



# 2023

## Annual Report



**HeartWorks**  
WE BUILD HEARTS

# who we are

At HeartWorks, we are dedicated to developing, testing, and delivering innovative therapies to cure congenital heart defects, empowering families to lead full and enriching lives. As the world's largest collaborative network focused on this mission, we bring together a consortium of experts, the FDA, and CHD families to advance our efforts with unwavering trust and commitment.

Our work is more than just medical innovation; it's about making a meaningful difference in the lives of our HeartWarriors and their families. By advancing cutting-edge treatments and providing vital support, we help create lasting memories and enhance the quality of life for those affected by congenital heart defects.

Your support is crucial in driving this mission forward and achieving our goal of a world where every child with a congenital heart defect has the chance to thrive.



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# our mission

At HeartWorks, our mission is more than just a statement—it's our driving force. We are a dedicated, multidisciplinary team of physicians, researchers, and allied health professionals united by a singular goal: to revolutionize the treatment of HLHS and other congenital heart defects.

We are on a quest to unravel the mysteries of heart disease, pushing the frontiers of knowledge and applying groundbreaking solutions to improve patient outcomes. Our focus on developing innovative cell-based therapies aims to delay or prevent heart failure, offering new hope to those affected by HLHS.

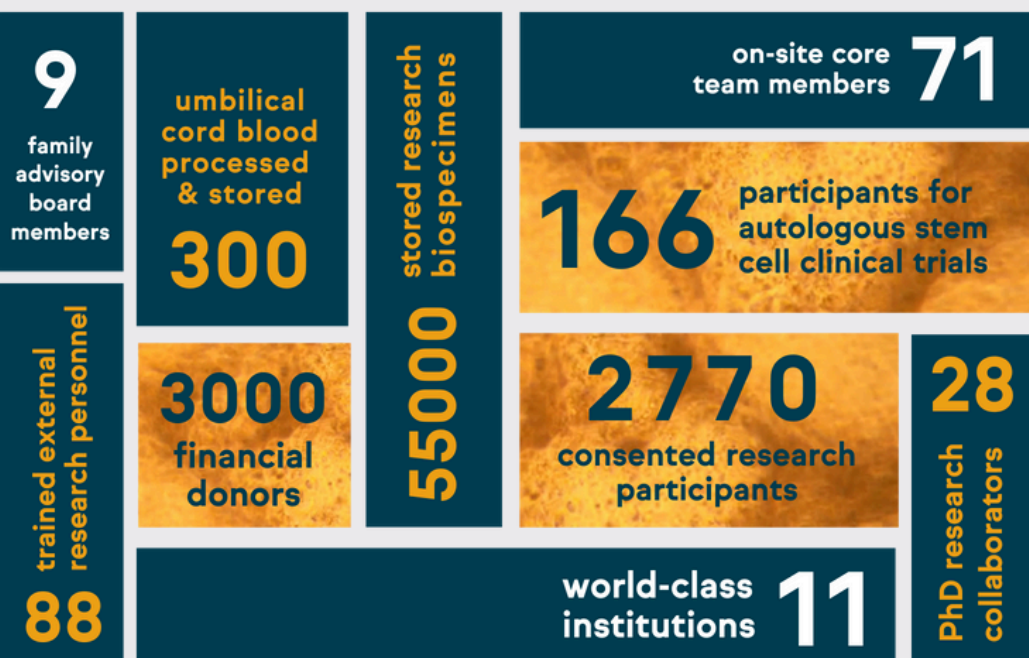
Through the HLHS Consortium, we're expanding our reach and accelerating progress. By pooling expertise and resources from leading cardiovascular programs across the country, we're shortening the gap between research breakthroughs and real-world applications. Our collaborative approach is setting new standards in the field and transforming lives with every step forward.



# 2023 highlights

This year, we've achieved remarkable milestones that bring us closer to our vision of curing congenital heart defects:

- **Bioengineered Cardiomyocyte Clinical Trial:** On August 12, 2022, we received FDA approval to conduct a pioneering phase I clinical trial using engineered heart cells for adults with congenital heart disease. With 408 candidates screened, we're diligently working to meet enrollment criteria and are refining our approach to ensure more patients benefit from this groundbreaking study.
- **ReGen CardiaCord Trials:** We completed patient enrollment for our ReGen CardiaCord trials in Glenn and Fontan patients. While phase IIb results were inconclusive, preclinical data shows promise, guiding us toward future trials and potential advancements in umbilical cord blood therapies.
- **HeartWorks-Sponsored Longitudinal Study:** We're designing a longitudinal study to track the health outcomes of past clinical trial participants, thanks to collaborative support from HLHS Consortium members. This study will provide valuable insights and guide future research directions.
- **Innovative Preclinical Research:** Our team is making strides in developing a bionic pump for pediatric use and advancing studies on cell-based therapies and immune suppression protocols. These efforts are laying the groundwork for future clinical applications and expanding our understanding of heart repair.



## Basic Research and Development

Critical advances in medicine often start with basic research studies that lead to new and better therapies. At HeartWorks, the Research and Development (R&D) Team is at the forefront of these studies. A major focus of the R&D team is characterizing key features and functions of cells in the bioengineered cardiomyocyte preparations used in our cell-based therapies.

The processes by which skin cells collected from patients are converted into induced pluripotent stem cells (iPSCs) and then selectively differentiated into functional cardiomyocytes (heart muscle cells) are highly complex. The bioengineered cell products obtained from this manufacturing process contain various sub-types of cardiomyocytes. To better understand the molecular nature and clinical potential of these cardiomyocyte subtypes, the R&D team has developed sophisticated methods to determine the key characteristics of individual cells in these preparations.

In 2023, the team introduced two key approaches: gene sequencing, which reveals which genes are "turned on and off" during these complex processes, and the determination of electrical properties, which are critical to understanding how cardiomyocytes contribute to heart function in patients. The ultimate goal of these genetic and electrical studies is to develop preparations of patient-derived cardiomyocytes that will optimize heart muscle function and overall patient outcomes.

## Manufacturing

A foundational component of HeartWorks' novel bioengineered cell therapies is our manufacturing team. They manage the intricate multi-step processes required to convert patient skin cells into induced pluripotent stem cells (iPSCs), expand these stem cells exponentially, and ultimately differentiate them into functional cardiomyocytes (heart muscle cells) for use in our therapies.

The development of robust, FDA-approved procedures for these critical tasks has been ongoing throughout the history of HeartWorks. Without this exceptional manufacturing program, HeartWorks would not be able to conduct its clinical trials. Significant progress has been made in 2023, as reflected in the diagram below, which illustrates the yield of cardiomyocytes for each sample:

2015	2017	2019	2023	future
100K cells	4M cells	300M cells	3B cells	+++

The dramatic increase in capacity—from a few million cells per sample in 2017 to three billion cells per sample in 2023—demonstrates the innovation, productivity, and quality of our manufacturing operation. In 2023, the team expanded its capability by increasing the number of vessels used for each sample preparation, proving to be a more effective strategy than enlarging vessel size or redesigning vessels. Additionally, process advancements included more elegant synchronization of manufacturing activities within the facility to optimize productivity.

Looking ahead, as patient numbers and new trials drive increased demand, the team plans to incorporate bioreactors. These advanced systems will utilize optimized conditions within a vessel to bring together the necessary biological components, conditions, and cells for the efficient production of cardiomyocytes.

### Introducing the Co-op at HeartWorks

HeartWorks is set to launch the Co-op in February, an initiative aimed at improving patient care and advancing therapies for congenital heart disease (CHD). This patient-driven centralized database will streamline the management of medical records, allowing families to securely access and share their information across providers.

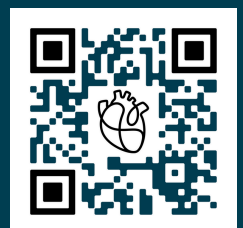
For pediatric patients, keeping track of medical histories is particularly challenging due to multiple specialists. The Co-op will enable families to control their records, facilitating better communication with healthcare providers.

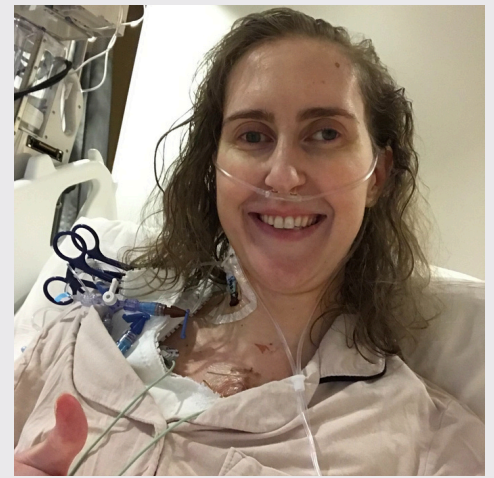
On the research side, the Co-op will address barriers clinicians face in accessing patient data, enhancing the design of clinical trials and increasing patient involvement. With participant consent, HeartWorks physicians and researchers will have access to vital medical histories, ultimately leading to more effective therapies.

Visit our website to learn more and stay updated as we approach the launch!



the  
co-op  
@HeartWorks





## Creating Memories with Heart: Lauren's Journey with HeartWorks

At 36, Lauren embodies resilience and hope, navigating life with a unique set of challenges due to her congenital heart defects. Born with Tricuspid Atresia, Hypoplastic Right Ventricle, a large VSD, and multiple muscular ASDs—essentially, half a functioning heart—Lauren's journey has been anything but ordinary. Her heart has required three open-heart surgeries, numerous procedures, and a lifetime of ongoing medical care. Despite these hurdles, Lauren's spirit remains unbroken, and her desire to live fully shines through.

HeartWorks has had the privilege of supporting individuals like Lauren, helping them create meaningful and joyful memories despite the trials they face. This year, we are thrilled to share how our mission has intersected with Lauren's remarkable story and how we strive to help her continue making cherished memories.

Lauren's life is a testament to the power of perseverance. Despite the difficulties she has encountered, she remains a beacon of positivity and hope. She enjoys the simple pleasures of life, from collecting coins and pressed pennies to indulging in a good comedy or romance film. Lauren's past is rich with experiences, from playing piano and participating in family theater to earning a varsity letter in bowling. Today, she is a homemaker, a passionate advocate for congenital heart defects (CHDs) and mental health, and a dedicated member of the CHD community—her “second family.”

One of Lauren's greatest joys is re-learning to play the piano, a pursuit that resonates deeply with her past interests. Through HeartWorks, Lauren has had the opportunity to participate in events and programs designed to create lasting memories. We are proud to support her journey, ensuring that her days are filled with moments of joy and connection. Lauren's story is a powerful reminder of why HeartWorks exists. We are committed to helping individuals like her build and celebrate life's precious moments. Whether it's through providing access to special events, supporting personal goals, or simply offering a compassionate community, our mission is to enhance the quality of life for those we serve.

As Lauren continues to embrace life with a hopeful heart, she remains an inspiration to all who know her. Her story is a reflection of the incredible impact that a supportive community and dedicated organization can have. We are honored to play a part in Lauren's journey and look forward to many more years of helping individuals like her create beautiful memories.

Thank you for your support, which makes it possible for us to continue our vital work. Together, we can ensure that stories like Lauren's continue to be filled with hope, joy, and cherished moments.

## Cora's Heart Journey: A Story of Strength and Resilience

In September 2020, baby Cora's life began with extraordinary challenges. Born with double inlet left ventricle, transposed great arteries, and coarctation of the aorta, Cora's journey has been a testament to courage and the transformative power of medical care and support. At just four days old, Cora underwent the Norwood procedure, a critical surgery for her condition. Her recovery was initially complex, marked by seizures, a paralyzed diaphragm, and a paralyzed vocal cord. She required a G-tube for feeding and spent six weeks in the hospital before her courageous return home.

Her path to health continued with the Glenn procedure in February 2021. Despite the surgery's challenges, including the development of chylothorax and an extended hospital stay, Cora's spirit remained strong. The road to recovery was not without its hurdles, but each step forward was a testament to her resilience and the care provided by her medical team and support network. Most recently, in July 2024, Cora faced another significant milestone: the Fontan procedure. While she again encountered chylothorax, it resolved swiftly, allowing her to return home on a low-fat diet and continue her journey toward better health.

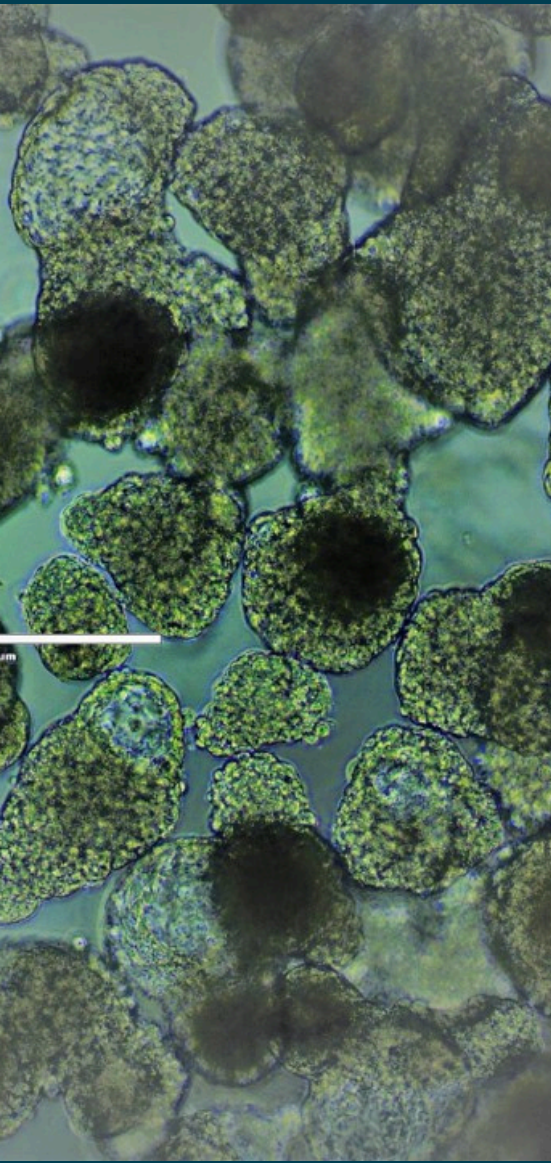
Cora's story is a powerful example of the challenges faced by families with complex congenital heart conditions and the incredible strength of the children who endure them. Her journey highlights the importance of comprehensive care, the support of a dedicated medical team, and the love and perseverance of her family.

At HeartWorks, we are honored to be part of Cora's journey and to support families like hers through the ups and downs of managing congenital heart defects. Our work is dedicated to improving the lives of children and families affected by heart conditions, ensuring they receive the care and support they need at every step of their journey.

We invite you to join us in supporting families like Cora's by getting involved, participating in our programs, or making a donation. Your support helps us continue to provide essential services and create positive outcomes for those we serve. To read more stories of courage and hope, or to find out how you can contribute, please visit our website or contact us directly.







## program priorities

Our program priorities reflect our commitment to advancing science and improving patient care. Here's where we stand:

- **Preclinical Studies:** We are focused on porcine (pig) models to assess and mitigate arrhythmia risks from cell-based therapies, streamlining our approach to enhanced clinical outcomes.
- **Immunosuppression Protocols:** We've completed a crucial study on a three-drug immune suppression regimen in porcine models, laying the groundwork for future large-scale studies and potential FDA pathways.
- **Clinical Trials:** Ongoing efforts include refining our CardiaCord protocols and optimizing left ventricular cardiomyocyte production. We're committed to ensuring these trials meet their objectives and bring us closer to clinical application.
- **Preclinical Innovations:** We're advancing our research on bionic pumps and cell-based therapies, aiming to develop solutions that can be tested and implemented in clinical settings.

### **Case Study: With our Partner Team at the Todd and Karen Wanek Family Program for Hypoplastic Left Heart Syndrome**

#### **A Life Transformed: Travis Kelchen's Journey**

Travis Kelchen's story is a testament to the impact of our innovative approaches. Diagnosed with Ebstein anomaly, Travis faced a critical moment when his heart condition worsened. Thanks to the groundbreaking ECMO intervention developed with our support, he was stabilized and ultimately received a life-saving heart transplant.

This regenerative approach, tested in preclinical models and refined through our program, provided Travis with a new lease on life. His successful recovery and return to normal activities underscore the transformative potential of our research and the dedication of our multidisciplinary team.

## Publications & Presentations

Birker K., Ge S., Kirkland N.J., et al. (2023). Mitochondrial MICOS complex genes, implicated in hypoplastic left heart syndrome, maintain cardiac contractility and actomyosin integrity. *Elife*. 2023;12:e83385. Published 2023 Jul 5. doi:10.7554/eLife.83385

Min-Hwang, C., Secreto, F. & Nelson, T.J. (2023). Gene Expression Analysis of Clinical-Grade Cardiomyocyte Lineage Cells Generated in Bioreactors from Induced Human Pluripotent Stem Cells via Single-Cell RNA Sequence Assays. *Keystone Symposia*. Poster Presentation.

Odogwu-Nkechi, M. (2023). Gene Expression Signature in Right Ventricular Pressure Overload Porcine Model Administered Autologous Umbilical Cord Blood-Derived Mononuclear Stem Cell Therapy. *American Society of Human Genetics*. Abstract.

Oommen, S. (2022). Preclinical Safety and Long-Term Survival of Human iPSC-Derived Cardiomyocytes Supporting Clinical Trials in the Treatment of Univentricular Congenital Heart Disease. *International Society for Stem Cell Research*. Abstract.

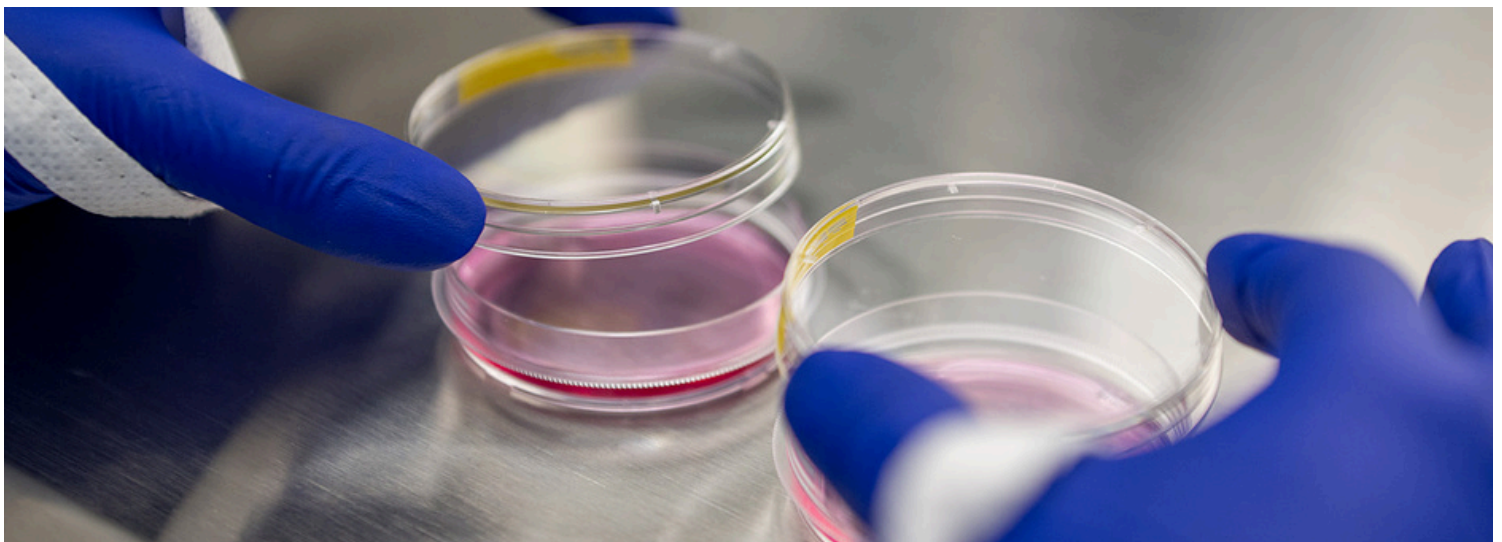
Oommen, S. (2022). Preclinical Safety and Long-Term Survival of Human iPSC-Derived Cardiomyocytes Supporting Clinical Trials in the Treatment of Univentricular Congenital Heart Disease. *Single Ventricle Investigator Meeting*. Presentation.

Oommen, S., Cantro Peral, S., Qureshi, M.Y., et al. (2022). Autologous Umbilical Cord Blood-Derived Mononuclear Cell Therapy Promotes Cardiac Proliferation and Adaptation in a Porcine Model of Right Ventricle Pressure Overload. *Cell transplantation*, 31. <https://doi.org/10.1177/09636897221120434>

Theis, J.L., Niaz, T., Sundsbak, R.S., et al. (2022). CELSR1 Risk Alleles in Familial Bicuspid Aortic Valve and Hypoplastic Left Heart Syndrome. *Circulation: Genomic and Precision Medicine*, 15(2), E003523. <https://doi.org/10.1161/CIRCGEN.121.003523>

Theis, J.L., & Olson, T.M. (2022). Whole Genome Sequencing in Hypoplastic Left Heart Syndrome. *Journal of Cardiovascular Development and Disease*, 9(4), [117]. <https://doi.org/10.3390/jcdd9040117>

Theis, J.L., Shatila, S.D.H., Fogarty, Z.C., et al. (2023). Genome-Wide Association and Inheritance-Based Analyses Implicate Unconventional Myosin Genes in Hypoplastic Left Heart Syndrome. *Circulation: Genomic and Precision Medicine*, 16(1), E003761. <https://doi.org/10.1161/CIRCGEN.122.003761>



# Governance and Leadership

## Board of Directors

Townsend (Tom) Porter  
Matthew Nelson  
Dr. Timothy Nelson

## Family Advisory Council

Erin Borkowski  
Hannah Elizabeth Brewer  
Tara Chamberlain  
Jack McArtney  
Michelle Waletzko  
Jessica Marra  
Holly Thorne  
Kalee Plowman  
Katie Pieper  
Kelly DiMaggio  
Karlyn Tejada Brolsma  
Jenny Kiel

## Leadership Council

Launching in 2024: For more information,  
contact Amy Deshler at [Amy@webuildhearts.org](mailto:Amy@webuildhearts.org)





# Looking Forward

## Charting Our Future

As we look ahead, HeartWorks is poised for exciting advancements. The past year has been a transformative period, shifting our focus from basic research to the demands of a product-driven approach.

We're expanding our team with new hires, including Dr. Bin Zhang, an expert in Fontan procedures, and are actively seeking a preclinical director to lead our research efforts. Our commitment to developing safe and effective solutions for HLHS remains unwavering, and we're excited about the new projects and innovations on the horizon.

Our dedication to producing breakthrough therapies is matched only by our resolve to overcome the challenges that lie ahead. With continued collaboration and support, we're confident in our ability to achieve our goals and make a lasting impact in the field of congenital heart disease.



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