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Arrowhead Pharmaceuticals, Inc. (ARWR-NASDAQ)

ARWR: Updates on Plozasiran and Zodasiran at AHA 2023…

Based on our probability adjusted DCF model that takes into account potential future revenues from the company's development products, ARWR is valued at $84/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 (12/05/23)	$24.93
Valuation	**$84.00**

OUTLOOK

On November 29, 2023, Arrowhead Pharmaceuticals, Inc. (ARWR) announced financial results for the fourth quarter and full fiscal year 2023 that ended September 30, 2023. The company recently presented new Phase 2 clinical data for the ongoing SHASTA-2 and MUIR studies of plozasiran (ARO-APOC3) and the ARCHES-2 study of zodasiran (ARO-ANG3) at the American Heart Association Scientific Sessions 2023. Each drug continues to have a favorable safety profile with plozasiran treatment leading to substantial reductions in triglycerides and remnant cholesterol and zodasiran treatment leading to substantial reductions in triglycerides and LDL-cholesterol. The company will be deciding which compound to take into a cardiovascular outcome trial (CVOT) that is expected to launch in the middle of 2024.

SUMMARY DATA

52-Week High	**$41.38**
52-Week Low	**$23.22**
One-Year Return (%)	**-10.00**
Beta	**0.89**
Average Daily Volume (sh)	**903,923**
Shares Outstanding (mil)	**107**
Market Capitalization ($mil)	**$3,106**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**66**
Insider Ownership (%)	**5**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**41.8**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2020 Estimate	**-10.7**
P/E using 2021 Estimate	**-9.4**

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

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2023	62.6 A	146.3 A	15.8 A	16.1 A	240.7 A
2024	50.0 E	50.0 E	50.0 E	50.0 E	200.0 E
2025					250.0 E
2026					300.0 E

Earnings per Share

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2023	-$0.39 A	$0.46 A	-$0.96 A	-$1.04 A	-$1.92 A
2024	-$0.58 E	-$0.61 E	-$0.64 E	-$0.65 E	-$2.48 E
2025					-$1.96 E
2026					-$1.57 E

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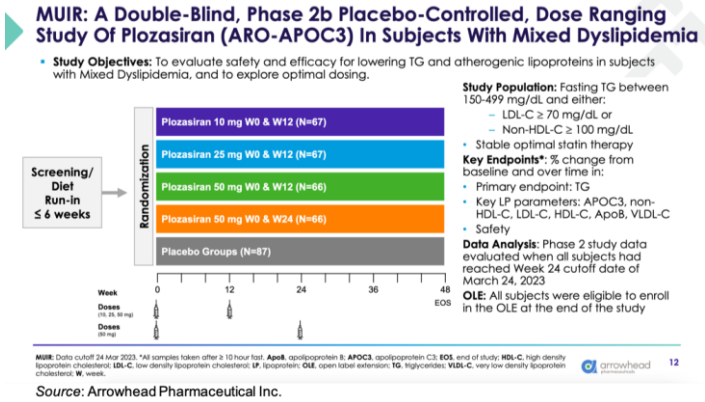
WHAT'S NEW

Business Update

Updated Clinical Data for Cardiometabolic Candidates Presented at AHA 2023

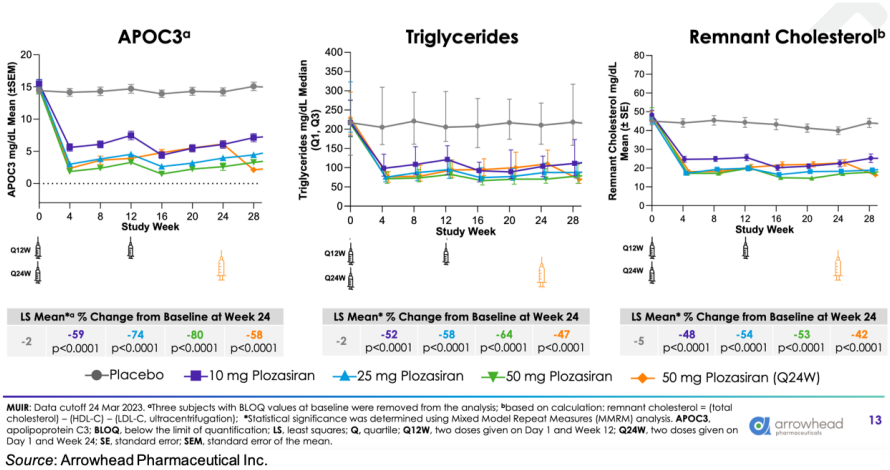
On November 13, 2023, Arrowhead Pharmaceuticals Inc. (ARWR) announced new clinical data for the Phase 2 SHASTA-2 and MUIR studies of plozasiran (ARO-APOC3) and the ARCHES-2 study of zodasiran (ARO-ANG3) were presented at the American Heart Association (AHA) Scientific Sessions 2023. The company also held a virtual analyst and investor event to discuss the data. A copy of the presentation can be found here.

ARO-APOC3, an Investigational RNAi Therapeutic, Silences APOC3 and Reduces Atherosclerosis-Associated Lipoproteins in Patients with Mixed Dyslipidemia: MUIR Study Results
MUIR is a Phase 2b double blind, placebo controlled, dose ranging study of plozasiran in subjects with mixed dyslipidemia, defined as fasting triglycerides (TG) between 150-499 mg/dL and either LDL-C ≥ 70 mg/dL or non-HDL-C ≥ 100 mg/dL. Study subjects were treated with plozasiran 10 mg, 25 mg, or 50 mg at Week 0 and Week 12, plozasiran 50 mg at Week 0 and Week 24, or placebo. The key endpoints of the study are the change from baseline in TG, APOC3, HDL-C, LDL-C, ApoB, and VLDL-C.



Source: Arrowhead Pharmaceutical Inc.

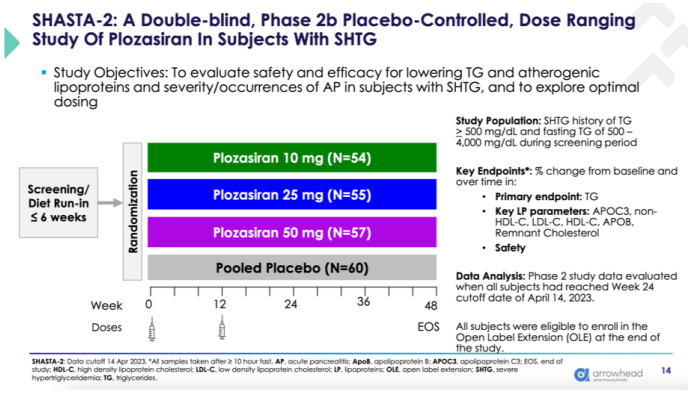
The following slide shows that plozasiran treatment results in substantial and durable reductions in triglycerides and triglyceride-rich lipoproteins. At the 50 mg Q12W dose, APOC3 levels were reduced an average of 80%, triglycerides were reduced an average of 64%, and remnant cholesterol was reduced an average of 53%. In addition, HDL-C was increased an average of 51%. As the following graphs show, these results were significantly different compared to the placebo group that experienced little to no change in the measured parameters.



Source: Arrowhead Pharmaceutical Inc.

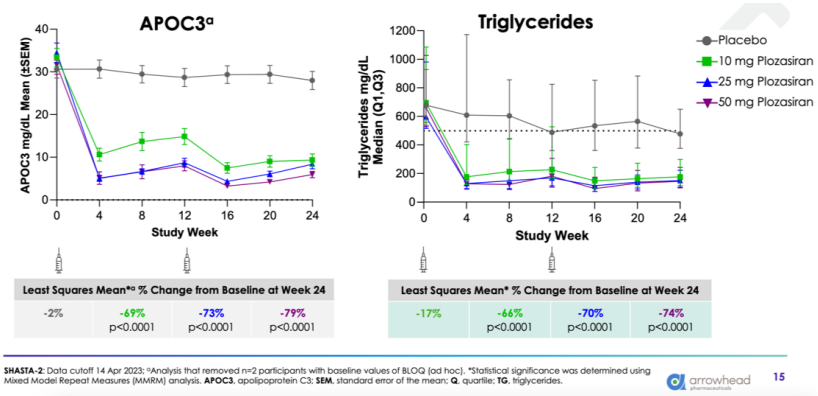
ARO-APOC3, an Investigational RNAi Therapeutic, Silences APOC3 and Reduces Triglycerides to Near Normal Levels in Patients with Severe Hypertriglyceridemia: SHASTA-2 Study Results

SHASTA-2 is a Phase 2b double blind, placebo controlled, dose ranging study of plozasiran in subjects with severe hypertriglyceridemia (sHTG; circulating TG ≥ 500 mg/dL). Study subjects were treated with placebo or plozasiran 10 mg, 25 mg, or 50 mg at Week 0 and Week 12. The primary endpoint of the trial is the percent change from baseline in TG, with key secondary endpoints examining the levels of APOC3, non-HDL-C, LDL-C, HDL-C, ApoB, and remnant cholesterol.



Source: Arrowhead Pharmaceutical Inc.

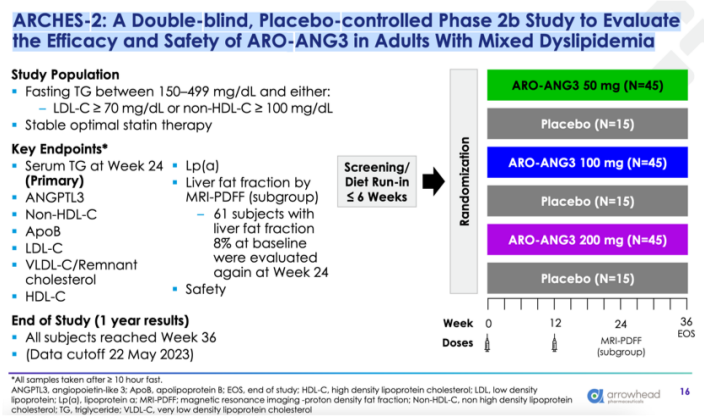
The following slide shows the significant decreases in APOC3 and TG. Patients treated with 50 mg plozasiran experienced an average decrease of 79% in APOC3 and 74% in TG at Week 24. In addition, 91% of patients experienced a reduction in TG to below 500 mg/dL. Treatment with 50 mg plozasiran also led to an average reduction in remnant cholesterol of 58% and an increase in HDL-C of 68%. There was a 76% increase in LDL-C, however this could possibly be due to lipolysis of triglyceride-rich lipoproteins that we believe could be managed effectively.



Source: Arrowhead Pharmaceutical Inc.

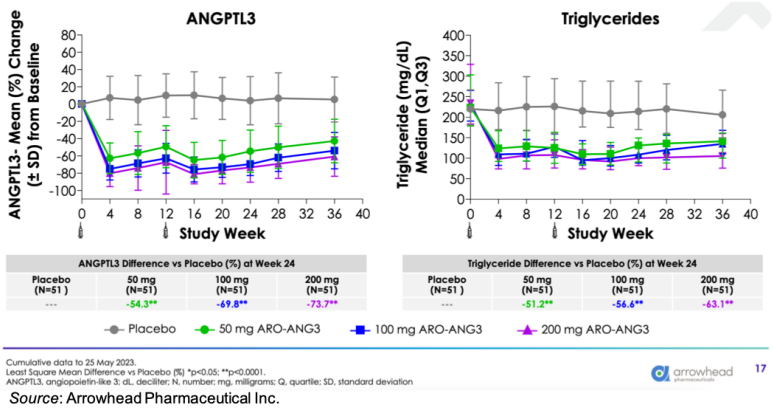
ARCHES-2: A Double-blind, Placebo-controlled Phase 2b Study to Evaluate the Efficacy and Safety of ARO-ANG3 in Adults with Mixed Dyslipidemia

ARCHES-2 is a double blind, placebo controlled Phase 2b trial that is evaluating zodasiran (ARO-ANG3) in adults with mixed dyslipidemia (TG between 150-499 mg/dL and either LDL-C ≥ 70 mg/dL or non-HDL-C ≥ 100 mg/dL. The primary endpoint is the change in serum TG at Week 24 following treatment at Week 0 and Week 12 with either 50 mg, 100 mg, or 200 mg ARO-ANG3 or placebo. A subset of study subjects with liver fat ≥ 8% were also evaluated for liver fat fraction at Week 24.



Source: Arrowhead Pharmaceutical Inc.

The results of the study show that subjects treated with 200 mg zodasiran experienced a substantial decrease in ANGPTL3 (-74%) and TG (63%). In addition, at that dose level patients experienced a 20% decrease in LDL-C, an 82% decrease in remnant cholesterol, a 22% decrease in ApoB, and a 36% decrease in non-HDL-C. Lastly, for patients with a baseline liver fat ≥ 8% there was an approximate 29% decrease in liver fat as measured by MRI-PDFF.



Source: Arrowhead Pharmaceutical Inc.

The company is currently completing the Phase 3 PALISADE study of plozasiran in patients with familial chylomicronemia syndrome (FCS) and we anticipate the last patient visit to be in the second quarter of 2024. Beyond FCS, Arrowhead is going to focus on developing plozasiran in patients with sHTG with Phase 3 studies anticipated to begin in early 2024. After FCS and sHTG, there are opportunities for both plozasiran and zodasiran in larger indications. The company will be conducting a cardiovascular outcome trial (CVOT) that will likely launch in mid-2024. The plan had been to test plozasiran in a CVOT, however given the data for zodasiran in the mixed dyslipidemia patient population, the company now has to decide whether plozasiran or zodasiran would be a better candidate to advance in a CVOT trial. This decision should be made in the next couple of months.

Update on the Pulmonary Platform

Arrowhead's pulmonary platform currently consists of three candidates: ARO-RAGE, ARO-MMP7, and ARO-MUC5AC. All three candidates are currently in Phase 1/2a trials evaluating single and multiple doses in normal healthy volunteers and in patients. Thus far, 145 total subjects have received active drug via inhalation, with another 31 receiving ARO-RAGE via the subcutaneous route. There have been no patterns of drug-related adverse events, pulmonary adverse events (cough, shortness of breath, etc.), or adverse changes in lab or spirometry values. All chest x-rays have been normal and there has been no evidence of local lung inflammation based on BALF cell count.

The company had previously reported chronic toxicology issues with the first-generation ARO-ENaC candidate, which involved local lung inflammation in chronic rat and monkey toxicology studies. The cause

was determined to be macrophage overload syndrome, thus next-generation pulmonary candidates needed enhanced potency and increased duration of effect to reduce overall exposure.

The chronic toxicology results are now completed in both rodent and primates for ARO-RAGE and ARO-MMP7. The results show that the NOAELs (No Observed Adverse Effect Levels) suggest a sufficient safety margin to move both candidates into Phase 2 testing. The company will be meeting with regulators in 2024 to discuss the results seen thus far and to map out the path forward.

Clinical data for the ARO-RAGE program shows that normal volunteers experienced a mean 89% maximum knockdown (95% maximum knockdown) in circulating sRAGE after two doses of 184 mg ARO-RAGE. The next step for this program is to determine if RAGE knockdown leads to favorable clinical outcomes in patients. The company is currently enrolling the top dose in mild-to-moderate asthma patients and has begun enrolling a cohort of asthma patients with a high baseline level of fractional exhaled nitric oxide (FeNO), which is a biomarker for IL-13 driven Type 2 inflammation in the lung. We anticipate FeNO data for the mild-to-moderate asthma patients in the coming months and for the patients with high baseline FeNO in the third quarter of 2024.

Financial Update

On November 29, 2023, Arrowhead announced financial results for fiscal year 2023 that ended September 30, 2023. The company reported revenue of approximately $240.7 million for fiscal year 2023 compared to approximately $243.2 million for fiscal year 2022. This revenue included the recognition of $30 million associated with the GSK license agreement, $163 million associated with the Takeda License Agreement, $23 million associated with the Horizon Licensing Agreement, and $25 million associated with the Amgen license agreement.

R&D expenses for the year ending September 30, 2023 were approximately $353.2 million compared to $297.3 million for the year ending September 30, 2022. The increase was primarily due to increased salaries, facilities-related expenses, the progression of pipeline candidates into and through clinical trials, R&D discovery expenses, and non-cash stock-based compensation. G&A expenses for fiscal year 2023 were $92.5 million compared to $124.4 million for fiscal year 2022. The decrease was primarily due to decreased non-cash stock-based compensation.

Arrowhead exited fiscal year 2023 with approximately $403.6 million in cash, cash equivalents, and investments. As of November 20, 2023, Arrowhead had approximately 107.4 million shares outstanding and, when factoring in stock options and restricted stock units, a fully diluted share count of approximately 113.9 million.

Conclusion

The data for the company's cardiometabolic programs continues to be very encouraging and we look forward to the Phase 3 data for plozasiran in FCS as well as additional Phase 3 development plans for both compounds. The company has an important decision to make regarding which compound to move into a CVOT trial, and we expect an update on that in the next couple of months. We believe the pulmonary program has been substantially de-risked with the positive chronic toxicology data for ARO-RAGE and ARO-MMP7 and we look forward to the FeNO data for ARO-RAGE as well as an update on the Phase 2 plans for those compounds after the company is able to meet with regulators. Lastly, the company has initiated another clinical program with ARO-DM1, which is being evaluated as a treatment for Type 1 myotonic dystrophy, which brings the current total to 15 clinical programs as Arrowhead moves toward its "20 in '25" goal of having 20 clinical stage or marketed products by the year 2025. After advancing our model ahead one year our valuation now stands at $84 per share.

PROJECTED FINANCIALS

Arrowhead Pharmaceuticals, Inc.	FY2023 A	Q1FY24 E	Q2FY24 E	Q3FY24 E	Q4FY24 E	FY2024 E	FY2025 E	FY2026 E
Revenue	$240.74	$50.00	$50.00	$50.00	$50.00	$200.00	$250.00	$300.00
YOY Growth	*456.1%*	*-65.8%*	*216.0%*	*210.6%*	*-79.2%*	*2520.3%*	*48.1%*	*918.5%*
Total Revenues	**$240.7**	**$50.0**	**$50.0**	**$50.0**	**$50.0**	**$200.0**	**$250.0**	**$300.0**
YOY Growth	*456.1%*	*-65.8%*	*216.0%*	*210.6%*	*-79.2%*	*2520.3%*	*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	**$240.7**	**$50.0**	**$50.0**	**$50.0**	**$50.0**	**$200.0**	**$250.0**	**$300.0**
Gross Margin	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*	*100.0%*
R&D	$353.2	$90.0	$92.0	$94.0	$96.0	$372.0	$375.0	$380.0
% R&D	*146.7%*	*180.0%*	*184.0%*	*188.0%*	*192.0%*	*186.0%*	*150.0%*	*126.7%*
Salary and G&A	$92.5	$22.0	$23.0	$24.0	$24.0	$93.0	$95.0	$100.0
% SG&A	*38.4%*	*44.0%*	*46.0%*	*48.0%*	*48.0%*	*46.5%*	*38.0%*	*33.3%*
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	**($205.0)**	**($62.0)**	**($65.0)**	**($68.0)**	**($70.0)**	**($265.0)**	**($220.0)**	**($180.0)**
Operating Margin	*-85.2%*	*-*	*-*	*-*	*-*	*-132.5%*	*-88.0%*	*-60.0%*
Other Income (Net)	($1.5)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Pre-Tax Income	**($206.5)**	**($62.0)**	**($65.0)**	**($68.0)**	**($70.0)**	**($265.0)**	**($220.0)**	**($180.0)**
Net Taxes (benefit)	$2.8	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Net Loss Attributable to Noncontrolling Interest	$4.0	$0.0	$0.0	$0.0	$0.0	$0.0		
Reported Net Income	**($205.3)**	**($62.0)**	**($65.0)**	**($68.0)**	**($70.0)**	**($265.0)**	**($220.0)**	**($180.0)**
Net Margin	*-85.3%*	*-*	*-*	*-*	*-*	*-132.5%*	*-88.0%*	*-60.0%*
Reported EPS	**($1.92)**	**($0.58)**	**($0.61)**	**($0.64)**	**($0.65)**	**($2.48)**	**($1.96)**	**($1.57)**
YOY Growth	*-*	*-*	*-*	*-*	*-*	*-*	*-*	*-*
Basic Shares Outstanding	106.8	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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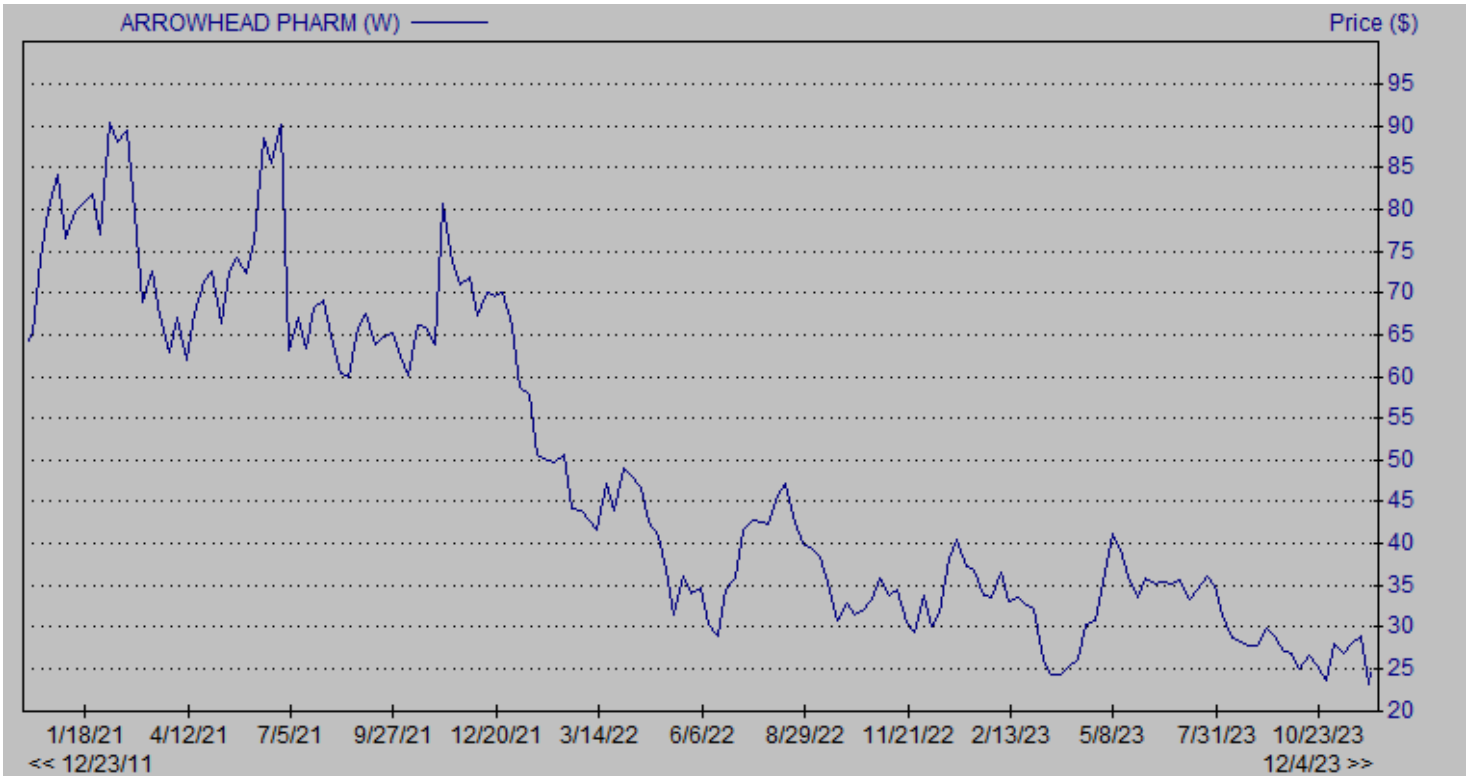

Source: Zacks SCR

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