



# FULL SPEED AHEAD

*New Cell Therapy Facility is the Latest in a Line of Promising Biomedical Manufacturing Projects*

It's no easy feat to manufacture potentially lifesaving treatments. Doing so requires a team with the expertise and dedication to surmount the many obstacles that stand between design and distribution.

At the Frederick National Laboratory for Cancer Research, the Biopharmaceutical Development Program (BDP) has risen to that challenge. In less than 12 months, it established a new capability to produce a personalized cell therapy for children with acute myeloid leukemia, a particularly aggressive blood cancer.

## **In Record Time**

Although that might seem like an eternity for cancer patients and their families, the facility's launch was impressive, given the scientific and regulatory complexity of the process.

"You can't just come in off the street and do this [cell therapy]," said Trevor Broadt, BDP quality control manager, adding that it can take a year alone for staff to be trained and cleared to do the work.

The BDP uses an engineered virus to infect certain white blood cells taken from a patient—called T cells—to make them cancer killers. The virus causes the T cells to develop a special protein, a "chimeric antigen receptor," on their surface, which enables them to bind to a certain protein on the patient's leukemia cells. These weaponized CAR T cells are then infused back into the patient, where they embark on a "search-and-destroy mission" to find, attach to, and kill the cancer cells.

Production must go flawlessly, or the batch of cells will be ruined. It also must be done in a laboratory that complies

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with the FDA's current Good Manufacturing Practice regulations, which delineate laboratory specifications and ensure consistent processes that support reproducibility and minimize chances for error. The BDP was already following these standards but had to quickly set up new equipment and methods to accommodate the personalized cell manufacturing.

The Division of Cancer Treatment and Diagnosis and intramural laboratories at the National Cancer Institute, along with collaborators at the Center for Cellular Engineering at the National Institutes of Health, supported and helped with the accelerated setup.

"It is very exciting that we went from having no direct experience with personalized cell therapies to clinical manufacturing in less than two years. That would be considered extremely rapid for our industry," said Broadt.



**Trevor Broadt, M.S.**

Trevor Broadt leads the quality control team at the Biopharmaceutical Development Program at the Frederick National Laboratory.

## Building on a Legacy

Though it's new to cell therapy, the BDP is no stranger to developing innovative biological agents for NCI preclinical and clinical trials.

A modified poliovirus to treat brain cancer was an idea in a laboratory until NCI asked the BDP to take on the project more than 10 years ago. Duke University researchers sought to move "PVSRIPO"—a combination of the Sabin type 1 polio vaccine strain and a rhinovirus—into early clinical trials for glioblastoma. The BDP developed manufacturing processes and product testing assays so the virus could be reliably reproduced for the trial.

The trial's results appeared in the *New England Journal of Medicine* in 2018. Roughly 21 percent of patients with recurrent stage 4 glioblastoma treated with PVSRIPO survived for at least three years after the treatment, compared to 4 percent of a historical cohort.

Other treatments have been transferred to industry and are now being given to patients.

The FDA approved the immunotherapy Unituxin (dinutuximab) in 2015 for high-risk pediatric neuroblastoma. Lumoxiti (moxetumomab pasudotox) was approved in 2018 for patients with refractory hairy cell leukemia. Both were championed by NCI and began their clinical development in the BDP.

None of the BDP's projects came with an instruction manual. Through collaboration and craft, the BDP determined whether the goal was possible, worked out how to make it a reality, and developed the technology to do it.

It's never easy, but as the BDP's record shows, sometimes it's exactly what's needed to make emerging therapies possible for patients.

## Collaborate with the Frederick National Laboratory

The Frederick National Laboratory for Cancer Research is a shared national resource whose mission is to enable solutions to biomedical research questions and overcome challenges to progress. We actively establish partnerships among our scientists and external researchers in government, academia, industry and the nonprofit research community.

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