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Saying No to Penelope

Father Seeks Experimental Cancer Drug, But a Biotech Firm Says Risk Is Too High

By **GEETA ANAND**

NEW YORK -- John London, a successful hedge-fund executive, is desperate to save his 4-year-old daughter, who suffers from a rare cancer. She clings to life at New York University Medical Center here, sucking her thumb and clutching her favorite teddy bear.

For the past month, Mr. London has been begging a small biotechnology firm to allow Penelope to be treated with an experimental cancer drug that might help. Mr. London has received high-powered support: Several legislators, including House Speaker Nancy Pelosi, have lobbied the company and its board to make the drug available. The Food and Drug Administration isn't blocking the way.



London family

Neotropix Inc. of Malvern, Pa., says it would like to help, but the drug may not be safe for a child and dispensing it would be bad business. "For us to provide the drug to this child would be to put at significant risk a small company with limited financial resources," says P. Sherrill Neff, managing partner of Quaker BioVentures, a major investor in the firm, which is trying to tie up a vital round of financing of about \$20 million. "You could delay the opportunity for lots of patients to get this drug if you sidetrack it for one patient," he says.

The deadlock reflects an increasing tension between individual patients and companies using the revolution in understanding biology to develop new medicines. Ideas for treating deadly diseases are proliferating, and the Internet carries hints of promising results into the homes of dying patients. They are pushing for the chance to bypass the laborious approval process and receive quick access to experimental drugs when all else has failed.

In the U.S. Court of Appeals in Washington last month, a lawyer for a patient-advocacy group argued that patients' constitutional rights are violated when they are deprived of medicines in testing that could save their lives. The Abigail Alliance for Better Access to Developmental Drugs wants the FDA to allow patients to buy drugs in testing directly from companies and to allow the companies to profit from the sale. A three-judge appellate panel last year ruled in favor of the alliance. The FDA appealed the case to the full appellate court, which is scheduled to rule later this year.

Lawyers for the FDA argued that broad access to experimental drugs could harm patients and undermine the incentive for them to participate in clinical trials, the studies companies are required to perform in humans to prove safety and efficacy.

"This is a huge dilemma we face as a society -- it's moral and it's ethical," says Patty Delaney, director of the FDA's cancer liaison program. "We have the incredible pain of an individual -- sometimes it's a 4-year-old child, which pulls at everyone's morality -- versus the societal issue of what happens if a small biotech company diverts its resources to a child or ill mother?"

Mr. London, 40 years old, was raised in Manhattan and spent seven years at Highbridge Capital Management, one of the largest hedge funds in the world. He co-founded SuttonBrook Capital in 2002 with \$30 million in capital and built it into a \$2 billion hedge fund. On a blind date in 2001, he met his wife, Catherine, a free-lance writer and editor. They married the next year, and she gave birth to Penelope, their first child, on July 6, 2002.

Growth in the Ribs

Penelope was 16 months old when she was diagnosed with neuroblastoma, a rare cancer that develops from nerve tissue and often appears first in the adrenal glands. By the time her parents noticed a growth under her ribs and took her to Mount Sinai Hospital, the disease already had spread to her lymph nodes, liver and bones.

Four days later, Ms. London delivered the couple's second child, a boy named Oliver.

Doctors told the Londons that Penelope had a particularly aggressive form of neuroblastoma and stood just a 25% chance of being cured. Over the next year, she underwent high-dose chemotherapy, radiation, a bone-marrow transplant and surgery.

A few weeks after the treatment ended, the family went on vacation to the Atlantis Paradise Resort, a hotel with a marine park in the Bahamas. They had just gotten off the plane when they noticed a lump on Penelope's neck. They tried to ignore it and enjoy the vacation, taking turns holding her in the underwater tanks for hours to indulge her fascination with the giant stingrays.



Soon after they returned to Manhattan, they discovered the cancer was back. Radiation shrank the tumors in Penelope's neck and skull, but the cancer broke through again after several months, in what would become a pattern. Each time Penelope's cancer progressed, the Londons tried a new treatment -- moving toward therapies earlier and earlier in human testing. Some treatments put her cancer into remission, others kept it in check for weeks, and some didn't work at all.

Mr. London combed the Internet and connected via Web sites with parents of other children with neuroblastoma. When he heard of promising research, he phoned the physicians or scientists involved, pressing them about whether their work could benefit Penelope.

Several times, the Londons say, their doctors told them they were out of options and advised them to take Penelope home to enjoy the time they had left. "More than John, I was willing not to try anything else because I just wanted Penelope to be comfortable," says Mrs. London. "But John just couldn't do that. And many times, he was right. Penelope would not be alive today if it weren't for him."

"Penelope was still laughing those deep belly laughs of hers, still running around and looking healthy," says Mr. London. "I just couldn't give up on her."

Not wanting to miss time with his daughter, Mr. London stopped going regularly to work at the Manhattan office of SuttonBrook. Running his hedge fund from Penelope's bedside at home, he often stayed up all night devouring medical research papers. One day, sifting through 600 papers that were presented at a conference, he read about an antibiotic used overseas that appeared to help a child with neuroblastoma. Pediatric-cancer specialist Giselle Sholler wrote that the child's cancer went into remission after being treated with the antibiotic plus chemotherapy. Dr. Sholler agreed to treat Penelope.

The combination therapy seemed to work, says Dr. Sholler, an assistant professor at the University of Vermont who had been studying the potential treatment in mice. The walnut-size lump over Penelope's collarbone shrank to less than the size of a pea, Dr. Sholler says. For three months, as Penelope's curly brown hair began to grow

back, she played like any other child, dressing her dolls, making vanilla pudding with her older half-sister, Isabelle, and teasing the family cat, Charlotte.

"She had an incredible ability to bounce back," says Elizabeth Raetz, a pediatric oncologist at NYU Medical Center who has been treating Penelope and advising the family since she was diagnosed.

Through the struggle, Mr. London grew close to the parents of other children with neuroblastoma. "I felt so alone in going beyond what the medical establishment wanted me to do, that the parents of other sick kids were the only ones I could truly relate to," he says. He invested \$100,000 in a fund that is paying for Dr. Sholler to test the antibiotic in combination with chemotherapy in a clinical trial. Dr. Sholler has enrolled eight patients in her trial and most have had their tumors shrink without many side effects, she says, although she cautions that the tests are still at a very early stage.

"John's passion for finding a cure for this disease and his daughter made this trial happen," she says. "And all of these children are seeing a better quality of life."

Cancer Breaks Through

Last November, Penelope's cancer broke through again. After unsuccessfully trying two other experimental drugs, Mr. London was particularly anxious when a parent emailed him in March about Neotropix's therapy.

The experimental medicine is a virus that strikes pigs and appears, in early test-tube and mouse experiments, to attack certain cancer cells in humans. The approach is new and risky, Neotropix Chief Executive Peter Lanciano notes, because it involves injecting a virus into humans that they presumably haven't been exposed to before. The drug is still in its earliest phase of trials for safety. It was tested in just six human beings over the past year. The company hopes to finish the first stage of testing over the next 18 months, giving the virus to another 49 patients, most with small-cell lung cancer.

Mr. Lanciano says that the week he took over as CEO nine months ago, the FDA put Neotropix's trial on hold because the first patient died. Only after four months of testing and analysis was Neotropix able to resume its trial, having demonstrated that the patient died from cancer and not the therapy.

That delay was on Mr. Lanciano's mind when Mr. London and his supporters began calling. The CEO says he wanted to help, but he thinks the drug is too early in testing to be used safely by a child. To give Penelope the dose that was effective in mice, he says he would have to multiply the top dose used in humans so far by 100,000 times. Normally drug companies are careful to raise the experimental dosage in small increments to detect side effects before they become lethal.

"The question is: Can we really help or would we do more harm?" asks Mr. Lanciano.

Mr. London argues this is a risk worth taking. "We're not talking of testing an unproven drug in a child who is perfectly healthy and running around," he says. "My daughter is already in so much pain and is so sick she can't get out of bed. If anything has a prayer of saving her, how can you argue it's not the right thing to do?"

Investors have put about \$14 million into Neotropix, which was founded in 2003 by a former Novartis AG scientist. Last year, Mr. Lanciano, a former executive at several biotech companies, took the helm.

Mr. Lanciano and Neotropix board members have expressed concern that the FDA will force Neotropix to put its trial on hold again if Penelope dies. FDA officials called Neotropix and reassured the company that this isn't the case, Mr. Lanciano says. A colleague of Mr. London who is an internist had approached the FDA and asked it to deliver that message.

Despite the verbal assurances, the CEO says he is still worried. "You never have the ability to wash your hands of any adverse events the patient has," says Mr. Lanciano.

FDA officials, agreeing only to speak generally about the issue, said the agency would not hold a company accountable for the death of a very sick patient receiving therapy as a desperate effort.

"The FDA has good appreciation for the fact that we're dealing with people mortally ill and this is a last-ditch effort," says Richard Klein, director of the agency's HIV program. The notion that the FDA would halt trials over a death in such circumstances is "more of a myth, or urban legend," he says.

Nonetheless, "there aren't any absolutes," says Ms. Delaney, the FDA's cancer liaison. "We can never say: 'We won't pay any attention to safety' " when a patient gets a drug.

The Neotropix board held several meetings on the question of giving the drug to Penelope, Mr. Lanciano says. At one point, the board called an ethicist for an opinion. Urged on by the London family, patient groups and politicians, including the staff of House Speaker Pelosi and Pennsylvania Gov. Edward Rendell, lobbied on behalf of giving the drug to the child.

On April 18, the Neotropix board decided not to provide the drug. Yet calls from politicians and Mr. London's supporters continued, Mr. Lanciano says. Finally, four days later, a Sunday, Mr. Lanciano sent out an email, copying them all.

"Tremendous pressure has been brought to bear on all levels of the company" to try to get it to change its position, he said in the email. "We will not do so."

Mr. Lanciano, 50, says he sympathized, having lost his wife several weeks earlier to cancer at age 51. He tried to get her in clinical trials for pancreatic-cancer treatments, but she didn't qualify, he says.

"If I were that father and mother with a dying 4-year-old, I'd be doing exactly the same thing," says Mr. Neff, the partner at the venture-capital firm that has invested in Neotropix. "There is no right answer," he says. "But in a small company with limited financial resources and a high risk profile, you really have to reduce the risks to drug development."

Mr. London is now trying a new avenue. A day after Neotropix turned down Penelope, a friend Mr. London met on a parents' Web site told him about another company, Jennerex Biotherapeutics, also with a virus in the earliest phase of human testing for cancer. Mr. London reached the company's chief executive, David Kirn, on his cellphone and the two spoke for an hour. Dr. Kirn, a cancer specialist, agreed to provide his experimental drug to Penelope if a hospital would agree to administer it.

"If you are in the position where a loved one is dying of a disease, it is impossible to understand how any company can withhold something potentially beneficial," says Dr. Kirn. He says his company has raised \$10 million so far, mainly from individual investors who leave medical decisions entirely up to him.

William Carroll, director of pediatric oncology at NYU Medical Center, said Saturday he's trying to get permission to treat Penelope with Jennerex's experimental virus at his hospital. He needs approval from several hospital committees that monitor clinical trials and biosafety because the treatment is a live virus. That process would normally take months.

Dr. Kirn is pitching in to make the case. "We're asking hospitals to compress a six-month procedure into a week and that's very difficult," Dr. Kirn says. "You're asking them to bless a plan with less than the full data that is normally available. But you're asking them to do it for a heroic cause -- to try to save a child."

Running Out of Time

Mr. London knows the family may have run out of time.

Wearing pink pajamas in a ninth-floor room at NYU Medical Center last week, Penelope, frail and partly bald, tucked her favorite stuffed bear under her arm as she watched an Animal Planet television show about a sick walrus that was saved. She cried now and again, sending her parents rushing over. A bowl of half-eaten oatmeal sat on the table; Mrs. London asked a friend to make it with extra butter to try to fatten up her daughter. Mr. London's computer was open to the Web site he uses to keep family and supporters updated about Penelope.

The Londons brought Penelope to the medical center Wednesday because her pain medicine wasn't working. They thought she needed stronger drugs to stay comfortable. The plan was to switch her to methadone, a powerful narcotic, and take her home.

On Friday night, after Penelope had struggled for two days with the pain, her eyes lit up when her big sister, Isabelle, appeared in the doorway. The little girl, who hadn't gotten out of bed in days, pulled herself up -- batting away the outstretched arms of her parents -- and wobbled over to sit on the cot beside her sister. Later, when Dr. Raetz, the oncologist, stopped by, she found Penelope, her arm shaking a little, putting the numbers of a block puzzle into the right spaces, not randomly but meticulously, in ascending order. "She's a very determined little girl," Dr. Raetz said.

"We go into this with our eyes open," Mr. London said, talking in another room out of Penelope's earshot. "The chance of anything bringing her back from the abyss now is very low. But the only thing I know for sure is if we don't treat her, she will die."

Mr. London and his wife say they are searching Penelope's big brown eyes for clues as to how long she wants to continue to battle for life.

For now, says Mr. London: "We see she still wants to fight."