Zacks Small-Cap Research
Sponsored – Impartial - Comprehensive

September 10, 2024
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: PALISADE Phase 3 Results Published in NEJM…

Based on our probability adjusted DCF model that takes into account potential future revenues from the company's development products, ARWR is valued at $70/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 (09/10/24)	$21.76
Valuation	**$70.00**

OUTLOOK

On September 2, 2024, Arrowhead Pharmaceuticals, Inc. (ARWR) announced results from the Phase 3 PALISADE study of plozasiran in patients with familial chylomicronemia syndrome (FCS). The trial met its primary endpoint and all key secondary endpoints, including statistically significant reductions in triglycerides (TGs), apolipoprotein C-III (APOC3), and the incidence of acute pancreatitis. The data were presented in a late-breaking oral presentation at the European Society of Cardiolog (ESG) Congress 2024 and simultaneously published in *The New England Journal of Medicine*. Based on these results, Arrowhead will be filing a New Drug Application before the end of 2024 and plans to seek regulatory approval in other jurisdictions thereafter.

SUMMARY DATA

52-Week High	**$39.48**
52-Week Low	**$21.20**
One-Year Return (%)	**-25.53**
Beta	**0.94**
Average Daily Volume (sh)	**1,179,030**
Shares Outstanding (mil)	**124**
Market Capitalization ($mil)	**$3,337**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**63**
Insider Ownership (%)	**5**
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 2024 Estimate	**-5.1**
P/E using 2025 Estimate	**-5.7**

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)
2023	62.6 A	146.3 A	15.8 A	16.1 A	240.7 A
2024	3.6 A	0.0 A	0.0 A	50.0 E	53.6 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	-$1.24 A	-$1.02 A	-$1.38 A	-$0.47 E	-$4.07 E
2025					-$1.76 E
2026					-$1.42 E

© Copyright 2024, Zacks Investment Research. All Rights Reserved.

WHAT'S NEW

Business Update

Phase 3 PALISADE Results Published in The New England Journal of Medicine

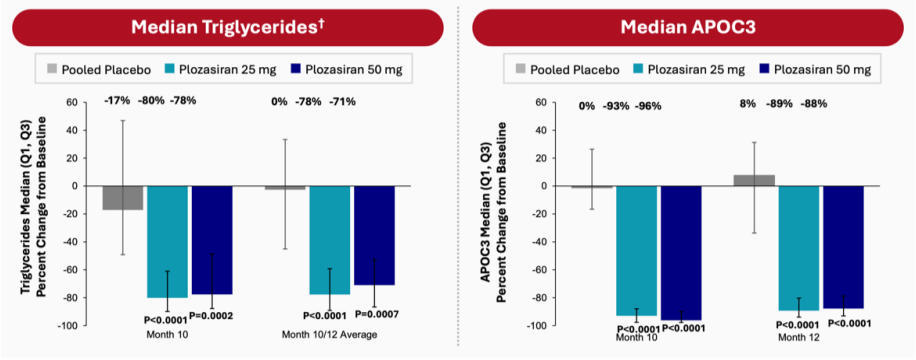
On September 2, 2024, Arrowhead Pharmaceuticals, Inc. (ARWR) announced results for the Phase 3 PALISADE trial of plozasiran in patients with familial chylomicronemia syndrome (FCS). The results were presented in a late-breaking oral presentation at the European Society of Cardiology (ESC) Congress 2024 and also published in *The New England Journal of Medicine* (Watts *et al.*, 2024). The company held an investor call on September 3, 2024 and the slides for it can be found here. Plozasiran was also recently granted Breakthrough Therapy designation by the U.S. FDA. It previously received Orphan Drug Designation and Fast Track Designation by the FDA along with Orphan Drug Designation by the European Medicines Agency.

The PALISADE trial enrolled 75 patients with persistent chylomicronemia, with or without a genetic diagnosis of FCS, who were randomized to subcutaneous plozasiran at 25 mg (n=26), 50 mg (n=24), or placebo (n=25) every three months for 12 months. Inclusion criteria included a history of multiple triglyceride (TG) measurements above 1000 mg/dL (11.3 mmol/L) along with at least one of the following: prior genetic testing diagnosis for FCS; recurrent episodes of acute pancreatitis; recurrent hospitalizations for severe abdominal pain without other explainable cause; history of childhood pancreatitis; or family history of HTG-induced acute pancreatitis. The following table shows the baseline characteristics for the patients, including the median baseline TG level of 2044 mg/dL across all cohorts.

Characteristic	Pooled Placebo (N=25)	Plozasiran 25 mg (N=26)	Plozasiran 50 mg (N=24)
Mean (SD) Age, years	47 (14)	48 (14)	43 (11)
Female, n (%)	11 (44)	14 (54)	13 (54)
Male, n (%)	14 (56)	12 (46)	11 (46)
White, n (%)	19 (76)	19 (73)	17 (71)
Mean (SD) BMI, kg/m^2	25 (4)	26 (4)	25 (5)
Median (Q1, Q3) APOC3, mg/dL	39 (29, 50)	39 (27, 44)	30 (18, 37)
Mean (SD) APOC3, mg/dL	40 (18)	39 (17)	33 (20)
Median (Q1, Q3) Triglyceride, mg/dL	2053 (1435, 2755)	2008 (1204, 3361)	1902 (1434, 2948)
Median (Q1, Q3) Triglyceride, mmol/L	23 (16, 31)	23 (14, 38)	22 (16, 33)
Mean (SD) Triglyceride, mg/dL	2272 (1141)	2350 (1375)	2492 (1523)
Mean (SD) Triglyceride, mmol/L	26 (13)	27 (16)	28 (17)
Receiving Statins n (%)	11 (44)	11 (42)	12 (50)
Fibrates, n (%)	16 (64)	19 (73)	15 (63)
Omega-3 fatty acids, n (%)	6 (24)	9 (35)	7 (29)
Diabetes or Pre-diabetes, n (%)	11 (44)	10 (39)	7 (29)
Genetic Confirmation of FCS, n (%)	14 (56)	14 (54)	16 (67)
Previous episode of pancreatitis, n (%)	22 (88)	23 (89)	22 (92)

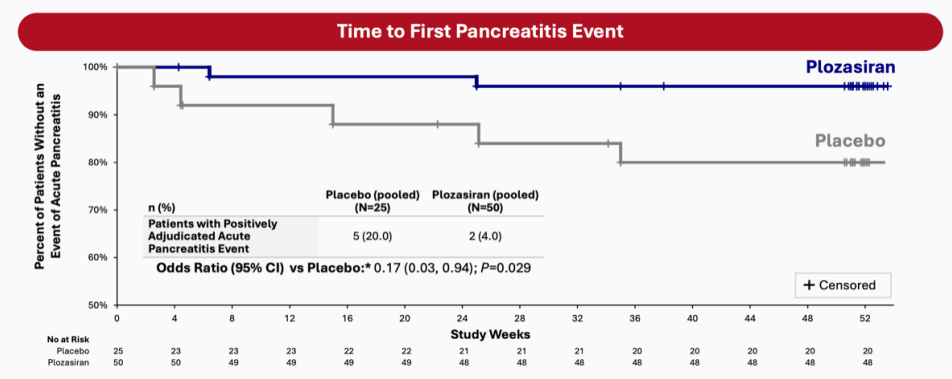
Source: Arrowhead Pharmaceuticals, Inc.

The following graphs show the median reduction in triglycerides and level of APOC3. At the ten-month time point, the median reduction in fasting triglycerides was -80% in the 25 mg cohort, -78% in the 50 mg cohort, and -17% for the placebo cohort (P<0.001). The reduction in APOC3 was -93% in the 25 mg cohort, -96% in the 50 mg cohort, and -1% in the placebo group (P<0.001).



Source: Arrowhead Pharmaceuticals, Inc.

An important secondary efficacy endpoint compared the incidence of positively adjudicated acute pancreatitis (AP) in a pre-specified pooled analysis of the 25 mg and 50 mg plozasiran groups versus the pooled placebo group. Of the 38 suspected cases of acute pancreatitis that were referred for adjudication, nine episodes in seven patients were positively adjudicated. The results showed an 83% reduction in the risk of developing acute pancreatitis for plozasiran-treated patients compared to those treated with placebo. A total of two cases occurred in two of 50 patients (4%) receiving plozasiran versus seven cases that occurred in five of 25 patients (20%) receiving placebo (OR 0.17; *P*=0.03).



Source: Arrowhead Pharmaceuticals, Inc.

The following table provides the summary of adverse events during the trial. There was a higher rate of serious or severe adverse events in the placebo group, no changes were seen in platelet counts, and there were no deaths reported in the study.

	Pooled Placebo (N=25)	Plozasiran	
		25 mg (N=26)	50 mg (N=24)
Patients with Any TEAEs	20	23	20
Most Common TEAEs, N (%)			
Abdominal Pain	5 (20)	7 (27)	6 (25)
COVID-19 Infection*	0 (0)	5 (19)	7 (29)
Nasopharyngitis	3 (12)	5 (19)	2 (8)
Headache	2 (8)	3 (12)	5 (21)
Nausea	2 (8)	4 (15)	3 (13)
Back Pain	2 (8)	3 (12)	2 (8)
Upper respiratory tract infection	2 (8)	3 (12)	2 (8)
Diarrhea	2 (8)	1 (4)	4 (17)
Severe TEAEs	5 (20)	3 (12)	3 (13)
Serious TEAEs	7 (28)	5 (19)	2 (8)
Deaths	0 (0)	0 (0)	0 (0)
Premature Discontinuations	6 (24)	3 (12)	2 (8)
HbA1c, mean (SD)			
Baseline	6.1 (1.33)	5.7 (0.90)	5.59 (1.15)
Month 12	6.2 (1.17)	5.98 (1.00)	5.83 (1.56)
Platelet count, 10^9/liter, mean (SD)			
Baseline	217.9 (80.5)	204.4 (70.4)	192.9 (50.7)
Mean change from baseline at Month 10	25.9 (38.2)	28.7 (61.2)	-4.4 (48.2)
Mean change from baseline at Month 12	8.6 (47.5)	-4.3 (40.8)	-8.7 (50.8)

Source: Arrowhead Pharmaceuticals, Inc.

Comparison with Olezarsen

Ionis Pharmaceuticals' is developing olezarsen, an antisense oligonucleotide that targets *APOC3*. Ionis recently reported that the NDA for olezarsen for the treatment of FCS was accepted for Priority Review with a PDUFA date of December 19, 2024. The results from the Phase 3 BALANCE trial of olezarsen in FCS were recently published in *The New England Journal of Medicine* (Stroes *et al*., 2024). While difficult to perform cross-trial comparisons, the following chart provides some of the parameters and outcomes for the Phase 3 trials for olezarsen and plozasiran.

	Plozasiran			Olezarsen		
	Placebo	25 mg	50 mg	Placebo	50 mg	80 mg
Dosing	Q3M			Q4W		
No. Subjects	25	26	24	23	21	22
Male (%)	56%	46%	46%	48%	29%	50%
BMI	25±4	26±4	25±5	24.2±4.1	22.4±3.5	25.1±6.0
TG - mean (mg/dL)	2272±1141	2350±1375	2492±1523	2596±1256	2684±1235	2613±1499
TG - median (mg/dL)	2053 (1435-2755)	2008 (1204-3361)	1902 (1434-2948)	2493 (334-5436)	2679 (779-5965)	2086 (683-6898)
APOC - mean (mg/dL)	40±18	39±17	33±20	27.7±11.7	27.7±10.5	27.5±11.6
History of AP	88%	89%	92%	65%	71%	77%
Genetic Confirmation FCS	56%	54%	67%	100%	100%	100%
TG Reduction - 6 mo	N/A	N/A	N/A	-	LSM vs PBO: -22.4% (P=0.08)	LSM vs PBO: -43.5% (P<0.001)
TG Reduction - 10 mo	Median: -17%	Median: -80%	Median: -78%	N/A	N/A	N/A
TG Reduction - 12 mo	Median: 0%	Median: -78%	Median: -71%	-	LSM vs PBO: -43.8%	LSM vs PBO: -59.4%
APOC3 Reduction - 6 mo	N/A	N/A	N/A	-	LSM vs PBO: 65.5%	LSM vs PBO: 73.7%
APOC3 Reduction - 10 mo	Median: 0%	Median: -93%	Median: -96%	N/A	N/A	N/A
APOC3 Reduction - 12 mo	Median: 8%	Median: -89%	Median: -88%	N/A	LSM vs PBO: 77.1%	LSM vs PBO: 81.3%
AP Events (No. patients)	9 (7)	1 (1)	1 (1)	11 (7)	1 (1)	1 (1)
Odds Ratio	Odds Ratio: 0.17, *P*=0.03			Rate Ratio: 0.12		

Source: Ionis Pharmaceuticals, Inc.; Arrowhead Pharmaceuticals, Inc.; Stroes *et al*., 2024; Zacks SCR

A few points that we think are worthwhile for investors to consider include:

- Olezarsen is dosed once every four weeks while plozasiran is dosed once every three months
- All of the subjects in the olezarsen study had genetically confirmed FCS, while between one-half to two-thirds of subjects in the plozasiran trial had generically confirmed FCS
- The triglyceride and APOC3 reductions were greater for plozasiran than for olezarsen (with the caveat of median vs. mean values reported), with less variability over time for plozasiran than for olezarsen.
- Plozasiran showed a statistically significant decrease in the risk of developing acute pancreatitis (AP), however the olezarsen trial was not powered for statistical significance but still showed a favorable rate ratio.

Overall, we believe the plozasiran results are highly competitive and should position the product to do well in the FCS market.

Conclusion

The results from the Phase 3 PALISADE trial of plozasiran in FCS are very encouraging and we believe the drug compares quite favorably to olezarsen, which has a PDUFA date of December 19, 2024 for FCS. We look forward to the company filing the NDA for plozasiran and additional information on plans for its potential commercial launch next year. With no changes to our model our valuation remains at $70 per share.

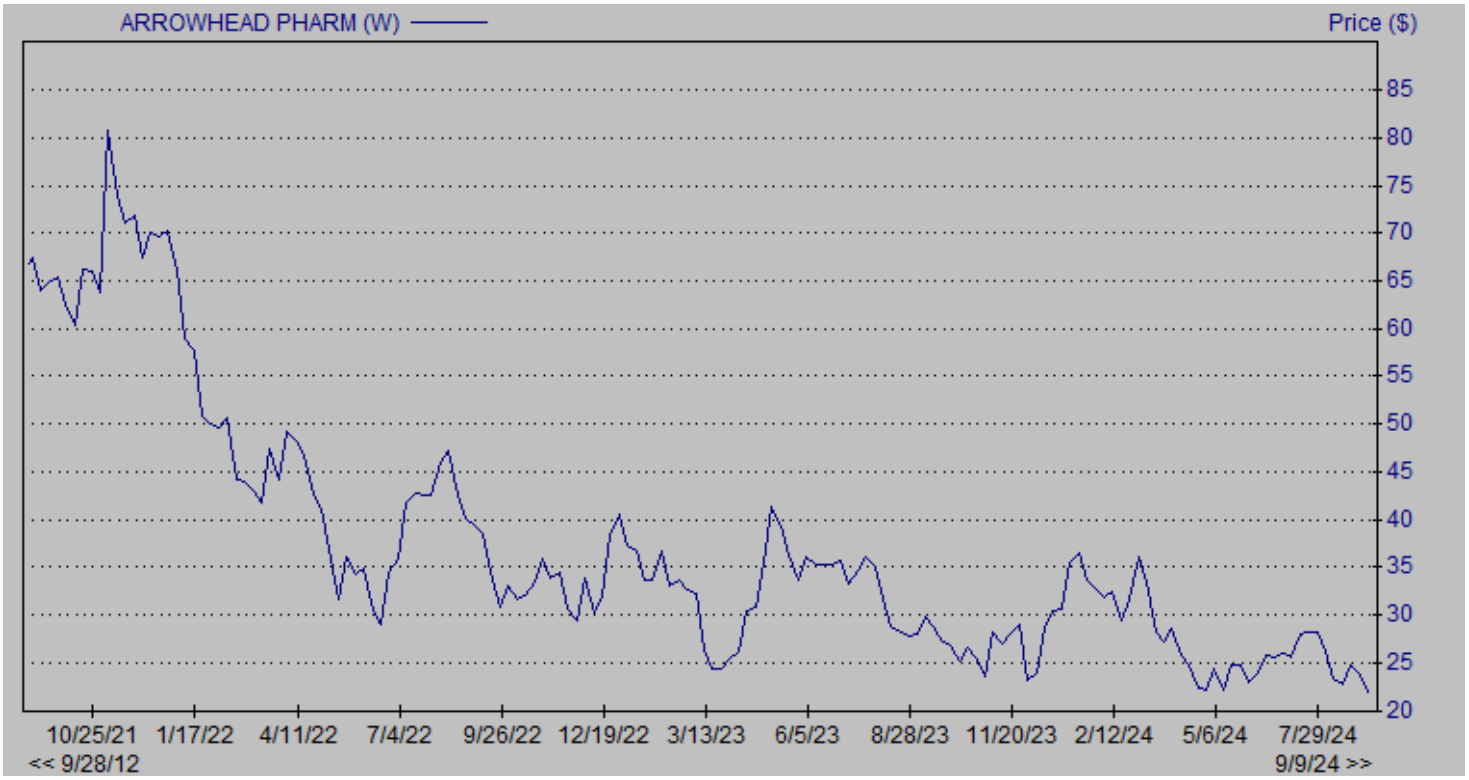
PROJECTED FINANCIALS

Arrowhead Pharmaceuticals, Inc.	FY2023 A	Q1FY24 A	Q2FY24 A	Q3FY24 A	Q4FY24 E	FY2024 E	FY2025 E	FY2026 E
Revenue	$240.74	$3.55	$0.00	$0.00	$50.00	$53.55	$250.00	$300.00
YOY Growth	*456.1%*	*-97.6%*	*-100.0%*	*-100.0%*	*-79.2%*	*601.6%*	*48.1%*	*918.5%*
Total Revenues	**$240.7**	**$3.6**	**$0.0**	**$0.0**	**$50.0**	**$53.6**	**$250.0**	**$300.0**
YOY Growth	*456.1%*	*-97.6%*	*-100.0%*	*-100.0%*	*-79.2%*	*601.6%*	*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**	**$3.6**	**$0.0**	**$0.0**	**$50.0**	**$53.6**	**$250.0**	**$300.0**
Gross Margin	*100.0%*	*100.0%*	*#DIV/0!*	*#DIV/0!*	*100.0%*	*100.0%*	*100.0%*	*100.0%*
R&D	$353.2	$116.5	$101.1	$152.4	$85.0	$455.0	$375.0	$380.0
% R&D	*146.7%*	*3280.5%*	*#DIV/0!*	*#DIV/0!*	*170.0%*	*849.7%*	*150.0%*	*126.7%*
Salary and G&A	$92.5	$23.6	$25.1	$23.7	$24.0	$96.4	$95.0	$100.0
% SG&A	*38.4%*	*664.7%*	*#DIV/0!*	*#DIV/0!*	*48.0%*	*180.0%*	*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%*	*#DIV/0!*	*#DIV/0!*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Operating Income	**($205.0)**	**($136.5)**	**($126.2)**	**($176.1)**	**($59.0)**	**($497.9)**	**($220.0)**	**($180.0)**
Operating Margin	*-85.2%*	*-*	*-*	*-*	*-*	*-929.7%*	*-88.0%*	*-60.0%*
Other Income (Net)	($1.5)	($2.1)	($0.8)	$2.2	$0.0	($0.8)	$0.0	$0.0
Pre-Tax Income	**($206.5)**	**($138.7)**	**($127.0)**	**($174.0)**	**($59.0)**	**($498.7)**	**($220.0)**	**($180.0)**
Net Taxes (benefit)	$2.8	$3.3	$0.0	$0.0	$0.0	$3.3	$0.0	$0.0
Net Loss Attributable to Noncontrolling Interest	$4.0	$2.5	$1.7	$3.2	$0.0	$7.4	$0.0	$0.0
Reported Net Income	**($205.3)**	**($132.9)**	**($125.3)**	**($170.8)**	**($59.0)**	**($488.0)**	**($220.0)**	**($180.0)**
Net Margin	*-85.3%*	*-*	*-*	*-*	*-*	*-911.2%*	*-88.0%*	*-60.0%*
Reported EPS	**($1.92)**	**($1.24)**	**($1.02)**	**($1.38)**	**($0.47)**	**($4.07)**	**($1.76)**	**($1.42)**
YOY Growth	*-*	*-*	*-*	*-*	*-*	*-*	*-*	*-*
Basic Shares Outstanding	106.8	107.4	123.3	124.2	124.3	119.8	125.0	127.0

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

© Copyright 2024, Zacks Investment Research. All Rights Reserved.

HISTORICAL STOCK PRICE



Source: Zacks SCR

© Copyright 2024, Zacks Investment Research. All Rights Reserved.

DISCLOSURES

The following disclosures relate to relationships between Zacks Small-Cap Research ("Zacks SCR"), a division of Zacks Investment Research ("ZIR"), and the issuers covered by the Zacks SCR Analysts in the Small-Cap Universe.

ANALYST DISCLOSURES

I, David Bautz, PhD, hereby certify that the view expressed in this research report accurately reflect my personal views about the subject securities and issuers. I also certify that no part of my compensation was, is, or will be, directly or indirectly, related to the recommendations or views expressed in this research report. I believe the information used for the creation of this report has been obtained from sources I considered to be reliable, but I can neither guarantee nor represent the completeness or accuracy of the information herewith. Such information and the opinions expressed are subject to change without notice.

INVESTMENT BANKING AND FEES FOR SERVICES

Zacks SCR does not provide investment banking services nor has it received compensation for investment banking services from the issuers of the securities covered in this report or article.
Zacks SCR has received compensation from the issuer directly, from an investment manager, or from an investor relations consulting firm engaged by the issuer for providing non-investment banking services to this issuer and expects to receive additional compensation for such non-investment banking services provided to this issuer. The non-investment banking services provided to the issuer includes the preparation of this report, investor relations services, investment software, financial database analysis, organization of non-deal road shows, and attendance fees for conferences sponsored or co-sponsored by Zacks SCR. The fees for these services vary on a per-client basis and are subject to the number and types of services contracted. Fees typically range between ten thousand and fifty thousand dollars per annum. Details of fees paid by this issuer are available upon request.

POLICY DISCLOSURES

This report provides an objective valuation of the issuer today and expected valuations of the issuer at various future dates based on applying standard investment valuation methodologies to the revenue and EPS forecasts made by the SCR Analyst of the issuer's business.
SCR Analysts are restricted from holding or trading securities in the issuers that they cover. ZIR and Zacks SCR do not make a market in any security followed by SCR nor do they act as dealers in these securities. Each Zacks SCR Analyst has full discretion over the valuation of the issuer included in this report based on his or her own due diligence. SCR Analysts are paid based on the number of companies they cover. SCR Analyst compensation is not, was not, nor will be, directly or indirectly, related to the specific valuations or views expressed in any report or article.

ADDITIONAL INFORMATION

Additional information is available upon request. Zacks SCR reports and articles are based on data obtained from sources that it believes to be reliable, but are not guaranteed to be accurate nor do they purport to be complete. Because of individual financial or investment objectives and/or financial circumstances, this report or article should not be construed as advice designed to meet the particular investment needs of any investor. Investing involves risk. Any opinions expressed by Zacks SCR Analysts are subject to change without notice. Reports or articles or tweets are not to be construed as an offer or solicitation of an offer to buy or sell the securities herein mentioned.

CANADIAN COVERAGE

This research report is a product of Zacks SCR and prepared by a research analyst who is employed by or is a consultant to Zacks SCR. The research analyst preparing the research report is resident outside of Canada, and is not an associated person of any Canadian registered adviser and/or dealer. Therefore, the analyst is not subject to supervision by a Canadian registered adviser and/or dealer, and is not required to satisfy the regulatory licensing requirements of any Canadian provincial securities regulators, the Investment Industry Regulatory Organization of Canada and is not required to otherwise comply with Canadian rules or regulations.