

Spring 2021



## *Youngest Successful* **CAR-T Cancer Immunotherapy in Buffalo**

“She’s a bundle of joy, she’s a blessing. she’s just life.” That’s what Cariori Mayfield of Niagara Falls says about his 2-year-old daughter, Chasity. It’s been over a year since she went through a complex series of therapies at the Roswell Park Oishei Children’s Cancer and Blood Disorders Program to treat the leukemia she was diagnosed with at only 5 weeks old.

Chasity’s battle with leukemia began in the fall of 2018, when her parents became concerned that the persistent vomiting, irritability and skin discoloration they saw in their newborn could be signs of something serious. After a few trips to the pediatrician, they took her to the Oishei Children’s Hospital, where Kara Kelly, MD, pediatric oncologist and Roswell Park Oishei Children’s Cancer and Blood Disorders Program Chair, would diagnose Chasity with an aggressive, treatment-resistant blood cancer, acute lymphocytic leukemia (ALL).

“When we got the news, it was just like, ‘How?’” recalls Chasity’s mom, Shawanda Prather. “I felt a pain in my stomach that I had never felt before.”

Following the diagnosis, the family endured even more stressful news. Her treatment team determined that her leukemia was marked by a gene mutation that made it even less likely that she would respond to standard chemotherapies, and more likely that the cancer would recur.

“This particular type of leukemia, when it presents in babies as young as Chasity — the prognosis is terrible, with typically only about 20 to 30 percent being able to make it,” says Dr. Kelly. “I knew we needed something different, something that the leukemia cells were not going to be resistant to.”

That’s where CAR T therapy came in.

### **Immunotherapy Treatment Provides Hope**

Few centers in the country are approved to offer CAR T, short for chimeric antigen receptor T-cell therapy, but Roswell Park is thanks to our cutting-edge facilities and comprehensive care. CAR T therapy involves removing a patient’s own immune cells, bolstering them to make them more effective at recognizing and killing cancer cells, and infusing them back into the patient with the goal of providing long-term protection against cancer.

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To learn more about the impact of your support, visit [RoswellPark.org/giving](https://RoswellPark.org/giving)

Roswell Park is one of very few centers in the United States equipped to offer clinical trials of a full range of immunotherapies, including many that were developed right here.





## Donor-Funded Translational Research Position Proves Key to Roswell Park Success

Roswell Park's Drs. Pawel Kalinski and Shipra Gandhi

As he ticks off a list of six different clinical trials he is currently collaborating on with Shipra Gandhi, MD, Pawel Kalinski, MD, PhD, Vice Chair for Translational Research in the Department of Medicine and Rustum Family Professor for Molecular Therapeutics and Translational Research, says, with understated humor, "We keep ourselves busy."

You may have read about Dr. Gandhi in the Spring 2020 issue of Donor Dollars at Work. Thanks to donor giving, Dr. Gandhi was Roswell Park's first designated Translational Researcher funded by the Release the Breakthroughs campaign. Just a few years ago, the Roswell Park Alliance Foundation was presented with the need to fund positions like this and immediately saw its importance.

As a translational researcher, Dr. Gandhi serves as a "bench-to-bedside" bridge, using the results of laboratory research to develop clinical trials that will lead to techniques and tools to help improve, extend and save lives of cancer patients. And, in a little over a year, Dr. Gandhi, has indeed proven herself more than worthy of donor support.

### At the bedside....

Two days each week, you will find Dr. Gandhi "at the bedside," assessing Roswell Park patients who are participating in her clinical trials for breast cancer. "Working directly with the patients is both gratifying and humbling," says Dr. Gandhi. "When a treatment is working, it helps to see our efforts making a positive difference in a person's life. When I see firsthand that a treatment is not working, it motivates me to go back to the lab and figure out why, and then try to develop strategies to improve the treatment's efficacy," says Dr. Gandhi.

### ...and the bench

At "the bench," Dr. Gandhi has collaborated with Dr. Kalinski and other researchers to develop, garner funding, implement and analyze several clinical trials and projects, including:

- **Testing a vaccine in combination with immune modulating strategy to treat cancer in patients with triple negative and HER2 positive breast cancer.** This phase 2 trial, set to begin soon, is the first to assess the effectiveness of a three-pronged strategy combining distinct immunotherapy approaches for breast cancer. "Our strategy uses a unique combination of biologic agents to make tumors visible to the immune system by making them look like tissue that's been infected by a virus. We've never tested them all together before in patients, but the findings from earlier clinical and preclinical studies lend strong support for assessing this combination even in the most aggressive and hard-to-treat cancer types," says Dr. Kalinski.

Dr. Kalinski is the overall Principal Investigator (PI) and Dr. Gandhi is Roswell Park's PI for this \$6.42 million Breakthrough Award, in partnership with researchers from the Moffitt Cancer Center in Tampa, and funded by the Department of Defense's Breast Cancer Research Program. **Dr Kalinski emphasized that the donor funding of Dr. Gandhi's position was pivotal in winning this award.** Explaining that without proof of a person with the right experience who has contributed to the development of the basic concepts, has prepared the clinical trial and who can take care of critical patients, monitoring them for any potential side effects, it would be impossible to even think about pursuing and attracting outside funding for this work.

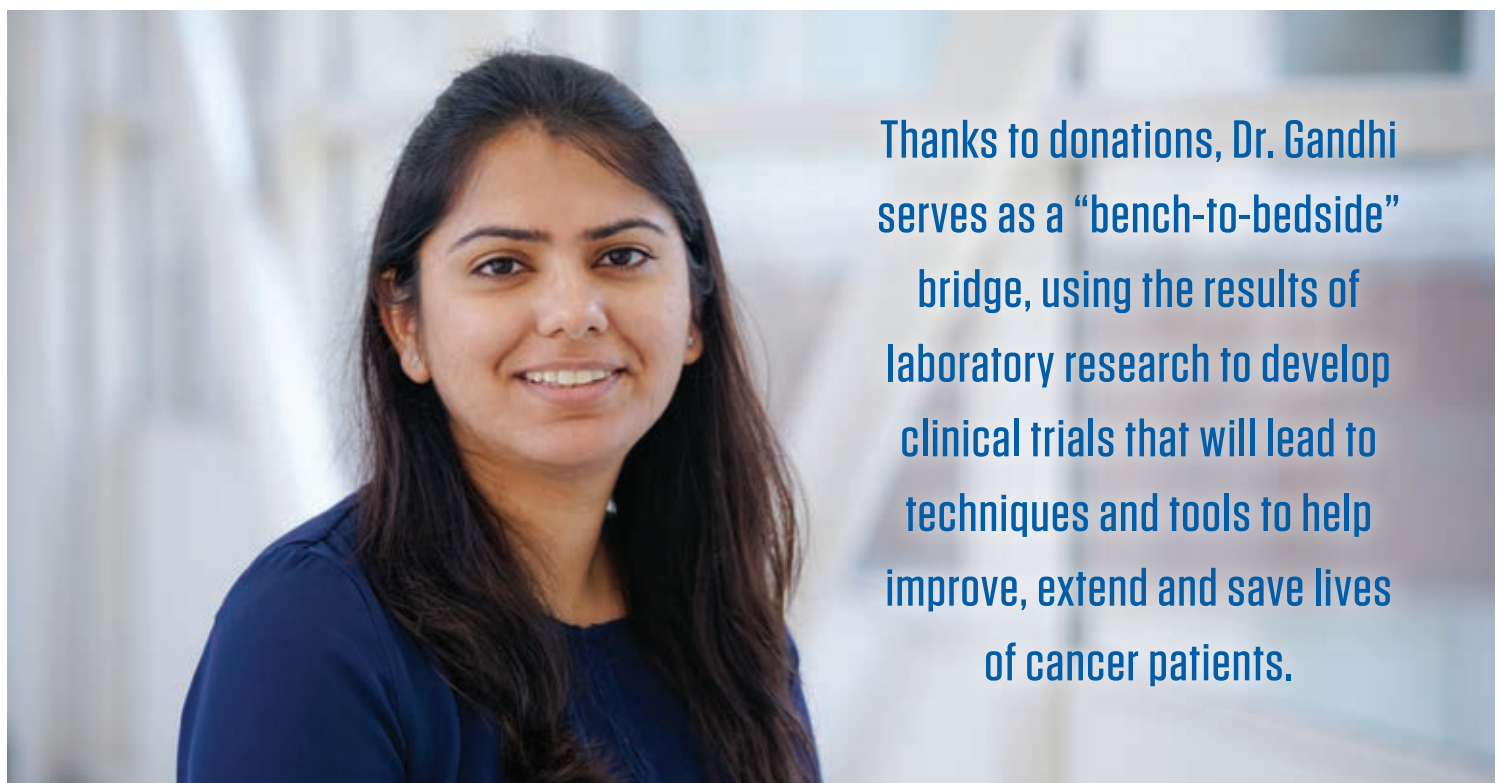
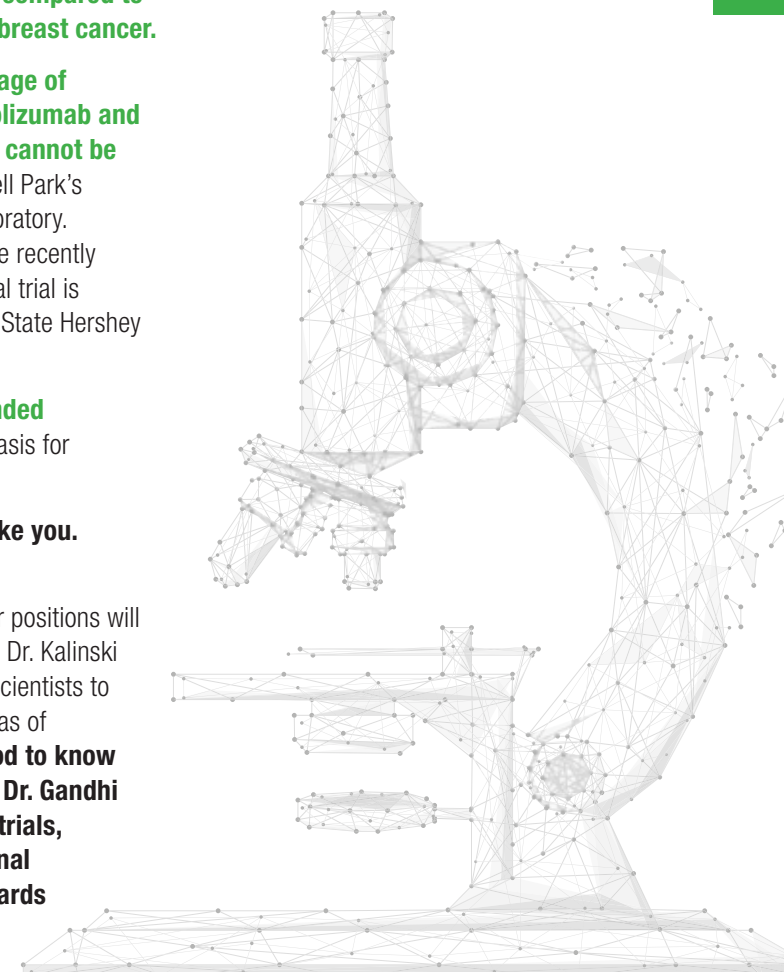
- **A phase 1 trial that studies how well chemokine modulation therapy and standard chemotherapy given before surgery work in treating patients with early stage triple negative breast cancer (TNBC).** Cytokines are small secreted proteins released by cells, and have a specific effect on the interactions and communications between cells. This trial is partially supported by a donor-funded grant and from the Clinical and Translational Science Institute Pilot award given to Dr. Gandhi.

- **A randomized phase 2 study to evaluate if a combination of drugs (T-DM1 and palbociclib) improves progression-free survival compared to using only T-DM1 in patients with metastatic HER2 positive breast cancer.**
- **A phase 1b/2 trial that studies the side effects and best dosage of propranolol hydrochloride when given together with pembrolizumab and how well they work in treating patients with melanoma that cannot be removed by surgery.** This trial is a collaborative effort with Roswell Park's Dr. Repasky and is based on novel preclinical findings from her laboratory. Encouraging preliminary findings from the phase 1 clinical trial were recently published in Clinical Cancer Research 2020 and the phase 2 clinical trial is ongoing at three other centers including the Cleveland Clinic, Penn State Hershey and Emory University.
- Additionally, Dr. Gandhi just received her own **prestigious NCI-funded career-KL2 career development** award to study the molecular basis for chemo-resistant tumors.

All of this important work is being achieved thanks to donors like you.

### Paving the Way for Additional Researchers

Given Dr. Gandhi's success, it's hoped that more transitional researcher positions will be added at Roswell Park in the near future with donor support. In fact, Dr. Kalinski notes that Roswell Park has brought on two additional junior clinician-scientists to work with senior researchers and expand research and trials in the areas of colorectal cancer, pancreatic cancer and esophageal cancer. **"It is good to know that, thanks to donors to the Roswell Park Alliance Foundation, Dr. Gandhi was able to fully devote her time to so many important clinical trials, and that her success may pave the path for additional transitional researchers here, so we can expand our research and work towards better outcomes for cancer patients,"** says Dr. Kalinski.

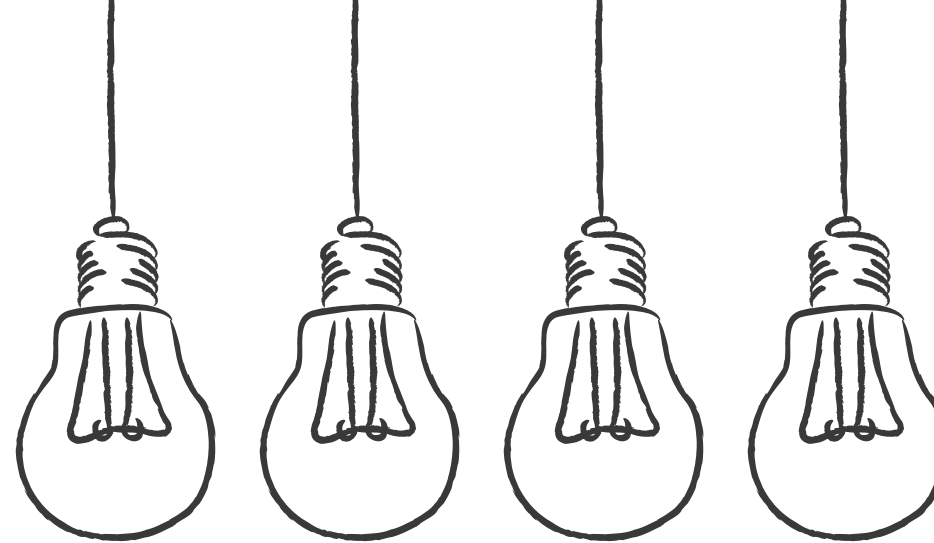


Thanks to donations, Dr. Gandhi serves as a "bench-to-bedside" bridge, using the results of laboratory research to develop clinical trials that will lead to techniques and tools to help improve, extend and save lives of cancer patients.



# 5 Promising Ideas Moving Ahead

## THANKS TO DONOR GIVING



The Roswell Park Alliance Foundation has awarded over 500 grants to promising research studies thanks to donors like you.

Change doesn't happen in a vacuum. It requires energy and motivation, encouragement and support. And that's just what you provide to researchers at Roswell Park who work every day to change the cancer landscape.

Donations from generous supporters like you allow Roswell Park to award critical seed funding that helps these big, bright ideas develop into new treatments and ideas that could change how cancer is diagnosed and treated.

This past fall, our Scientific Advisory Committee (SAC) awarded five grants to Roswell Park researchers to explore ideas that have the potential to make a significant impact on the cancer landscape.



### The role of mitochondrial unfolded protein response in resistant prostate cancer

Although significant progress has been made to treat localized prostate cancer, the biology of and treatment strategies for aggressive or resistant prostate cancer are not fully developed. Dr. Chandra will examine whether Hsp60, a mitochondria residence protein, promotes prostate cancer progression and whether this protein could be targeted for prevention of prostate cancer recurrence. **Ultimately, this study could change how prostate cancer is treated by creating alternative treatment options for men.**

*led by Dhyan Chandra, PhD, Department of Pharmacology and Therapeutics*



### Do anti-anxiety drugs promote pancreatic cancer progression?

Many people might not recognize the term 'benzodiazepines' but it is a commonly prescribed class of anti-anxiety drugs and Dr. Feigin believes it may modify a cancerous tumor and promote the progression of pancreatic cancer. Often, these anti-anxiety medications are prescribed to cancer patients during treatment to help alleviate anxiety and insomnia as well as post-traumatic stress disorder. While past research has been done on benzodiazepines' role in increasing an individual's risk of developing cancer, Dr. Feigin's study is unique in studying its impact on cancer progression. **The long-term goal of this research is to change how anti-anxiety medications are prescribed to pancreatic cancer patients or those individuals at risk of developing pancreatic cancer** to slow the progression and improve the efficacy of the patient's treatment plan.

*led by Michael Feigin PhD, Department of Pharmacology and Therapeutics*



### New combination therapy for colorectal and esophageal cancers with p53 abnormalities

Cancer of the large bowel, esophagus and stomach are leading causes of cancer-related death in the United States. Abnormalities in a gene called p53 are found in up to half of diagnoses of these cancers and often contributes to poor prognosis. **Currently, there is no therapy effectively and selectively targeting these cancers and medications being used provide limited long-term benefit. Dr. Fountzilas's study is testing a completely new strategy** targeting cancers with p53 abnormalities using two already FDA-approved drugs that have not been combined before. Preliminary studies demonstrated that this strategy can selectively target tumor cells, protects healthy cells and can work at lower dose of drugs therefore limiting side effects, decreasing costs and improving quality of life. This study will test this novel combination for the first time in patients and then determine the right dose and establish a bank of patient-derived material for better understanding and predicting individual patient response in the future.

*led by Christos Fountzilas, MD, Department of Medicine*



### Approach Targeting PTEN Loss in Pediatric Sarcoma

Rhabdomyosarcoma (RMS), a type of pediatric sarcoma, is the most common type of soft tissue cancer in children and adolescents. While patients with localized RMS see success with conventional therapy, there has been no significant improvements in cure rates for patients with metastatic or relapsed RMS. That's why Dr. Mal identified the need to develop novel, targeted and safer therapeutic approaches for these high-risk pediatric patients, specifically looking at the tumor suppressant PTEN's impact on cancer cells. **Success in this study could provide a more effective and less toxic alternative to treatment strategies and change therapeutic management for all pediatric cancer patients with high-risk RMS.**

*led by Asoke Mal PhD, Department of Cell Stress Biology*



### Epigenetic dysregulation of cellular identity as a path to recurrence in prostate cancer

Prostate cancer cells depend on androgen signaling to survive and thrive. That's why prostate cancer initially responds to androgen deprivation therapy but unfortunately, nearly all patients relapse and are then resistant to the initially successful therapy. Roswell Park researchers have insights on how cancer cells switch their identity from androgen-dependent to indifferent to androgen. Taking that knowledge, this research project, led by Dr. Smiraglia, aims to better understand the process of identity switching in cancer cells to allow for the development of novel therapeutic strategies to interfere with the process. The interference **could lead to the development of new therapies that will reduce prostate cancer recurrence rates.**

*led by Dominic Smiraglia PhD, Department of Cancer Genetics and Genomics*

THIS GRANT MADE POSSIBLE BY FUNDS RAISED BY

THE 11 DAY POWER PLAY


THIS GRANT MADE POSSIBLE BY THE EXCELSIOR FUNDRAISERS IN THE 2020



On average, every \$1 donated to Roswell Park for cancer research results in another \$13 in external grant awards.







## Roswell Park donors provide SurVaxM expanded access for compassionate use and enrollment in next phase of SurVaxM brain cancer clinical trial

**M**ore time to live a quality life with loved ones, and more hope for the future; these are things that most cancer patients want more than anything else.

But, for many patients with glioblastoma, time and hope have been in short supply over the years. Glioblastoma is a notoriously aggressive brain cancer that, with standard therapy, has a median survival rate of only 15 months.

### SurVaxM Successes

Enter SurVaxM, a brain tumor vaccine developed in 2012 by Roswell Park's Drs. Robert Fenstermaker and Michael Ciesielski. Thanks to generous support from Roswell Park donors, Phase 1 and 2 trials of SurVaxM were opened in 2014 and 2016, respectively, with results showing significantly increased overall survival in patients with both recurrent glioblastoma and newly diagnosed glioblastoma.

"In the phase 1 trial, seven out of eight patients with recurrent glioblastoma had increased overall survival, extending the standard time of recurrence from seven months to sixteen months, and one patient had and continues to have complete remission," says Dr. Ciesielski.

"In the phase 2 trial, 55% of the 63 newly diagnosed glioblastoma patients from Roswell Park, Dana Farber and Cleveland Cancer Clinics who were treated with SurVaxM were alive two years from diagnosis, compared to 27% on standard therapy," says Dr. Ciesielski. "Those are promising statistics, made possible thanks to donor support."



Roswell Park's Drs. Robert Fenstermaker and Michael Ciesielski

### What's Next for the SurVaxM Trial?

The next proposed phase of the SurVaxM clinical trial is a randomized controlled trial (RCT) that mirrors the current studies for patients with newly diagnosed glioblastoma, adding a control and increasing enrollment of up to 240 patients over 24 months in as many as 20 different cancer centers across the country. Major funding for phase 2b of this clinical trial will be funded thanks to donations, and the trial is set to open in the coming months.

*Think about that for a moment; 240 cancer patients and their families across the United States will have hope and more time thanks to your support.*

### Expanded Access for Compassionate Exemption Cases

But what about glioblastoma patients who wish to be treated with SurVaxM now but do not qualify for the currently open SurVaxM trials? That's where compassionate use exemptions come in, and that's where, **once again, donations to Roswell Park are helping to provide time and hope for these patients.**

Dr. Ciesielski noted that there are currently only a few small phase 1 studies involving SurVaxM at Roswell Park, including a trial for pediatric patients with brain tumors (partially funded by

the Alliance Foundation), and separate trials for patients with multiple myeloma and neuro endocrine tumors (NET). "With no other open trials for glioblastoma in the United States, each patient who did not meet the requirements for phase 1 or 2b of our current trials but wished to be treated with the SurVaxM vaccine had to apply for a compassionate care exemption through Roswell Park's Internal Review Board (IRB) and the FDA," says Dr. Ciesielski.

"Unfortunately, this is a time-consuming process that requires many resources and levels of approval. So, in 2019, Roswell Park's IRB recommended that we focus on applying for and receiving FDA permission to open expanded access for SurVaxM, which allows for compassionate care exemptions, but does not need individual approvals from the FDA and IRB for each patient." Additionally, the Roswell Park Alliance Foundation granted funds to synthesize 3,000 doses of the SurVaxM vaccine specifically to undertake more compassionate exemption cases and ultimately to provide a vaccine for SurVaxM expanded access trial once a required randomized clinical trial was open.

As of press time, Dr. Ciesielski noted that Roswell Park was filing the last of the necessary documentation for FDA expanded access approval, and was expecting final approval in the upcoming weeks.

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Chasity is one of the youngest patients to successfully receive CAR T therapy. These types of immunotherapy treatments are on the cutting-edge of care and several are made possible thanks to donations to the Roswell Park Alliance Foundation.

Patients who receive CAR T-cell therapy will be treated at Roswell Park's Bill and Jane Greene Transplant and Cellular Therapy (TCT) Center, a donor-supported expansion of the former Blood and Marrow Transplant Clinic through donations to the Release the Breakthroughs Capital Campaign. The TCT medical team, which includes national leaders in their fields, have significant experience in recognizing and managing the side effects of immunotherapies.

In early 2019, Chasity's blood stem cells were collected, re-engineered and infused back into her under the guidance of Dr. Kelly, pediatric oncology/cellular therapy specialist Meghan Higman, MD, PhD, pediatric critical care specialist Bree Kramer, DO, transfusion medicine expert Joanne Becker, MD, and the TCT Center.

"This was kind of the equivalent of a Hail Mary approach," recalls Dr. Kelly. "But we also knew it was her best chance for putting her cancer in remission, and she'd already proven that she was a strong baby, a real fighter."

Tense nights, a few days' stay in the Pediatric Intensive Care Unit at Oishei Children's Hospital, additional treatments and a long road to recovery followed. But the treatment team quickly saw reason to be hopeful.

"One Friday night, I just couldn't sleep. So I quickly

logged into the computer and looked up her labs, and she had turned the corner," Dr. Kelly says. "You could see that the leukemia cells were dying, that they were being killed off by the CAR T cells. And by the end of the weekend, she was so much better. She had clearly responded to the therapy."



**Roswell Park is home to one of  
the largest phase I clinical trials  
programs in New York State.**

The treatment team determined that Chasity should have another very intensive therapy, stem cell transplant, also known as blood and marrow transplant, or BMT, to decrease the chances that her leukemia would return.

### **A Bright Future for a Miracle Baby**

Now almost 2, walking, talking, and showing no evidence at all of the leukemia that once wracked her body, Chasity has two birthdays to celebrate: October 4, the anniversary of her birth, and July 24, the day she got a new immune system thanks to a half-match transplant of donor cells from her oldest sister, Vataeya.

"We knew our baby was in great hands with the nurses, the doctors, the counselors, all the support staff, the donors," says Shawanda. "We felt very lucky to have this program a half-hour's drive away. They gave us our baby back."

"I look at her as our little miracle," says Dr. Higman. "We had a baby who had high-risk disease, whose leukemia relapsed twice, whose ethnicity is itself a risk factor. By all of us working together, this family walked through this process and are on the other end with a beautiful, healthy child and are doing well. And I think that's one of the best gifts we can give anybody."