

TRION Pharma Exposing Cancer to the Power of Immune Response



TRION Pharma is a privately held biopharmaceutical company that has established a novel approach to cancer immunotherapy. The company's unique family of trifunctional antibodies, called Triomab[®], simultaneously activates multiple immune defense mechanisms against cancer. As a result, tumor cells are specifically destroyed with hitherto unknown potency and precision. Moreover, the patient's immune system seems to emerge from Triomab[®] treatment with improved, long-term cancer immunity – an effect that can otherwise only be achieved through vaccination. In 2009, Removab[®] (catumaxumab), the most advanced candidate of the Triomab[®] family, received EU market approval for the intraperitoneal treatment of malignant ascites. Removab[®] is not only the first drug indicated for the treatment of malignant ascites, but also the first approved bispecific, trifunctional antibody worldwide. It is marketed by TRION's partner Fresenius Biotech.

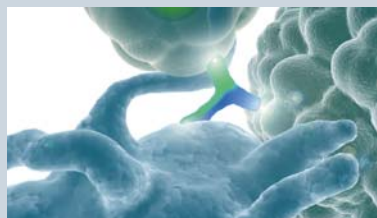
From Genuine Science to Professional Development

TRION Pharma is the first German biotech company that has advanced a novel therapeutic antibody from the bench to the bedside. Triomab[®] development dates back to the 1990s with the pioneering work of **TRION** founder Horst Lindhofer and his team at the Helmholtz Zentrum Munich, Germany. In 1998, Lindhofer decided to set up two sister companies – **TRION Research** and **TRION Pharma** – in order to develop his novel approach to its full potential and make therapeutics available to cancer patients. While the smaller entity, **TRION Research**, focuses on the generation of novel Triomab[®] candidates and clinical analytics, **TRION Pharma** manages process development, in-house GMP manufacturing and is actively involved in clinical development. Intellectual property rights surrounding Triomab[®] were exclusively licensed from the Helmholtz Zentrum Munich at the time of **TRION's** foundation, and have since been continuously expanded by the company to include, for example, design and production, individual candidates and corresponding analytics. Today, an extensive portfolio of worldwide IP rights secures the company's unique and independent position in the world of monoclonal antibodies.

Strategic Alliance with Fresenius

Early on, **TRION Pharma** entered into a collaboration with Fresenius Biotech for the development of three Triomab[®] candidates. Within the alliance, Fresenius Biotech is responsible for clinical development, marketing and sales. **TRION Pharma** is in charge of process development and manufacturing and is actively involved in all development stages up to market approval. **TRION** will receive royalties upon commercialization. This strategy has enabled the company to pursue a continuous path of growth, largely independent of capital market conditions. **TRION** has further Triomab[®] candidates in early stages of development, for which the company holds full commercial rights. These provide additional prospects for growth.

Today, **TRION Pharma** employs a staff of about 130. **TRION Research** currently has a team of eleven employees.



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Triomab® Platform

Three specificities in one molecule

Trifunctional antibodies (Triomab®) combine the halves of two distinct full-size antibodies, a tumor-specific mouse antibody and a T cell specific rat antibody, in one molecule. The resulting molecule can simultaneously bind to a tumor cell, a T cell and, via its unique Fc-region, to an accessory cell of the innate immune system.



Enabling the immune system to fight cancer

The tri-cell complexes mediated by Triomab® antibodies trigger several major immune defense cascades at the same time, including: i) the activation of cytotoxic T cells, ii) the activation of accessory cells such as monocytes, macrophages and natural killer cells, and iii) the induction of long lasting immunity mediated by antigen-processing and antigen-presenting cells.

Orchestrated immune response

Taken together, these combined mechanisms achieve what no other drug has so far been capable of: tumor cells are precisely recognised and presented to the immune system for destruction, despite the many immune evasion mechanisms seen in tumors.

Pipeline generation

Due to their unique mode of action, Triomab® antibodies add a new quality to currently available treatments – even if directed against well-established therapeutic targets. The building blocks of Triomab® antibodies are easily adapted to various indications. A number of candidates are currently in pre-clinical or clinical development in different cancer indications.

GMP manufacturing

The specific design of Triomab® antibodies ensures correct matching of corresponding halves during production. TRION has established a highly efficient, robust and fully scalable manufacturing pro-

cess to provide GMP material for clinical trials and world market supply. A further in-house GMP facility has recently been opened.

Rapid transition to clinic and markets

TRION's expertise in process development and manufacturing enables the advancement of new Triomab® candidates swiftly from preclinical stage to the clinic. Clinical development focuses initially on advanced stages in niche indications, such as malignant ascites, in order to speed up time to market.

Broad potential

In a second development phase, broader indications are addressed, exploiting the full therapeutic and commercial potential of the compounds. Some of the most advanced Triomab® candidates target antigens such as HER2 or EpCAM, which are frequently overexpressed in the most common forms of cancer. These trifunctional antibodies may therefore be applicable to a broad range of cancer indications, in early as well as late stages of disease.

Triomab®	Pre-clinical	Phase I	Phase II	Phase III	Market
Removab® (catumaxomab)					Malignant Ascites EU
					Malignant Ascites US
					Ovarian Cancer EU/US
					Gastric Cancer EU
Rexomun® (ertumaxomab)					Metastatic Breast Cancer EU/US
Lymphomun™					B-Cell Lymphoma
Ektomun™					Melanoma

■ partnered with Fresenius ■ partnered with TRION Research

