

SAN DIEGO BUSINESS JOURNAL

Drug Combination Targets Brain Cancer

BIOTECH: UC Hospitals Host Tocagen Clinical Trials

■ By JULIE GALLANT

An investigational treatment for recurrent brain cancer developed by San Diego-based **Tocagen Inc.** is being studied in trials under way at UC San Diego Moores Cancer Center.

Six patients have enrolled since November in the study at the Moores Cancer Center, which is among a handful of leading sites working with the investigational treatment along with UCLA, UC San Francisco, The Cleveland Clinic and Henry Ford Hospital.

The trial is investigating the use of Toca 511, a virus that is injected into a brain tumor where it is designed to replicate for four weeks before the patient takes Toca FC (which contains flucytosine) extended-release tablets that act as a precursor to a powerful chemotherapy drug.

Toca 511 is a retroviral replicating vector that is designed to deliver a fungal gene cytosine deaminase, or CD, selectively to cancer cells. After allowing time for the administered Toca 511 to spread through the cancerous tumor those cancer cells expressing the CD gene can convert flucytosine into the anti-cancer drug 5-fluorouracil, while normal cells cannot activate the flucytosine. In this study, patients receive cycles of oral Toca FC monthly for up to six months.

"We take a virus and inject it in the tumor and this virus propagates and spreads throughout the tumor," said Dr. **Santosh Kesari**, Ph.D., director of neuro-oncology at Moores Cancer Center.

Kesari said the follow-up with the Toca FC tablets improves the chance of delivering chemotherapy to the cancerous tumors while reducing the chance of affecting bone marrow and other organs.

Patients in Need

Kesari said the trials are geared toward patients who have a grade three or grade four glioma, the most aggressive forms of brain tumors with poor survival rates. The

TOCAGEN INC.

CEO: Dr. Harry E. Gruber.

Revenue: Pre-revenue.

No. of local employees: 38.

Investors: Privately funded.

Headquarters: San Diego.

Year founded: 2007.

Company description: Tocagen Inc. is a clinical stage biopharmaceutical company pursuing the discovery, development and commercialization of gene transfer products for the treatment of cancer.

Key factors for success: The company is initially focusing on treatments for patients with advanced cancer for whom no adequate treatments currently exist. Toca 511 and Toca FC, the company's lead investigational combination product, is being evaluated in clinical trials in patients with recurrent high grade glioma (such as glioblastoma multiforme).

trials are particularly suited to patients who have tumors that recur after standard treatments with radiation and Temodar have been attempted.

The current standard of care for a newly diagnosed, high-grade glioma includes surgically removing as much of the tumor as possible, followed by radiation therapy and chemotherapy with an alkylating agent. Despite these measures, the tumor often recurs, making the Tocagen trial a high priority.

The phase one trials at the Moores Cancer Center are expected to continue through the end of this year, Kesari said.

Tocagen CEO and co-founder Dr. **Harry E. Gruber** said the Toca 511 and Toca FC therapies are based on technology scientists discovered at UC San Diego as far back as 1984. Gruber was involved in the initial collaborations along with Dr. **Theodore Friedmann**, a UCSD professor, and **Douglas J. Jolly**, Ph.D., who is now executive vice president of research and pharmaceutical development and co-founder at Tocagen. Their work led to the formation of San Diego-based gene therapy company Viagene in 1987, which was eventually acquired by **Chiron Corp.** Tocagen was founded in 2007 shortly after

'We believe we are developing a platform for developing a number of anticancer treatments.'

— Dr. Harry E. Gruber
CEO, Tocagen Inc.

licensing the technology from UCLA and the University of Southern California.

Grant Funding

Earlier animal studies have shown Toca 511 and Toca FC to be effective in extending the life expectancy in mouse models of brain cancer from 30 days to as long as the duration of the experiments, which in some cases was seven months, said Gruber, who adds that benefits have been shown in other cancer types in animals.

"We believe we are developing a platform for developing a number of anticancer treatments," Gruber said.

Although Tocagen, a biopharma focused on commercializing treatments for cancer, declined to disclose investment figures, some of the funding to develop the treatments and to run the clinical trials has been provided through grants to the company from the American Brain Tumor Association, the National Brain Tumor Society and Accelerate Brain Cancer Cure.

Gruber said Moores Cancer Center was chosen as one of the research sites because it has an excellent team focused on neuro-oncology, or brain cancer, and experience in clinical trials, particularly in using viruses to treat brain cancer.

"It's important for San Diego to realize there's such a high-quality group of clinicians dedicated to advancing the treatment options for brain cancer patients," Gruber said.