



U.S. Court of Appeals decision has stalled a Minnesota teen's quest to get access to experimental drugs for a rare neurological condition. Jacob Gunvalson has Duchenne muscular dystrophy (DMD), a fatal disease that wears down skeletal and cardiac muscle tissue.

A panel of federal judges in Philadelphia has halted a lower court ruling that would have forced PTC Therapeutics, a biopharmaceutical company, to provide PTC124 to the 16-year-old, who is in the mid-stage of his disease.

In August, the Federal District Court in Newark had ordered the New Jersey-based company to provide the information necessary to begin a single-patient study on Jacob. The latest legal development means the court's order is put on hold until PTC Therapeutic's appeal is heard.

The drug is now undergoing clinical trials, but Jacob is not eligible to participate because he can no longer walk. As a result, the Gunvalsons are seeking a "compassionate-use exemption" for access to the drug outside of the trial. They believe PTC124 is their best chance to give Jacob a longer life and maintain that company officials promised them the drug.

Stuart W. Peltz, Ph.D., PTC Therapeutics' president and CEO, denies promising the drug to the Gunvalsons. And he claims a compassionate-use exemption would slow down the trials. "Our greatest concern in clinical development is performing the trial as fast and fairly as possible so that all patients will have equitable access to the drug," says Dr. Peltz.

Compassionate-use exemptions for drugs that lack data on safety or efficacy in the target disease may also put drug trials on shaky ethical grounds, according to Dr. Merit E. Cudkowicz, M.D., associate professor of neurology at Harvard Medical School. Full-scale clinical trials typically include one group that takes the experimental drug and another group that takes a placebo.

"If you do a clinical trial without knowing whether a drug works, then it's ethical to have a placebo group," Dr. Cudkowicz says. But if a drug is known to be effective, it's unethical to deny it to people in a trial. "It's hard to say that it's okay to divide people up into those who get the drug and others who don't, and later allow more to join a compassionate-use group," she explains.

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NEUROBICS Can you figure out the common expression represented by each picture?











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Sharon Hesterlee, Ph.D., vice president of translational research for the Muscular Dystrophy Association, says it's not uncommon for parents of children with terminal diseases to be "very, very anxious" to gain access to experimental drugs. She notes that families who have pushed for new therapies may be disappointed when drug trials are developed and include strict eligibility rules.

"We've long had an issue with the boys with Duchenne," says Dr. Hesterlee. "When they stop walking, they are no longer eligible for clinical trials. The parents and sometimes the boys themselves feel they are forgotten."

The PTC124 trial measures drug efficacy in part on how boys perform in a six-minute walk.

Dr. Hesterlee believes that granting compassionate-use exemptions may not be the best solution to the problem. Instead, she says, researchers need to develop ways to measure improvement in boys with DMD who cannot walk. Dr. Peltz of PTC Therapeutics says the company has met with key opinion leaders to

explore clinical parameters for additional clinical trials for DMD patients who were excluded from the current trial.

The Gunvalsons' lawsuit, however, is not aimed at the company's clinical trial procedures. Rather, the brief filed in the case argues that Jacob should be given an exemption to get the drug because top company officials had promised it to him. The case may rest on whether the Gunvalsons can prove such promises were made, according to Richard Samp, chief counsel at the Washington Legal Foundation, a public interest law firm that advocates for patients' rights in the drug approval process. (Neither Samp nor the Washington Legal Foundation is involved in the Gunvalson lawsuit.)

Even if the U.S. Court of Appeals rules in the Gunvalsons' favor, Jacob may still be unable to take PTC124 immediately. Under federal regulations, the Food and Drug

Administration and an institutional review board would have to approve the request for treatment. But for now, the legal battle is being closely watched by both the pharmaceutical industry and patient advocacy groups. —Lisa Phillips

"When [the boys with Duchennel stop walking, they are no longer eligible for clinical trials."





SCREENING ROOM

Diminished Capacity

(Plum Pictures, 2008; directed by Terry Kinney)

ow much are memories worth? That's the million-dollar question that Diminished Capacity explores by drawing a parallel between baseball nostalgia and memory loss. Chicago newspaper editor Cooper Zerbs (Matthew Broderick), afflicted with short-term memory loss after sustaining a concussion, heads home to Missouri to visit his aging Uncle Rollie (Alan Alda), a baseball memorabilia collector suffering from Alzheimer's disease. Rollie shows Cooper a rare 1909 Chicago Cubs baseball card he wants to selland soon the men are off to Chicago for a memorabilia convention, with Cooper's high school sweetheart, Charlotte (Virginia Madsen), in tow.

In legal parlance, "diminished capacity" refers to a plea by which the defendant argues that he or she should not be held criminally liable for breaking the law because of impaired mental function. If successful, it results in the defendant being convicted of a lesser offense.

While the film's premise is interesting—a middleaged man finds himself in a situation similar to that of his elderly uncle, who is unwilling to acknowledge his inability to take care of himself—the lead character is bland, and Broderick seems miscast in the role. The film is also enervated by implausible plot turns and a lack of chemistry between Broderick and Madsen.

On the plus side, Alda brings a poignancy to his role, especially as he realizes the implications of his forgetfulness; more of the film should have been devoted to his character's struggle with Alzheimer's. Baseball fans will enjoy the inside jokes about the Cubs. But viewers looking for an insightful movie probing the ephemeral nature of memory may be disappointed with this rambunctious comedy-drama.

Verdict? Guilty, by reason of diminished capacity.

—Elizabeth Stump

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