Nuwellis Announces the Submission of the AVOID-HF Clinical Analysis as a Late Breaking Clinical Trial at HFSA

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The Finkelstein-Schoenfeld Method of Win Ratios Analysis Provides New Insights Into Superiority of Ultrafiltration over Diuretics in Treating Fluid Overloaded Heart Failure Patients Resistant to Diuretics

MINNEAPOLIS, July 26, 2022 (GLOBE NEWSWIRE) -- Nuwellis, Inc. (Nasdaq: NUWE) a commercial-stage company focused on improving the quality of life for people with fluid overload, today announced the submission of the AVOID-HF clinical study analysis using the Finkelstein-Schoenfeld method of Win-Ratios (WR) as a Late Breaking Clinical Trial at the Heart Failure Society of America's (HFSA) 2022 Annual Scientific Meeting in September.

The AVOID-HF (**A**quapheresis **V**ersus Intraven**o**us Diuret**i**cs an**d** Hospitalization for **H**eart **F**ailure) prospective, multicenter, randomized controlled trial tested the hypothesis that patients hospitalized for heart failure (HF) and treated with ultrafiltration would have a longer time to their first heart failure event within 90 days after hospital discharge compared to those receiving IV loop diuretics. The study was trending favorably when the study sponsor terminated it before reaching full enrollment for reasons unrelated to patient safety or clinical futility. At the time, analysis of the AVOID-HF trial data was inconclusive due to the lower-than-planned sample size. However, newer statistical methods like the Finkelstein-Schoenfeld method of hierarchical Win Ratios increase statistical precision to evaluate the clinical benefit and demonstrate significance between treatment arms with the added benefit of requiring a smaller study sample size.

"The Finkelstein-Schoenfeld method of hierarchical Win Ratios provides a critical framework for evaluating the data obtained from the 221 patients enrolled in the AVOID-HF study," said Dr. Sean Pinney, Professor of Medicine and Co-Director of the Heart and Vascular Center at The University of Chicago Medicine. "We were finally able to evaluate the role of ultrafiltration in treating these fluid overloaded heart failure patients and share our findings with the medical community."

Heart failure can disrupt normal kidney function and lower the ability to remove sodium from the body, resulting in excessive water retention that can ultimately lead to fluid overload. Over 1 million heart failure hospitalizations occur annually in the United States, and fluid overload is the predominant cause in 90% of the patients. Furthermore, nearly one-quarter of heart failure patients will be readmitted to the hospital within 30 days of their initial discharge, and half will be readmitted within 6 months.[1] In addition to the higher mortality rate associated with repeat hospitalizations for existing patients with HF[2], hospitals receive no reimbursement for patients that are readmitted within 30 days of initial discharge. According to Premier Applied Sciences data, the average total unreimbursed cost per inpatient encounter is $24,027, which highlights the importance of reducing unscheduled 30-day readmissions.

"The Win-Ratios analysis of the AVOID-HF clinical study will provide additional evidence to support the use of ultrafiltration to treat fluid-overloaded heart failure patients," said Nestor Jaramillo, Jr., President and CEO of Nuwellis. "We're grateful to Drs. Pinney, DeVita, and Costanzo, the authors of this manuscript, for leading this reanalysis of the AVOID-HF data. As a company, we are committed to the ultimate goal of making Aquadex therapy the standard of care for fluid management in heart failure patients that are resistant to diuretics. We hope the AVOID-HF Win-Ratios analysis is accepted as a Late Breaking Clinical Trial at HFSA, and we are excited to share these results with the broader heart failure community."

In addition to the AVOID-HF Win-Ratios analysis and submission, Nuwellis recently announced the first patient enrolled in its REVERSE-HF clinical study evaluating the clinical benefit and economic value of its Aquadex® ultrafiltration therapy in comparison to intravenous (IV) diuretics for the treatment of fluid overload in patients with worsening heart failure. Nuwellis also submitted information on REVERSE-HF to HFSA's Clinical Trials Central, as a currently enrolling heart failure randomized controlled trial.

About Nuwellis
Nuwellis, Inc. (Nasdaq: NUWE) is a medical device company dedicated to transforming the lives of patients suffering from fluid overload through science, collaboration, and innovation. The Company is focused on developing, manufacturing and commercializing the Aquadex SmartFlow® system for ultrafiltration therapy. Nuwellis is headquartered in Minneapolis, with a wholly-owned subsidiary in Ireland.

About the Aquadex SmartFlow® System
The Aquadex SmartFlow system delivers clinically proven therapy using a simple, flexible and predictable method of removing excess fluid from patients suffering from hypervolemia (fluid overload). The Aquadex SmartFlow system is indicated for temporary (up to 8 hours) or extended (longer than 8 hours in patients who require hospitalization) use in adult and pediatric patients weighing 20 kg or more whose fluid overload is unresponsive to medical management, including diuretics. All treatments must be administered by a health care provider, within an outpatient or inpatient clinical setting, under physician prescription, both having received training in extracorporeal therapies.

Forward-Looking Statements
Certain statements in this release may be considered forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including without limitation, statements regarding the new market opportunities and anticipated growth in 2022 and beyond. Forward-looking statements are predictions, projections and other statements about future events that are based on current expectations and assumptions and, as a result, are subject to risks and uncertainties. Many factors could cause actual future events to differ materially from the forward-looking statements in this release, including, without limitation, those risks associated with our ability to execute on our commercialization strategy, the impact of the COVID-19 pandemic, the possibility that we may be unable to raise sufficient funds necessary for our anticipated operations, our post-market clinical data collection activities, benefits of our products to patients, our expectations with respect to product development and commercialization efforts, our ability to increase market and physician acceptance of our products, potentially competitive product offerings, intellectual property protection, our

ability to integrate acquired businesses, our expectations regarding anticipated synergies with and benefits from acquired businesses, and other risks and uncertainties described in our filings with the SEC. Forward-looking statements speak only as of the date when made. Nuwellis does not assume any obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

[1] Costanzo MR et al. J Am Coll Cardiol. 2017 May 16;69(19):2428-2445

[2] Andrew H Lin et al. Mil Med. 2017 Sep.

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