advance its clinical programs.

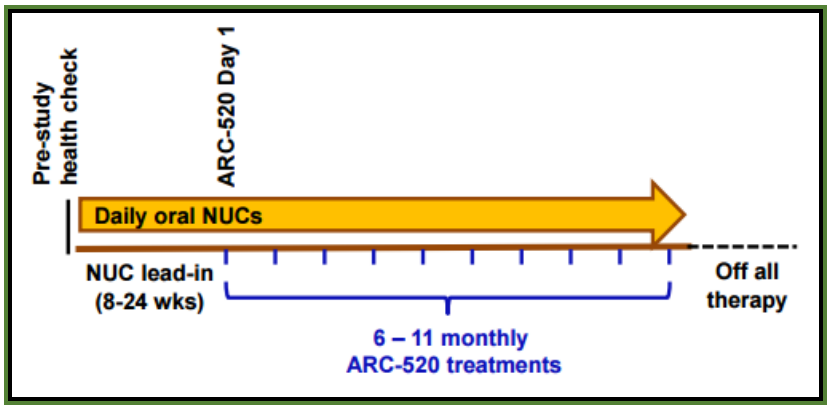
Update on ARC-520 Chimpanzees Study

On December 7, 2015, Arrowhead presented chimpanzees data of ARC-520 at HEP DART 2015.

The Chimpanzee Study

The study included nine chimpanzees (5 males, 4 females; 9-37 years-old) chronically infected with HBV. Deep sequencing and phylogenetic analyses indicated that the HBV sequence is a chimpanzee variant of human HBV. At start of study, five chimps were HBeAg positive (HBeAg+), baseline DNA 8-9 log10 IU/mL serum; and four were HBeAg negative (HBeAg-), baseline DNA ≤3 log10 IU/mL. HBsAg levels ranged from 250-3190 µg/mL in HBeAg+ chimps and from 1.2-200 µg/mL in HBeAg- chimps.

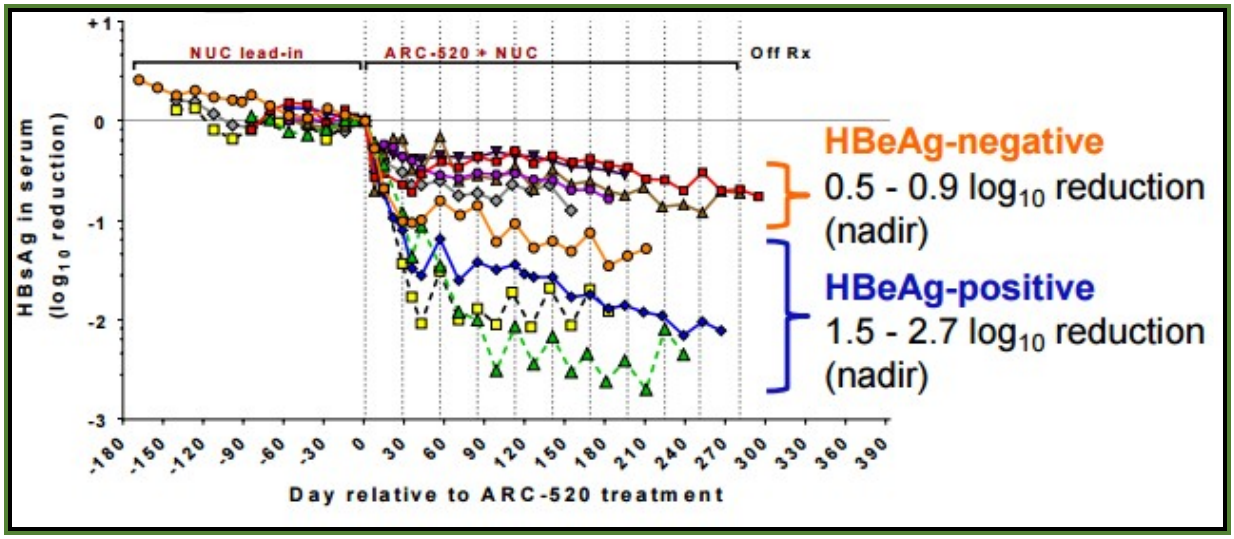
To reduce viral replication prior to treatment with ARC- 520, chimps were treated for 8-24 weeks with entecavir (ETV) or in one case (chimp Michele) with ETV+ tenofovir (TDF). Following the NUC lead-in period, animals were administered ARC-520 intravenously at 4- week intervals (q4w). Dose levels were 2, 3, or 4 mg/kg ARC-520, along with maintenance doses of ETV or ETV+TDF. Chimps were monitored for up to 31 weeks off all treatment.



The Data

Data showed that NUC only therapy had minimal effect on serum HBsAg levels while ARC-520+NUC demonstrated deep reduction in HBsAg levels. HBsAg was reduced at nadir in HBeAg+ chimps by 2.1 log10 (avg.) and in HBeAgchimps by 0.7 log10 (avg.) by treatment of NUC+ARC-520. Serum HBsAg was deeply reduced in HBeAg+ chimps, less so in HBeAg- chimps.

Molecular biology approaches were used to elucidate the differences in HBV biology in the HBeAg+ vs. HBeAg- chimps. The HBeAg+ chimps had high levels of cccDNA in the liver, whereas almost all the HBV DNA in the liver of HBeAg- chimps (95%) appeared to be integrated.

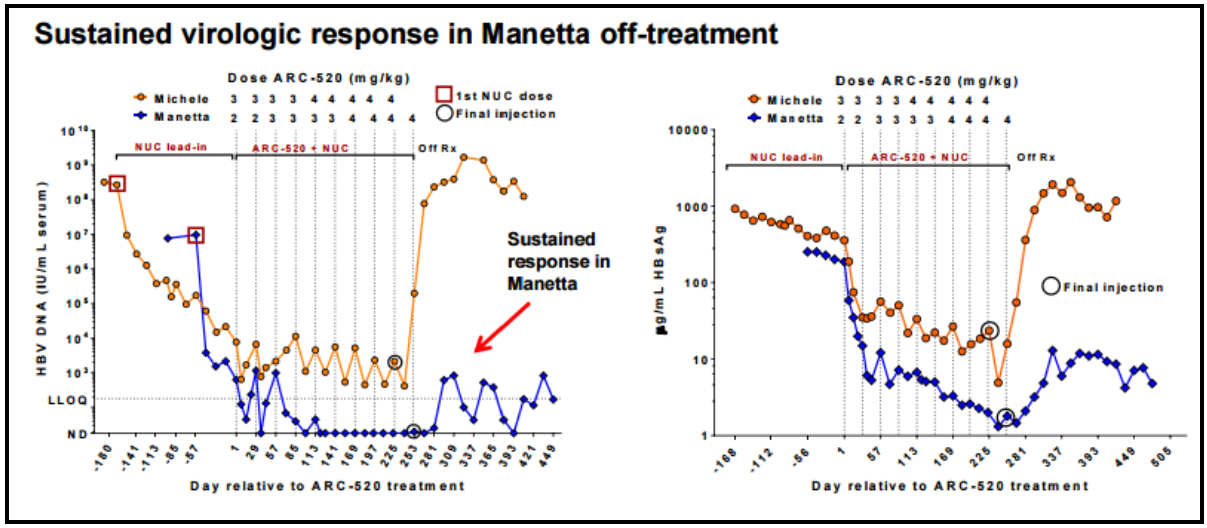


Specifically, two HBeAg positive chimps, Manetta and Tattoo, seroconverted for HBeAg.

Chimp Manetta exhibited deep decreases in HBV DNA, RNA and viral proteins during ARC-520/NUC treatment. The sustained induction of CXCL9 in Manetta was associated with a therapeutic ALT flare (218 U/L) followed by HBeAg seroconversion. Sustained virologic improvements were still observed 31 weeks after all treatment was removed. At this final time point, serum HBV DNA was 5 log10 lower, HBsAg was 1.7 log10 lower, and liver HBV RNA was 99% lower than pre-study.

Tattoo had decreasing levels of HBeAg prior to and during NUC lead-in. Anti-HBe first detected 28 days prior to 1st ARC-520 injection. HBeAg lost following 1st ARC-520 dose and was sustained off-therapy.

8 out of 9 chimps exhibited episodes of serum cytokine CXCL9 elevation. For 7 chimps these occurred during ARC-520 treatment and in one chimp (Tattoo) these coincided with seroclearance of HBeAg that began prior to study. In Manetta and Michele, IFN-gamma induction on ARC-520 treatment was followed by induction of chemokines CXCL9 and CXCL10.



HBV suppresses the immune system to allow chronic HBV infection. Interferon gamma (IFN-γ) is a key antiviral cytokine critical to innate and adaptive immune responses. IFN-γ produced by natural killer cells and natural killer T cells induces the chemokines CXCL9 and CXCL10 to mediate a T-cell response. An elevation of CXCL9 in the chimps studied is a promising sign of immune system reactivation.

Our Takeaway

We are impressed by the data presented at HEP DART 2015 showing that in chronically HBV-infected chimpanzees treated with ARC-520 **in combination** with nucleoside analogs, 7 of 9 (78%) exhibited signs of immune reactivation, which is likely a necessary step for achieving a functional cure of chronic HBV. One chimpanzee also exhibited an on-treatment therapeutic ALT flare and sustained virologic improvements 31 weeks off all treatment.

The higher response rate is a big deal. We believe the elevations in T-cell responsive serum cytokines observed in this study represent a strong proof of principle that ARC-520 can begin the process of immune reconstitution that can lead to functional cure.

These data are particularly encouraging when combined with the recent **Phase IIa** human data of ARC-520. The Phase IIa data showed that ARC-520 can dramatically reduce s-antigen, e-antigen, and core-related antigen in humans after a single dose.

New Findings from the Ongoing ARC-520 Phase IIa HBV Study

The Background

The Phase IIa trial **(Heparc-2001)** began doing patients on March 24, 2014 in Hong Kong. The ongoing Phase IIa is a randomized, double blind, placebo controlled study. The original trial plan was to enroll patients in three dose cohorts (1, 2, and 3 mg/kg) with patients receiving either ARC-520 or placebo **in combination with entecavir**. The trial expanded into four doses (1, 2, 3, and 4 mg/kg) in 7 cohorts later with the last three cohorts in HBeAg positive patients. Patients are randomized to placebo or ARC-520 at a ratio of 1:3 and continue daily entecavir. **Primary endpoints** will be safety and tolerability as well as depth and duration of surface antigen knock down. Patients will be followed until surface antigen levels return to baseline.

Cohort	Prior NUCs?	Pat Type	ARC-520 dose	Active	Placebo	Status
1	Yes	HBeAg neg	1.0 mg/kg	6	2	Complete/Unblinded
2	Yes	HBeAg neg	2.0 mg/kg	6	2	Complete/Unblinded
3	Yes	HBeAg neg	3.0 mg/kg	6	2	Complete/Unblinded
4	Yes	HBeAg neg	4.0 mg/kg	6	2	Complete/Unblinded
5	Yes	HBeAg pos	4.0 mg/kg	6	2	Complete/Unblinded
6	Yes	HBeAg pos	2 x 2.0 mg/kg	6	0	Ongoing/Open label
7	No	HBeAg pos/neg	4.0 mg/kg	6 pos/6 neg	0	Ongoing/Open label

New cohorts

Updated Data Presented at AASLD

In November 2015, Arrowhead presented updated data from the above **Phase IIa** clinical study at The AASLD Liver Meeting 2015.

In the clinical study, 58 patients with chronic HBV received doses of 1mg/kg - 4 mg/kg of ARC-520 in 7 cohorts. The cohorts varied by ARC-520 dose, HBeAg status, and prior NUC treatment status. The primary objective of the study was to measure the depth and duration of HBsAg reduction in response to a single dose or two doses (cohort 6) of ARC-520 in combination with entecavir. Arrowhead also assessed safety and tolerability and additional secondary and exploratory endpoints.

In this presentation, Dr. Yuen and co-authors showed that in the Heparc-2001 clinical study, ARC-520 in combination with entecavir achieved maximum reductions of HBsAg, HBV DNA, HBeAg, and core-related antigen (HBcrAg) of 1.9 logs (99%), 4.3 logs (99.995%), 1.7 logs (98%), and 1.2 logs (93.7%), respectively.

HBeAg-positive, treatment naïve patients achieved consistent reductions in HBsAg with a mean maximal reduction of 1.5 logs (96.8%). ARC-520 caused a direct antiviral effect after a single dose that was still evident after 57 days, which was the last time-point available.

Consistent with findings from the chimpanzee study, HBeAg-positive treatment naïve patients experienced a greater relative reduction in HBsAg than patients that were HBeAg-negative or treatment experienced. One transitional patient in cohort 7 was HBeAg-positive at baseline and became HBeAg-negative at days 3 to 43. This patient experienced an intermediate response initially, however HBsAg continued to trend downward through day 57, the last time-point available.

The explanation: NUC treatment and HBeAg loss are associated with sharp reduction in cccDNA. As cccDNA is reduced, integrated DNA emerges as unexpected source of persistent HBsAg production.

Since ARC-520 is specifically designed to silence cccDNA, it shows deep knockdown of cccDNA derived gene products such as HBeAg. However, ARC-520 would not be expected to silence most integrated-derived HBsAg. NUC-naïve HBeAg-positive patients are expected to be richest in cccDNA.

ARC-520 was well tolerated with no serious adverse events (AE), no dose limiting toxicities, no discontinuations due to medication AEs. A modest occurrence rate (23%) of AEs were all deemed unrelated to study drug. No AE occurred more than once. There were no AEs amongst 10 patients receiving placebo. There was a low occurrence rate of abnormal laboratory tests, with no observed relationship to timing or dose.

The rationale for testing ARC-520 in HBeAg positive patients is based on **Chimp study** we discussed above. Clearly, from these chimp data and the data from the ARC-520 Phase IIa trial, ARC-520 seems to work better in the HBeAg positive subjects.

New Development Plan for the HBV Program

Based on the chimp data and data from the Phase IIa trial, Arrowhead updated its new development plan for its HBV program.

ARC-520 will continue development including focus on the significant market of **e-antigen positive**, **treatment-naïve** chronic HBV patients.

The company plans to initiate **Phase IIb** trial **Heparc-2008** (**Monarch cohorts**). The MONARCH study is a multicenter, open-label study to evaluate ARC-520 administered alone and in combination with other therapeutics in patients with chronic hepatitis B virus infection. The primary outcome measure is the percentage of patients achieving a 1-log reduction in hepatitis B surface antigen (HBsAg) compared to baseline. Secondary outcome measures include the percentage of patients achieving HBsAg loss and time to HBsAg loss based on qualitative assay, percentage of patients achieving anti-HBs seroconversion and time to anti-HBs seroconversion (antibody to HBsAg), percentage of patients achieving a 1-log reduction in HBsAg and achieving a HBsAg level less than 100 IU/L, as well as other outcome measures.

The initial **six cohorts** are each planned to consist of up to twelve treatment naïve patients. Patients in cohort 1 will receive ARC-520 as monotherapy once every 4 weeks for 48 weeks (13 doses). Patients in cohorts 2-6 will be stratified by e-antigen status and HBV genotype. They will receive the same regimen of ARC-520 for 48 weeks in combination with daily entecavir for 60 weeks and pegylated interferon alpha 2a (PEG IFN) for 48 weeks. MONARCH is designed to allow for new cohorts to be added that test additional dosing regimens and different combinations as new agents become available for study.

On Jan 7, 2016, the company dosed the first patient in the Phase IIb MONARCH combination study of ARC-520 for the treatment of chronic HBV infection. The clinical trial is currently enrolling patients at multiple centers in Australia and New Zealand. This study is intended to identify one or more combinations of ARC-520 and other therapeutic agents that can potentially lead to a functional cure of chronic HBV.

We expect to see deep knockdown of all gene products, especially in HBeAg positive patients.

It is estimated in the U.S. that 95% of people chronically infected with HBV are currently NUC-naïve and at least 50% of them are likely to be HBeAg-positive. In West Europe, 90% of estimated CHB patients are naïve, and about 33% of them are HBeAg positive. The effect on HBsAg in NUC-naïve HBeAg-positive patients makes this group especially attractive to study and a key focus for multi-dose studies going forward.

Arrowhead also has nominated a new candidate **ARC-521,** which is being developed to target both cccDNA and also integrated DNA, which appears to be a more significant producer of HBsAg in patients who have been treated with NUCs or who are **e-antigen negative**.

ARC-521 is also derived from the company's DPC platform; therefore, its safety profile is expected to be similar to ARC-520. While ARC-520 is designed to target cccDNA, ARC-521 is designed to target both cccDNA and integrated DNA. Therefore, ARC-521 is a complement to ARC-520.

In HBeAg-negative chimps predicted to have higher levels of integrated DNA, administration of ARC-521 led to 99% (2 logs) of additional HBsAg reduction. The Company expects to file an **IND** or equivalent for ARC-521 by **mid-2016.**

Update on Phase IIb of ARC-520 for HBV

The Heparc-2004 Study

In April 2015, the FDA cleared the multiple-dose **Phase IIb** clinical study of ARC-520 for the treatment of chronic hepatitis B infection.

The clinical study, titled **Heparc-2004**, 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 (HBsAg) decline in response to multiple doses of ARC-520 compared to placebo in patients with chronic, immune active HBV infection as a measure of drug activity. **Secondary objectives** are to measure safety and tolerability and pharmacokinetics of ARC-520, and to evaluate the effect of ARC-520 on entecavir or tenofovir pharmacokinetics, in addition to other exploratory safety and pharmacodynamic objectives.

Originally, Arrowhead proposed a **parallel design** multiple-dose **Phase IIb** study testing doses of 2 mg/kg and 4 mg/kg simultaneously. However, in January 2015, the FDA placed a partial clinical hold on the program. In order to proceed with the proposed parallel design study, the FDA requested that the Company provide additional information including data from the single-dose Phase IIa study in patients who receive 1-4 mg/kg ARC-520, data from an ongoing multiple-dose non-clinical study, and data from Heparc-2004 which is now cleared to begin.

The Heparc-2002 and Heparc-2003 Study will Continue

During the summer of 2015, ARC-520 was approved in **Germany and Hong Kong** for two additional **Phase IIb** multiple-dose studies, which will be conducted **in parallel**.

The two studies (**Heparc-2002** and **Heparc-2003**) will enroll patients with chronic HBV infection that are e-antigen (HBeAg) negative and HBeAg positive, respectively. Each study is a multicenter, randomized, double-blind, placebo-controlled, multi-dose study intended to evaluate two dose levels in parallel of ARC-520 in combination with entecavir or tenofovir in patients with immune active chronic HBV infection. The 2002 trial will enroll up to 60 and the 2003 will enroll 90 patients. In each study, patients will be randomized to receive four doses, once every 4 weeks, of either 1 mg/kg ARC-520, 2 mg/kg ARC-520, or placebo at a ratio of 1:1:1.

Per protocol, for each patient, the duration of the study is approximately 33 weeks, from screening to the Day 169 follow-up visit. For each study, a planning interim analysis will be performed when 54 patients have completed their Day 71 visit. This analysis will be used to plan future studies only and will not impact the enrollment or conduct of Heparc-2002 and -2003. Based on the interim results, the company will decide whether higher multiple-doses would be likely to lead to increased activity, in which case higher doses may be evaluated in one or more additional studies.

The **primary objective** of the 2002 and 2003 studies is to evaluate the depth of hepatitis B surface antigen (HBsAg) decline in response to multiple doses of ARC-520 compared to placebo as a measure of drug activity. **Secondary objectives** include the assessment of safety and tolerability and multi-dose pharmacokinetics of ARC-520 when co-administered with entecavir or tenofovir, in addition to other exploratory objectives.

In addition, the company is engaged with regulatory authorities from South Korea to open additional sites for these studies.

Update on the ARC-AAT Program

In late February 2015, Arrowhead initiated a **Phase I** clinical trial of ARC-AAT for the treatment of liver disease associated with Alpha-1 Antitrypsin Deficiency (AATD) in **Australia**.

The Phase I trial is a multi-center, randomized, placebo-controlled, double-blind, single dose-escalation study to evaluate the safety, tolerability, pharmacokinetics of ARC-AAT and the effect on circulating alpha-1 antitrypsin (AAT) levels. 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 (normal saline). The study will consist of **two parts**, with **Part A** planned to be conducted in healthy volunteers and **Part B** planned to be conducted in patients with PiZZ genotype AATD. In Part A, dose escalation will proceed until the achievement of certain target knockdown parameters. That target is at least 30% reduction of serum AAT levels in 3 subjects or greater than 60% reduction in a single subject. When these AAT knockdown parameters are achieved, dose escalation in healthy volunteers (Part A) is planned to stop and dosing in patients with AATD (Part B) is planned to begin at the highest dose level used in Part A and then dose escalation will proceed. Participants will be evaluated for 28 days following dosing with additional follow-up every 2 weeks until AAT levels return to baseline.

Part A of the study in healthy volunteers has dosed up to 5 mg/kg and is not precluded from going higher. In early July 2015, Arrowhead began dosing the first patient in Part B of the Phase I clinical trial. It is likely that Part A in healthy volunteers will complete before Part B in patients, so the company may report top-line data from Part A **later in the year** and prior to Part B. The timing of this release will depend on the number of dose levels that the company decides to study.

While the Phase I continues, Arrowhead is also preparing to begin a pilot **Phase IIa** multiple dose study. This study will look at the effect on circulating levels of AAT after multiple doses of ARC-AAT. The company also intends to take biopsies to determine the effect on the hepatocyte level. This study should get underway this year.

ARC-AAT has been granted orphan drug designation (ODD) by both the FDA and the European Medicines Agency.

Arrowhead has signed an agreement with the Alpha-1 Project (TAP), a subsidiary of the **Alpha-1 Foundation**. Under the terms of the agreement, TAP will partially fund the development of ARC-AAT. In addition to the funding, TAP will make its scientific advisors available to Arrowhead, assist with patient recruitment for clinical trials thanks to the Alpha-1 Foundation Patient Research Registry, and engage in other collaborative efforts that support the development of ARC-AAT.

ARC-AAT is Arrowhead s second clinical candidate, which further de-risks its pipeline. In the absence of specific therapy other than liver transplant for AATD associated liver disease, we believe RNAi holds great potential.

Pipeline further Expanded by New Candidates

In September, 2015, Arrowhead nominated **ARC-HIF2** as its first therapeutic candidate delivered using a new Dynamic Polyconjugate™ (DPC™) designed to target tissues outside of the liver. Arrowhead believes that ARC-HIF2, which uses RNA interference to silence transcription factor hypoxia-inducible factor 2α (HIF-2α), is a promising new candidate for the treatment of clear cell renal cell carcinoma **(ccRCC).**

ARC-HIF2 is designed to inhibit the production of HIF-2α, which has been linked to tumor progression and metastasis in ccRCC. Using ARC-HIF2 in a preclinical ccRCC tumor model, mice treated with weekly injections led to greater than 80% knockdown of HIF-2α mRNA in tumors. Furthermore, tumors from treated mice exhibited statistically significant reductions in size and weight, extensive tumor cell death,

reduction in the tumor-expressed VEGF-A biomarker, and destruction of the blood vessels feeding the tumors.

The company presented positive preclinical data at the European Cancer Congress 2015 (ECC2015) in Vienna on September 27 in a poster titled "HIF-2α targeting with a novel RNAi delivery platform as therapy for renal cell carcinoma," (abstract #353).

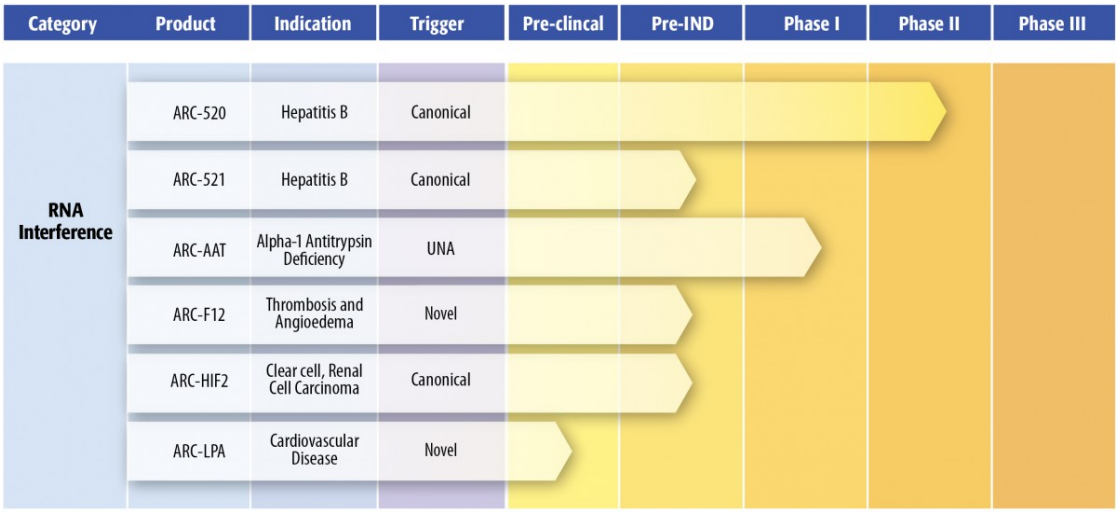
The company is in the process of manufacturing scale up to allow for initiation of IND-enabling studies. Timing for anticipated regulatory submission will be announced in the future.

In October 2015, Arrowhead presented data from a new program, **ARC-LPA**, which is designed to reduce production of apolipoprotein A (apo(a)), a key component of lipoprotein(a) (LPa). LPa has been genetically linked with increased risk of cardiovascular diseases, independent of cholesterol and LDL levels.

Using a new **subcutaneous delivery** construct that Arrowhead has developed, an initial lead compound has achieved up to 90% knockdown of apo(a) in mice.

Arrowhead is also developing a preclinical program **ARC-F12** for hereditary angioedema.

With a platform technology, we believe the pipeline can be further expanded with ease.



We Remain Bullish on Arrowhead's Shares

We maintain our Buy rating on Arrowhead shares, but reduce our 12-month price target to $10 from previous $15 due to the current market condition.

Arrowhead has been busy in 2015 to move forward with its clinical programs. We believe the company's lead HBV program ARC-520 is a viable drug for chronic HBV patients and the addition of ARC-521 further expands its HBV franchise.

In the area of HBV therapy under development, we think Arrowhead is substantially ahead of its competitors. The company's ARC-520 has the strong advantage of positive data from the long term chimp study and dozens of patients. ARC-520 also has a favorable safety profile. Given the 5 ongoing Phase II studies, we believe that if a breakthrough in HBV is going to occur in the next 12 months it should come from Arrowhead.

The acquisition of Novartis' RNAi development portfolio significantly expands and complements the company's current RNAi assets and will provide the opportunity to rapidly expand its clinical pipeline in the coming years.

Arrowhead has a strong balance sheet. As of December 31, 2015, the company held $76.6 million in cash and investment, which can support the company's operations into fiscal 2017 according to our financial model.

We believe current market price of Arrowhead shares does not reflect the intrinsic value of the company.

Based on the current development plan, we expect Arrowhead will be able to initiate **pivotal Phase III** trial of ARC-520 in late 2016 or early 2017, and data should be available in late 2017. NDA could be filed in late 2017, and the FDA approval is in late 2018 or early 2019.

We estimate Arrowhead will become profitable in fiscal 2019 with an EPS of $0.68 based on revenue of $210 million. We think a P/E ratio of 30x is appropriate for Arrowhead considering its growth in the next few years. Based on this P/E multiple, we think Arrowhead should be valued at $10.00 per share using 25% discount for 3 years. Our price target values Arrowhead at $600 million in market cap, which we think is appropriate and fare compared to its peers.

We think ARC-520 is the primary value driver in near- and mid-term for Arrowhead. The successful development of ARC-520 is critical to Arrowhead because the HBV market offers opportunities for substantial revenues, and because validation of the Company's RNAi delivery technology opens broad opportunities both for other therapeutic programs and licensing opportunities.

In this regard, the ongoing Phase IIa study and the initiation of the multiple Phase IIb studies of ARC-520 represent an important milestone for Arrowhead in achieving its long term growth goal. One of the attractive features of RNAi and of DPCs specifically is once the safety profile in man for the delivery system has been established; additional targets and candidates can be studied rapidly. Therefore, the Phase II trials of ARC-520 will provide the company with the data needed to accelerate the development of its pipeline and bring additional candidates into the clinic.

PROJECTED INCOME STATEMENT

	2015 (Sept)					2016 (Sept)					2017 (Sept)	2018 (Sept)	2019 (Sept)
$ in millions except per share data	Q1	Q2	Q3	Q4	FYE	Q1	Q2	Q3	Q4	FYE	FYE	FYE	FYE
Revenue	$0.17	$0.04	$0.12	$0.04	$0.38	$0.04	$0.04	$0.04	$0.04	$0.16	$0.50	$5.00	$210.00
YOY Growth						-	-	-	-	-	*205.3%*	*900.0%*	*4100.0%*
Total Revenues	**$0.17**	**$0.04**	**$0.12**	**$0.04**	**$0.38**	**$0.04**	**$0.04**	**$0.04**	**$0.04**	**$0.16**	**$0.50**	**$5.00**	**$210.00**
YOY Growth	*297.1%*	*0.0%*	*182.9%*	*-1.7%*	*118.3%*	*-74.4%*	*-8.6%*	*-67.7%*	*-8.6%*	*-57.1%*	*205.3%*	*900.0%*	*4100.0%*
Cost of Revenue	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.1	$0.8	$29.4
Gross Income	**$0.2**	**$0.0**	**$0.1**	**$0.0**	**$0.4**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.2**	**$0.4**	**$4.3**	**$180.6**
Gross Margin	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*85.0%*	*85.0%*	*86.0%*
R&D	$17.7	$21.8	$7.5	$10.4	$57.4	$10.3	$12.5	$14.5	$17.0	$54.3	$75.0	$55.0	$60.0
% R&D	*10392.0%*	*49791.0%*	*6052.8%*	*23752.8%*	*15028.8%*	*23631.6%*	*31250.0%*	*36250.0%*	*42500.0%*	*33184.0%*	*15000.0%*	*1100.0%*	*28.6%*
Salary and G&A	$5.2	$5.2	$5.4	$8.6	$24.5	$5.9	$6.5	$7.0	$7.5	$26.9	$30.0	$37.5	$50.0
% SG&A	*3067.0%*	*11973.2%*	*4363.6%*	*19680.4%*	*6409.7%*	*13420.6%*	*16250.0%*	*17500.0%*	*18750.0%*	*16410.1%*	*6000.0%*	*750.0%*	*23.8%*
Other expenses	$2.3	$2.7	$3.2	$4.4	$12.6	$3.2	$2.5	$2.5	$2.5	$10.7	$8.5	$10.0	$12.0
% Other	*1349.9%*	*6067.7%*	*2607.8%*	*10017.0%*	*3290.3%*	*7256.4%*	*6250.0%*	*6250.0%*	*6250.0%*	*6518.9%*	*1700.0%*	*200.0%*	*5.7%*
Operating Income	**($25.1)**	**($29.6)**	**($16.0)**	**($23.3)**	**($94.1)**	**($19.3)**	**($21.5)**	**($24.0)**	**($27.0)**	**($91.7)**	**($113.1)**	**($98.3)**	**$58.6**
Operating Margin	-	-	-	-	-	-	-	-	-	-	-	-	*27.9%*
Other Income (Net)	$2.5	$0.9	$0.1	($5.4)	($1.9)	$0.1	($0.2)	($0.2)	($0.1)	($0.4)	($0.5)	($0.5)	($0.5)
Pre-Tax Income	**($22.6)**	**($28.7)**	**($15.9)**	**($28.8)**	**($96.0)**	**($19.3)**	**($21.6)**	**($24.2)**	**($27.1)**	**($92.1)**	**($113.6)**	**($98.8)**	**$58.1**
Net Taxes (benefit)	$0.0	$0.0	$0.0	($4.0)	($4.0)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	*0.0%*	*0.0%*	*0.0%*	*14.0%*	*4.2%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Reported Net Income	**($22.6)**	**($28.7)**	**($15.9)**	**($24.7)**	**($91.9)**	**($19.3)**	**($21.6)**	**($24.2)**	**($27.1)**	**($92.1)**	**($113.6)**	**($98.8)**	**$58.1**
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	-	-
Net Margin	-	-	-	-	-	-	-	-	-	-	-	-	-
Weighted avg. Shares Out	*54.7*	*55.7*	*59.5*	*59.5*	*57.4*	*59.5*	*62.0*	*65.0*	*68.0*	*63.6*	*75.0*	*80.0*	*85.0*
Reported EPS	**($0.41)**	**($0.51)**	**($0.27)**	**($0.42)**	**($1.60)**	**($0.32)**	**($0.35)**	**($0.37)**	**($0.40)**	**($1.45)**	**($1.51)**	**($1.23)**	**$0.68**
YOY Growth	-	-	-	-	-	-	-	-	-	-	-	-	-
One-time charge	$2.54	$0.95	$0.06	($5.44)	($1.89)	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00
Non GAAP Net Income	**($20.0)**	**($27.7)**	**($15.9)**	**($30.2)**	**($93.8)**	**($19.3)**	**($21.6)**	**($24.2)**	**($27.1)**	**($92.1)**	**($113.6)**	**($98.8)**	**$58.1**
Non GAAP EPS	**($0.37)**	**($0.50)**	**($0.27)**	**($0.51)**	**($1.64)**	**($0.32)**	**($0.35)**	**($0.37)**	**($0.40)**	**($1.45)**	**($1.51)**	**($1.23)**	**$0.68**

Source: Company filing and Zacks estimates

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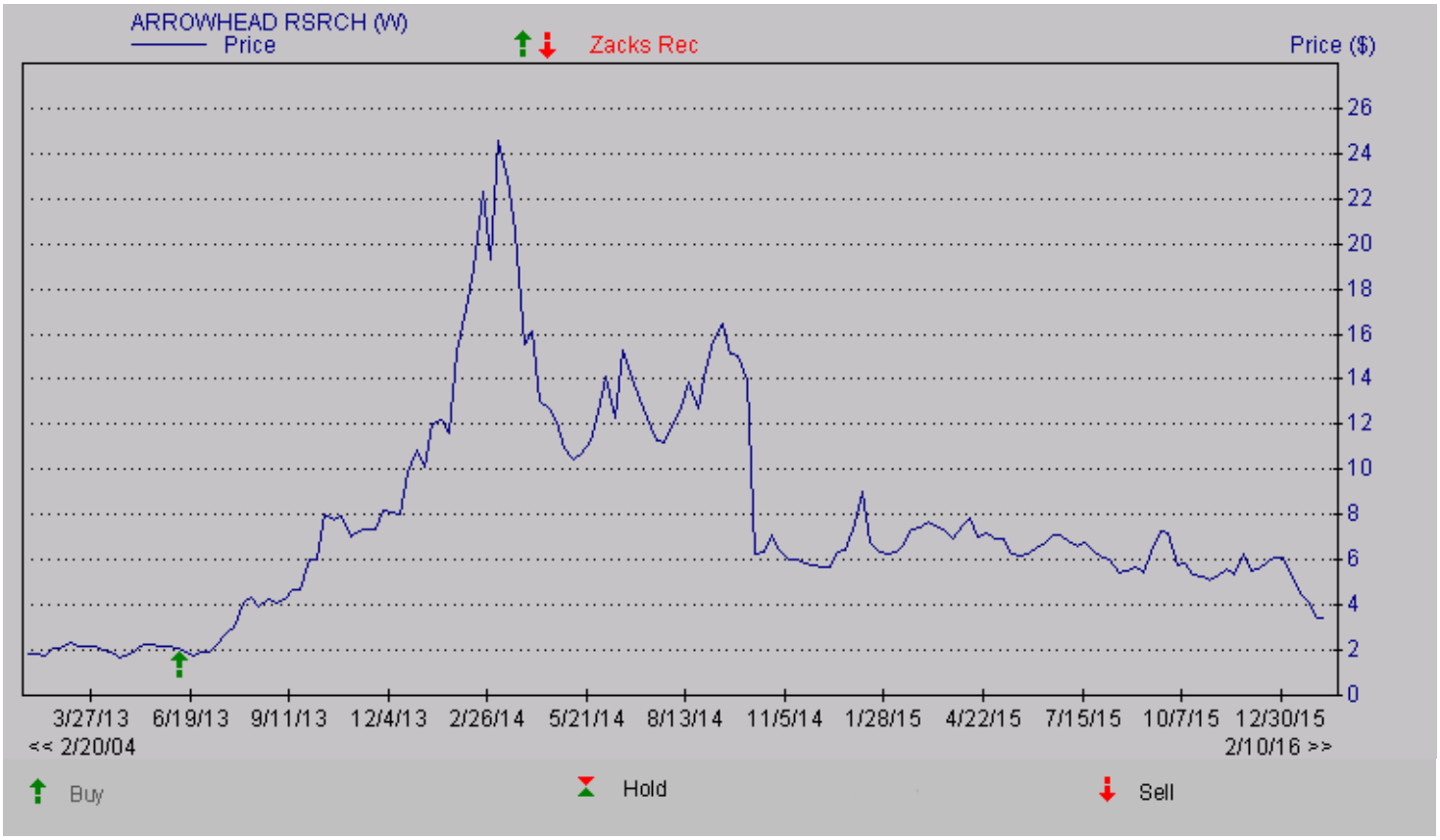

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