TRI-INSTITUTIONAL
THERAPEUTICS DISCOVERY INSTITUTE

LakePharma
The Biologics Company

"When we have partnerships with CROs, we are the most successful if we put the collective brain power together in order to find a solution. With LakePharma, we really feel like we are interacting with scientists who are invested in our projects, and we trust their approaches and listen to their suggestions. We have a very high success rate for biologics discovery projects with LakePharma – and we did not give them easy targets; that's for sure."

-Ivo Lorenz, Ph.D., Vice President of Biologics, Tri-Institutional Therapeutics Discovery Institute, New York, NY

Climbing the mountain to reach drug discovery

Academic research is rich with innovative ideas to treat diseases. However, reaching the bedside with a life-improving drug requires a mountain of resources and investigational tools. On the other hand, there is the private sector of drug discovery that is alertly searching for its own next big target. How do we breach the barriers between target discovery and drug discovery?

Bridging partners to invent therapies

The unique and fascinating model of the Tri-Institutional Therapeutic Discovery Institute (TDI; http://tritdi.org) in New York, NY provides industry-scale infrastructure, resources, and support for three world-class academic institutions: Memorial Sloan Kettering Cancer Center, The Rockefeller University, and Weill Cornell Medicine. This all-star alliance seamlessly catalyzes the transformation of academic discoveries into entrepreneurial ventures and drug discovery.

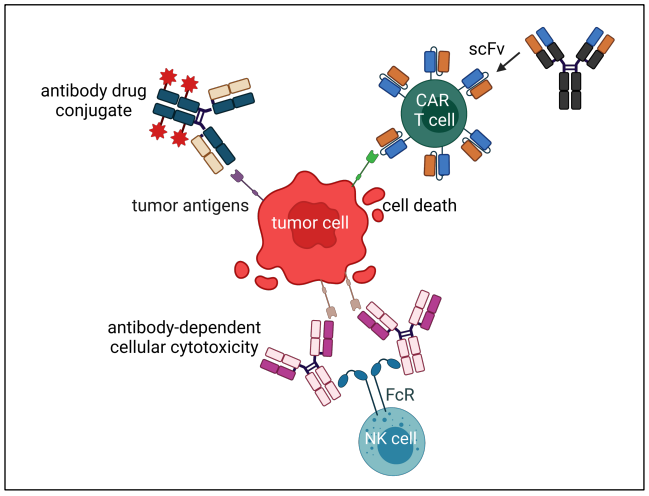
TDI Biologics focuses on antibody- and protein-based therapies against targets discovered by their academic researchers to bring novel molecules from the bench to the bedside. In addition to antagonist or agonist antibodies modulating cellular functions, cutting-edge projects at TDI utilize antibody-drug conjugates (ADC), antibody-dependent cellular cytotoxicity (ADCC), and chimeric antigen receptor (CAR) T cells. These approaches are effective in treating many cancers.

To expand their capacity to develop the best therapies for diseases with unmet medical need, TDI was looking for a strong CRO partner with expertise in antibody discovery. For several years, TDI has been collaborating extensively with LakePharma's Antibody Center (https://hybridoma.com; https://lakepharma.com) in San Carlos, CA to discover novel monoclonal antibodies (mAbs) with key antigen-binding features needed for effective therapeutic approaches for cancer and other indications.

"LakePharma has a very enthusiastic team. One of my favorite things is that they are flexible with their approaches, are always keen to take on new things, and adapt as the project changes. With LakePharma, there are discussions and adjustments to the approach accordingly. That is important when you are trying to get an immune response going. I respect the science going on there." *-David Andrew, Ph.D.*, Director of Biologics Lead Identification
Tri-Institutional Therapeutics Discovery Institute, New York, NY

Cancer immunotherapy modalities need special and diverse antibodies

Cancer immunotherapies offer a more targeted approach compared to systemic chemo- and radiation therapies, and require mAbs to specifically confer cytotoxicity to tumors. ADCs comprise a tumor antigen-specific mAb conjugated to a cytotoxic drug or radioactive label. Effective ADCs require receptor internalization for killing. ADCC leverages natural killer (NK) cell recognition of Fc-receptors (FcR) and their cytotoxic effector mechanisms. CARs are synthetic chimeric proteins introduced into a patient's T cells where they commandeer antigenic specificity and redirect and activate T cells to kill tumor cells. To selectively target the tumor, CARs contain a single-chain variable fragment (scFv) ectodomain derived from a tumor antigen-binding mAb. In contrast to ADCs, CAR designers may wish to select scFvs that do not trigger receptor internalization. Further, scFvs based on human variable domain sequences are less



antigenic than mouse-derived antibodies, and thus resistant to efficacy-dampening anti-CAR responses *in vivo*. Thus, to maximize success and mitigate risk in CAR T development, a diverse selection of humanized target-binding mAbs are desired.

> *"We worked on very diverse mechanisms with LakePharma. Because of LakePharma's broad immunization approaches, we were able to find what we needed for multiple applications. In one example, some antibodies were utilized for CARs, some antibodies were used for radioimmunotherapy, and another set of antibodies was used for ADC approaches. All three modalities were covered with a single discovery campaign run with LakePharma with different antibodies against the same target!"*
>
> *-David Andrew, Ph.D.,* Director of Biologics Lead Identification
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> *-Ivo Lorenz, Ph.D.*, Vice President of Biologics

The art of antibody discovery

TDI's strategic and hopeful biologics portfolio needed diverse panels of mAbs, and LakePharma was just the right partner to deliver both humanized and fully human antibodies! Significantly, in a series of over 10 successful campaigns in three years, the Antibody Center team at LakePharma leveraged their vast experience and expertise to hand select the appropriate animal strains, and to implement their advanced proprietary approaches for immunizations of DNA, protein, and cellular immunogens, generating and screening thousands of hybridomas. In addition, antibodies from various TDI programs were successfully humanized by LakePharma. The outcome: the discovery and optimization of potent, target-specific, fully human or humanized mAbs using proven screening methods, custom antibody characterization assays, and state-of-the-art binding studies.

> *"The project management at Lake Pharma is excellent; I always feel like I know where the project is through their online client portal."*
>
> *-David Andrew, Ph.D.*
> Director of Biologics Lead Identification

> *"We successfully humanized a half dozen antibodies with LakePharma, and we have had a 100% success rate with an efficient approach and fast timeline. "*
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> *- Ivo Lorenz, Ph.D.*
> Vice President of Biologics

Pipeline excitement builds

The partnership between TDI and LakePharma's Antibody Center teams led to an abundance of novel mAb discoveries that are now in the pipeline for preclinical and clinical studies, awaiting their turn to show their potential in humans in the coming years.

> *"We have worked with LakePharma on several hybridoma, phage display, and antibody engineering campaigns, including ADC, ADCC, and CAR T programs. These have gone forward to successful applications in vitro and in vivo, and in some cases further to clinical partnerships for TDI and the academic institutions with Fortune 100 pharma or biotech companies."*
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> *-Ivo Lorenz, Ph.D.*, Vice President of Biologics
> Tri-Institutional Therapeutics Discovery Institute, New York, NY

To see an example of the spirit of collaborative scientists from the Tri-Institutional Therapeutics Discovery Institute and LakePharma making great things happen for CAR T development, click on this link:

Poster presentation at Antibody Engineering and Therapeutics conference 2019

To learn more about hybridoma technologies, please visit:

HYBRIDOMA.COM
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