HLS Therapeutics Inc.

News Release

New REDUCE-IT® Analyses Show VASCEPA® (Icosapent Ethyl) Benefit in High-Risk Cardiovascular Disease Patient Subgroups

4/8/2024

- Findings Presented on VASCEPA Utility in REDUCE-IT Patient Subgroups by Baseline High/Low Lp(a), LDL-C Levels
- Lp(a) Results Published Simultaneously in the Journal of the American College of Cardiology (JACC)

TORONTO, April 8, 2024 /CNW/ - HLS Therapeutics Inc. (HLS or the Company) (TSX: HLS), a pharmaceutical company focusing on addressing unmet needs in the treatment of psychiatric disorders and cardiovascular disease, today highlighted two data presentations at the 73rd Annual Scientific Sessions of the American College of Cardiology (ACC.24) describing the effects of VASCEPA (icosapent ethyl) on reducing Major Adverse Cardiovascular Events (MACE) in patients with baseline high or low Lipoprotein(a) [Lp(a)] levels, as well as reducing the risk of cardiovascular (CV) events in patients irrespective of baseline LDL-C level. The REDUCE-IT analysis results relating Lp(a) concentrations with CV risk were also published online today in the Journal of the American College of Cardiology (JACC).

"These new findings provide additional important evidence about the clinical utility of VASCEPA and further demonstrate its value in reducing cardiovascular events in at-risk patients in key subgroups," said Craig Millian, CEO of HLS. "Our partner Amarin Corporation (Amarin) (NASDAQ:AMRN), continues to generate exciting new research and insights from the REDUCE-IT trial, which build on the already vast body of evidence supporting the clinical benefits of VASCEPA."

The subgroup analyses and their key findings are outlined below:

Icosapent Ethyl Reduces MACE in Patients with Elevated Triglycerides and High or Low Lipoprotein(a) Concentrations: A REDUCE-IT Subanalysis

High Lp(a) concentrations are associated with increased CV event risk, even when LDL-C levels are well-managed. There are no treatments currently approved to reduce residual CV risk on top of contemporary medical therapy in patients with high Lp(a) levels.

In this post hoc analysis of REDUCE-IT, the relationship between continuous baseline Lp(a) concentration and risk of MACE was analyzed in models that also accounted for baseline LDL-C, baseline triglycerides (TG), and double-blind treatment.

REDUCE-IT participants were randomized to receive either 2g twice daily of icosapent ethyl (IPE) or matching placebo and followed for a median 4.9 years. In this subanalysis, there were 7,026 REDUCE-IT patients with baseline Lp(a) data and a median Lp(a) value of 11.6 (Q1-Q3: 5.0-37.4) mg/dL. Results showed that baseline Lp(a) had a strong and significant relationship with MACE irrespective of baseline LDL-C, baseline TGs, and treatment assignment, and that the benefit of IPE was consistent across Lp(a) concentrations. Importantly, the treatment benefit of IPE was evident across subgroups with both high (≥50 mg/dL) and low (<50 mg/dL) Lp(a) concentrations. Specifically, for first MACE, the relative IPE treatment effects for Lp(a) ≥50 mg/dL and <50 mg/dL were HR 0.79 (95% CI 0.64-0.97; P=0.0248) and HR 0.75 (95% CI 0.66-0.84; P<0.0001), respectively. Absolute risk reductions at 5 years with IPE were 6.5% and 5.7% for Lp(a) ≥50 mg/dL and <50 mg/dL, respectively.[1]

Limitations include that participants in REDUCE-IT were not selected on the basis of their baseline Lp(a) concentration and that not all REDUCE-IT patients had available baseline Lp(a) data.

"In this analysis, IPE showed a clear clinical benefit for patients with both high and low Lp(a) levels. IPE provided a relative risk reduction of 21% among patients with an Lp(a) level of ≥50 mg/dL and 25% for those patients with an Lp(a) level of <50 mg/dL," said Dr. Michael Szarek, professor, Division of Cardiology, University of Colorado School of Medicine and a faculty member at CPC Clinical Research. "These findings are important, as high baseline Lp(a) concentrations are a predictor for MACE, and this analysis reinforces IPE's clinical benefit in these at-risk patient sub-populations."

The analysis and its findings were published simultaneously online in **JACC**.

Efficacy of Icosapent Ethyl for Reducing Cardiovascular Outcomes by Baseline Low Density Lipoprotein Cholesterol Level

Elevated low-density lipoprotein cholesterol (LDL-C) is a well-established major CV risk factor supported by clinical

evidence showing decreased atherosclerotic disease events when LDL-C is therapeutically lowered. Recent international guidelines recommend lowering LDL-C to <55 mg/dL in those patients who are at very high risk for a future CV event.

In this post hoc analysis, investigators explored REDUCE-IT data to determine if IPE reduces CV outcomes among high-risk CV patients irrespective of baseline LDL-C. Patients were stratified by LDL-C <55 vs ≥55 mg/dL. The primary outcome was a composite of CV death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or unstable angina.

Among statin-treated REDUCE-IT patients with baseline LDL-C data, 1,058 (12.9%) had LDL-C <55 mg/dL and 7,117 (87.1 %) had LDL-C ≥55 mg/dL. The primary outcome rate among patients with LDL-C <55 mg/dL was 16.2% in the IPE group and 22.8% in the placebo group, HR 0.66 (95% CI 0.50-0.87; P=0.003). Findings were consistent in the LDL-C ≥55 mg/dL subgroup, with rates of 17.4% in the IPE group and 21.9% in the placebo group, HR 0.76 (95% CI 0.69-0.85; P<0.0001). No significant interaction by baseline LDL-C was observed.

Limitations are that randomization was not stratified by baseline LDL-C, however, baseline characteristics were similar among the two baseline LDL-C subgroups. REDUCE-IT patients were on statin therapy, but with low rates or unavailability of other lipid therapies such as ezetimibe, proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitors, or small interfering RNA (siRNA) therapies.

"As we know, LDL-C is a well-established major CV risk factor. These data are important and show that among adults with increased CV risk and elevated TGs, icosapent ethyl clearly reduced the rate of CV outcomes irrespective of baseline LDL-C, including in those with very well controlled LDL-C <55 mg/dL," said Deepak L. Bhatt, MD, MPH, MBA, Director of Mount Sinai Fuster Heart Hospital.

All analyses highlighted above were funded by Amarin. Dr. Deepak L. Bhatt served as the principal investigator for REDUCE-IT and his institution received research funding from Amarin.

About REDUCE-IT®

REDUCE-IT was a global cardiovascular outcomes study designed to evaluate the effect of VASCEPA in adult patients with LDL-C controlled to between 41-100 mg/dL (median baseline 75 mg/dL) by statin therapy and various cardiovascular risk factors including persistent elevated triglycerides between 135-499 mg/dL (median baseline 216 mg/dL) and either established cardiovascular disease (secondary prevention cohort) or diabetes mellitus and at least one other cardiovascular risk factor (primary prevention cohort).

REDUCE-IT, conducted over seven years and completed in 2018, followed 8,179 patients at over 400 clinical sites in

11 countries with the largest number of sites located within the United States. REDUCE-IT was conducted based on a special protocol assessment agreement with FDA. The design of the REDUCE-IT study was published in March 2017 in Clinical Cardiology.[2] The primary results of REDUCE-IT were published in The New England Journal of Medicine in November 2018.[3] The total events results of REDUCE-IT were published in the Journal of the American College of Cardiology in March 2019.[4] These and other publications can be found in the R&D section on Amarin's website at **www.amarincorp.com**.

ABOUT CARDIOVASCULAR DISEASE

Worldwide, cardiovascular disease (CVD) remains the #1 cause of mortality of men and women.

Controlling bad cholesterol, also known as LDL-C, is one way to reduce a patient's risk for cardiovascular events, such as heart attack, stroke or death. However, even with the achievement of target LDL-C levels, millions of patients still have significant and persistent risk of cardiovascular events, especially those patients with elevated triglycerides. Statin therapy has been shown to control LDL-C, thereby reducing the risk of cardiovascular events by 25-35%.[5] Significant cardiovascular risk remains after statin therapy. People with elevated triglycerides have 35% more cardiovascular events compared to people with normal (in range) triglycerides taking statins.[6, 7, 8.]

ABOUT VASCEPA (ICOSAPENT ETHYL) CAPSULES

VASCEPA capsules are the first-and-only prescription treatment comprised solely of the active ingredient, icosapent ethyl (IPE), a unique form of eicosapentaenoic acid. VASCEPA was approved by Health Canada and added to Health Canada's Register of Innovative Drugs and benefits from data protection for a term of eight years, as well as being the subject of multiple issued and pending patents based on its unique clinical profile. HLS in-licensed the exclusive rights to VASCEPA for the Canadian market from Amarin.

ABOUT HLS THERAPEUTICS INC.

Formed in 2015, HLS is a pharmaceutical company focused on the acquisition and commercialization of late-stage development, commercial stage promoted and established branded pharmaceutical products in the North American markets. HLS's focus is on products targeting the central nervous system and cardiovascular therapeutic areas. HLS's management team is composed of seasoned pharmaceutical executives with a strong track record of success in these therapeutic areas and at managing products in each of these lifecycle stages. For more information visit: **www.hlstherapeutics.com**

FORWARD LOOKING INFORMATION

This release includes forward-looking statements regarding HLS and its business. Such statements are based on the

current expectations and views of future events of HLS's management. In some cases the forward-looking statements can be identified by words or phrases such as "may", "will", "expect", "plan", "anticipate", "intend", "potential", "estimate", "believe" or the negative of these terms, or other similar expressions intended to identify forward-looking statements, including, among others, statements with respect to HLS's pursuit of additional product and pipeline opportunities in certain therapeutic markets, statements regarding growth opportunities, expectations regarding financial performance, and the NCIB and ASPP. The forward-looking events and circumstances discussed in this release may not occur and could differ materially as a result of known and unknown risk factors and uncertainties affecting HLS, including risks relating to the specialty pharmaceutical industry, risks related to the regulatory approval process, economic factors and many other factors beyond the control of HLS. Forward-looking statements and information by their nature are based on assumptions and involve known and unknown risks, uncertainties and other factors which may cause HLS's actual results, performance or achievements, or industry results, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statement or information. Accordingly, readers should not place undue reliance on any forward-looking statements or information. A discussion of the material risks and assumptions associated with this release can be found in the Company's Annual Information Form dated March 13, 2024, and Management's Discussion and Analysis dated March 13, 2024, both of which have been filed on SEDAR and can be accessed at **www.sedarplus.ca**. Accordingly, readers should not place undue reliance on any forward-looking statements or information. Except as required by applicable securities laws, forward-looking statements speak only as of the date on which they are made and HLS undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events, or otherwise.

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