



figure 1

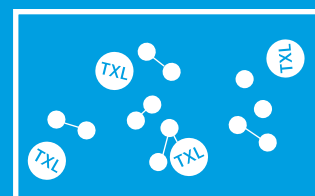


figure 2

XYOTAX is a proprietary biologically enhanced drug conjugate in which the chemotherapy agent paclitaxel is linked to a polyglutamate polymer [figure 1]. The paclitaxel-polymer conjugate allows the drug to circulate through the blood stream with minimal activity, reducing unwanted side effects in healthy tissue. Tumor blood vessels are more porous than normal blood vessels, allowing XYOTAX to pass from vessels into tumor cells, where it is trapped. Once inside the cancer cell, the biodegradable polymer is metabolized, releasing active paclitaxel [figure 2] and leading to cancer-cell death.

XYOTAX™

In 2005, we made substantial progress in advancing XYOTAX (paclitaxel poliglumex) toward the market as a treatment for non-small cell lung cancer (NSCLC). Lung cancer is the leading cause of cancer death for both men and women, and more than 80 percent of lung cancers are diagnosed as NSCLC. Despite intensive efforts to improve lung cancer outcomes, one-year and two-year survival rates for all lung cancer patients are only about 40 percent and 25 percent, respectively. For patients who have a poor performance status, survival rates are even worse.

In the first half of 2005, we presented data from more than 1,700 patients who participated in the STELLAR phase III NSCLC clinical trials. Although the three STELLAR trials did not meet their primary endpoints of superior overall survival compared with the control chemotherapies, they provided important data that will support our efforts to commercialize XYOTAX. In all three studies, XYOTAX demonstrated efficacy similar to standard therapies. There was more convenient dosing and, depending on the dose, a lower rate of severe side effects and a decreased need for supportive care.

In a pooled analysis of the STELLAR 3 and STELLAR 4 trials, there was a statistically significant improvement in survival in women treated with XYOTAX compared with controls. In addition to providing compelling data about the potential utility of XYOTAX in the treatment of NSCLC, this result raised important questions about the impact of gender on cancer therapy. Further analyses of the data have enabled us to begin answering those questions, and highlight the importance of considering biological factors in developing effective treatment strategies.

The female hormone estrogen may enhance the biodistribution and cellular metabolism of XYOTAX. As a result, women with tumors that express the estrogen receptor may receive a higher effective dose of XYOTAX compared with men, resulting in enhanced responses to the drug.

Based on these data, we initiated a confirmatory phase III trial (PIONEER) that will assess survival of chemotherapy-naïve women with NSCLC who have poor performance status (ECOG PS2) when treated with XYOTAX or paclitaxel as a single agent. We are targeting the second half of 2006 for submission of a New Drug Application (NDA) for XYOTAX in the United States for women with NSCLC who are PS2, as well as a Marketing Authorisation Application (MAA) in Europe for men and women with NSCLC who are PS2.

Additionally, we advanced the development of XYOTAX as a potential treatment for ovarian cancer. In March 2005, the Gynecologic Oncology Group (GOG), a premier clinical trials cooperative, initiated a landmark pivotal phase III trial designed to evaluate the impact of monthly maintenance XYOTAX therapy on progression-free survival and overall survival in ovarian cancer patients who have achieved a complete response following standard first-line chemotherapy. The tolerability of XYOTAX may enable maintenance therapy in this indication. Previous evaluation of paclitaxel maintenance therapy required toxicity-related dose reduction. Enrollment in this 1,500-patient study is ongoing and is expected to continue throughout 2006.

“Clinical trials that exploit new data on the biology of lung cancer in women are long overdue. Outcomes will be instrumental in developing tailored therapies, possibly based on gender but even more so on the molecular biology of the disease. The exploratory data from the initial XYOTAX studies are provocative and validate the design of the PIONEER study.”

Kathy Albain, M.D., Professor of Medicine, Hematology/Oncology and Director, Thoracic Oncology and Breast Clinical Research, Loyola University Health System

“The composite analysis of STELLAR 3 and 4 provide strong support for superior efficacy of XYOTAX in women with normal estrogen levels.”

James A. Bianco, M.D., President, Chief Executive Officer, CTI

“It is important to note that XYOTAX has shown improved survival in women, but also has similar efficacy to standard agents in men, with notable safety and convenience advantages over existing therapies in both men and women, particularly when used as a single agent.”

Jack W. Singer, M.D., Chief Medical Officer, CTI

“There is some exciting emerging evidence of the role of estrogen in measuring the risk of and treating lung cancer. We are optimistic that this breakthrough science will translate into **targeted lung cancer treatments for women**, and we can give this patient group the medical attention they need.”

Joan Schiller, M.D., Melanie Heald Professor of Medical Oncology, University of Wisconsin Comprehensive Cancer Center;
President, Women Against Lung Cancer

“XYOTAX is better tolerated than many other cytotoxic agents. It is virtually never associated with alopecia or nausea. These considerations, plus the short infusion time (10 to 20 minutes), make XYOTAX an attractive chemotherapeutic agent.”

Philip D. Bonomi, M.D., Director of Medical Oncology, Rush-Presbyterian-St. Luke's Medical Center

“These data are intriguing and provide a strong scientific **link between estrogen and the effectiveness of XYOTAX**, a biologically enhanced chemotherapy agent, in treating women with lung cancer. These findings open the door to a new avenue of clinical research for gender-specific therapy.”

Mark A. Socinski, M.D., Associate Professor of Medicine, Multidisciplinary Thoracic Oncology Program,
Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill

“As somebody who works as a mental health therapist, I believe this experience has helped me to connect on a very different level with my patients. I understand now what it means to be in pain or to feel despair. Having cancer is a terrifying experience, but I think it has helped me find purpose in my life.”

Cheryl Ferguson, XYOTAX clinical trial patient



Cheryl Ferguson

Both of my parents died of cancer, and I have to admit that I always suspected I would get cancer too. But it was still shocking to hear that I had lung cancer. I had always been athletic. I had a degree in physical education and worked at health clubs for a while. I had never been a big smoker, but I had a bad habit of smoking in place of eating meals, which was apparently the worst decision I ever made.

I was diagnosed with stage IIIA lung cancer on my husband's birthday in 2003. I went through all the stages of grief and loss. I hoped for the best, but I really was expecting the worst. I had radiation and chemotherapy — cisplatin and etoposide. It was a really difficult regimen, and I had to stop working. My hair fell out and I just felt sick all the time, and the infusions took several hours. After this treatment, I had surgery and had no evidence of disease. I was feeling good, getting my strength back, and even went back to work. After about a year, the cancer recurred. I asked my oncologist about experimental protocols and that's how I found out about the XYOTAX trial.

I entered the XYOTAX trial in October 2004, and it was a completely different experience from my first chemotherapy

regimen. The infusions took a lot less time, I kept my hair, and I had the energy to maintain my normal daily routine. In the spring of 2005, I developed neuropathy in my feet, and my doctor recommended that I discontinue the trial. I felt so good that I wanted to stay in, but I took his advice.

Today, I am doing well, and my disease appears to be stable. I developed brain metastases in December 2004, but they responded to radiation. Now I am volunteering as a mental health counselor and maintaining an active lifestyle. In my career, working with people who struggle to cope with life's challenges, I've realized that a positive attitude is incredibly powerful. I used that power to get through those awful months of my initial therapy, to find a clinical trial that could help, and to appreciate everything I've been given.

Having cancer gave me a totally different perspective on life. I'm not afraid anymore. I've renewed my faith, and I love stronger now than I did before I got sick. I made a list of all the things I want to do. I've taken up oil painting, and I'm even thinking about taking tap-dancing lessons. Do you know anybody who can teach a persistent, passionate 46-year-old to tap dance?