CASE STUDY
A prospective, multicenter, single-arm, clinical cohort study to systematically characterize the risk-benefit profile of a NEW implantable cardiac device in a carefully selected cohort of children with severe heart failure, managed according to a standardized treatment protocol.

Planned enrollment
The study will enroll a total of 48 subjects in 2 cohorts based on body surface area at 14 pediatric centers in the United States and Canada.

Treatment allocation
Children aged 0 to 16 years with severe heart failure due to 2-ventricle heart disease and actively listed for heart transplant comprise the primary study cohort, in which the NEW device will be implanted. The control population is a propensity-matched retrospective cohort of children supported with the STANDARD device.

Primary endpoints
Efficacy: Survival to heart transplantation or ventricular recovery, where survival is defined as the time from implant to the time of 1 of 3 events: cardiac transplantation, death, or recovery, where recovery is the longer of hospital discharge or 30 days post-explant with acceptable neurological status.

Safety: Incidence of serious adverse events per day of mechanical support.

Secondary endpoints
Efficacy:
- Number of days of transplant-eligible survival
- Survival to hospital discharge

Safety:
- Incidence rate and scope of neurological adverse events
- NEW device technical performance

Eligibility
Inclusion criteria
- Severe NYHA functional class IV (or Ross class IV) heart failure refractory to optimal medical therapy
- Two-ventricle circulation (eg, cardiomyopathy or congenital heart disease such as repaired anomalous left coronary from the pulmonary artery)
- Age 0-16 years and weight 3-60 kg
- BSA: cohort 1 b0.7 m^2, cohort 2 0.7-1.5 m^2

Exclusion criteria

- Weight b3.0 kg or N1.5 m^2
- Unfavorable cardiac anatomy including
  - Single-ventricle lesions, restrictive cardiomyopathy, apical VSD or other hemodynamically significant lesion
  - Mechanical aortic valve or severe aortic or pulmonary valve insufficiency
- Evidence of intrinsic renal disease (serum creatinine N3× ULN for age) unless caused by acute heart failure in judgment of PI (ie, reversible)
- Evidence of intrinsic hepatic disease (total bilirubin, AST/ALT N5× ULN for age) unless caused by acute heart failure (reversible) in judgment of PI
- Evidence of intrinsic pulmonary disease (eg, chronic lung disease or respiratory distress syndrome) requiring chronic ventilation unless caused by acute heart failure and reversible in judgment of PI
- STANDARD DEVICE support N10 days or CPR for N30 minutes within 48 hours of implant
- Stroke within the past 30 days or congenital CNS malformation associated with bleeding
- Documented coagulopathy or hematologic disorder causing fragility of blood cells or hemolysis
- Active infection within 48 hours of implantation defined by a positive blood culture or temperature N38°C and WBC N15000
- Documented HIV infection or life-limiting malignant disease
- Psychiatric or behavioral disease with high likelihood for noncompliance

Study schedule
Baseline Assessments

- Medical history
- Hemodynamic data: Heart Rate, Blood pressure
- Echocardiogram
- Laboratory results
- Medication data

Procedure Assessments

- Implanted pump sizes
- Concomitant cardiac surgery
- Procedure time

Follow-up Visits (while on device)
2 Weeks, 1 Month, 6 Weeks, 3 Months, 6 Months and every 3 months if subject remains on device

- Subject status including heart failure classification
- Hemodynamic data: Heart Rate, Blood pressure

- Echo results: Available age appropriate parameters (i.e. LVSF, LVEDD, LVEF, RVEF)
- Laboratory values
- Medication data
- Device Settings and Information: Rate, Systolic duration, Mode of operation
- Pump Replacement data: Dates and reasons for replacements

Data collection time windows

Pre-Implant Evaluation	Within 48 hours prior to implant
Implant	During implant procedure
2 Weeks follow-up	Days 12-16 Post-Implant
1 Month follow-up	Days 23-37 Post-Implant
6 Weeks follow-up	Days 37-47 Post-Implant
3 Months follow-up	Days 76-104 Post-Implant
6 Months follow-up	Days 166-194 Post-Implant
9 Months follow-up	Days 256-284 Post-Implant
12 Months follow-up	Days 335-395 Post-Implant

Follow-up Visits (post-explant)
30 day or hospital discharge, whichever is longer, and 1 year
- Subject status including heart failure classification
- Hemodynamic data: Heart Rate, Blood pressure
- Echocardiogram
- Laboratory values
- Medication data

Statistical methods
The study sample size is determined by the sample size required to meet the safety end point, given that establishing reasonable safety of the NEW DEVICE is the primary regulatory requirement for HDE approval. A sample size of 24 subjects followed up for 100 days each provides >80% to conclude that, with a 1-sided α = .025 test, the serious adverse event rate for the NEW device (assumed to 0.21 per patient-day) is <0.25 per patient-day, a pre-specified performance goal established by agreement between the sponsor and FDA. Therefore, a total enrollment of 48 subjects (24 per size- based cohort) would be enrolled and implanted with the NEW device. For the efficacy end point (survival to HT or recovery), a propensity score analysis will be performed to match the NEW device patients to STANDARD device patients in a 1:2 ratio. Twenty-four patients in each NEW device cohort will provide >99% power to test the hypothesis that survival on the NEW device is different from survival in the propensity score–matched cohort of children supported with STANDARD device.