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David Bautz, PhD
312-265-9471
dbautz@zacks.com

scr.zacks.com
10 S. Riverside Plaza, Chicago, IL 60606

Arrowhead Pharmaceuticals, Inc. (ARWR-NASDAQ)

ARWR: Enrollment Complete in PALISADE Phase 3 Trial of ARO-APOC3 in FCS…

Based on our probability adjusted DCF model that takes into account potential future revenues from the company's development products, ARWR is valued at $80/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 (08/10/23)	$29.01
Valuation	**$80.00**

OUTLOOK

On August 7, 2023, Arrowhead Pharmaceuticals, Inc. (ARWR) announced financial results for the third quarter of fiscal year 2023 that ended June 30, 2023. During the quarter, the company hosted an R&D Day to discuss the "20 in 25" goal of having 20 clinical stage or marketed products in the year 2025. The company also recently completed enrollment in the PALISADE Phase 3 clinical trial of ARO-APOC3 in familial chylomicronemia syndrome (FCS). We anticipate the trial completing in the second quarter of 2024, with a topline data readout shortly thereafter. Positive results would set up the company to begin the NDA process in the second half of 2024. Phase 2 data for both ARO-APOC3 and ARO-ANG3 are expected at the American Heart Association meeting in November 2023 and 'End-of-Phase 2' meetings are likely before the end of 2023.

SUMMARY DATA

52-Week High	**$48.31**
52-Week Low	**$23.68**
One-Year Return (%)	**-38.22**
Beta	**0.96**
Average Daily Volume (sh)	**941,518**
Shares Outstanding (mil)	**107**
Market Capitalization ($mil)	**$3,110**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**67**
Insider Ownership (%)	**5**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**54.6**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2020 Estimate	**-17.5**
P/E using 2021 Estimate	**-12.2**

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

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2022	27.4 A	151.8 A	32.4 A	31.6 A	243.2 A
2023	62.5 A	146.3 A	15.8 A	50.0 E	304.6 E
2024					250.0 E
2025					300.0 E

Earnings per Share

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2022	-$0.60 A	$0.42 A	-$0.68 A	-$0.81 A	-$1.67 A
2023	-$0.39 A	$0.46 A	-$0.97 A	-$0.48 E	-$1.40 E
2024					-$1.38 E
2025					-$1.08 E

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WHAT'S NEW

Business Update

Update on Cardiometabolic Candidates

The company's two cardiometabolic candidates, ARO-APOC3 and ARO-ANG3, are currently being studied in multiple ongoing clinical trials. The U.S. FDA has granted Fast Track designation to ARO-APOC3 for reducing triglycerides in adult patients with familial chylomicronemia syndrome (FCS) after previously being granted Orphan Drug designation by both the FDA and the EMA. ARO-APOC3 is currently being studied in the following trials:

PALISADE: This is a Phase 3, double blind, placebo controlled trial in patients with FCS. These patients have fasting triglyceride levels >880 mg/dL. Target enrollment of 72 patients has completed and patients are being assigned to one of four dose cohorts in a 2:1:2:1 manner (ARO-APOC3 25 mg, volume-matching placebo, ARO-APOC3 50 mg, volume-matching placebo). The primary endpoint of the trial is the percent change from baseline at month 10 in fasting triglycerides (TGs). Secondary and exploratory endpoints will include the change in lipid parameters, incidence of acute pancreatitis, and other measures. We anticipate study completion in the second quarter of 2024, a data readout shortly thereafter, and then preparation for a new drug application (NDA).

SHASTA-2: This is a Phase 2b, double blind, placebo controlled trial in patients with severe hypertriglyceridemia (SHTG; TG > 500 mg/dL). The primary endpoint of the trial is the safety and efficacy of ARO-APOC3 as determined by the percent change from baseline in fasting TGs at week 24. The trial is fully enrolled with 229 subjects. We anticipate topline results being reported at the American Heart Association meeting in November 2023.

MUIR: This is a Phase 2b, double blind, placebo controlled trial in adults with mixed dyslipidemia, which is defined as having TG between 150 and 500 mg/dL and non-HDL cholesterol > 100 mg/dL or LDL cholesterol >70 mg/dL. The primary objective is to evaluate the safety and efficacy of ARO-APOC3 as determined by the percent change from baseline in fasting TGs at week 24. Enrollment of 353 patients has been reached. We anticipate topline results being reported at the American Heart Association meeting in November 2023.

The Phase 3 plan for SHTG includes two separate studies: SHASTA-3 and SHASTA-4. SHASTA-3 will be a randomized, double blind, placebo controlled, 12-month study with approximately 600 patients with TG>500 mg/dL. SHASTA-4 will examine the effect of ARO-APOC3 in a more severe population (approximately 200 patients) that is at high-risk of developing pancreatitis. That study will last two years and will be powered to detect the difference in the incidence of pancreatitis. Positive data from that study could enable label expansion to include the indication of pancreatitis risk reduction, which is a key clinical outcome relevant to patients and payers.

The Phase 3 plan for mixed dyslipidemia will be a cardiovascular outcomes trial (COVT) called CASCADE. This study will enroll patients with a high risk for cardiovascular disease driven by high TGs, high LDL cholesterol, and low HDL cholesterol. Currently, the company is planning to run this trial on its own.

ARO-ANG3 targets the angiopoietin like protein 3 (ANGPTL3). ANGPTL3 loss-of-function mutations lead to low levels of LDL, VLDL, HDL, and TG (Musunuru *et al*., 2010), with one study showing an ANGPTL3 loss of function associated with a 34% reduction in odds of coronary artery disease (CAD) (Stitziel *et al*., 2017). Arrowhead is currently testing ARO-APOC3 in the following clinical trials under the VISTA program:

ARCHES-2: This is a Phase 2b, double blind, placebo controlled trial in adults with mixed dyslipidemia (patients are defined just as those in the MUIR trial). The primary objective is to evaluate the safety and efficacy of ARO-ANG3 and to select a dosing regimen for later stage trials in this patient population. Three dose levels of ARO-ANG3 (50 mg, 100 mg, 200 mg) were tested. Patients received a subcutaneous injection

on day 1 and week 12. The trial completed with a total of 204 patients and the company is currently in the process of generating and analyzing study data, which we anticipate being reported later this year.

GATEWAY: This is a Phase 2, open-label trial in 18 patients with homozygous familial hypercholesterolemia (HoFH). Patients were randomized 1:1 to receive two doses of 200 or 300 mg ARO-ANG3 on Day 1 and Day 84 and evaluated over a 36-week period. The study is fully enrolled and interim data were presented at the 91st European Atherosclerosis Society Congress on May 2023. Results showed that at week 20, administration of 200 mg or 300 mg ARO-ANG3 on day 1 and day 84 led to mean reductions in LDL cholesterol of 48.1% and 44.0%, respectively. These reductions were achieved on top of continued standard of care, including statins, ezetimibe, PCSK9 inhibitors, and apheresis. The results were comparable to an approved monoclonal antibody treatment that targets ANGPTL3, however ARO-ANG3 has a more convenient dosing regimen of one subcutaneous injection every three months compared to a once-monthly intravenous infusion for the antibody treatment.

Continued Encouraging Data for ARO-RAGE

At the company's R&D day, updated data for the Phase 1/2 clinical trial of ARO-RAGE was presented. ARO-RAGE is being developed to reduce production of the receptor for advanced glycation end products (RAGE) as a potential treatment for inflammatory diseases such as asthma. Importantly, thus far there have been no reported serious or severe adverse events, no study withdrawals or drug discontinuations due to adverse events, and safety labs have shown no patterns of adverse changes. In addition, there has been no change in the pattern of airway immune cells and all chest X-rays have been normal. These safety results have been consistent in the ARO-MMP7 and ARO-MUC5AC programs as well.

At the highest dose of 184 mg there was a mean reduction in soluble RAGE (sRAGE) of up to 76% and a maximal reduction of 91% following just a single dose. The 184 mg inhaled dose also achieved a mean reduction of 90% and a maximal reduction of 95% in BALF. These data are highly encouraging and provide compelling evidence for gene silencing in the lung using an inhaled siRNA. In addition, these results are supportive of positive results being likely in the company's other pulmonary programs (ARO-MUC5AC, ARO-MMP7, and additional undisclosed preclinical programs).

The company is currently waiting for the final rat data for the ARO-RAGE chronic GLP toxicology study. For ARO-MMP7, the No Observed Adverse Effect Level (NOAEL) was the highest dose that was tested in the chronic rat toxicology study. The highest dose is what the company believes would be substantially greater exposure than would be applied to humans. For ARO-RAGE, while the final results are not in, the company indicated the NOAEL will likely be the highest dose tested. Data from the 9-month monkey toxicology study is still forthcoming for both candidates, however the company believes the rat is the more sensitive species for the pulmonary toxicology studies (based on what was seen with ARO-ENAC), thus it is very encouraging that the rat studies appear to be quite positive.

Financial Update

On August 7, 2023, Arrowhead announced financial results for the third quarter of fiscal year 2023 that ended June 30, 2023. The company reported revenue of approximately $15.8 million for the third quarter of fiscal year 2023 compared to approximately $32.4 million for the third quarter of fiscal year 2022. The change in revenue in the current period relates primarily to the collaboration agreements with Takeda, Horizon, Amgen, and GlaxoSmithKline (GSK). R&D expenses for the quarter ending June 30, 2023 were approximately $94.8 million compared to $72.1 million for the quarter ending June 30, 2022. The increase was primarily due to increased candidate costs due to progression of the company's pipeline of candidates along with increased R&D discovery costs. G&A expenses for the third quarter of fiscal year 2023 were $23.8 million compared to $33.1 million for the third quarter of fiscal year 2022. The decrease was primarily due to lower non-cash, stock-based compensation.

Arrowhead exited the third quarter of fiscal year 2023 with approximately $494.5 million in cash, cash equivalents, and investments. As of July 31, 2023, Arrowhead had approximately 107.2 million shares outstanding and, when factoring in stock options and restricted stock units, a fully diluted share count of approximately 113.9 million.

Conclusion

Arrowhead is well on its way to achieving its “20 in 25” goal with continued positive developments for a number of its development candidates. We look forward to Phase 2 results for the company’s cardiometabolic candidates at the AHA meeting in November 2023. The ARO-RAGE data continues to impress, and we view it as de-risking for the entire pulmonary program. With no changes to our model our valuation remains at $80 per share.

PROJECTED FINANCIALS

Arrowhead Pharmaceuticals, Inc.	FY2022 A	Q1FY23 A	Q2FY23 A	Q3FY23 A	Q4FY23 E	FY2023 E	FY2024 E	FY2025 E
Revenue	$243.23	$62.55	$146.27	$15.83	$50.00	$274.64	$250.00	$300.00
YOY Growth	*469.7%*	*-58.8%*	*351.3%*	*-49.9%*	*-79.4%*	*534.4%*	*48.1%*	*918.5%*
Total Revenues	**$243.2**	**$62.5**	**$146.3**	**$15.8**	**$50.0**	**$274.6**	**$250.0**	**$300.0**
YOY Growth	*469.7%*	*-58.8%*	*351.3%*	*-49.9%*	*-79.4%*	*534.4%*	*48.1%*	*918.5%*
Cost of Revenue	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Gross Income	**$243.2**	**$62.5**	**$146.3**	**$15.8**	**$50.0**	**$274.6**	**$250.0**	**$300.0**
Gross Margin	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*
R&D	$297.3	$83.7	$74.9	$94.8	$79.0	$332.3	$310.0	$320.0
% R&D	*122.2%*	*133.8%*	*51.2%*	*598.8%*	*158.0%*	*121.0%*	*124.0%*	*106.7%*
Salary and G&A	$124.4	$21.0	$23.2	$23.8	$24.0	$92.0	$100.0	$110.0
% SG&A	*51.2%*	*33.6%*	*15.9%*	*150.2%*	*48.0%*	*33.5%*	*40.0%*	*36.7%*
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	**($178.5)**	**($42.1)**	**$48.2**	**($102.7)**	**($53.0)**	**($149.7)**	**($160.0)**	**($130.0)**
Operating Margin	*-73.4%*	-	-	-	-	*-54.5%*	*-64.0%*	*-43.3%*
Other Income (Net)	$5.8	$0.3	($0.5)	($0.7)	$1.5	$0.7	$6.0	$6.0
Pre-Tax Income	**($172.7)**	**($41.8)**	**$47.7**	**($103.4)**	**($51.5)**	**($149.0)**	**($154.0)**	**($124.0)**
Net Taxes (benefit)	$3.8	$0.0	$1.0	$0.7	$0.0	$0.0	$0.0	$0.0
Tax Rate	*-2.2%*	*0.0%*	*-2.1%*	*-0.7%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Reported Net Income	**($176.5)**	**($41.8)**	**$48.7**	**($104.1)**	**($51.5)**	**($149.0)**	**($154.0)**	**($124.0)**
YOY Growth	-	-	-	-	-	-	-	-
Net Margin	*-72.6%*	-	-	-	-	*-54.3%*	*-61.6%*	*-41.3%*
Reported EPS	**($1.67)**	**($0.39)**	**$0.46**	**($0.97)**	**($0.48)**	**($1.40)**	**($1.38)**	**($1.08)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	105.4	106.0	106.8	107.0	107.2	106.8	112.0	115.0

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

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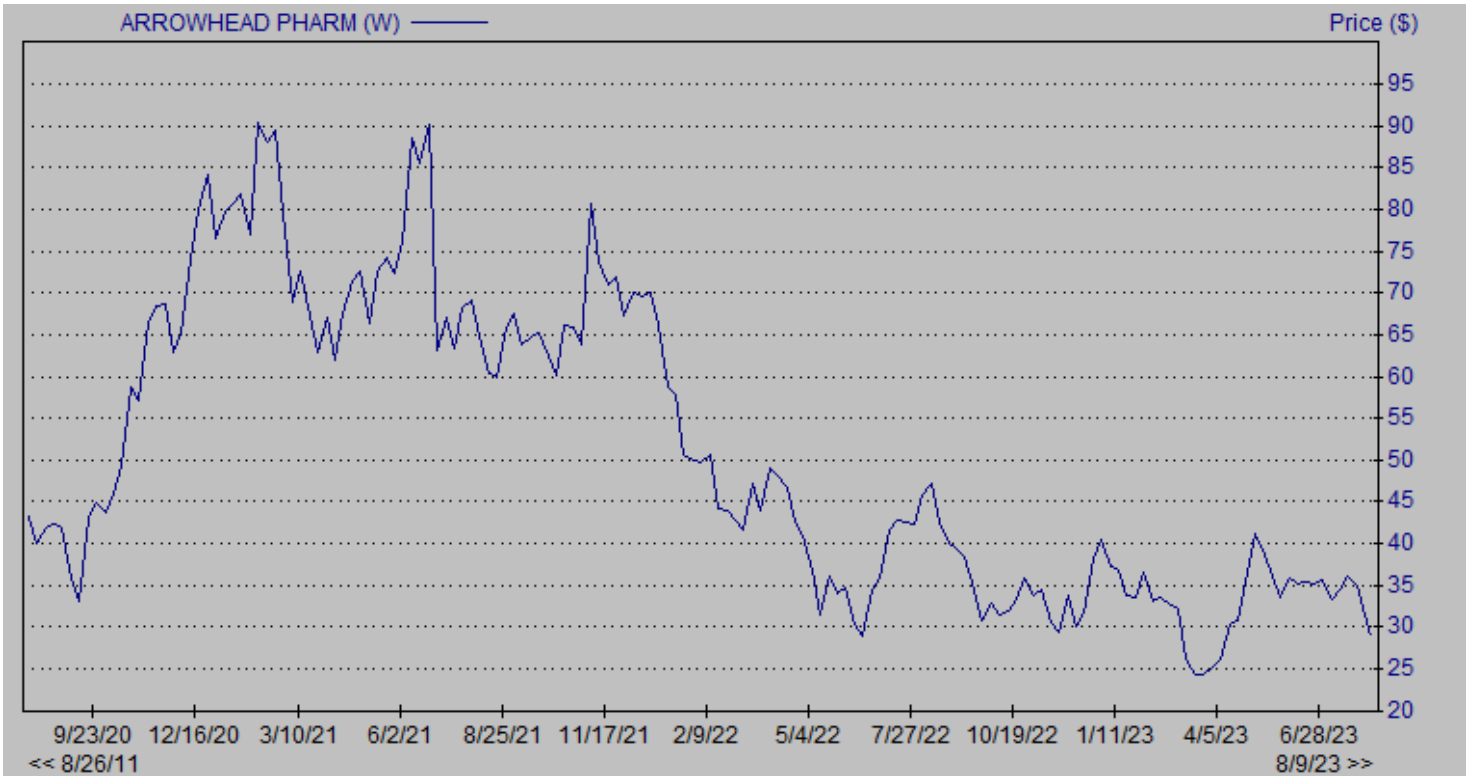
HISTORICAL STOCK PRICE



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