



2015 IMPACT REPORT TO BEN'S GIFT, INC.

Accelerating the Pace of Research

Children's National is deeply grateful to Ben's Run for its visionary and growing support. As described below, funds generated through Ben's Run have provided timely investments in the pioneering research led by physician-scientist Kirsten Williams, MD. An emerging pediatric oncology leader, Dr. Williams focuses on children with chemotherapy-resistant leukemia—those for whom all other treatments, including bone marrow transplantation (BMT), have failed. Harnessing her clinical and research expertise, Dr. Williams is creating novel therapies and tools to overcome the gravest prognoses in childhood cancer today.

Year after year, funds generated by volunteers and participants in Ben's Run have helped Dr. Williams and her team gain crucial understanding of why BMT sometimes fails to defeat cancer, how drugs and emerging immunotherapy treatments could help a child's body successfully fight residual disease, and which patients are most likely to relapse (giving clinicians a "head start" to act before recurring cancer cells have time to multiply!). Philanthropic investment from Ben's Run is pushing scientific boundaries so every child has the best possible chance for a long, healthy life.

LEVERAGING PRIOR RESEARCH INVESTMENTS

Project 1: Improving Early Detection and Treating Cancer Relapse

Dr. Williams used her initial grant from Ben's Run (2013) to develop a blood test that could reveal a rare leukemia cell circulating in the blood (CD34 chimerism). Because this test was a simple blood draw, it spared patients from painful and invasive marrow biopsy, which requires inserting a needle in their hip. Furthermore, because CD34 chimerism is a simple blood test, doctors can also monitor their patients more frequently, providing an extraordinary "head start" to begin treatment should the cancer return. In conjunction with this test, the team also wrote and opened a clinical trial to administer a combination of two drugs to help the new transplanted cells more effectively kill any remaining leukemia. This trial has both monitored and even treated a patient after relapse. This trial was the patient's only chance to treat the leukemia at this early stage! Our team is committed to building on the new scientific knowledge yielded through this project to find new ways to identify leukemia cells at the lowest level possible and with the least amount of invasive testing for children.



A stark reality: 90 percent of children with leukemia who relapse after BMT die of their disease.

Why is treating relapse after BMT so difficult?:

Patients undergoing BMT need the new immune cells to kill the leukemia. However, these immune cells can also hurt healthy tissues, so medicines are strategically used to control this immune "military" response. What is really needed is the ability to identify patients who require the full force of the immune response and then give marching orders to remove restrictions on their power in a positive way—so that only the anti-leukemia forces are activated to kill the leukemia cells. Current diagnostic tools cannot detect residual disease soon enough to muster the immune cells to have a fighting chance to defeat the leukemia.

Our Vision: To overcome current scientific limitations to caring for these children—first by identifying who needs to take further risks to cure the leukemia after BMT and then developing the sophisticated targeted "military" strategy. Our team's experimental approaches are leading the way to novel solutions to identify and treat relapse in real-time. By acting immediately, when the cancer burden is still low, we believe we can help these children survive!



Project 2

Objective 1: Predicting Relapse before It Happens (completed)

Prior funds from Ben's Run (2014) helped advance the ability to use a novel imaging test called 18Flurothymidine (FLT) to predict relapse. This simple diagnostic tool is neither invasive nor painful, and it shows the entire space where leukemia can hide (in contrast to the CD34 chimerism blood test or the marrow biopsy which samples only one spot). Dr. Williams was the first to show that FLT could identify the presence of healthy new bone marrow and distinguish this from recurrence of the leukemia in the post-BMT patient in adults. These studies have demonstrated that this approach can predict leukemia relapse up to 80 days sooner than biopsy—well before it is currently detectable in children even using the most sophisticated tests. In addition, in two-thirds of the cases, FLT predicted where in the patient's body the cancer would relapse, offering new opportunities for intervention.



Status: Funds from Ben's Run were crucial to developing and testing this early detection tool in adults (a step required before it can be applied to children). The team has already translated its preliminary data into an article that is currently being submitted to a high-level medical journal. When published, the article will recognize Ben's Run for providing critical early seed funding.

Objective 2: Bringing FLT Technology to Children in Need (ongoing)

Dr. Williams' research team now seeks to bring FLT technology to children, using this noninvasive and painless test to determine the presence of residual leukemia versus healthy cell growth (using reduced radiation appropriate for children). Her team is greatly encouraged by the predictive accuracy found in the adult study of the experimental scans in terms of both likelihood of relapse and location in the body. These results suggest the potential to use these scans to precisely target treatments and minimize damage to healthy cells—critically important to protecting children's health for a lifetime.



Status: Over the past year, Dr. Williams assembled an extensive cross-disciplinary team to execute this work and has pursued necessary approvals to open this trial. Her initial aim is to enroll three children, a critical first step to collecting the preliminary data required to secure additional private and federal funding to take the research to scale. A thorough internal review, including by the Radiation Safety Committee, was completed and approved in mid-November 2015; the team immediately began patient enrollment. In addition, Dr. Williams is collaborating with our world-class immunotherapy team to add a targeted leukemia treatment (pending additional funding; proposed for 2016).



PROPOSAL FOR 2016 FUNDS: INTEGRATING A POWERFUL IMMUNOTHERAPY APPROACH

To significantly enhance the imaging and detection work described above, Dr. Williams seeks to integrate an immunotherapy component to the scope of work. Undertaken in close collaboration with Catherine Bollard, MBChB, MD, the trial will provide patients with personalized, potentially lifesaving, cellular products. Dr. Bollard's ongoing research has shown that our team can "train" a BMT donor's cells so that they recognize multiple proteins expressed on leukemia cells (but not on healthy cells). This multi-target approach gives the remaining cancer less opportunity to escape an immune attack and minimizes the risk of harm to healthy tissues.

Based on the team's experience in adults, they hypothesize that the experimental scans will identify sites of residual leukemia better than standard biopsies, providing the greatest opportunity to reveal the treatment's success. Given the high mortality of relapse of acute leukemia after BMT, it is critical to develop new approaches for early diagnosis and to improve understanding of relapse biology. The resulting data will allow us to better treat and evaluate the response to immunotherapy not only for patients with leukemia but, ultimately, for any patient with relapse of cancer after BMT. Proceeds from the 2016 Ben's Run would facilitate the use of this new immunotherapy for children and evaluate its success using Dr. Williams' novel imaging technique.

Status: To translate this approach to children, we must first demonstrate its safety in adults. An adult trial now underway has enrolled three participants; two must reach a six-week safety mark for the team to pursue FDA approval to include children. Although one adult left the trial due to unrelated complications, one has already reached the required six-week goal. A second adult is expected to reach that milestone in mid-November. At that point, Dr. Williams will have the required data to submit to the FDA, a key next step to extending the research trial to a pediatric population.

OUR HEARTFELT THANKS!

Philanthropic investment in cancer research is critical to improving overall survivability and helping children thrive. Although private funding is limited, its strength is that it can be used to take calculated risks—sparking the transformation from the laboratory to the child's bedside. Childhood cancers collectively receive only four percent of U.S. federal research funding, making individual donations essential to pushing scientific boundaries and catalyzing innovation. Proceeds generated by Ben's Run are essential to filling this gap, advancing experimental research to the stage that a viable NIH application can be submitted. Thank you for being such an important partner in our work to turn promising science into real solutions for kids.

Every Dollar Counts: How Each Participant's Contribution Leads to Lifesaving Breakthroughs for Kids with Cancer

