UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

Current Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **March 26, 2024**

Nuwellis, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**001-35312**	**No. 68-0533453**
(State or Other Jurisdiction of Incorporation or Organization)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

12988 Valley View Road, Eden Prairie, MN 55344
(Address of Principal Executive Offices) (Zip Code)

(952) 345-4200
(Registrant's Telephone Number, Including Area Code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	NUWE	Nasdaq Capital Market

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On March 11, 2024, Nuwellis, Inc. (the "Company") filed its Annual Report on Form 10-K for the fiscal year ended December 31, 2023 (the "Form 10-K") with the U.S. Securities and Exchange Commission ("SEC"). This Current Report on Form 8-K (this "Report") is being filed solely to replace Part I, Item 1: Business of our Form 10-K, with the Business section as set forth below.

Except as described below, no other changes have been made to the Form 10-K, and this Report does not otherwise amend, update or change the financial statements or other disclosures in the Form 10-K. This Report speaks as of the filing date of the Form 10-K and does not (i) reflect events, results or developments that occurred or facts that became known after the filing date of the Form 10-K or (ii) modify or update those disclosures affected by subsequent events, results, developments or facts. Among other things, forward-looking statements made in the Form 10-K have not been revised to reflect events, results or developments that occurred or facts that became known to us after the date of the Form 10-K, and such statements should be read in conjunction with our filings with the SEC subsequent to the Form 10-K. This Report should be read in conjunction with the Company's other filings with the SEC subsequent to March 11, 2024.

Item 1. Business

Overview

We are a medical technology company dedicated to transforming the lives of patients suffering from fluid overload through science, collaboration, and innovative technology. The company is focused on developing, manufacturing, and commercializing medical devices used in ultrafiltration therapy, including the Aquadex FlexFlow® and the Aquadex SmartFlow® systems (collectively the "Aquadex System"). The Aquadex SmartFlow® system is indicated for temporary (up to eight 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.

Please note that selected authors in the citations below are either current consultants to the Company or were previously compensated consultants. Each author typically is required to disclose any actual or potential conflicts of interests at the time they submitted their written manuscript to the potential publication. Dr. Sean Pinney for example, is the principle investigator under the Company's current REVERSE heart failure clinical study. Additionally, Dr. Maria Rosa Costanzo, joined the Company's Board of Directors in September, 2019, though many of her cited publications preceded her membership on the Board of Directors. Since joining the Company's Board, Dr. Costanzo has declined any equity ownership in the Company, although she has accepted cash remuneration for her Board and Committee participation.

Fluid Overload

Fluid overload, also known as hypervolemia, is a condition in which there is too much fluid in the blood, vital organs, and interstitial space, and generally refers to the expansion of the extracellular fluid volume. Although the body does need some amount of fluid to remain healthy, too much can cause an imbalance and damage to an individual's health.[1]

The signs and symptoms of fluid overload are not always the same in each patient and may vary. However, possible signs and symptoms of fluid overload include pulmonary edema/pleural effusion, peripheral edema, anasarca (swelling of the skin) ascites, jugular vein distention and dyspnea.[2] Medical conditions or diseases where excess fluid accumulates in the body are heart failure, kidney failure, nephrotic syndrome, cirrhosis, or burn injuries/trauma. Individuals may also suffer from temporary fluid overload following certain surgical procedures, such as cardiac surgery.[3] The diagnosis of fluid overload can be made through a variety of tests/exams such as a physical exam (weight, presence of pulmonary rales, and edema), blood chemistry, natriuretic peptides, liver enzymes, hemoglobin and hematocrit, blood volume analysis, and/or bioimpedance analysis.[4] Fluid overload has a significant association with the combined events of death, infection, bleeding, arrhythmia, and pulmonary edema[5] and is a leading cause of hospital readmissions with patients suffering from heart failure and patients following cardiac surgery.[6]

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[1] Murugan R et al. Nature Rev Nephrol. 2020; 1-14.

[2] Koratala A et al. Cardiorenal Med. 2022;12(4):141-154.

[3] Vaara ST et al. *Crit Care*.2012; 16: 1-11.

[4] Koratala A et al Cardiorenal Med. 2022;12(4):141-154

[5] Stein, A, et. al. Critical Care, 2012:16:R99.

[6] Iribarne A, et al. Ann Thorac Surg. 2014; 98(4): 1274-80.

The condition of fluid overload is often observed in patients with heart failure and secondary oliguric states,[7] although in pediatric patients, fluid overload is associated with significant increases in mortality.[8] [9] Congestion or fluid overload, the hallmark of decompensated heart failure or HF, is the primary reason for hospitalization in 90% of these patients.[10] [11] For this reason, diuretics have been the cornerstone of heart failure treatment for more than 50 years.[12] Over the past 20 years, approaches to treatment have changed dramatically.[13]

These dramatic improvements include new medications and new technologies, such as ultrafiltration, to help treat fluid overload. Each year there are over 1 million heart failure hospitalizations in the United States, and 90% of those hospitalizations are due to symptoms of fluid overload.[14] These patients are hospitalized on average for 8 days at a cost of approximately $24,000, as to which reimbursement does not cover the full cost.[15]

Treatments for Fluid Overload

Diuretics

Treatment for fluid overload has traditionally been achieved through use of oral or loop diuretics which may be accompanied by use of other categories of medications, such as angiotensin-converting enzyme (ACE) inhibitors, sodium-glucose co-transporter 2 (SGLT-2) inhibitors, Aldosterone receptor antagonists (MRAs), beta-blockers, and inotropic drugs. Chronic diuretic use has been associated with increased long-term mortality and hospitalizations in a wide spectrum of chronic systolic and diastolic HF patients.[16] We believe that diuretics, particularly at high doses, may be deleterious to patients. Additionally, between 10-40% of heart failure patients are refractory to diuretics,[17] with diuretic resistance associated with a higher risk of in-hospital worsening of heart failure, increase mortality after discharge, and a 3-fold increase in rehospitalization rates.[18] In addition, patients with heart failure and cardiorenal syndrome have diminished response to loop diuretics, making these agents less effective at relieving congestion.[19] Also, long term use of diuretics has been associated with kidney damage.[20] One study found that approximately 40% of heart failure patients have poor diuretic response.[21] This poor response is possibly due to noncompliance or high intake of salt, poor drug absorption, insufficient kidney response to drug, and reduced diuretic secretion.[22] Despite treatment with loop diuretics, patients are frequently hospitalized and treated for recurrent symptoms and signs of fluid overload.

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[7] Ronco C, Costanzo MR, Bellomo R, et al. (2010) Fluid Overload Diagnosis and Management. Basel, Switzerland: Karger.
[8] Sutherland SM, et al. *Am J Kidney Disease*. 2010; 5(2): 316-25.
[9] Gillespie RS, et al. *Ped Nephro*. 2004; 19(12): 1394-99.
[10] Kazory A & Costanzo MR. *Adv Chronic Kidney Dis*. 2018; 25(5): 434-442.
[11] Fonarow GC. Rev Cardiovasc Med. 2003; 4: s21-30.
[12] Kamath SA. *Int J of Nephrol*. 2011; 1-6.
[13] Ellison DH. *Cardio*.2001;96:132-143
[14] Costanzo MR, et al. J Am Coll Cardiol. 2017 May 16;69(19):2428-2445.
[15] Gheorghiade M, et al. *Eur Heart J Suppl*. 2005; 7:B13- 19.
[16] Ahmed A, et al. *Eur Heart J.* 2006 Jun;27(12):1431-9.
[17] Testani JM, Hanberg JS, Cheng S et al. *Circ Heart Fail*. 2016; 9(1): e002370.
[18] Costanzo MR, et al. *J Am Coll Cardiol*. 2017;69(19):2428-2445.
[19] Kamath SA. *Int J of Nephrol*. 2011: 1-6.
[20] Felker MG & Mentz RJ. *J Am Coll Cardiol*. 2012;59(24):2145-53.
[21] Testani JM. *Circ Heart Fail*. 2016 Jan;9(1):e002370.
[22] Hoorn EJ & Ellison DH. *Am J Kidney Dis*. 2017;69(1):136-142.

Nearly one-half of hospitalized patients with heart failure are discharged with residual fluid excess after receiving conventional diuretic therapies.[23] Additionally, one study found that 24% of such patients were readmitted to the hospital within 30 days of their discharge, and up to 42-50% were readmitted at 90 days and 6 months respectively.[24] [25] Regardless of diuretic strategy, 42% of acutely decompensated heart failure subjects in the DOSE (Diuretic Optimization Strategies Evaluation) trial reached the composite endpoint of death, rehospitalization, or emergency department visit at 60 days.[26] We believe that there is an association of chronic loop diuretic therapy and greater resource utilization at hospitals.[27] Therefore, an alternative therapy to help stabilize or improve patient care is needed.

Ultrafiltration.

Ultrafiltration, or aquapheresis, is an alternative therapy to diuretics for fluid removal in patients with volume overload. Ultrafiltration has been a well-documented technique in the treatment of fluid overload in heart failure patients for over 20 years.[28] We believe that ultrafiltration is a safe and effective therapy to treat fluid overload and congestion by removing the overload of fluid and congestion by removing extra fluid and salt.[29] With ultrafiltration, medical practitioners can specify and control the amount of fluid to be extracted at a safe, predictable, and effective rate. The use of ultrafiltration therapy in subgroups of patients, such as heart failure and post-cardiac surgery, has demonstrated clinical benefits in treating fluid overload signs and symptoms. In addition to the clinical benefits of ultrafiltration, we believe the data suggests that the therapy provides economic advantages. One hospital cost analysis demonstrated a total cost savings of $3,975per patient when using ultrafiltration as compared to diuretic therapy over 90 days.[30]

The Aquadex System

The Aquadex System is designed and clinically proven to simply, safely, and precisely remove excess fluid (primarily excess salt and water) from patients suffering from fluid overload who have failed diuretic therapy.

With the Aquadex System, medical practitioners can specify and control the amount of fluid to be extracted at a safe, predictable, and effective rate. The Aquadex System has been shown to have no clinically significant impact on electrolyte balance, blood pressure or heart rate.[31] [32] Unlike other forms of ultrafiltration, which typically require administration specifically by a nephrologist, the Aquadex System may be prescribed by any physician and administered by a healthcare provider, both of whom have received training in extracorporeal therapies. The Company estimates it has treated nearly 26,000 patients across all three (3) of our customer categories, since it reintroduced the Aquadex System to the U.S. market in 2016.

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[23] Orso D, et al. *Eur Rev Med Pharmacol Sci*. 2021 Apr;25(7):2971-2980.

[24] Costanzo MR, et al. *J Am Coll Cardiol*. 2017;69(19):2428- 2445.

[25] Thandra A, et al. *Clin Invest*. 2023; 365(2): 145-51.

[26] Felker GM, et al. *N Engl J Med*. 2011; 364:797-805.

[27] Costanzo MR, et al. *J Am Coll Cardiol*. 2007; 49(6):675-683.

[28] Agostoni PG, et al. *J Am Coll Cardiol*. 1993; 21(2):424-431.

[29] Kazory A, et al. *Cardiorenal Med*. 2023;13(1)1-8.

[30] Costanza MR, et. al. *Value Health*. 2018; 21 (Suppl 1):S167.

[31] SAFE Trial: Jaski BE, et al. J Card Fail. 2003; 9(3): 227-231.

[32] RAPID Trial: Bart BA, et al. *J Am Coll Cardiol*. 2005; 46(11): 2043-2046.

Benefits of the Aquadex System

The Aquadex System offers a safe approach to treating fluid overload and:

- In a single center, retrospective analysis of 335 consecutive patients, patients in whom there was follow-up for 12 months, there were 1.74 fewer rehospitalizations for HF in the year following UF when compared to the 12 months preceding UF;
- Rehospitalizations at 30 days with Aquadex were 12.4% compared with the national average at 30 days of 24%;
- Reduces length of hospital stay when initiated early, resulting in average savings of $3,975 (14%);[33]
- Stabilizes or improves cardiac hemodynamics;[34] [35]
- Safe, easy-to-use, and flexible in application;
- Provides complete control over rate and total volume of fluid removed by allowing a medical practitioner to specify the amount of fluid to be removed from each individual patient;
- Can be performed via peripheral or central venous access;
- Predictably removes excess isotonic fluid (extracts water and sodium while sparing potassium and magnesium; decrease risk of electrolyte abnormalities);[36] [37]
- No significant changes to kidney function;[38]
- The use of continuous hematocrit monitoring and SvO2 sensor provides guided-therapy ultrafiltration.[39]
- Following ultrafiltration, neurohormonal activation is reset toward a more physiological condition and diuretic efficacy is restored;[40]
- Provides highly automated operation with only one setting required to begin therapy;
- Utilizes a single-use, disposable auto-loading blood filter circuit that facilitates easy set-up; and
- Has a built-in console that guides the medical practitioner through the setup and operational process.

Components of the Aquadex System

The Aquadex System consists of:

- A console, a piece of capital equipment containing electromechanical pumps, an LCD screen and stand;
- A one-time disposable blood circuit set, an integrated collection of tubing, filter, sensors, and connectors that contain and deliver the blood from and back to the patient; and
- A disposable catheter, a small, dual-lumen, extended length catheter designed to access the peripheral venous system of the patient and to simultaneously withdraw blood and return filtered blood to the patient.

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[33] Costanza MR, et. al. Value Health. 2018; 21 (Suppl 1):S167.
[34] Boga M, et al. *Perf*. 2000; 15:143-150.
[35] Kiziltepe U, et al. *Ann Thorac Surg* 2001;71:684-93.
[36] Kazory A, et al. *Cardiorenal Med*. 2023;13(1)1-8.
[37] Agostoni PG et al. *J Am Coll Cardiol*. 1993;21(2):424-31.
[38] Kazory A, et al. *Cardiorenal Med*. 2023;13(1)1-8.
[39] Starr MC, et al. *Pediatric Nephrology*. 2024; 39(2):597-601.
[40] Costanzo MR, et al. *J Am Coll Cardiol*. 2005; 46(11): 2047-51.

Our Market Opportunity

The Aquadex System is indicated for the treatment of patients suffering from fluid overload who have failed medical therapy including diuretics, or patients that can benefit from a predictable mechanical way to remove excess fluid (isotonic fluid). We are currently focusing our commercial activities in three primary clinical areas where fluid overload is prevalent: heart failure, critical care, and pediatrics.

Heart Failure

Heart disease is the leading cause of death in the United States and other developed countries. In fact, approximately 50% of patients who develop heart failure die within five years of diagnosis. The five-year mortality rate for heart failure, regardless of heart function, is approximately 75% across all phenotypes.[41] Approximately 6.7 million Americans over 20 years of age have heart failure, and the prevalence is expected to rise to 8.5 million Americans by 2030.[42] Based on the Atherosclerosis Risk in Communities Study from 2005 to 2013, conducted by the National Heart, Lung and Blood Institute, there are an estimated 960,000 new heart failure cases annually.[43] Annual hospitalizations for heart failure exceed one million in both the United States and Europe, and more than 90% are due to symptoms and signs of fluid overload.[44] In addition, approximately 68% of the patients are discharged with sub-optimal results.

Heart failure is a syndrome that can have an acute onset or is a progressive disease caused by impairment of the heart's ability to pump blood to the various organs of the body. Patients with heart failure and fluid overload commonly experience shortness of breath, fatigue, difficulty exercising and swelling of the legs. The heart becomes weak or stiff and enlarges over time, making it harder for the heart to pump the blood needed for the body to function properly. The severity of heart failure depends on how well a person's heart pumps blood throughout the body.[45]

According to a nationwide study of over 140,000 patients suffering from acute decompensated heart failure, over 38% of patients discharged were still symptomatic and about half of the patients were discharged with less than five pounds lost.[46] This clinical evidence from the ADHERE registry shows patients are discharged too early, while still showing evidence of fluid overload.

As a result of not fully having their fluid imbalance properly addressed prior to discharge from the hospital, patients are frequently being readmitted, with one study showing 30-day readmissions of 24% and 6-month readmissions of 44%.[47] [48]

Heart failure often requires inpatient treatment, and it carries a huge economic burden in the United States, costing the nation an estimated $60.2 billion each year, with hospital costs accounting for 62% of the economic burden.[49] As the population ages, healthcare expenditures are expected to increase substantially.[50] Therefore, therapies aimed at treating congestion and fluid overload are essential from a patient care and healthcare economics perspective.

To remove the excess fluid, patients suffering from heart failure may receive ultrafiltration therapy in two settings: (i) *inpatient care:* provided to a patient admitted to a hospital, extended care facility, nursing home or other longer-term care facility; and (ii) *outpatient care:* provided to a patient who is not admitted to a facility, but receives treatment at a doctor's office, clinic, or hospital outpatient department.

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[41] Shah, K, et al. *J Am Coll Cardiol*. 2017 Nov, 70 (20) 2476-2486.
[42] Bozhurt B, et al. *J Card Fail*. *J Card Fail*. 2023; 29(10): 1412-42.
[43] Benjamin EJ, et al. *Circ*. 2017;135:00-00. (e378).
[44] Fonarow GC, et al. *Rev Cardiovasc Med*. 2003; 4: s21-30.
[45] Arrigo M et al. *Nat Rev Dis Primers*. 2020; 6(16):1-15.
[46] Fonarow et al. *Rev Cardiovasc Med*. 2003;4: Suppl 7:S21-30.
[47] Costanzo MR, et al. *J Am Coll Cardiol*. 2017 May 16;69(19):2428-2445.
[48] Sax D, et al. J Card Fail. 2022: 28(10): 1545-59.
[49] Voigt J, et al. *Clin Cardiol*. 2014;37(5): 312-321.
[50] Heidenreich PA, et al. *Circ Heart Fail*. 2013;6(3):606-619.

Hospitals in the United States also face potential penalties for heart failure readmissions. As part of the Patient Protection and Affordable Care Act of 2012, as amended (the "Affordable Care Act"), Medicare instituted the Hospital Readmissions Reduction Program, which penalizes hospitals with high 30-day readmission rates for heart failure and other common diseases and procedures. This penalty can be as high as 3% of reimbursement for all Medicare admissions. Technologies that help reduce readmissions, such as the Aquadex System, can help hospitals mitigate these penalties.[51]

The Company believes the total U.S. heart failure market is approximately $1 billion[52] and that roughly 30% of its revenue is derived from the treatment of heart failures patients.

Critical Care

Patients suffer from fluid overload in connection with a variety of critical care procedures and treatments, including cardiac surgery, cardiogenic shock, liver and other organ transplants, ventricular assist device ("VAD") implants, extra corporeal membrane oxygenation ("ECMO") therapy, sepsis, liver disease and severe burns. According to the National Center for Health Sciences, over 7.3 million cardiovascular operations are performed each year in the United States, including an estimated 340,000 coronary-artery bypass grafting ("CABG") procedures,[53] Cardiac surgery is associated with a degree of fluid overload due to cardiopulmonary bypass.[54] Intravenous fluid therapy is an integral treatment for patients undergoing surgery and in critical care units.[55] Fluid overload in post-cardiac surgery can readily occur because surgery can affect the pumping actions of the heart, leading to postoperative hemodynamic instability.[56] The condition often remains symptomless for several days until clinical symptoms become apparent, when treatment is almost always too late and ineffective.[57]

Major complications after cardiac operations are associated with an increased risk for operative death, longer hospital length of stay, and higher rates of discharge to a location other than home.[58]

Hospital readmissions are a common problem in cardiac surgery and remain high. Approximately 20% of patients who undergo cardiac operations require readmission, an outcome with significant health economic implications. Volume overload was among the top three most prevalent causes for first readmission within 30 days and beyond 30 days.[59] It is estimated that 13.5% of post cardiac surgery patients are readmitted due to fluid overload within 30 days of discharge. Positive research has been recently published demonstrating the value of ultrafiltration in high-risk coronary artery bypass grafting surgery.[60] It is also encouraging to see ultrafiltration being recommended for cardiac surgery patients who are unresponsive to diuretics in a recently published turnkey order set proposed by the Enhanced Recovery After Surgery ("ERAS") Society consensus guidelines.[61]

The Company believes it can expand use cases for the Aquadex System, without any additional clinical trial or other labeling changes at the U.S. Food and Drug Administration ("FDA") to support its use in the applications identified immediately above.

The Company believes the total U.S. critical care failure market is approximately $900 million.[62] In 2023, the Company derived approximately 40% of its revenue from the treatment of critical care patients.

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[51] McIlvennan C et al. *Circ*. 2015; 131(20): 1796-1803.

[52] See Appendix to Company Investor Presentation filed with the SEC on Form 8-K/A, dated January 9, 2024.

[53] https://idataresearch.com/new-study-shows-approximately-340000-cabg-procedures-per-year-in-the-united-states/.

[54] Kruger A et al. *J Cardiovasc Dev Dis*. 2023;10(6);263-78.

[55] Bowdish ME, et al. *Ann Thorac Surg*. 2021;111(6):1770-1780.

[56] Xu J, et al. *Medicine*. 2015.94(33):e1360.

[57] Xu J, et al. *Medicine*. 2015;94(33):e1360.

[58] Crawford TC, et al. *Ann Thorac Surg*. 2017;103:32-40.

[59] Iribane A, et al. *Ann Thorac Surg*. 2014;98:1274-80.

[60] Beckles DL et al. *J Card Surg*.2022; 37: 2951-57.

[61] Engelman D, et al. *Ann Thorac Surg*. 2023;115:11-5A

[62] See Appendix to Company Investor Presentation filed with the SEC on Form 8-K/A, dated January 9, 2024.

Pediatrics

Many of the conditions and procedures faced by adult patients also occur in pediatric patients, such as cardiac surgery, organ transplants, heart failure and ECMO therapy. Similar to adult patients, these conditions and procedures may lead to fluid overload. While incidence data is not readily available, it is estimated that there are approximately 10,000 to 14,000 pediatric patients with heart failure.[63] Fluid overload drives pediatric morbidity and mortality risk in critically ill patients. In one pediatric study, a 3% increase in mortality was observed for every 1% increase in fluid overload, and children who are more than 20% fluid overloaded have an odds ratio for mortality of 8.5 compared to children who are less than 20% fluid overloaded.[64] [65]

The Company believes that the total U.S. pediatric market for fluid overload is approximately $130 million.[66] In 2023, the Company derived approximately 30% of its revenue from the treatment of pediatric patients.

While the Aquadex System is only FDA cleared for the treatment of pediatric patients weighing 20 kg or more, the Company is aware that many children's hospitals in the U.S. are modifying the way that the Aquadex System is used in a manner that is deemed to be off-label by the Company and FDA in order to provide dialysis to neonates and other premature infants who weigh less than 20 kg and who were born either without kidneys or without normal kidney function. These patients typically have very few other treatment options given the large extracorporeal blood volume required by standard dialysis machines the need for blood priming of the dialysis circuit and the use of large catheters. By comparison, the Aquadex extracorporeal blood volume is only 35 ml.

It is because of this unmet medical need the Company has undertaken the development of a dedicated Continuous Renal Replacement Therapy ("CRRT") device intended for patients weighing between 2.5 and above kg. See - Product Development Activities below.

Growing Clinical Evidence

In December 2021, we launched the REVERSE-HF prospective, multicenter, randomized controlled trial (RCT) to evaluate ultrafiltration compared to IV diuretics in patients with heart failure. This RCT is currently being conducted at sixteen clinical sites nationwide, and patient enrollment began in June 2022. As of February 10, 2024, there are 91 patients enrolled in this RCT. The primary effectiveness endpoint is the time to first HF Event within 30 days, as a comparison between Aquadex therapy and IV Loop Diuretics. The Company intends to target a total of 20 sites and hopes to be fully enrolled by the middle of 2025 with a total of 372 patients enrolled. The protocol for REVERSE-HF permits an interim data analysis once enrollment reaches 80% of its targeted enrollment, and the Company hopes to complete analysis of the primary endpoint and to publish the results in the second half of 2025.

Secondary endpoints will be analyzed as a comparison between Aquadex and IV Loop Diuretics:

- Composite win ratio analysis of Cardiovascular (CV) mortality, HF events, and quality of life within 30 days:
    - CV mortality
    - HF event
    - Change in Kansas City Cardiomyopathy Questionnaire (KCCQ) score
- Time to first HF event within 90 days
- Time to first HF event or all-cause death within 90 days
- HF events within 30 and 90 days
- Treatment crossovers

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[63] Jayaprasad, N. *Heart Views*. 2016; 17(3): 92-99.

[64] Sutherland SM, et al. *Am J Kidney Dis*. 2010; 55(2):315-25.

[65] Gillespie RS, et al. *Ped Nephro*. 2004; 19(12):1394-99.

[66] See Appendix to Company Investor Presentation filed with the SEC on Form 8-K/A, dated January 9, 2024.

In December 2022, a third-party, real-world retrospective study of 335 patients treated with the Aquadex FlexFlow® System, "*Ten Year Experience with Ultrafiltration for the Management of Acute Decompensated Heart Failure,*"[67] compared previous randomized controlled clinical trials with ultrafiltration and demonstrated that ultrafiltration compares favorably in reducing heart failure rehospitalizations, renal function response, and weight/volume loss. The study found ultrafiltration to be safe with regard to renal function despite the cohort in this study being sicker than those studied in other clinical trials, and that Ultrafiltration can be a safe and effective strategy for decongestion in clinical practice wherein the benefits outweigh the potential risks of kidney dysfunction requiring hemodialysis and major bleeding events.[68] Additionally, another 2022 peer-reviewed publication advocates for early clinical application of ultrafiltration in diuretic resistant patients.[69] Jain et al. pooled data from seven randomized controlled trials of ultrafiltration with a total of 771 patients and concluded that extracorporeal ultrafiltration is associated with more efficient fluid and sodium removal compared with medical therapy, hence leading to a reduction in readmission rates and a potential salutary impact on financial burden associated with the care of heart failure patients.[70] Compared to diuretics, ultrafiltration provided predictable, adjustable, and more efficient fluid removal - without clinically adverse impacts on renal function, demonstrating a 14% cost reduction at 90-days achieved due to reduced readmissions.[71]

The AVOID-HF trial was initiated by Baxter International, Inc. ("Baxter") in 2016. AVOID-HF was designed to prospectively address the question of patient outcomes when treated with ultrafiltration versus intravenous diuretics for acute decompensated heart failure. Trial design assumptions indicated that 810 patients would need to be randomized to achieve adequate statistical power. However, the study was terminated by Baxter at 224 patients, apparently for business reasons unrelated to patient outcomes or device safety. Despite being underpowered, the results of AVOID-HF indicated distinct trends toward reduced time to heart failure events within 90 days, favoring the ultrafiltration group over diuretics. In addition, pre-specified secondary endpoints demonstrated significant reductions in heart failure rehospitalizations and days in the hospital and cardiovascular events at 30 days. No significant differences were observed in creatinine level between the groups during treatment and up to 90 days following treatment. In totality, AVOID-HF provided evidence that had AVOID-HF been followed to completion, it is our belief that the trial would likely have met its primary endpoint of improved outcome in acute decompensated heart failure patients.[72]

One 2019 peer reviewed paper reported on a multicenter, retrospective case series of children who received kidney replacement therapy ("KRT") with an ultrafiltration device.[73] Patients were grouped according to weight and primary disease state (e.g. kidney, cardiac or other) and received one of three treatment modalities. The study found that of the 72 patients who weighed less than 10 kg, 43 or 60% survived to the end of therapy or transitioned to another modality of kidney support. 23 or 32% survived to hospital discharge. Among patients who weighed between 10-20 kg, 13 or 100% survived to the end of KRT treatment. Among patients who weighed more than 20 kg, 33 or 97% survived to KRT discontinuation and 23 or 68% survived to hospital discharge.[74]

Product Development Activities

As we expand our commercialization efforts in the pediatric market, we are developing a CRRT device, branded Vivian, to address the unmet and specific needs of pediatric patients weighing 2.5kg and above who do not have functioning kidneys and who need kidney replacement therapy for survival. Approximately 10,300 children AKI. Of these, over 1800 are neonates. Funded in part by a $1.7 million grant from the National Institute of Health, the Company completed preliminary engineering testing for its dedicated pediatric system in the fourth quarter of 2023. The Company intends to submit an IDE with the FDA in the third quarter of 2024, with U.S. commercialization of this product expected in the fourth quarter of 2025.

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[67] Watson R, et al. *Am Heart J Plus: Cardiol Res & Pract 24*. 2022; 1-6.

[68] Watson R, et al. *Am Heart J Plus: Cardiol Res & Pract 24*. 2022; 1-6.

[69] Kazory et al. *Cardiorenal Med*. 2023;13:1-8.

[70] Kazory A, et al. *Cardio Renal Med*. 2023.12(1):1-8.

[71] Costanzo MR, et al. *Val in Health.* 2018: 21(1): s167.

[72] Costanzo MR, et al. *JACC: Heart Failure*. 2016;4(2):95-105.

[73] Menon S, et al. *Clin J Am Soc Nephrol*. 2019;14(10):1432-1440.

[74] Menon S, et al. *Clin J Am Soc Nephrol*. 2019;14(10):1432-1440.

Corporate Development Activities

SeaStar License and Distribution Agreement

On December 27, 2022, we entered into an exclusive license and distribution agreement (the "Distribution Agreement") with SeaStar Medical Holding Corporation ("SeaStar"), pursuant to which SeaStar appointed the Company as its exclusive distributor for the sale and distribution of SeaStar's Selective Cytopheretic Device ("SCD-PED") product throughout the United States following the receipt by SeaStar from the FDA of a written authorization to market such product for pediatric use pursuant to the Humanitarian Device Exemption (HDE) application submitted by SeaStar. The SCD-PED will provide a new therapy option for children weighing 10 kilograms or more who have acute kidney injury (AKI) and sepsis or a septic condition requiring continuous kidney replacement therapy (CKRT) in a hospital intensive care unit.

Pursuant to the Distribution Agreement, SeaStar received an upfront payment, and is entitled to milestone payments upon achievement of certain milestones and royalties on gross sales of the SCD- PED product. The Distribution Agreement has an initial term commencing on December 27, 2022 and shall end on the three (3) year anniversary from the date that is the earlier of (a) ninety (90) days after SeaStar receives FDA authorization to market such SCD- PED product for pediatric use and (b) the first commercial sale of the SCD-PED product. The term of the Distribution Agreement may be automatically extended for additional terms of one (1) year and for a total of two (2) extensions. Each party has the right to terminate the Distribution Agreement for material breach if such breach is not cured within ninety (90) days after written notice. SeaStar has additional rights to terminate the Distribution Agreement in accordance with other terms set forth in the Distribution Agreement.

On October 31, 2023, we announced that SeaStar received an Approvable Letter from the FDA for its SCD-PED. The Approvable Letter indicated that SeaStar Medical's HDE application substantially meets the requirements for an Approval Order and outlined remaining administrative steps that must be finalized before the HDE can be active for commercialization. For the SCD-PED, these include revisions to product labeling and minor modifications to the post-approval study plan.

Recent Developments

On December 7, 2023, we received a letter (the "Notice") from the Listing Qualifications Department (the "Staff") of the Nasdaq Stock Market ("Nasdaq") informing us that because the closing bid price for our common stock listed on Nasdaq was below $1.00 for 30 consecutive trading days, we were not in compliance with the Minimum Bid Price Requirement for continued listing on the Nasdaq Capital Market, as set forth in Nasdaq Marketplace Rule 5550(a)(2) (the "Minimum Bid Price Rule").

In accordance with Nasdaq Marketplace Rule 5810(c)(3)(A), the Company has a period of 180 calendar days from December 7, 2023, or until June 4, 2024, to regain compliance with the Minimum Bid Price Requirement. If at any time before June 4, 2024, the closing bid price of the Company's common stock closes at or above $1.00 per share for a minimum of 10 consecutive trading days (which number days may be extended by Nasdaq), Nasdaq will provide written notification that the Company has achieved compliance with the Minimum Bid Price Requirement, and the matter would be resolved.

The Notice also disclosed that in the event the Company does not regain compliance with the Minimum Bid Price Rule by June 4, 2024, the Company may be eligible for additional time. To qualify for additional time, the Company would be required to meet the continued listing requirement for market value of publicly held shares and all other initial listing standards for Nasdaq, with the exception of the bid price requirement, and would need to provide written notice of our intention to cure the deficiency during the second compliance period, by effecting a reverse stock split, if necessary. If the Company meets these requirements, Nasdaq will inform the Company that it has been granted an additional 180 calendar days. However, if it appears to the Staff that the Company will not be able to cure the deficiency, or if the Company is otherwise not eligible, Nasdaq will provide notice that the Company's securities will be subject to delisting.

The Company intends to continue actively monitoring the closing bid price for the Company's common stock between now and June 4, 2024, and it will consider available options to resolve the deficiency and regain compliance with the Minimum Bid Price Requirement. If the Company does not regain compliance within the allotted compliance period, including any extensions that may be granted by Nasdaq, Nasdaq will provide notice that the Company's common stock will be subject to delisting. The Company would then be entitled to appeal that determination to a Nasdaq hearings panel. There can be no assurance that the Company will regain compliance with the Minimum Bid Price Requirement during the 180-day compliance period, secure a second period of 180 calendar days to regain compliance, or maintain compliance with the other Nasdaq listing requirements.

Our Strategy

Our vision is to transform the lives of patients suffering from fluid overload through science, collaboration and innovation. We provide healthcare professionals with a reliable, predictable, and easy-to-use mechanical pump and filtration system to remove excess fluid in fluid overloaded patients. We believe that our technology will provide a competitive advantage in the fluid management market by providing improved clinical benefits and reducing the cost of care relative to other treatment alternatives.

Our strategic focus is to demonstrate a strong business model by driving revenue growth. Growing revenue is the key metric employees, stockholders and potential investors will use to judge our performance. Our field-based employees include both sales representatives and clinical education specialists in 9 sales territories in the United States. We also have distribution agreements in several countries in Europe, South America, the Middle East, and Asia. We intend to focus on the acute needs of fluid overloaded patients in cardiac surgery and other areas of critical care, while continuing to support heart failure patients in the inpatient setting, and the outpatient setting. With our "FDA 510(k) clearance for use in pediatric patients weighing 20kg or more, we have expanded our commercialization efforts to treatments for pediatric patients.

Critical Care: After we launched a marketing campaign focused on the benefits of the Aquadex System in treating patients suffering from fluid overload following cardiac surgery procedures, such as CABG surgery, valve repairs and replacements procedures, VAD implants and other cardiac surgical procedures. We then realigned our salesforce to further focus on the acute needs of fluid overloaded patients in the critical care setting. We believe that we will continue to grow revenue in this faster-growing segment of our business by leveraging the synergies between heart failure cardiologists and cardiovascular surgeons, traditional technology adoption rates of cardiac surgeons, and product purchase cycle of the cardiac surgical and other critical care centers at large hospitals.

Pediatrics: Ultrafiltration is used by physicians to treat fluid overload in various conditions in pediatric patients, including heart failure, cardiac surgery,[75] ECMO therapy[76], solid organ transplantation,[77] and kidney replacement therapy for neonatal patients. In February 2020, the Company received FDA 510(k) clearance for the Aquadex System to include pediatric patients who weigh 20kg or more. With this clearance, we expanded our commercialization efforts to include promotion to physicians and hospitals who treat this pediatric population, and we are investing in the development of new clinical evidence around use of ultrafiltration in pediatric patients, including the ULTRA-Peds pediatrics registry, a multi-center, single-arm study. We are also investing in the development of a new dedicated pediatric device, to further address the needs of the pediatric population, and in clinical studies supporting the use of this device.

Heart Failure In-Patients: Heart failure patients suffering from fluid overload may be treated in an inpatient setting, such as a hospital, extended care facility or nursing home. Historically, our commercial efforts have been primarily focused on use of the Aquadex System in the inpatient setting in large hospital accounts. We intend to continue to support our sales efforts on inpatient facilities, leveraging the clinical benefits and economic advantages of using the Aquadex System over diuretic therapy. We are investing in additional clinical evidence supporting the use of ultrafiltration in patients with decompensated heart failure including a multicenter, randomized controlled trial, the REVERSE-HF study, comparing ultrafiltration and IV diuretics.

Heart Failure Out-Patients: Further, we intend to expand the use of the Aquadex System with heart failure patients in the outpatient setting, such as an infusion clinic or hospital outpatient department (e.g., observation unit). On January 1, 2022, the American Medical Association granted a new and dedicated Category III Current Procedural Terminology (CPT) code, 0692T, for Therapeutic Ultrafiltration. Healthcare providers can utilize this code when using Aquadex to deliver ultrafiltration to adult and pediatric patients weighing more than 20kg. In addition, the new CPT code provides additional reimbursement for therapeutic ultrafiltration administered in the outpatient setting and will facilitate the migration of the therapy to this setting for a subset of the patient population due to hospital economic and patient quality of life benefits. Continued focus on driving positive coverage policies for various targeted payers will be an ongoing strategy for the Company.

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[75] Elliott MJ. *Ann Thorac Surg*. 1993;56:1518-22.

[76] Selewski DT, et al. *Crit Care Med*. 2012; 40(9): 2694-2699.

[77] Riley AA. *BMC Nephrology*. 2018; 19:268-80.

Outside the United States, the Aquadex System is sold by independent specialty distributors who in turn sell to hospitals and clinics in their geographic regions. We currently have distribution relationships in Austria, Belarus, Brazil, Colombia, Czech Republic, Germany, Greece, Hong Kong, India, Indonesia, Israel, Italy, Panama, Romania, Singapore, Slovak Republic, Spain, Switzerland, Thailand, United Arab Emirates and the United Kingdom. We intend to continue to establish distribution partners in additional countries outside of the United States. We received CE Mark Certification for our 24-Hour Blood Circuit Set in January 2022 to be used with the Aquadex SmartFlow® system. The CE marking (as defined below) allows us to market the 24-hour Blood Circuit in the European Union (EU) and all other countries that recognize this certification. This new circuit will help us expand access to ultrafiltration among patients who need no more than 24 hours of therapeutic ultrafiltration in the inpatient setting. Additionally, this circuit can provide a more economical solution for hospitals to treat patients in the outpatient/ambulatory setting, where therapy can be delivered for up to 8 hours. Such use in the outpatient setting provides us with the flexibility to better meet the clinical and healthcare economic needs of European markets, while at the same time improving lives by seeking to prevent hospitalizations.

Besides driving near-term revenue growth through sales of the Aquadex System, we intend to develop product enhancements to improve performance and customer satisfaction. We have projects designed to improve venous access for the Aquadex catheter and enhance the functionality of the hematocrit sensor that is part of the Aquadex console. As we expand our commercialization efforts in the pediatric market, we are developing a CRRT console to address the unmet and specific needs of pediatric patients who do not have functioning kidneys and need kidney replacement therapy for survival.

Sales and Marketing

As of December 31, 2023, we had 24 full-time employees in sales and marketing. We have 9 sales territories in the United States. Our U.S. field salesforce includes sales managers, account managers and clinical education specialists who provide training, technical and other support services to our customers. Following the acquisition of the business associated with the Aquadex System (the “Aquadex Business”) from Baxter in August 2016, our direct salesforce was focused initially on re-engaging hospital accounts that had ordered Aquadex blood sets in prior years, re-educating customers on the therapy, and assessing each hospital’s use of the Aquadex System to gain additional opportunity for increased utilization, primarily in heart failure. In 2018, we expanded our commercialization efforts to include post-cardiac surgery. In September 2019, we realigned our salesforce to further focus on the acute needs of fluid overloaded patients in the critical care setting, while still supporting heart failure. We expanded our commercialization efforts to include pediatrics, following receipt of 510(k) clearance of the Aquadex system to include pediatric patients who weigh 20kg or more in February 2020.

In the United States, our target customers for the Aquadex System include healthcare systems and academic hospitals specializing in advanced treatment of chronic heart failure and/or critical care patients. With the FDA 510(k) clearance of the Aquadex SmartFlow® system for patients weighing over 20kg, we are also targeting pediatric hospitals. Our largest customer represented 13.9% of our 2023 annual revenue. The loss of this customer would have a material adverse effect on our revenue.

Clinical Experience

Several large-scale, multi-center, randomized, controlled trials have evaluated the use of ultrafiltration using the Aquadex System on patients with acute decompensated heart failure compared to standard-of-care treatment with intravenous diuretics. These trials followed early-stage studies which primarily focused on safety of ultrafiltration treatment with the Aquadex System.

The UNLOAD trial enrolled 200 patients and showed that average weight and fluid loss were greater in the ultrafiltration group 48 hours following randomization. No differences were noted in symptoms of dyspnea between the groups. In addition, through 90 days of follow-up, the ultrafiltration group experienced fewer re-hospitalizations and unscheduled medical visits for heart failure, while renal function assessed by serum creatinine level was not significantly different between the groups.

The CARRESS trial studied 188 randomized acute decompensated heart failure patients over the course of 96 hours and found no difference in weight loss and an increase in creatinine level relative to the control group treated with intravenous diuretics. The creatinine increase was interpreted as a sign of potential worsening renal function in the ultrafiltration group. We believe that the trial results were impacted by centers unfamiliar with the use of ultrafiltration therapy, that more than one third of the ultrafiltration group received diuretics instead of ultrafiltration, ultrafiltration rates were fixed rather than utilizing adjusted ultrafiltration rates according to patient characteristics whereas diuretic doses were titrated based on urine output, and that the diuretic regimen employed was not representative of standard-of-care.[78] In addition, subsequent analyses of the CARRESS study cohort have been published since the original study results. One protocol analysis showed that ultrafiltration had higher net fluid loss and weight reduction compared to intravenous diuretics, and there were no significant differences in long-term outcomes.[79] An additional sub-study analysis on urinary biomarkers showed that although further worsening creatinine levels were reported, decongestion and renal function recovery at 60 days were superior in patients with increased tubular injury markers.[80] The data suggests that the benefits of decongestion may outweigh modest or transient increases in serum creatinine during ultrafiltration. Thus, we believe that a change in creatinine should not dissuade the use of ultrafiltration.

Disparate results between UNLOAD and CARRESS led to initiation of the AVOID-HF trial by Baxter. AVOID-HF was designed to prospectively address the question of patient outcomes when treated with ultrafiltration versus intravenous diuretics for acute decompensated heart failure. Trial design assumptions indicated that 810 patients would need to be randomized to achieve adequate statistical power. However, the study was terminated by Baxter at 224 patients, apparently for business reasons unrelated to patient outcomes or device safety. Despite being underpowered, the results of AVOID-HF indicated distinct trends toward reduced time to heart failure events within 90 days, favoring the ultrafiltration group over diuretics. In addition, pre-specified secondary endpoints demonstrated significant reductions in heart failure rehospitalizations and days in the hospital and cardiovascular events at 30 days. No significant differences were observed in creatinine level between the groups during treatment and up to 90 days following treatment. In totality, AVOID-HF recapitulated the results of both UNLOAD and CARRESS while providing evidence that had AVOID-HF been followed to completion, it is our belief that the trial would likely have met its primary endpoint of improved outcome in acute decompensated heart failure patients.

In November 2020, we launched the ULTRA-PEDs pediatrics registry, a multi-center, single-arm study conducted at seven clinical sites, and closed in October 2023 with 97 patients enrolled and the data is currently being analyzed.

In May 2021, a third-party systemic evaluation of eight randomized controlled trials, *"Ultrafiltration is better than diuretic therapy for volume-overloaded acute heart failure patients: a meta-analysis,"*[81] studied the effectiveness of ultrafiltration therapy compared to diuretics in 801 patients hospitalized with acute decompensated heart failure. The meta-analysis demonstrated ultrafiltration increases fluid removal and weight loss and reduces rehospitalization and the risk of worsening heart failure in congestive patients, suggesting ultrafiltration is a safe and effective treatment option for volume-overloaded heart failure patients.

In December 2021, we launched the REVERSE-HF prospective, multicenter, RCT to evaluate ultrafiltration compared to IV diuretics in patients with heart failure. This RCT is currently being conducted at nine clinical sites nationwide, and patient enrollment began in June 2022.

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[78] Urban S, et al. *Adv Clin Exp Med*. 2021;30(7):737-746.

[79] Grodin JL, et al. *Eur J of Heart Fail*. 2018;20(7):1148-1156.

[80] Rao VS, et al. *Circ Heart Fail*. 2019;12 (6):e005552.

[81] Urban S, et al. *Adv Clin Exp Med*. 2021;30(7):737-746.

In February 2022, a third party retrospectively reviewed and concluded, *"The Use of Ultrafiltration as a fluid management strategy for High-Risk Coronary Artery Bypass Grafting,"*[82] that ultrafiltration is a safe and effective modality to manage fluid balance in a patient population with relatively high Society of Thoracic Surgery ("STS") scores, but a prospective multicenter study would be warranted in this patient cohort.

A reanalysis of the AVOID-HF data was presented at the Annual Scientific Session of the Heart Failure Society of America in September 2022, *"Revisiting The Aquapheresis Versus Intravenous Diuretics And Hospitalizations For Heart Failure (AVOID-HF) Trial: Further Evidence Supporting Aquapheresis To Reduce Heart Failure Events,"*[83] using the novel Finkelstein-Schoenfeld method of hierarchical win ratio (WR) to explore cardiovascular mortality and heart failure events. Adjustable ultrafiltration (AUF) was compared to adjustable loop diuretics (ALD) with respect to a primary composite endpoint of CV mortality within 90 days, HF event within 30 days, and time to first heart failure event within 90 days, with HF event defined as HF rehospitalization, unscheduled outpatient or emergency department treatment with IV loop diuretics or vasoactive drugs, or unscheduled outpatient ultrafiltration. The WR analysis yielded results favoring ultrafiltration, demonstrating that AUF is safe and more effective than ALD in reducing CV mortality and subsequent HF events for hospitalized heart failure patients. The results of the reanalysis were presented as a Late Braking Clinical Trials podium presentation at the Technology and HF Therapeutics Conference in March 3-5, 2024, in Boston. The results demonstrated statistical significance in the reduction of HF events and HF hospitalizations at 30 days.

In December 2022, a third-party, single center, real-world retrospective study of 335 consecutive patients treated with the Aquadex FlexFlow® System, *"Ten Year Real World Experience with Ultrafiltration for the Management of Acute Decompensated Heart Failure,"*[84] compared previous randomized controlled clinical trials with ultrafiltration and demonstrated that ultrafiltration compares favorably in reducing heart failure rehospitalizations (2.14 hospitalizations per year before Aquadex versus 0.4 hospitalizations per year one year after Aquadex), renal function response, and weight/volume loss. The study found ultrafiltration to be safe with regard to renal function (unchanged) despite the cohort in this study being sicker than those studied in other clinical trials, and that UF can be a safe and effective strategy for decongestion in clinical practice wherein the benefits outweigh the potential risks of kidney dysfunction requiring hemodialysis and major bleeding events.

In January 2023, we began designing an IDE clinical study for the Company's dedicated pediatric device currently under development. The design was reviewed with FDA in May 2023 and the study is anticipated to begin enrollment in 2024.

In September, 2023, a third-party, single center case study review of pediatric patients showed the Aquadex System successfully treated small patients without hemodynamic instability or other complications, demonstrating that therapy is an effective treatment option for fluid overload. Patient treatment was guided with the continuous hematocrit monitoring function built within the Aquadex System, supporting safe and effective fluid removal in critically ill pediatric patients.[85]

In November 2023, a retrospective cease series and literature review conducted by The Mount Sinai Hospital, "*Utilization of aquapheresis among hospitalized patients with end-stage liver disease: A case series and literature review,"*[86] utilization of ultrafiltration from January 2020 through July 2023 in patients with decompensated cirrhosis in the intensive care unit (ICU) found that the introduction of ultrafiltration earlier in a patient's hospital course may reduce the risk of kidney injury and diuretic-induced electrolyte derangement and reduce the risk of development of sequential organ failures in patients with decompensated cirrhosis.

Research and Development

Research and Development costs include activities related to development, design, and testing improvements to the Aquadex System and potential related products. The Aquadex system software may require periodic modifications for feature additions and performance improvements. We will make such design changes as needed based on proactive and reactive mechanisms. Research and development costs also include expenses related to our clinical research.

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[82] Beckles D. et al. *J of Card Surg. Fail*. 2022; 37(10): 2951-2957.

[83] Pinney S, et al. Poster from Heart Failure Society of America Meeting; October 2022; Washington, DC.

[84] Hass DC, et al. *Amer Heart J Plus Cardio Res & Pract* 2022; 24:1-6 (100230).

[85] Starr MC, et al. Pediatric Nephrology, September 2023.

[86] Crismale, J. et al. *Clinical Transplantation*, 2024; 38:e15221.

In 2021 we initiated a product development project designed to enhance the functionality of the hematocrit sensor that is part of the Aquadex console. In 2021, we also initiated a product development project to develop a pediatric continuous renal replacement therapy device. We successfully completed functional system prototypes in 2022 and preliminary engineering testing 2023. We are also evaluating diagnostic tools for physicians to use during an Aquadex therapy to more precisely determine the amount of excess fluid to be removed, the rate of ultrafiltration, and when to stop therapy as dry weight is approached.

Manufacturers and Suppliers

We manufacture the Aquadex System at our 23,000 square foot facility in Eden Prairie, Minnesota. We have manufactured the Aquadex SmartFlow® console and blood circuits since its development in 2019. We purchase parts and components for the Aquadex System from third-party manufacturers and suppliers. We believe that our current manufacturing facility is suitable and adequate to meet anticipated manufacturing demands, and that, if necessary, suitable additional or substitute space will be available to accommodate expansion of our operations.

Intellectual Property

We have submitted patent applications to establish an intellectual property portfolio through which we seek to protect our system and technology. In connection with our acquisition of the Aquadex Business, we entered into a patent license agreement with Baxter for patents used in connection with the Aquadex System to make, have made, use, sell, offer for sale and import the Aquadex System in the "field of use."

The rights granted to us under the patent license agreement will automatically revert to Baxter in the event we cease operation of the Aquadex Business or we file for, have filed against us, or otherwise undertake any bankruptcy, reorganization, insolvency, moratorium, or other similar proceeding. We estimate that the last expiring patent licensed from Baxter has a term to mid-2025.

In addition to the licensed patents, Nuwellis has company owned patents, including 3 patents issued within the last two years. The first patent issued in the last two years is related to multiple features of the Aquadex system. The second patent issued in the last two years is related to support for neonatal and pediatric patients. The third patent issued in the last two years is related to a wearable appliance to increase vein diameter and venous flow for peripheral ultrafiltration.

Further, 2 issued patents are assigned to Nuwellis in the United States directed to the C-Pulse® Heart Assist System (the "C-Pulse System") for treatment of Class III and ambulatory Class IV heart failure of which the last expiring issued U.S. patent has a term to 2026. Given the strategic refocus away from the C-Pulse System and toward the Aquadex System, we have chosen to limit the maintenance of issued C-Pulse System related patents to those innovations that are of high value. Further, we have elected to emphasize important jurisdictions rather than maintain protection in multiple countries.

Still further, Nuwellis has 1 patent assigned to it related to a heart assist device that utilizes aortic deformation. Additionally, Nuwellis has 3 patents assigned to it related to wraps for a heart assist device or a blood vessel.

In addition, we have thirteen pending patent applications in Europe and in the US. The thirteen applications cover nine different areas. The first application involves a support device for an arm of a patient. The second application includes multiple features and capabilities to assist patient fluid balance and to enhance usability for healthcare providers. The third application involves features and functions for ultrafiltration for pediatric patients. The fourth application involves a wearable appliance to increase vein diameter and venous flow for peripheral ultrafiltration. The fifth application involves plasma and blood volume measurement to guide ultrafiltration therapy. The sixth application involves a dual-lumen ultrafiltration catheter for enhanced peripheral access. The seventh application involves guidance of ultrafiltration therapy based on one or more diagnostic parameters. The eighth application involves a system for ensuring maintenance of peripheral venous flow during ultrafiltration and other continuous kidney replacement therapy ("CKRT") modalities. The ninth application enhances patient fluid balance through control of an ultrafiltration system.

We also have filed a family of patent applications related to our dedicated pediatric device in development. This has resulted in 2 issued United States patents, 6 pending United States patent Applications and a pending international patent application filed under the Patent Cooperation Treaty.

Our pending and future patent applications may not issue as patents or, if issued, may not issue in a form that will provide us any financial return. Even if issued, existing or future patents may be challenged, narrowed, invalidated or circumvented, which could limit our ability to obtain commercial benefits from them.

At this time, we are not a party to any legal proceedings that relate to patents or intellectual property rights or any other subject matter.

Competition

Competition from medical device companies and medical device divisions of healthcare companies, pharmaceutical companies and gene- and cell-based therapies is intense and expected to increase. The vast majority of patients with fluid overload receive pharmacological treatment (diuretics) as the standard of care. There are no direct competitors for the Aquadex System in heart failure or critical care in the United States, other than diuretics. Other systems, such as Baxter's Prismaflex, a filter-based device that is approved for continuous renal replacement therapy for patients weighing 20kg or more with acute renal failure and/or fluid overload, represent indirect competitors, as they can only be used to conduct ultrafiltration with significant limitations. In pediatrics, the Carpediem system distributed by Medtronic is indicated for use in acute kidney injury or fluid overloaded patients requiring hemodialysis or hemofiltration therapy, and Baxter's HF20 Set is authorized under an Emergency Use Authorization to deliver CRRT to treat patients of low weight (8-20kg) in an acute care environment during the COVID-19 pandemic. Additionally, Medtronic and DaVita have recently formed a joint venture, called Mozarc Medical, to pursue a variety of kidney applications across each of our customer categories.

Our ability to compete effectively depends upon our ability to demonstrate the advantages of ultrafiltration as compared to diuretics, a pharmacological treatment that is currently the standard of care. In addition, we need to distinguish the Aquadex System from the indirect competition of other devices that can also be used to conduct ultrafiltration.

Third-Party Reimbursement

In the United States, our products are purchased primarily by customers such as hospitals or other healthcare providers. Customers bill various third-party payers for covered services provided to patients. These payers, which include federal healthcare programs (e.g., Medicare and Medicaid), state healthcare programs, private health insurance companies, and managed care organizations, then reimburse our customers based on established payment formulas that consider part or all of the costs associated with these devices and the related procedures performed.

While the agency responsible for administering the Medicare program, the Centers for Medicare and Medicaid Services, has not issued a favorable national coverage determination under its Investigational Device Exemption Studies Program for ultrafiltration using the Aquadex System, a number of private insurers have approved reimbursement for use of the products included in the Aquadex System for specific indications and points of service. In addition, patients and providers may seek insurance coverage on a case-by-case basis. On January 1, 2022, a new and dedicated Category III Current Procedural Terminology (CPT) code, 0692T, became effective for Therapeutic Ultrafiltration. Healthcare providers can utilize this code when using Aquadex to deliver ultrafiltration to adult and pediatric patients weighing more than 20kg. The new CPT code provides additional reimbursement for therapeutic ultrafiltration administered in the outpatient setting.

Legislative proposals can substantially change the way healthcare is financed by both governmental and private insurers and may negatively impact payment rates for our system. Also, from time to time, there are numerous legislative, regulatory and other proposals both at the federal and state levels that may impact payment rates for our system. It remains uncertain whether there will be any future changes that will be proposed or finalized and what effect, if any, such legislation or regulations would have on our business. However, in the United States and international markets, we expect that both government and third-party payers will continue to attempt to contain or reduce the costs of healthcare by challenging the prices charged, or deny coverage, for healthcare products and services.

Government Regulations

Regulation by governmental authorities in the United States and foreign countries is a significant factor in the manufacture and marketing of our current system and any future products and in our ongoing research and development activities. In particular, medical devices are subject to rigorous preclinical testing as a condition of 510(k) clearance by the FDA and by similar authorities in foreign countries. Any proposed products will require regulatory clearance/approval prior to commercialization.

United States

The Federal Food, Drug, and Cosmetic Act ("FDC Act") and the FDA's implementing regulations govern medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Medical devices and their manufacturers are also subject to inspection by the FDA. The FDC Act, supplemented by other federal and state laws, also provides civil and criminal penalties for violations of its provisions. We manufacture and market medical devices that are regulated by the FDA, comparable state agencies and regulatory bodies in other countries.

Unless an exemption applies, each medical device we intend to commercially distribute in the U.S. will require 510(k) clearance.

510(k) Clearance. To obtain 510(k) clearance for a medical device, an applicant must submit a premarket notification to the FDA demonstrating that the device is "substantially equivalent" to a predicate device legally marketed in the United States. A device is substantially equivalent if, with respect to the predicate device, it has the same intended use and has either (i) the same technological characteristics or (ii) different technological characteristics and the information submitted demonstrates that the device is as safe and effective as a legally marketed device and does not raise different questions of safety or effectiveness. A showing of substantial equivalence sometimes, but not always, requires clinical data. The 510(k) clearance process cannot exceed 90 days from the date the FDA accepts the 510(k) submission After a device has received 510(k) clearance for a specific indication for use, any modification to that device that could "significantly affect its safety or effectiveness," such as a significant change in the design, materials, method of manufacture or which results in "major change" to the product performance, may require a new 510(k) clearance. The determination as to whether new 510(k) is needed is initially left to the manufacturer; however, the FDA may review this determination to evaluate the regulatory status of the modified product at any time and may require the manufacturer to cease marketing the modified device until 510(k) clearance is received.

The Aquadex FlexFlow system was granted FDA 510(k) clearance for commercial use on June 3, 2002. On February 4, 2020, we received 510(k) clearance of the Aquadex SmartFlow® system for use in adult and pediatric patients weighing 20 kg or more whose fluid overload is unresponsive to medical management. The Aquadex SmartFlow incorporates diagnostic tools for physicians to use during an Aquadex therapy to more precisely determine the amount of excess fluid to be removed, the rate of ultrafiltration, and when to stop therapy as dry weight is approached.

Clinical Trials. To obtain FDA clearance to market certain devices, clinical trials may be required to support a 510(k) application. Premarket clinical trials generally require submission of an application for an IDE to the FDA prior to commencing the trial. FDA approval of an IDE allows clinical testing to go forward but does not bind the FDA to accept the results of the trial as sufficient to prove the product's safety and efficacy, even if the trial meets its intended success criteria.

All clinical trials must be conducted in accordance with regulations and requirements collectively known as "Good Clinical Practices". Good Clinical Practices include, but is not limited to, the FDA's IDE regulations, which describe the conduct of clinical trials with medical devices. They also prohibit promotion, test marketing or commercialization of an investigational device and any representation that such a device is safe or effective for the purposes being investigated. Good Clinical Practices also include the FDA's regulations for institutional review board approval and for protection of human subjects (such as informed consent), as well as disclosure of financial interests by clinical investigators. Required records and reports are subject to inspection by the FDA.

The results of clinical trials may be unfavorable or, even if the intended safety and efficacy success criteria are achieved, may not be considered sufficient for the FDA to grant clearance of a product. The commencement or completion of any clinical trial may be delayed or halted or be inadequate to support clearance of a 510(k) application for numerous reasons.

Continuing Regulation. After a device is cleared for use and placed in commercial distribution, numerous regulatory requirements continue to apply. These include:

- establishment registration and device listing upon the commencement of manufacturing;
- the Quality System Regulation ("QSR"), which requires manufacturers, including third-party manufacturers, to follow the FDA design control regulations;
- labeling regulations, which prohibit the promotion of products for unapproved or "off-label" uses and impose other restrictions on labeling and promotional activities;
- medical device reporting regulations, which require that manufacturers report to the FDA if a device may have caused or contributed to a death or serious injury or malfunctioned in a way that would likely cause or contribute to a death or serious injury if malfunctions were to recur;
- corrections and removal reporting regulations, which require that manufacturers report to the FDA field corrections; and
- product recalls or removals if undertaken to reduce a risk to health posed by the device or to remedy a violation of the FDC Act caused by the device that may present a risk to health.

In addition, the FDA may require a company to conduct post-market studies or order it to establish and maintain a system for tracking its products through the chain of distribution to the patient level.

Failure to comply with applicable regulatory requirements, including those applicable to the conduct of clinical trials, can result in enforcement action by the FDA, which may lead to any of the following sanctions:

- warning letters or untitled letters;
- fines, injunctions and civil penalties;
- product recall or seizure;
- unanticipated expenditures;
- delays in clearing or refusal to clear products;
- withdrawal or suspension of FDA clearance;
- orders for physician notification or device repair, replacement or refund;
- operating restrictions, partial suspension or total shutdown of production or clinical trials; or
- criminal prosecution.

We and our contract manufacturers are also required to manufacture our products in compliance with Current Good Manufacturing Practice requirements set forth in the QSR. The QSR requires a quality system for the design, manufacture, packaging, labeling, storage, installation and servicing of marketed devices, and includes extensive requirements with respect to quality management and organization, device design, buildings, equipment, purchase and handling of components, production and process controls, packaging and labeling controls, device evaluation, distribution, installation, complaint handling, servicing and record keeping. The FDA enforces the QSR through periodic announced and unannounced inspections that may include the manufacturing facilities of subcontractors. If the FDA believes that we or any of our contract manufacturers or regulated suppliers are not in compliance with these requirements, it can shut down our manufacturing operations, require recall of our products, refuse to clear or approve new marketing applications, institute legal proceedings to detain or seize products, enjoin future violations or assess civil and criminal penalties against us or our officers or other employees. Any such action by the FDA would have a material adverse effect on our business.

European Union

In order to import and sell our products in member countries of the European Union, or EU, medical devices currently must comply with the essential requirements of the European Union Medical Devices Directive (Council Directive 93/42/EEC). Compliance with these requirements is a prerequisite to be able to affix the Conformité Européene, or CE, Mark ("CE Mark") to our products, without which they cannot be sold or marketed in the EU. To demonstrate compliance with the essential requirements we must undergo a conformity assessment procedure, which varies according to the type of medical device and its classification. Except for low-risk medical devices (Class I non-sterile, non-measuring devices), where the manufacturer can issue an EC Declaration of Conformity based on a self-assessment of the conformity of its products with the essential requirements of the European Union Medical Devices Directive, a conformity assessment procedure requires the intervention of a "Notified Body", an organization accredited by a member state of the EU to conduct conformity assessments. Depending on the relevant conformity assessment procedure, the Notified Body would typically audit and examine the technical file and the quality system for the manufacture, design and final inspection of our devices. The Notified Body issues a certificate of conformity following successful completion of a conformity assessment procedure conducted in relation to the medical device and its manufacturer and their conformity with the essential requirements. This certificate entitles the manufacturer to affix the CE Mark to its medical devices after having prepared and signed a related EC Declaration of Conformity.

The EU Medical Device Regulation 2017/745 ("MDR") was adopted in April 2017. The MDR replaces the existing Medical Device Directives (MDD 93/42/EEC and AIMDD 90/385/EEC). The new MDR went into effect on May 26, 2021, and the new CE Mark product must comply with new MDR or AIMDD 90/385/EEC after this date. As of May 26, 2021, companies that have devices on the market with CE Mark under MDD 93/42/EEC or AIMDD 90/385/EEC must meet the transitional provisions of the new MDR. Devices lawfully placed on the market under MDD 93/42/EEC or AIMDD 90/385/EEC before May 26, 2021, may continue to be made available on the market until May 27, 2024, provided the CE Mark was issued prior to this date, the manufacturer continues to comply with either one of the directives, and that no significant changes are made in the design and intended purpose of the applicable medical device. Recently EU parliament issued an amendment and approved the new timeline for EU MDR compliance. The new timeline is now December 31, 2028. All medical devices entering the EU after December 31st, 2028, will need to have a new CE Mark under the MDR, even if they have been on the market previously under the MDD/AIMDD. The amendment also removes the date after which devices can no longer be made available ("sell-off" deadline). Legacy devices can therefore continue to be made available on the market and put into service after 26/05/2025. This removal applies unconditionally: devices that will not be brought into compliance with the MDD regulation are also beneficiaries. Manufacturers are required to update their technical documentation and processes to meet the new MDR regulations. Nuwellis received the CE Mark for Aquadex SmartFlow® on January 13, 2020. Nuwellis received the renewal certificate to include the 24-Hour blood circuit on September 3, 2021. Our CE certificate for Aquadex SmartFlow® System is under MDD/93/42 EEC and is valid through May 26, 2024, which allows us to sell the Aquadex SmartFlow® System into the EU and satisfy future distribution demand. We plan before May 26, 2024, file a formal application and sign a contract with our Notified Body, GMED, for Aquadex SmartFlow certification to new MDR and extend our EC certificate beyond May 26, 2024.

Any one or more of these factors associated with international operations could increase our costs, reduce our revenues, or disrupt our operations, which could have a material adverse effect on our business, financial condition, and results of operations.

Employees

As of December 31, 2023, we had 59 employees all of whom are full time. None of our employees are covered by a collective bargaining agreement. We consider relations with our employees to be good.

Legal Proceedings

We are not currently subject to any legal proceedings.

Company History

Prior to July 2016, we were focused on developing the C-Pulse System for treatment of Class III and ambulatory Class IV heart failure. In August 2016, we acquired the Aquadex Business from a subsidiary of Baxter. In September 2016, we announced a strategic refocus of our strategy that included halting all clinical evaluations of the C-Pulse System related technology to fully focus our resources on our recently acquired Aquadex Business. On April 27, 2021, we announced that we were changing our name from CHF Solutions, Inc. to Nuwellis, Inc. to reflect the expansion of our customer base from treating fluid imbalance resulting from congestive heart failure to also include critical care and pediatrics applications.

Corporate Information

Nuwellis, Inc. was incorporated in Delaware on August 22, 2002. We began operating our business in November 1999 through Sunshine Heart Company Pty Limited, which dissolved as a wholly owned Australian subsidiary of Nuwellis, Inc. in 2020. Our common stock began trading on Nasdaq on February 16, 2012.

Our principal executive offices are located at 12988 Valley View Road, Eden Prairie, Minnesota 55344, and our telephone number is (952) 345-4200. Our website address is www.nuwellis.com. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K and amendments to reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act will be made available free of charge on our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. These reports are also available on the SEC's website, www.sec.gov. The information on, or that may be accessed through, any websites noted herein is not incorporated by reference into and should not be considered a part of this Annual Report on Form 10-K.

We are a "smaller reporting company" under federal securities laws. For as long as we continue to be a smaller reporting company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies, including, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than $250 million or (ii) our annual revenue was less than $100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700 million. As long as we remain a smaller reporting company and non-accelerated filer, we are exempt from the attestation requirement in the assessment of our internal control over financial reporting by our independent auditors pursuant to section 404(b) of the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act") but are required to make our own internal assessment of the effectiveness of our internal controls over financial reporting.

Except as described above, no other changes have been made to the Form 10-K, and this Report does not otherwise amend, update or change the financial statements or other disclosures in the Form 10-K. This Report speaks as of the filing date of the Form 10-K and does not (i) reflect events, results or developments that occurred or facts that became known after the filing date of the Form 10-K or (ii) modify or update those disclosures affected by subsequent events, results, developments or facts. Among other things, forward-looking statements made in the Form 10-K have not been revised to reflect events, results or developments that occurred or facts that became known to us after the date of the Form 10-K, and such statements should be read in conjunction with our filings with the SEC subsequent to the Form 10-K. This Report should be read in conjunction with the Company's other filings with the SEC subsequent to March 11, 2024.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: March 26, 2024

NUWELLIS, INC.

By: /s/ Nestor Jaramillo, Jr
Name: Nestor Jaramillo, Jr.
Title: President and Chief Executive Officer