Progress Update from Dr. Slotkin
January 2026

We are making real progress — both in the laboratory and in the clinic — in understanding and treating desmoplastic small round cell tumors (DSRCT). It is my pleasure to share updates with you here.

Growing Patient Volume

In 2025, we witnessed a doubling of the volume of patients with DSRCT who come to MSK Kids for care. Our team typically treats about 10 to 15 new patients annually, and as of October, that number has already risen to 30 in 2025. This increase allows us to not only help more patients and their families, but also presents an opportunity for our team to learn more about the disease than ever before — insights that will benefit even more patients and their families in the future.

Expanding Our Team

We have expanded our DSRCT program by hiring a technician who oversees the collection of DSRCT tissue samples from the operating room and prepares them for analysis. This role is also critical to building and maintaining our DSRCT registry.

Additionally, our team now includes a dedicated nurse practitioner who coordinates all aspects of DSRCT patient care, ensuring families experience a more seamless and streamlined treatment journey.

Advancing New Treatments

Our researchers continue to conduct clinical trials evaluating new treatments for DSRCT. My hope is to have two new drugs approved for this disease within the next five years.

- **Prexasertib plus irinotecan.** In a phase 1-2 clinical trial assessing this drug combination in patients with DSRCT that came back or kept growing despite prior treatment, we found that about one in three patients responded to prexasertib plus irinotecan. To our knowledge, this is the first time a targeted therapy was incorporated into DSRCT treatment to achieve this magnitude of response. Prexasertib alone was also very active against tumors in the lab of Dr. Andrew Kung. This study was published in *JCO Oncology Advances* in April 2025. The prexasertib research program is now being overseen by a small pharmaceutical company, which assured me the drug would eventually get approved once they are more established.

- **Fam-trastuzumab deruxtecan (Enhertu®).** This drug has improved the treatment of advanced breast cancer and other tumors that make too much of a protein called HER2, such as stomach cancer and some types of lung cancer. It even has some activity against tumors that make low levels of HER2, such as DSRCT. Since this drug is already FDA approved, we were able to assess it in 16 patients with persistent DSRCT without conducting a clinical trial. All patients

experienced either tumor shrinkage or a halting of tumor growth, with minimal side effects. We presented this data at the American Society of Clinical Oncology 2025 Annual Meeting, the largest gathering of cancer professionals in the world. These results suggest that fam-trastuzumab deruxtecan is active in DSRCT and support a formal clinical trial, which we are planning with the Children's Oncology Group.

- **Lurbinectedin (Zepzelca®).** MSK researchers were the first to identify a unique genetic defect used to diagnosis DSRCT: *EWS-WT1*, which is the abnormal fusion of two genes. Lurbinectedin is a targeted therapy that inhibits the EWS-WT1 protein and is used to treat small cell lung cancer. I am now co-directing a phase 1 clinical trial of lurbinectedin in children with solid tumors, including Ewing sarcoma. We want to see how we can minimize these side effects by altering the dosing quantity and schedule for lurbinectedin.

- **TORL-1-23.** I am also leading a phase 1 clinical trial to find the best dose of TORL-1-23 in patients with advanced solid tumors, including DSRCT. TORL-1-23 is made of two parts. One part binds to a protein on cancer cells called Claudin 6, which plays a role in cancer cell growth and can be found in high levels in DSRCT tissue. The other part is an anti-cancer drug that enters and kills the cells, with less risk of harming normal cells. We are excited to see how patients respond to this new drug.

- **Treating liver tumors.** One of the biggest challenges is DSRCT that has spread to the liver. We are exploring the use of hepatic arterial infusion — giving chemotherapy through a pump — for patients with DSRCT that has spread to that organ. The advantage of this approach is that it delivers anti-cancer drugs directly into the liver, sparing the rest of the body from the traditional side effects of chemotherapy.

At MSK Kids, our team cares for patients with some of the rarest and most challenging pediatric cancers in the world. Thanks to the commitment of generous supporters like The Brett Tashman Foundation, we can conduct research that gives hope to young patients and their families.

The strides we are making against DSRCT are possible because of the commitment and dedication of families like yours turning profound loss into meaningful action.