WHAT IS CANCER IMMUNOTHERAPY?

Cancer immunotherapy is one of the most important medical advances of our time, and the first approach with the potential to generate long-lasting regressions for all types and stages of cancer. It harnesses the body's own powerful immune system and mobilizes its highly refined disease-fighting arsenal to eliminate cancer cells. The immune system produces specialized disease-fighting cells that circulate throughout the body, continually seeking out and destroying "foreign" agents. The similarity between cancer cells and healthy tissues blindfolds the immune system, which allows cancer to elude detection. Cancer immunotherapies overwhelm cancer's evasive strategies, to ensure that a powerful, precise and adaptable immune attack is focused on tumors anywhere in the body.

It has many advantages over previous types of cancer treatments:

- **Precise:** Immunotherapy has the potential to kill cancer cells without harming healthy tissue.
- **Systemic:** The immune system can home in on cancer and attack tumors anywhere in the body.
- **Dynamic:** As tumors evolve, the immune system adapts in tandem, sustaining protection from cancer.
- **Powerful:** The immune system can successfully eliminate even large and advanced tumors.
- **Durable:** Immune cells "remember" cancer cells to keep them from coming back.
- **Universal:** Immune system-based treatments have the potential to be effective for virtually all forms of cancer.
- **Synergistic:** Immunotherapy can enhance and complement the effectiveness of conventional cancer therapies.
- **Curative:** Patients treated with immunotherapies have achieved complete, long-lasting remissions of cancers that until recently were considered untreatable.

WHY NOW?

We are at an inflection point. The cancer immunotherapy field has made tremendous progress in just a few short years, much of it spearheaded by Parker Institute scientists. We now have a better ability to study cancer and its response to treatment at the molecular level, to genetically engineer cells as therapies, and have a greater understanding of the role of the immune system. In the 1990s, Parker Institute scientists Jim Allison, PhD, and Jeff Bluestone, PhD, independently discovered that, to prevent autoimmunity and overreactions, a molecule called CTLA-4 acts as a "brake" or checkpoint, on the immune response. This insight led to the development of drugs called "checkpoint inhibitors." First-generation checkpoint inhibitor drugs have achieved unprecedented responses in melanoma, lung and kidney cancers, and are being developed for virtually every other type of tumor.

In separate studies, the development of cancer-targeting T-cell therapies (termed CAR-Ts), pioneered by Carl June, MD, and others, has led to impressive results in several blood cancers in children and adults.

These breakthroughs have resulted in industry recognition and recent FDA approvals, further accelerating the field's progress. There is now a widespread consensus that the immune system is a promising mechanism to treat cancer. Immunotherapy was Science magazine's 2013 "Breakthrough of the Year," and the American Society of Clinical Oncology (ASCO) followed in 2016, naming cancer immunotherapy its advance of the year.

With recent scientific discoveries and the Parker Institute's pioneering organizational model, we expect to dramatically accelerate research breakthroughs and hasten the delivery of better treatments to patients.

WHAT WILL THE PARKER INSTITUTE'S RESEARCH FOCUS ON?

The Parker Institute's research efforts will span the entire field of cancer immunology, but the team will initially make big bets on three major cross-cutting collaborative research projects:

- **Best-in-class T-cells:** In cell-based therapies known as CAR-T (Chimeric Antigen Receptor T-cell) or TCR (T-cell Receptor) therapy, the immune system's main anti-cancer warriors, T-cells, are harvested from a patient's blood and genetically engineered to target proteins or peptides that are abundant in the patient's tumor. Billions of these modified cells are returned to the patient's bloodstream, where the cells seek out and attack tumors. Parker Institute scientist Carl June, MD, pioneered CAR-T therapy for acute lymphoid leukemia (ALL), which has been enormously successful: over 90 percent of ALL patients receiving CAR-T therapy achieved complete remission. The Parker Institute will develop laboratory and clinical studies that aim to identify the pathways and factors that modulate T-cell activity and survival, and develop a new generation of more effective T-cell therapies.

- **Checkpoint Blockade Non-Responder Biomarkers & Therapeutics:** "Checkpoint inhibitor" drugs "release the breaks" that the immune system has in place to prevent overreactions, so the immune system can attack cancers. First-generation drugs that target CTLA-4 and another checkpoint molecule called PD-1 have achieved unprecedented responses in melanoma, lung, and kidney cancers, and are being developed for virtually every other type of tumor. The Parker Institute team will research novel pathways and synergistic combination treatments to improve patient response rates and expand the treatment to more types of cancer.

- **Tumor Antigen Discovery:** Immune-boosting drugs include vaccines, therapeutic viruses, and substances designed to stimulate the immune system to recognize and more potently attack a patient's tumors. The Parker Institute team will use advanced DNA sequencing, antigenic peptide discovery efforts and immune monitoring

technologies to identify self and mutated proteins as novel antigens for tumor targeting, and then develop vaccines and CAR/TCR therapies against these targets. This could improve the effectiveness and broaden the applicability of vaccines and cellular therapies to many additional types of cancer.

FAST FACTS

- Each year, 14 million people are diagnosed with cancer and 8.2 million people die of cancer-related causes.
- There are well over 1,500 cancer immunotherapy drugs currently in the research and development pipeline, the second largest area of all drug development.

HOW DOES IMMUNOTHERAPY WORK?