1. Read the following three newspaper articles.
2. Identify the key ethical issues that arise in these articles.
3. Identify the individuals or groups who have been or might have been affected by the various actions taken by Tanox, Genentech, and Novartis since 1985 in connection with their efforts to develop certain anti-IgE antibodies such as Xolair(R) (omalizumab) and TNX 901.
4. For each ethical issue you chose to address write a set of moral principles upon which you will make your case. Provide some justification for these principles. What are the factual premises upon which you will base your argument?
5. Based on your analysis, provide a strong ethical argument to support or critique the actions taken by the various individuals or groups discussed in these articles.

This paper should be two–three pages typed and double spaced. Provide clear ethical arguments in favor of the position you support. Base your case on principles we have discussed this semester. Do not make arguments based on prejudice, personal emotions, patently false premises or principles, or the pronouncements of others. The paper is due on 6 December 2006.

Thursday, February 26 2004 - 9:02 AM
Tanox, Genentech and Novartis Settle Disputes Surrounding Xolair(R) And TNX-901

HOUSTON, Feb. 26 /PRNewswire-FirstCall

Tanox, Inc. (Nasdaq: TNOX), Novartis Pharma AG, an affiliate of Novartis AG (NYSE: NVS) and Genentech, Inc. (NYSE: DNA) announced today that they have settled all litigation among them and finalized the detailed terms of their three-party collaboration, begun in 1996, to develop and commercialize certain anti-IgE antibodies including Xolair(R) (omalizumab) and TNX-901.

The following details of the settlement were disclosed: Genentech and Novartis will each reimburse Tanox $3.3 million for a portion of its TNX-901 development costs; Tanox will relinquish any rights to manufacture Xolair and, in exchange, will receive payments tied to the quantity of Xolair produced; and Tanox will benefit from an accelerated forgiveness of a loan to finance the construction of its biologics manufacturing plant in the mid-1990s.

As in the original agreement, Genentech and Novartis share U.S. marketing rights for all collaboration products, while Novartis has marketing rights outside the U.S. The existing royalty and profit-sharing percentages will remain unchanged. Committees with representatives from all three companies have been established to cooperatively
oversee further development and commercialization of Xolair, and possibly other collaboration products.

"We are pleased to end the disputes with respect to Xolair and TNX-901 and look forward to working with Genentech and Novartis to further develop and support anti-IgE therapy for asthma and allergy," said Nancy Chang, CEO of Tanox.

Peanut allergy

The partners are committed to developing Xolair as the lead antibody for peanut allergy. An Investigational New Drug (IND) application for Xolair in this indication was filed with the U.S. Food and Drug Administration (FDA) in November 2003. Patient enrollment in a Phase II proof of concept clinical trial is expected to begin early this year.

About Tanox

Tanox, Inc. is a biopharmaceutical company with demonstrated expertise in monoclonal antibody technology. The Company is engaged in the discovery and development of therapeutic monoclonal antibodies designed to address significant unmet medical needs in the areas of asthma, allergy, inflammation and other diseases affecting the human immune system. In June 2003, the FDA approved Xolair(R) (omalizumab) For Subcutaneous Use for treatment of adults and adolescents (12 years of age and above) with moderate-to-severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids. Xolair, Tanox's first approved drug, is an anti-immunoglobulin E, or anti-IgE, antibody that was developed under a collaboration agreement among Genentech, Inc., Novartis Pharma AG and Tanox. This release and other information about Tanox, Inc. can be found on the World Wide Web at http://www.tanox.com.

This release contains certain "forward-looking statements" relating to the expected timing of patient enrollment in a Phase II proof of concept clinical trial. Those statements reflect the current views of Tanox with respect to future events and are subject to certain risks, uncertainties and assumptions. Many factors could affect the actual timing of trial enrollment, including but not limited to the discussions with the FDA, recruitment of investigators and study site initiation.
Silent Treatment
How Genentech, Novartis Stifled A Promising Drug

Biotech Firm Tried to Pursue Peanut-Allergy Injection, But Contract Got in Way
Zach Avoids a 'Kiss of Death'
By DAVID P. HAMILTON
Staff Reporter of THE WALL STREET JOURNAL
April 5, 2005; Page A1

NEWPORT NEWS, Va. -- For years, the onset of the peanut harvest was enough to send Zach Williams to the hospital.

Every fall, Zach's family would watch peanut dust rise from fields to the south and trigger his allergies, making him labor for air as fluid swelled his tissues and constricted his breathing passages. Some attacks laid him in a hospital bed for weeks, where he wore an oxygen mask as drugs dripped into his veins.

Five years ago Zach, then 15 years old, joined a clinical trial of an experimental drug called TNX-901, produced by Tanox Inc., a Houston biotechnology company. Monthly injections of the drug tamed Zach's runaway immune reactions. For the first time in years, his parents sent him to school without worrying that a peanut exposure might kill him.

More than 1.5 million Americans have an allergy to peanuts, and some can die in minutes if accidentally exposed. Food allergies lead to 30,000 emergency-room visits and more than 150 deaths a year, many the result of peanut exposure, says the Food Allergy and Anaphylaxis Network, a nonprofit organization in Fairfax, Va. If further testing had proven successful, TNX-901 might now be nearing approval as the first preventive treatment for these people.

Instead, the drug sits on the shelf, abandoned after Tanox's own corporate partners forced it to end development. The U.S. biotech giant Genentech Inc. and Swiss drug maker Novartis AG insisted that Tanox kill TNX-901 in favor of a Genentech drug called Xolair that has yet to prove effective against peanut allergy. When Tanox refused, its partners took it to court. The ensuing legal fight to kill TNX-901 spanned five years and consumed well over $100 million in legal fees.

The battle over TNX-901 highlights a common paradox in the drug business. While companies sell many drugs that help both patients and their bottom lines, they can sometimes also advance their commercial interests by stifling potential medical advances. That may mean postponing in-house projects to prevent competition with a drug the company already sells or demanding a halt to allegedly patent-infringing research at a rival.
TNX-901 represents an unusual twist on such cases: Genentech and Novartis, relying on disputed contract language, successfully blocked a third, independent company from moving ahead with a promising drug -- despite the absence of alternative treatments at the time. The long court record provides a window into the vigor with which big companies can fight to stop a potential breakthrough. "It's critical that we get that clinical trial...shut down," a lawyer representing Genentech told a judge in 2000, referring to the TNX-901 trial that Zach later joined.

No one knows whether TNX-901 would have ultimately proven successful. Regulatory approval would have required more rigorous testing. In the trial Zach joined, tests in more than 80 people showed that TNX-901 could bolster their tolerance to the equivalent of nine whole peanuts. Those receiving a placebo could tolerate less than half a peanut.

Novartis declined to make officials available for comment. Genentech officials cast the fight with Tanox as a straightforward contract dispute, and otherwise declined to comment.

Tanox itself, despite its long resistance, ultimately gave up and signed a settlement with Novartis and Genentech in February 2004. The three companies agreed to start testing Xolair as a peanut-allergy treatment. In a joint statement to The Wall Street Journal, the three say their current focus on Xolair is "the most rapid and efficient approach" for helping patients. Xolair, approved in 2003 as an asthma treatment, is now in mid-stage human trials for peanut allergy, and those tests may produce data sometime next year. Formal approval by the Food and Drug Administration for use in peanut allergy could take years more.

Like other food sensitivities, peanut allergy is growing more common in the U.S., particularly among children. A 2003 study found that the incidence of peanut allergy in children doubled between 1997 and 2002 for reasons no one fully understands.

LaDonna Williams knew her son Zach faced a lifetime of allergies almost from the moment he was born red and wheezing in 1985. Tests by Hugh Sampson, an allergy specialist then at Duke University, showed a severe allergy to peanuts. In subsequent years, Zach would keep his distance from outside food to avoid trace amounts of peanut or oil that might cling to utensils or cooking surfaces. When the family ate at a local Italian restaurant, Zach's mother would bring her own spaghetti and meatballs, ask for a plate and wash it in the bathroom before serving Zach's meal on it.

In 2000 Dr. Sampson, who had moved to Mount Sinai Medical Center in New York, called Ms. Williams with news of a potentially life-changing drug. It was TNX-901, and the Williamses jumped at the chance to enroll Zach in a clinical trial.

The odyssey of TNX-901 began with an allergy-prone molecular biologist, Tse-wen Chang, and his wife, Nancy, a fellow scientist. The Taiwanese couple founded Tanox in
1986 and soon embarked on a project to attack allergic inflammation. Their target: an immune-system antibody known as immunoglobulin E, or IgE.

Floating through the bloodstream and across mucous membranes, the Y-shaped IgE molecule sweeps up viral and bacterial particles in its outstretched arms, and then docks its tail to a particular immune-system cell. That alerts the body's defenses, usually triggering sneezing, rashes and watery eyes -- the body's somewhat crude initial attempt to expel invaders.

**Life-Threatening Reaction**

Unfortunately, in some people IgE also grabs innocuous substances such as pollen or peanut protein, making the body respond to a nonexistent threat. In some allergies, such as sensitivity to peanuts or penicillin, such reactions can escalate to life-threatening anaphylactic shock.

Other researchers had long tried to block IgE with experimental drugs but failed because the drugs themselves triggered allergic reactions. Tse-wen Chang thought Tanox could tailor-make a genetically engineered antibody that would latch onto IgE's tail, preventing it from docking and setting off an allergic reaction. Tanox scientists created several such antibodies. One was TNX-901.

Like many young biotech companies, Tanox was chronically short of cash. Nancy Chang, who handled the company's business side, looked for a corporate partner and found interest from Genentech and Ciba-Geigy of Switzerland, which later merged with another Swiss company in 1996 to become Novartis.

In 1989, Dr. Chang sent data and samples of an early anti-IgE antibody to Genentech, but talks with Genentech foundered. Tanox then signed a partnership with Ciba in mid-1990. Worried that the anti-IgE project might stall in Ciba's bureaucracy, Tanox negotiated a provision allowing it to move ahead with any antibody candidate that Ciba rejected.

A few years later, Genentech unveiled its own anti-IgE program, one that Dr. Chang says she considered suspiciously familiar. Tanox filed suit in Harris County district court in December 1993 accusing Genentech of misappropriating its work. The case dragged on into 1996, and Tanox officials began to fear that Genentech was outgunning them in the development race.

Eventually, the three companies reached a deal. Genentech, Ciba (soon to be renamed Novartis) and Tanox would combine their anti-IgE programs. Genentech and Ciba would take the lead in testing, manufacturing and selling any resulting drugs. Tanox, meanwhile, licensed its anti-IgE patents to the partnership in exchange for royalties and other rights. The deal explicitly incorporated the 1990 Ciba-Tanox pact -- but, significantly, it failed to
clarify whether Tanox still had the right to independently develop any anti-IgE drug rejected by the bigger partners.

The two big companies quickly chose Genentech’s anti-IgE antibody -- the future Xolair -- as the partnership's lead candidate. TNX-901 was relegated to backup status.

Tanox executives began to get frustrated when the bigger partners insisted on testing Xolair solely as an asthma and hay-fever treatment, says David Anderson, a former Tanox vice president. Tanox wanted to go after food allergies, too. In mid-1997, Tanox told Genentech and Novartis that it would assert its rights to study TNX-901 in medical conditions the collaboration wasn't addressing.

**Back to Court**

Tanox argued that Genentech and Novartis had effectively rejected TNX-901 -- triggering the old clause that said Tanox could research such drugs on its own. Not so, said the two big companies. They maintained that all anti-IgE drugs identified before the formation of the three-way collaboration belonged to the partnership, whether or not it was actively working on them.

In April 1999, Genentech and Novartis sued Tanox in federal district court and demanded that it stop working on TNX-901. Tanox refused, and soon after started the clinical tests of TNX-901 that involved Dr. Sampson and Zach Williams.

Zach joined the trial in October 2000. Several months later, a test revealed that his tolerance had risen substantially, apparently thanks to TNX-901. Zach's reactions to the dust from peanut harvests ceased. When he accidentally ate some jelly beans made in a factory that also processed peanuts, he didn't feel a thing.

For Ms. Williams, a 15-year burden lifted. She was no longer plagued by the fear that an unsuspecting girl would eat a peanut-butter candy, then grab her attractive son and plant a kiss on his lips. "It would literally be the kiss of death," she says.

Genentech and Novartis were worried about the commercial threat TNX-901 might pose to Xolair, court documents show. At the time, Genentech and Novartis weren't testing Xolair against food allergies, but their officials could foresee the possibility that they might end up competing against their own business partner.

In 2001, Genentech General Counsel Stephen Juelsgaard blasted "Tanox's unilateral decision to compete against the collaboration" and noted concerns that TNX-901 might "compete with the Xolair antibody." In a mid-2000 courtroom status conference, an outside lawyer for Genentech, Dana Haviland, told presiding U.S. district judge Marilyn Patel that Tanox's tests of TNX-901 threatened the "heart" of the collaboration and the coming launch of Xolair. "We really need to not have a competing product in the market from our strategic partner," Ms. Haviland said.
Judge Patel urged a settlement. One day she surveyed the attorneys in her courtroom and declared: "This is why you never had an agreement that you could agree upon. ...There are too many lawyers." Later, she added, "I can't imagine this is really helping, you know, further the cause of medicine and science or anything else."

On Oct. 9, 2001, Judge Patel ruled the partnership agreements allowed Tanox to pursue TNX-901. But Genentech and Novartis quickly asked the judge to suspend the case and let them proceed with arbitration, which Tanox had earlier sought. Judge Patel agreed. A year later, an arbitrator ruled that Tanox had no right to work on TNX-901. Nancy Chang decided to end a multiyear fight that she says had cost Tanox as much as $75 million.

"The biggest lesson was that money is more important than right or wrong," she said in an interview last year.

The joint statement by Genentech, Novartis and Tanox issued to the Journal says Dr. Chang's comments reflected a "general feeling about the legal system" and didn't specifically refer to the dispute with Genentech and Novartis. The statement says Tanox is "fully supportive" of the partnership's decision to pursue Xolair against peanut allergy.

As a bittersweet coda, Dr. Sampson and his team published findings from the TNX-901 trial in the New England Journal of Medicine in March 2003, triggering a wave of publicity and lifting the spirits of allergy sufferers. But the drug was on its last legs. In February 2004, the two sides settled remaining litigation. Tanox agreed to drop TNX-901 and forgo certain rights to Xolair in exchange for a payment of $6.6 million.

At the same time, Genentech and Novartis announced plans to test Xolair against peanut allergy. The drug is similar to TNX-901, so researchers like Dr. Sampson think it will also work well against food allergies. No one will know for certain, however, until results of that 150-person trial are released. Even if successful, the delay in bringing a peanut-allergy treatment to market would be significant since TNX-901 completed its similar trial in 2001.

The three-company statement defends the decision to go with Xolair, noting that it has an extensive safety record because it was tested in more than 6,000 asthma patients. It states that doctors and allergists are gaining experience with the drug and that Xolair can easily be manufactured in large quantities, neither of which was true of TNX-901.

Since Xolair is already approved as an asthma treatment, doctors could in theory prescribe it "off label" for peanut allergy as well. That might be risky, though, because no one knows the proper dose for peanut allergy. People receiving too low a dose might relax their watchfulness and end up in the emergency room. In addition, insurers generally don't cover off-label drug use so most patients would have to pay thousands of dollars a year out of pocket.
Tanox is now pursuing an AIDS treatment and drugs targeting asthma and inflammatory diseases. Nineteen years after its founding, the company is still unprofitable.

Tanox still supplies TNX-901 to former clinical-trial patients such as Zach Williams via the study's original researchers. But patients typically must travel at their own expense to clinics in New York City or Denver, and some have been asked to pay several hundred dollars a month to cover the cost of administering the drug.

Gregory Rogers, a 51-year-old Monument, Colo., carpenter who participated in a TNX-901 trial, stopped taking the drug last summer because he couldn't afford it. Other allergies like hay fever and a serious skin rash, once also suppressed by the drug, have come roaring back. "After having that [drug] for a while, I sure got spoiled," he says.

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Response by Genentech, Novartis and Tanox

Xolair Is the Better Drug for Peanut Allergy Therapy
May 19, 2005

We are writing to express our disappointment and strong exception to your page-one article "Silent Treatment: How Genentech, Novartis Stifled a Promising Drug" (April 5). The article included an incomplete discussion of the scientific facts regarding the development of a potential therapy for peanut allergies. Because science is at the center of our efforts to develop a treatment for peanut allergy, the article’s neglect of some important facts had the potential to be misleading to your readers.

Genentech, Novartis and Tanox together strived to identify the most promising medicine that could be brought to patients with peanut allergies most rapidly. The fundamental question was simply, what was the best way to develop an effective treatment for patients suffering from peanut allergy quickly and safely?

Two similar compounds with an identical mechanism of action -- Xolair, which was on the market, and TNX-901, in early development -- were considered as potential drug candidates to treat peanut allergy reactions. Because Xolair was already on the market and TNX-901 would require many years of development activities, Xolair was chosen as the most promising project.

It is imperative that we conduct the right trials to determine safety and efficacy. Xolair already has a record of safety and efficacy based on trials involving more than 6,000 patients as well as physician prescriptions for more than 40,000 patients. TNX-901 did not have a similar patient database. Secondly, Xolair already had a well-developed, FDA-approved manufacturing process and was on the market for a different indication. Therefore, the best way to move forward as quickly as possible for treating peanut allergies was to focus the trial program on Xolair.

Genentech, Novartis and Tanox have always focused on bringing innovative medicines to patients as quickly as possible, and we have kept this mission at the center of our efforts in developing a treatment for peanut allergies.

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