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Arrowhead Pharmaceuticals, Inc. (ARWR-NASDAQ)

ARWR: Biopsy Data from ARO-AAT Trial Before Year End 2020…

Based on our probability adjusted DCF model that takes into account potential future revenues from the company's development products, ARWR is valued at $58/share. This model is highly dependent upon the continued clinical success of those programs and will be adjusted accordingly based upon future clinical outcomes.

Current Price (08/10/20)	$40.23
Valuation	**$58.00**

OUTLOOK

On August 5, 2020, Arrowhead Pharmaceuticals, Inc. (ARWR) announced financial results for the third quarter of fiscal year 2020 and provided a business update. The company has completed dosing in the first cohort of patients in the AROAAT2002 study and collected the first 6-month repeat biopsy. We anticipate this data being announced before the end of 2020. Arrowhead received a $20 million milestone payment from Amgen following dosing of the first patient of AMG 890 in a Phase 2 trial. Dosing has also been completed in AROHSD1001, a Phase 1/2 clinical trial of ARO-HSD, which is being developed as a treatment for liver diseases such as NASH.

SUMMARY DATA

52-Week High	**$73.01**
52-Week Low	**$20.56**
One-Year Return (%)	**38.49**
Beta	**1.77**
Average Daily Volume (sh)	**949,811**
Shares Outstanding (mil)	**102**
Market Capitalization ($mil)	**$4,115**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**64**
Insider Ownership (%)	**4**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**362.7**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2020 Estimate	**-92.9**
P/E using 2021 Estimate	**-41.2**

Risk Level	**Average**
Type of Stock	**Large-Growth**
Industry	**Med-Drugs**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2019	34.7 A	48.2 A	42.7 A	43.3 A	168.8 A
2020	29.5 A	23.5 A	27.4 A	20.6 E	101.0 E
2021					73.2 E
2022					50.0 E

Earnings per Share

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2019	$0.13 A	$0.24 A	$0.21 A	$0.11 A	$0.69 A
2020	-$0.03 A	-$0.20 A	-$0.15 A	-$0.15 E	-$0.51 E
2021					-$0.74 E
2022					-$1.04 E

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WHAT'S NEW

Business Update

Arrowhead Pharmaceuticals Inc (ARWR) is developing medicines that cause gene silencing using RNA interference (RNAi), a specific means of inhibiting the expression of genes and stopping the production of a specific protein. The company has a deep and diverse pipeline consisting of the following development product candidates, including eight in-house programs and three partnered drugs, two with Johnson and Johnson (JNJ) and one with Amgen (AMGN).



Source: Arrowhead Pharmaceuticals, Inc.

Update on ARO-AAT

This is the company's second generation, subcutaneously administered RNAi therapeutic being developed as a treatment for the rare genetic liver disease, alpha-1-antitrypsin (AAT) deficiency. This program was granted Fast Track status by the FDA in June 2019 (which was in addition to Orphan Drug designation in the U.S. and E.U. granted in early 2018).

The company is currently conducting the SEQUOIA Phase 2/3 trial and the AROAAT2002 open label study. The 2002 study has now been fully enrolled, dosed, and six-month repeat biopsies have been performed for the first cohort of patients. We expect this biopsy data to be presented before the end of 2020. This data will represent the first biopsy data for a therapeutic targeting AAT deficiency, and while an effect on AAT monomer level is possible we do not anticipate histological effects showing an effect on AAT polymer content at this early of a time point.

Update on ARO-APOC3 and ARO-ANG3

ARO-APOC3 and ARO-ANG3 are Arrowhead's two wholly-owned cardiometabolic candidates that are in Phase 1/2 clinical trials and have enrolled close to 200 patients. Each study is evaluating single and multiple-doses of drug and we anticipate data from both studies being presented at scientific conferences in the second half of 2020.

ARO-APOC3 is targeted to apolipoprotein C-III (APOC3), a component of very low density lipoprotein (VLDL) and an inhibitor of lipoprotein lipase. This program is focused on treating patients with severe

hypertriglyceridemia and a history or high risk of pancreatitis. In support of targeting APOC3, an APOC3 loss-of-function mutation results in lower triglyceride (TG) levels (Jørgensen *et al*., 2014). Approximately 80-90% of APOC3 is produced in hepatocytes, thus making it an ideal target for the TRiM™ platform.

While some patients do have a single genetic cause of the disease, for example familial chylomicronemia syndrome (FCS) is caused by an impaired lipoprotein lipase and results in patients have TG levels >880 mg/dl, many patients have a polygenic disorder (multifactorial chylomicronemia, MCM) that is exacerbated by comorbidities, diet, and lifestyle and greatly increases the risk for pancreatitis. Both conditions are treated with currently available therapies and changes to diet/lifestyle, however adherence is difficult. While FCS is rare (prevalence is approximately 1 in 1 million [Brahm *et al*., 2015]), MCM is thought to affect up to 3.4 million Americans (Christian *et al*., 2011), although only a small percentage of those patients are currently on medication.

ARO-ANG3 is focused on treating patients with mixed dyslipidemia and potentially metabolic diseases through targeting angiopoietin like protein 3 (ANGPTL3). ANGPTL3 loss-of-function mutations lead to low levels of LDL, VLDL, HDL, and TG, with genome-wide association studies (GWAS) showing a reduced risk of cardiovascular disease (CVD). Just like APOC3, the majority of ANGPTL3 is produced in hepatocytes, also making it an ideal target for the TRiM™ platform.

Mixed dyslipidemia patients have both elevated TG and elevated LDL-cholesterol. There are an estimated 10-15 million mixed dyslipidemia patients in the U.S., making it a very large opportunity. While there are a number of treatments currently available, the ability for ARO-ANG3 to lower both TGs and LDL could lead to a better outcome than statins or PCSK9 inhibitors alone.

In the U.S. alone there are an estimated one million individuals with triglyceride levels greater than 1000 mg/dl, more than three million individuals with triglycerides greater than 500 mg/dl and less than 1000 mg/dl, and approximately 41 million individuals with triglycerides between 200-500 mg/dl. This represents an enormous market opportunity for both ARO-APOC3 and ARO-ANG3 and we look forward to the initial data from these programs later this year.

Update on ARO-HSD

ARO-HSD targets hydroxysteroid 17β-dehydrogenase 13 (HSD17B13), a member of the HSD17B family that is markedly upregulated in patients and mice with non-alcoholic fatty liver disease (NAFLD) (Su *et al*, 2019). Loss-of-function mutations in HSD17B13 provide the strongest known protection against NASH cirrhosis, alcoholic hepatitis, and cirrhosis (Abul-Husn *et al*., 2018). In the CDAA (choline-deficient, methionine-reduced, 60% fat) mouse model of non-alcoholic steatohepatitis (NASH), once-weekly treatment with 3 mg/kg ARO-HSD resulted in decreased steatosis, inflammation, and hepatocyte degeneration along with inhibition of liver fibrosis.

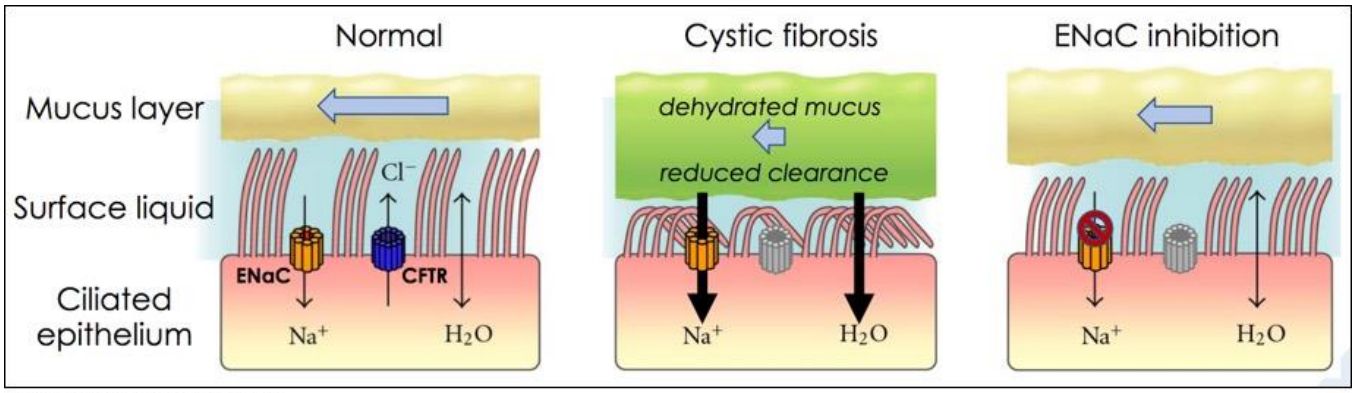
Arrowhead has initiated a Phase 1/2 clinical trial and completed dosing all healthy volunteer cohorts and will begin dosing patients with NASH or suspected NASH. Due to the fact that HSD17B13 is not a secreted protein the only way to assess proper target engagement is through liver biopsies. As long as there are not additional delays from the coronavirus pandemic we anticipate the company being in a position to present data in the first half of 2021.

Update on ARO-ENaC

In July 2020, Arrowhead held a KOL event about ARO-ENaC to discuss the current treatment landscape for patients with cystic fibrosis (CF) and the unmet medical need for those patients that aren't adequately helped with current therapies. Interested investors can access the event here.

ARO-ENaC targets the epithelial sodium channel (ENaC) and is being developed for the treatment of CF. CF patients have reduced clearance of dehydrated mucus due to a defect in the CFTR gene that conducts chloride ions across epithelial cell membranes. The lack of Cl^- movement and continued activity

of ENaC promotes the dehydration of mucus, however inhibiting the activity of ENaC improves this condition.



Source: Arrowhead Pharmaceuticals, Inc.

Multiple studies validate ENaC as a target in CF. A mutation that increases ENaC activity in patients with a mutation in only one CFTR allele ($CFTR^{+/-}$) causes atypical CF, thus suggesting that decreased ENaC activity could decrease CF pathophysiology (Rauh *et al*., 2010). A loss-of-function mutation in ENaC in pseudohypoaldosteronism (PAH) results in no sodium absorption from airway surfaces, a volume of airway surface liquid that is more than twice the normal value, and an increase in mucociliary clearance compared to healthy individuals (Kerem *et al*., 1999). Lastly, CF patients with a homozygous F508del mutation who live into their fifth or sixth decade of life were identified and found to have mutations in ENaC genes (Agrawal *et al*., 2017).

Thus far, Arrowhead has shown in preclinical models that ARO-ENaC can durably silence pulmonary αENaC expression in a dose dependent manner in rats and preserves lung clearance in a sheep mucostatic model of CF. While there have been many advancements in the treatment of CF patients, opportunities still exist to help those patients that either a) don't respond to treatment, and/or b) to enhance the response for those on standard of care therapies. Importantly, treatment targeting ENaC can be used in all CF patients, regardless of genotype.

The company has initiated a Phase 1/2 clinical trial in 24 healthy volunteers and up to 30 CF patients with dosing expected to begin in August 2020. We estimate that initial data from this trial could be available in the first half of 2021 and may include data on safety and tolerability along with functional outcomes such as forced expiratory volume (FEV1) and lung clearance index (LCI). Assuming the treatment is safe and effective, we believe a Phase 3 study could be initiated in 2021 in CF along with other trials in additional indications (COPD, asthma, pulmonary fibrosis).

Financial Update

On August 5, 2020, Arrowhead announced financial results for the third quarter of fiscal year 2020 that ended June 30, 2020. The company reported revenue of approximately $27.4 million for the third quarter of fiscal year 2020 compared to approximately $42.7 million for the third quarter of fiscal year 2019. This revenue is related to the recognition of a portion of the $252.6 million initial transaction associated with the agreements with Janssen.

R&D expenses for the three-month period ending June 30, 2020 were $32.6 million, compared to $19.3 million for the three-month period ending June 30, 2019. The increase was primarily due to increased manufacturing, clinical trials, and compensation expenses. G&A expenses for the third quarter of fiscal year 2020 were approximately $10.7 million, compared to approximately $4.8 million for the third quarter of fiscal year 2019. The increase was primarily due to increased stock-based compensation, salaries, and professional services.

Arrowhead exited the third quarter of fiscal year 2020 with approximately $464.6 million in cash, cash equivalents, short-term investments, and long-term investments. As of July 27, 2020, the company had approximately 102.3 million shares outstanding and, when factoring in stock options and restricted stock units, a fully diluted share count of approximately 109.6 million.

Conclusion

We are glad to see that there hasn't been a significant effect on any of the company's programs from the coronavirus pandemic and the company will have a number of data readouts over the next six months, including six-month biopsy data for ARO-AAT and initial readouts for both ARO-APOC3 and ARO-ANG3. With no changes to our model our valuation remains at $58 per share.

PROJECTED FINANCIALS

Arrowhead Pharmaceuticals, Inc.	FY2019 A	Q1FY20 A	Q2FY20 A	Q3FY20 A	Q4FY20 E	FY2020 E	FY2021 E	FY2022 E
Revenue	$168.80	$29.45	$23.53	$27.38	$20.62	$100.98	$73.22	$50.00
YOY Growth	*945.7%*	*-38.8%*	*-44.9%*	*-36.8%*	*-87.8%*	*191.4%*	*52.1%*	*17.1%*
Total Revenues	**$168.8**	**$29.5**	**$23.5**	**$27.4**	**$20.6**	**$101.0**	**$73.2**	**$50.0**
YOY Growth	*945.7%*	*-38.8%*	*-44.9%*	*-36.8%*	*-87.8%*	*191.4%*	*52.1%*	*17.1%*
Cost of Revenue	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Gross Income	**$168.8**	**$29.5**	**$23.5**	**$27.4**	**$20.6**	**$101.0**	**$73.2**	**$50.0**
Gross Margin	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*
R&D	$81.0	$23.4	$29.4	$32.6	$25.3	$110.7	$105.0	$110.0
% R&D	*48.0%*	*79.4%*	*125.1%*	*119.0%*	*122.8%*	*109.6%*	*143.4%*	*220.0%*
Salary and G&A	$26.6	$10.9	$16.3	$10.7	$12.2	$50.2	$52.2	$55.0
% SG&A	*15.7%*	*37.1%*	*69.4%*	*39.3%*	*59.3%*	*49.7%*	*71.3%*	*110.0%*
Other expenses	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
% Other	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Operating Income	**$61.2**	**($4.9)**	**($22.2)**	**($15.9)**	**($16.9)**	**($60.0)**	**($84.0)**	**($115.0)**
Operating Margin	*36.3%*	-	-	-	-	*-59.4%*	*-114.7%*	*-230.0%*
Other Income (Net)	$7.0	$2.2	$2.4	$2.3	$1.7	$8.7	$7.0	$6.0
Pre-Tax Income	**$68.1**	**($2.7)**	**($19.8)**	**($13.6)**	**($15.2)**	**($51.3)**	**($77.0)**	**($109.0)**
Net Taxes (benefit)	$0.2	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	*0.3%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Reported Net Income	**$68.0**	**($2.7)**	**($19.8)**	**($13.6)**	**($15.2)**	**($51.3)**	**($77.0)**	**($109.0)**
YOY Growth	-	-	-	-	-	-	-	-
Net Margin	*40.3%*	-	-	-	-	*-50.8%*	*-105.2%*	*-218.0%*
Reported EPS	**$0.69**	**($0.03)**	**($0.20)**	**($0.13)**	**($0.15)**	**($0.51)**	**($0.74)**	**($1.04)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	98.6	97.1	101.7	101.8	102.0	100.6	104.5	104.5

Source: Zacks Investment Research, Inc. *David Bautz, PhD*

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