UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

JACOB GUNVALSON, CHERI AND JOHN GUNVALSON, AS GUARDIANS FOR JACOB GUNVALSON, AND CHERI AND JOHN GUNVALSON, INDIVIDUALLY, Plaintiffs, v. PTC THERAPEUTICS, INC., Defendant.	Civil Action No. 08-3559 (WJM) (MF) *DOCUMENT FILED ELECTRONICALLY* Return Date to be set by the Court

BRIEF OF PLAINTIFFS JACOB, JOHN AND CHERI GUNVALSON IN SUPPORT OF THEIR MOTION FOR A PRELIMINARY INJUNCTION

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TABLE OF CONTENTS

PAGE

PAGE

TABLE OF AUTHORITIES

FEDERAL CASES

STATE CASES

FEDERAL STATUTES AND REGULATIONS

STATE STATUTES

PRELIMINARY STATEMENT

Plaintiff Jacob Gunvalson is a sixteen year-old boy with Duchenne Muscular Dystrophy ("DMD"), a rare and deadly condition marked by the steady deterioration of muscle tissue. Over the past year, Jacob, a straight A student, has gone from walking to being confined to a wheelchair and unable to lift a glass of water. Defendant PTC Therapeutics, Inc. ("PTC") manufactures a drug known as PTC124, which has successfully completed a number of clinical trials and has to date been effective in treating Jacob's type of DMD with no serious side effects.

Over the past few years, PTC repeatedly promised the Gunvalsons that Jacob would have access to PTC124, in part due to the efforts of Jacob's mother in obtaining federal grants for PTC. PTC even discouraged the Gunvalsons from participating in two short clinical trials of PTC124, advising them that Jacob would not be precluded from receiving PTC124 in any future trials based on this decision. The Gunvalsons relied upon and trusted PTC. Indeed, the Gunvalsons enjoyed a close relationship with PTC, and even stayed at the home of one of PTC's executives. There was no reason to doubt PTC's representations that Jacob would get access to PTC124. Now, PTC has established a long-term (96 week) clinical trial of PTC124, but has denied Jacob from participating solely because he was not part of the shorter clinical trial.

Even more inconceivable is that PTC has flagrantly and without explanation refused to acknowledge a federal regulation, 21 C.F.R. §312.34, that specifically addresses what are known as "compassionate uses" of new drugs, like PTC124, for seriously ill patients before they are brought to market. This refusal has come with full or imputed knowledge that the Director of the FDA's Neuro-Pharmacological Drug Products Division, Dr. Russell Katz, suggested Jacob seek such relief. Due to ongoing clinical trials of PTC124, PTC knows full well that in the best-case scenario, PTC124 will not be brought to market for at least two more years. Because of PTC's broken promises to the Gunvalsons, its cynical indifference as to whether Jacob lives or dies, and Jacob's deteriorating condition, plaintiffs seek preliminary relief from this Court. Without it, Jacob's condition will continue to worsen and, when he ultimately loses pulmonary function, Jacob will die.

By way of background, DMD is a disease that affects only one of every 7,000 children, and only 15% of those kids, or just one in more than 46,000, have a specific form of DMD and can potentially be helped by PTC124. Jacob is one of this very small group. Children with Jacob's type of DMD have a life expectancy of less than 25 years, and some die well before then. Historically, there has been little hope for individuals with Jacob's type of DMD. Some patients used another drug, Gentamicin, but PTC124 been shown to be substantially more effective than Gentamicin, with much less severe side effects.

Notwithstanding PTC's broken promises to the Gunvalsons, they are not trying to derail PTC124's ongoing clinical trials. Rather, concurrently with these trials, plaintiffs seek access to PTC124 through a "compassionate use" exception, which will enable Jacob to obtain PTC124, and provide PTC with additional data regarding the safety and efficacy of the drug without impacting clinical trial data at all. It is seemingly a win-win situation for all parties.

There are two types of compassionate uses: a "protocol exception" to an existing clinical study or a "single-patient IND." A "protocol exception" allows patients ineligible to participate in a study to be treated with an investigational drug alongside study members under the supervision of clinical researchers. Plaintiffs seek a preliminary injunction in part because a Phase IIa extension is about to commence in Cincinnati, and Jacob has an August 6 appointment to be examined and potentially approved as a "protocol exception" by Dr. Brenda Wong, the study supervisor. The only difference between the Phase IIa patients and Jacob is that Jacob was not part of the shorter clinical trial. Alternatively, a "single-patient IND" permits a physician to conduct an individualized study on just one patient. Dr. John Parkin, Jacob's physician, is prepared to apply to the FDA for approval to undertake a single-patient IND on behalf of Jacob.

These "compassionate uses" are specifically encouraged by the federal government. See 21 C.F.R. §312.34 (stating that the "**purpose of this section is to**

facilitate the availability of promising new drugs to desperately ill patients as early in the drug development process as possible, before general marketing begins, and to obtain additional data on the drug's safety and effectiveness") (emphasis added). Jacob satisfies all the criteria for receiving PTC124 under a compassionate use exception, and the FDA has encouraged Jacob to request such an exception. Jacob appears to be the perfect candidate for PTC124, especially because all clinical trials have been very successful in terms of safety and efficacy.

Accordingly, Jacob and his parents respectfully request that the Court order PTC to permit Jacob to participate as a "protocol exception" in a clinical study about to be undertaken at Cincinnati Children's Hospital. Alternatively, plaintiffs request that PTC be ordered to provide PTC124 to a physician to be used in a single patient IND if authorized by the FDA. As part of the conditions of an injunction, Jacob, John and Cheri Gunvalson will sign a full release concerning liability and any necessary "informed consent" document, pay for PTC124 and its administration, undertake the necessary applications to secure FDA approval for a "compassionate use" exception, and complete any other task necessary to secure Jacob access to PTC124.

Without this Court's intervention, Jacob looks forward to a ventilator and death.

STATEMENT OF FACTS

Jacob Gunvalson. Jacob Gunvalson is 16 years old, resides in Gonvick, Minnesota, and was born on October 5, 1991.[1] (Gunvalson Decl. ¶ 1.) He lives at home with his parents, Cheri and John, and his two siblings. (Id.) Cheri is a registered nurse with a Master's Degree in Adult Health Nursing and John is a farmer. (Id.) At an early age, Jacob began displaying symptoms of Duchenne Muscular Dystrophy. (Id. ¶ 2.) Since being diagnosed with DMD in 1999, Jacob has been treated with, among other medications, Gentamicin. (Id. ¶ 2 & Exh. D.)

Even after he was diagnosed, Jacob enjoyed riding go-karts, reading and playing video games. (Id. Exh. J.) Until this year, he was at the top of his academic class. (Id. ¶ 4.) He was able to walk without assistance until about a year ago. (Id.) Unfortunately, over the past year Jacob's condition has substantially deteriorated. (Id.) Since March 2007, he has been confined to a wheelchair and is losing his upper body strength. (Id.) As of today, Jacob cannot lift a glass of water, feed himself, use a urinal, and needs help even to sit up. (Id.)

Duchenne Muscular Dystrophy and the Nonsense Mutation. DMD is a progressive muscular disorder which is the most prevalent of the muscular dystrophies and the most common lethal genetic disorder diagnosed during childhood. (Id. Exhs. C, M.) One in every 7,000 children is born with DMD. (Id.

[1] A timeline of the most relevant facts for Jacob's claims and treatment is attached to this brief as an Appendix.

Exh. M.) The life expectancy for a child with DMD is under 25 years, with death usually caused by deterioration of the pulmonary system. (Id. ¶ 3.)

Approximately fifteen percent of children with DMD – approximately one of every 46,728 children – have the condition due to the presence of a "nonsense mutation" in the dystrophin gene. (Id. ¶ 5 & Exhs. E-F; Parkin Decl. ¶ 2 & Exh. A.) The nonsense mutation, which occurs in the X chromosome, instructs the ribosome within the dystrophin gene to prematurely stop the production of the protein which provides the connective structure for muscle tissue. (Gunvalson Decl. Exhs. C, G; Parkin Decl. Exh. A.) Because girls have two X chromosomes, and because only one working X chromosome is necessary to produce the protein, it is a disease that is carried by girls but affects boys. (Id.)

Jacob has had gene sequencing studies performed at Ohio State University, and the Eccles Institute of Human Genetics at the University of Utah, which both confirm that Jacob is one of the fifteen percent of DMD patients who have the nonsense mutation in the dystophin gene that stops the production of an amino acid that produces muscle tissue. (Id. ¶ 2 & Exhs. A-B.)

Current Treatment of DMD due to the Nonsense Mutation. There is currently no cure for DMD, nor is there an effective treatment currently in the marketplace. (Id. Exh. C.) There are some experimental treatments, however, that have been tried or are being evaluated. (Id. ¶ 6.) By far, the most promising

treatment is PTC124, a drug that allows the ribosome to direct that the dystrophin be produced to a mature cell. (Id. ¶ 7; Parkin Decl. ¶ 8 & Exh. A.) Another approach is the use of Gentamicin, an intravenously administered antibiotic that, in sufficient doses, is believed to allow the ribosome in the gene to continue to develop the protein for muscular connective tissue. (Gunvalson Decl. Exh. G.) Unfortunately, Gentamicin is less effective than PTC124, and can cause severe side effects, including "renal compromise." (Id. Exh. N.)

Jacob is one of less than ten American children with DMD who has been treated with Gentamicin, and he took the drug for approximately four years. (Id. ¶ 6.) However, according to Dr. Lee Sweeney, a physiology professor at the University of Pennsylvania Medical School who works with PTC and is the "primary investigator" for some of its trials, PTC124 is twelve times as effective as Gentamicin and may actually restore dystrophin to functional levels. (Id. ¶ 7.) Jacob's treatment with Gentamicin was terminated in part because he was told that to participate in a drug trial involving PTC124 he has to be free of Gentamicin for 90 days. (Id. ¶¶ 17, 25, 30 & Exh. N; Parkin Decl. ¶ 7; Hatch Decl. Exh. 8.)

Defendant PTC Therapeutics. PTC was started in 1998. (Id. Exh. 6.) It currently has about 100 employees and has spent over $100 million since it started. (Id.) In its 2006 SEC filing,[2] PTC stated it has not received revenue from any

[2] PTC subsequently withdrew its registration and stock offering.

product sales. (Id.) Initially, much of the company's revenue stream was from the federal government, amounting to over $25 million in grants.[3] (Id.) According to PTC, its most promising drug is PTC124. (Id.) The company has stated:

> We have generated significant losses as we have progressed our lead product candidates into clinical development and expect to continue to generate losses as we continue the clinical development of PTC124 and PTC299. Our net loss for 2005 was $22.9 million. As of December 31, 2005, we had a deficit accumulated during the development stage of $92.1 million.

(Id.) Funding from the government has therefore been very important to the viability of the company. PTC is currently the only company conducting clinical trials on any drug targeted at Jacob's form of DMD. (Gunvalson Decl. ¶ 8.)

Early on, PTC undertook a joint venture with a group known as the Parent Project for Muscular Dystrophy ("PPMD"). (Id. ¶ 8 & Exh. H.) PPMD is a organization of approximately 3,000 parents and relatives of muscular dystrophy children, fifty of whom contributed at least $25,000 for research. (Id.) PPMD collaborates with PTC in a partnership called "Project Catalyst." (Id. ¶ 9 & Exhs. H-I.) According to *Nature Biotechnology*, "Project Catalyst" created several benefits for PTC, including increased access to funding and advocacy power with the FDA. (Id. Exh. H) Indeed, Project Catalyst has raised over $3 million for

[3] After plaintiffs filed the Verified Complaint, PTC announced that it entered into an agreement with Genzyme Corporation to develop and commercialize PTC124. (Halpern Decl. Exh. A.) Under this agreement, Genzyme paid PTC $100 million, with additional milestone payments that could total $337 million. (Id.)

research for PTC, and PPMD parents have played a critical role in securing funding from the National Institutes of Health ("NIH"). (Id.)

Cheri Gunvalson, the "Heat Seeking Missile." In 2001, Cheri joined the Government Relations Board of PPMD. (Id. ¶ 10.) That year, she communicated with every member of Congress and persuaded 235 Congressman and 49 Senators to co-author the Muscular Dystrophy CARE Act, the only disease-specific legislation enacted by the 107th Congress, and was later described in the press as a "heat seeking missile for [Muscular Dystrophy] funds." (Id. ¶ 11 & Exh. J.)

Prior to passage of the Act, Muscular Dystrophy patients, on a per patient basis, received but a small fraction of grants and funds when compared to other diseases with similar morbidity outcomes. (Id. ¶ 12.) The law, sponsored by Minnesota Representative Colin Peterson and the late Senator Paul Wellstone, directed that the NIH increase Muscular Dystrophy research, which doubled the amount appropriated from $14.3 million in 2001 to $28 million in 2003, and doubled it again to $54 million in 2006. (Id. ¶ 12 & Exh. J.) It also required the NIH to establish and fund Centers of Excellence for the treatment of Muscular Dytrophy. (Id. ¶ 13.) After the Act was signed on December 18, 2001, Cheri served on the 2003 NIH review board to designate those Centers of Excellence. (Id.) Over the past five years, Cheri has continued to advocate to Congress, the NIH and the FDA in her effort to find a cure for the disease. (Id. ¶ 14.)

From 2003 through 2006, Cheri also worked on the preparation of annual Committee Reports, issued by the Senate Labor Health and Human Services Appropriations Committee, which give direction to the NIH concerning its funding decisions. (Id.) Cheri worked with Bettilou Taylor, the Committee staff administrator, to draft the annual report, and was extremely focused on making sure DMD received sufficient funding for research, particularly with PTC. (Id.)

In 2005, PTC began its the Phase I clinical trial of PTC124, primarily to determine patient tolerance to the drug. (Id. ¶ 15 & Exh. E.) The Phase I trial used healthy adults only, and as such, Jacob was not enrolled. (Id. ¶ 16.)

At this point, Cheri met with executives of PTC Therapeutics to urge them to file grant applications with the NIH. (Id. ¶ 15.) Dr. Langdon Miller, PTC's Chief Medical Officer, told Cheri that the applications were complicated and bureaucratic. (Id.) Having served on an NIH Peer Review Committee in 2003, Cheri was adamant that PTC was mistaken, that ten percent (10%) of the grant money was supposed to go to private companies, and that very few companies were applying for it. (Id.) Based on Cheri's direction and encouragement, PTC applied for government grants and has since received more than $25 million in federal funding, compared to just a fraction before that. (Hatch Decl. Exhs. 6-7.)

PTC Tells Jacob Not to Participate in the Phase II trial. After the Phase I trial yielded positive results, PTC commenced a Phase II trial on children

afflicted with Jacob's form of DMD in late 2005. (Gunvalson Decl. ¶ 17.) Patients in this trial were to receive a 28-day dosage of PTC124. (Id.) Prior to the trial's commencement, Cheri asked several PTC executives and agents whether Jacob should participate. (Id.) Although Jacob was eligible, both Dr. Richard Finkel, head of pediatric neurology at the Children's Hospital of Pennsylvania and the "primary investigator" for the trial, and Claudia Hirawat, PTC's Senior Vice President, told Cheri **not** to take Jacob off of Gentamicin – Jacob's then-current treatment, which had been providing him some benefit – due to the short duration that a trial participant would receive PTC124 and its unknown efficacy. (Id.)

Upon being asked, ***Hirawat assured Cheri that there would be no adverse effect on Jacob for not participating in the Phase II trial.*** (Id.) In reliance on these statements, the Gunvalsons did not attempt to enter Jacob in the Phase II trial nor to fulfill any prerequisites for it. (Id.)

Jacob's Experimental Treatment Options. In late 2004, PTC124 received "Orphan Drug" designation pursuant to the Orphan Drug Act (Gunvalson Decl. Exh. E), which applies to drugs designed to treat a "rare disease or condition." 21 U.S.C. §360bb(2) (emphasis added). Sponsors of Orphan Drugs, like PTC, are "encouraged" to "design protocols ... to permit the addition to the [clinical] investigations of persons with the disease ... who need the drug to treat the disease ... and who cannot be satisfactorily treated by available alternative drugs." 21

U.S.C. §360dd (emphasis added). Then, on March 30, 2006, PTC Therapeutics announced that the FDA had granted "fast track" status of PTC124's development. (Gunvalson Decl. ¶ 18, Exh. E.) A drug can only be "fast tracked" if it is intended for patients with "serious or life-threatening conditions." 21 U.S.C §356(a)(1). For a drug to receive "fast track" approval, the FDA must determine that the drug "is reasonably likely to predict clinical benefit." 21 U.S.C. §356(b)(1).

Around this time, too, it was clear that Jacob's condition was continuing to deteriorate. (Id. ¶ 19.) Concerned with this, Cheri looked for alternative solutions to help Jacob, one of which is a federal regulation that clearly fits Jacob's needs. (Id. ¶ 19.) Specifically, 21 C.F.R. §312.34(a) provides:

> During the clinical investigation of the drug, it may be appropriate to use the drug in the treatment of patients not in the clinical trials, in accordance with a treatment protocol or treatment IND. **The purpose of this section is to facilitate the availability of promising new drugs to desperately ill patients as early in the drug development process as possible, before general marketing begins, and to obtain additional data on the drug's safety and effectiveness.**

(emphasis added). See also 21 U.S.C. §360bbb(b) (providing one with a "serious disease" a method to obtain access to an investigational drug). Buoyed by this, Cheri went to Dr. John Parkin, Jacob's pediatrician, and asked him if he would apply on behalf of Jacob for a "compassionate use" exception from the FDA pursuant to this authority. (Gunvalson Decl. ¶ 19.) Under the federal regulation, to qualify for a "compassionate use" exception,

(i) The drug must be intended to treat a serious or immediately life-threatening disease;

(ii) There can be no comparable or satisfactory alternative drug or other therapy available to treat that stage of the disease in the intended patient population;

(iii) The drug must be under investigation in a controlled clinical trial under an IND in effect for the trial, or all clinical trials must have been completed; and

(iv) The sponsor of the controlled clinical trial must be actively pursuing marketing approval of the investigational drug with due diligence.

21 C.F.R. §312.34(b)(1). As discussed in detail later, Jacob's request for PTC124 easily meets all four of these criteria. However, the pharmaceutical company must still agree to make the drug available to the patient. (See Gunvalson Decl. Exh. L.)

Based on Cheri's entreaties, in March or April of 2006, Dr. Parkin wrote to Dr. Langdon Miller, PTC's Chief Medical Officer, requesting that the company make PTC124 available to him for a single-patient investigative study. (Id. ¶ 20; Parkin Decl. ¶ 5 & Exh. B.) On April 14, 2006, Dr. Miller responded by stating that Phase II clinical trials were being undertaken with PTC124 but their results would not be known until the end of 2006. (Parkin Decl. ¶ 6 & Exh. C; Gunvalson Decl. ¶ 20.) Wanting to avoid unacceptable risks, ***Dr. Miller said that once patient safety was confirmed with this clinical trial, PTC could then discuss Parkin's proposal.*** (Id.; Parkin Decl. ¶ 6 & Exh. C.)

On April 24, 2006, Cheri also received an email from Dr. Russell Katz, the head of the FDA's Neuro-Pharmacological Drug Products Division, suggesting that Jacob apply for a protocol exception or a single-patient IND (as had already been suggested by Dr. Parkin) in order to receive PTC124 without disturbing any of PTC's clinical trials. (Gunvalson Decl. ¶ 21 & Exh. L.)

The Phase IIa Trial and PTC Theraputics' First Promise to Provide PTC124 to Jacob. On July 13, 2006, the Gunvalsons attended the annual PPMD conference. (Id. ¶ 24.) While there, Jacob had a long conversation with PTC's Chief Medical Officer, Dr. Langdon Miller, and Senior Vice President, Claudia Hirawat. (Id.) The next day, the Gunvalsons had a private conference with Dr. Miller. (Id.) Dr. Miller expressed great appreciation for Cheri's work in Washington, as funding for PTC was critical to success of the company.[4] (Id. ¶ 24 & Exh. H.) During the conversation, Cheri asked Dr. Miller if Jacob would get PTC124. (Id. ¶ 24.) Dr. Miller replied that the boys in the first trial metabolized the drug faster than expected and PTC would need to do another 28-day trial at a higher dose. (Id.) He told her that they did not know the right dosage level yet and PTC needed to get the safety data back. (Id.) ***However, he reassured Cheri that, once positive results were back from the trial, Jacob would get the drug.*** (Id.)

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[4]As PTC has just received $25 million from the Cystic Fibrosis Foundation and $100 million from Genzyme, PTC's need to rely on the Cheri Gunvalsons of the world has diminished.

At this time, Cheri again asked PTC if Jacob should be in the second Phase IIa 28-day trial at the higher dosage. (Id. ¶ 25.) As she had before, Claudia Hirawat told Cheri not to discontinue Jacob's then-current Gentamicin treatment. (Id.) ***Hirawat also repeated that Jacob had no better or worse chance to be treated in the future based upon his non-enrollment in the Phase IIa trial.*** (Id.) The Gunvalsons did not place Jacob in the Phase IIa trial in reliance on PTC's medical advice, instructions and promises. (Id.)

More Promises by PTC Theraputics to Provide PTC124 to Jacob. On September 27, 2006, Cheri was recognized for her work in getting Congress and the NIH to fund DMD research at the National Genetic Alliance's annual gala in Washington, D.C. (Id. ¶ 26.) Claudia Hirawat, PTC's Senior Vice President, attended the Gala with Cheri. (Id.) Ms. Hirawat is in charge of PTC's corporate development and is directly responsible for fundraising and commercial development of the company. (Hatch Decl. Exh. 5.) At the event, Ms. Hirawat expressed great appreciation to Cheri for her work in getting federal funding for research of PTC124. (Gunvalson Decl. ¶ 26.) Cheri explained to Ms. Hirawat that she was frustrated with the delay in Jacob receiving access to PTC124. (Id.) ***In response, Hirawat assured Cheri that Jacob would get access to PTC124.*** (Id.)

The next day Cheri attended a conference in Philadelphia where PTC announced the successful results of its first study of PTC124 to the PPMD. (Id. ¶

27.) The drug appeared to be effective, by its production of dystrophin, and was reported to have no substantial side effects. (Id. Exh. M.) That evening, Dr. Stuart Peltz, the President and Chief Executive Officer of PTC, sat next to Cheri at a dinner held at the Loew's Hotel. (Id. ¶ 28.) Dr. Peltz thanked Cheri for her leadership in getting federal funding for DMD treatment. (Id.) She asked if Jacob could get PTC124, and ***Dr. Peltz promised her that Jacob would get it.*** (Id.)

In October 2006, a telephone conference call was set up between Cheri, Senior Vice President Claudia Hirawat, and Dr. Parkin. (Id. ¶ 29; Parkin Decl. ¶ 7.) ***During the conversation, Ms. Hirawat again said that Jacob would have access to PTC124.*** (Id.; Gunvalson Decl. ¶ 29.) During the discussion, it was also noted that Jacob was currently taking Gentamicin. (Id.; Parkin Decl. ¶ 7.) Ms. Hirawat explained that, to be enrolled in a PTC124 trial, Jacob would have to be off Gentamicin for at least 90 days. (Id.; Gunvalson Decl. ¶ 29.)

In or around March 2007, Jacob lost his ability to walk. (Id. ¶ 30.) Subsequently, he was examined by Dr. Brenda Wong, who was the "primary investigator" for the Phase IIa study of PTC124 at Cincinnati Children's Hospital. (Id.) Based on that examination and in reliance that Jacob would soon be enrolled in a PTC124 trial, the Gunvalsons discontinued Jacob's dosage of Gentamicin in the summer of 2007. (Id. ¶¶ 29-30 & Exh. N; Parkin Decl. ¶ 7.) Jacob had been taking Gentamicin to that point with positive results, but PTC124 was a more

promising treatment for his condition because it is more effective than Gentamicin and its side effects appear to be much less severe. (Gunvalson Decl. ¶ 30.)

On July 11, 2007, PTC and PPMD announced that PTC and the University of Pennsylvania had jointly received a $15.4 million research grant to develop PTC124. (Id. Exh. I.) Afterward, Cheri attended the PPMD conference in Philadelphia, and on July 14, again spoke with Dr. Peltz, PTC's CEO. (Id. ¶ 31.) Dr. Peltz once more thanked Cheri for her role in getting funding for Muscular Dystrophy research in general and PTC Therapeutics in particular. (Id.) Cheri asked Dr. Peltz if Jacob could get PTC124. (Id.) Although Dr. Peltz ***reiterated that Jacob would get access to PTC124,*** he also mentioned that Jacob should have been enrolled in one of the earlier clinical trials. (Id.; Ver. Compl. ¶ 31.)

Obviously distressed by Dr. Peltz's comment about the earlier trials, Cheri went to Senior Vice President Hirawat, who invited Cheri and Jacob to visit her at her home and tour the company headquarters. (Gunvalson Decl. ¶ 31.) ***While the Gunvalsons stayed at Ms. Hirawat's home, she again represented to Cheri and Jacob that the company would put Jacob in a different trial.***[5] (Id. ¶ 32.)

[5] The Gunvalsons consider Claudia Hirawat to be a friend. (Gunvalson Decl. ¶ 23.) For instance, in October 2007, Hirawat emailed Cheri, noting that she "was thinking of Jacob." (Id. Exh. O.) Two weeks later, Hirawat sent another email saying "[P]lease know I have all this [sic] photos of Jacob seating [sic] right here in fron [sic] of me, and consider all the Gunvalson's my personal friends, so please call and write to me ANYTIME! A big hug to the whole gang." (Id. Exh. P.)

In late 2007, PTC announced the results of its Phase IIa clinical trial. (Id. ¶ 34 & Exh. G.) The results were reported to be successful, with improved dystrophin presence, increased physical activity, and no serious side effects. (Id.)

Bolstered by this news, especially in light of Dr. Miller's earlier promises regarding proof of the safety and efficacy of PTC124, Cheri contacted PTC's patient liaison, Diane Goetz, about Jacob receiving PTC124 through a compassionate use exception. (Id. ¶ 35.) On November 26, 2007, ***Cheri spoke with Ms. Goetz, who told her that Jacob*** could not get PTC124 under an expanded use protocol but that he ***would be able to get the drug in a different way***. (Id.)

PTC Reneges on its Promises and Refuses to Provide PTC124 to Jacob. By late 2007, PTC announced that it was enrolling DMD patients in a Phase IIb clinical trial, which would be double-blinded, placebo-controlled, and multi-centered. (Id. Exh. V; Hatch Decl. Exh. 8.) However, Cheri was told by Ms. Hirawat that Jacob's status was still up in the air. (Gunvalson Decl. ¶ 36.) Distressed by this, Cheri emailed Diane Goetz to ask what Claudia had meant. (Id. ¶ 36 & Exh. Q.) On December 30, 2007, Goetz advised the Gunvalsons that Jacob would not qualify for the Phase IIb trial because patients were required to be ambulatory in order to measure their progress. (Id. ¶ 36 & Exh. R.) She also began to backpedal off PTC's commitment to Jacob by writing that PTC was looking for a new clinical trial in which Jacob could enroll. (Id.)

On January 1, 2008, Cheri replied to Ms. Goetz, explaining that Dr. Russell Katz, the director of the FDA's neuro-pharmacological division, suggested that Jacob receive PTC124 through a protocol exception and would consider an expedited review for the same. (Id. ¶ 38 & Exh. S.) On January 4, without explanation as to why Jacob could not receive a protocol exception, Ms. Goetz, on behalf of PTC, denied Cheri's request. (Id. ¶ 39 & Exh. T.)

Not satisfied with this response, Cheri contacted Bettilou Taylor, staff director of the Senate Labor, Health and Human Services Appropriations Committee. (Id. ¶ 40.) On January 14, Taylor sent Goetz an email specifically asking why PTC "won't grant a protocol exception for Jacob", especially because the FDA was "encouraging companies to grant exceptions to provide as much [information] as possible about the side effects from the drug". (Id. ¶ 40 & Exh. U.) Eleven days later, on January 25, 2008, Goetz responded to Taylor, again without explanation, that PTC would not provide PTC124 to Jacob in connection with a protocol exception. (Id.)

The "Compassionate Use" Exception for Treatment with Unapproved Drugs. The FDA allows patients who are not participants in a given clinical trial for unapproved investigational new drugs ("INDs") to gain access to these by virtue of expanded use protocols, or single-patient protocol exceptions. See 21 C.F.R. §312.34. Dr. Katz of the FDA elaborated on these possibilities to Cheri by

email. (Gunvalson Decl. Exh. L.) Significantly, Jacob clearly qualifies for a "compassionate use" exception under §312.34 because: 1) DMD is a serious or immediately life-threatening illness that PTC124 is intended to treat (Gunvalson Decl. Exhs. C, E, V); 2) There is no comparable or satisfactory alternative drug therapy beyond PTC124 to treat those with Jacob's type and extent of DMD (Id. Exhs. E, G, V); 3) PTC124 is still under investigation in a controlled clinical trial with an IND in effect for the trial (Id. Exh. V; Parkin Decl. Exh. D; Hatch Decl. Exhs. 4, 8); and 4) PTC Therapeutics is actively pursuing marketing approval for PTC124 with due diligence (Gunvalson Decl. Exhs. E, P; Halpern Decl., Exh. A.)

These "compassionate use" exceptions are not only permitted but **encouraged** by the FDA where the patient otherwise faces death or a serious debilitating condition. Indeed, as set forth in 21 C.F.R. §312.34(a), this is the very purpose of the exceptions. When advised of Jacob's situation, Dr. Russell Katz, the FDA's neurology chief, sent Cheri an e-mail with the following excerpt:

> In my opinion, the best option for your son would be to request a protocol exception. If approved by the sponsor, a protocol exception allows some patients who are ineligible to participate in a study to be treated with the investigational drug under the existing study IND at one of the study centers participating in the trial.

(Gunvalson Decl. Exh. L) (emphasis added).

The FDA has repeatedly made it clear that the use of an investigational drug, such as PTC124, in a patient for whom no effective therapy exists, like Jacob, is

appropriate.[6] (See, e.g., Hatch Decl. Exhs. 2, 3.) For instance, in January 2000, the FDA published an article in its Consumer Magazine entitled *Experimental Treatments? Unapproved but Not Always Unavailable*. (Hatch Decl. Exh. 1.) The article describes the availability of single-patient INDs as follows:

> If enough is known about the drug's safety, and there is some clinical evidence of effectiveness, FDA may allow a patient to become his or her own study. This so-called single-patient IND, or compassionate use IND, virtually ensures that any patient can get access to any investigational new drug.

(Id. (emphasis added)). In this case, there is evidence of PTC124's safety and effectiveness; Dr. Brenda Wong has stated, on behalf of PTC:

> [W]e are very encouraged by the promising results we have seen to date with PTC124. We believe that the safety profile of PTC124 and activity we have seen in the Phase 2a studies clearly support the initiation of this longer-term, registration-directed efficacy and safety study.

(Gunvalson Decl. Exh. V.)

Current PTC124 Clinical Trials. First, PTC is imminently starting a Phase IIa clinical trial extension at the Cincinnati Children's Hospital (and two other U.S. sites) in which children with Jacob's form of DMD will be provided PTC124 on a long-term basis, for 96 weeks. (Gunvalson Decl. ¶ 42.) However, the only children eligible for inclusion in the Phase IIa extension are those that

[6] Additionally, 42 U.S.C. §282(i)(3)(A) requires that PTC describe its policy on compassionate use exceptions on a governmental data bank. The website www.clinicaltrials.gov indicates that PTC may have ignored this statute and did not submit its expanded use protocol to the federal government. (Hatch Decl. ¶ 9.)

participated in the previous Phase IIa study. (Id.) Because the Gunvalsons were instructed by PTC not to enroll Jacob in the Phase IIa study and they did not do so in reliance on those instructions, Jacob is now ineligible to participate under the trial's protocol. (Id.) Ironically, several other non-ambulatory children with Jacob's form of DMD will be enrolled in the study. (Id.)

Second, PTC is running a Phase IIb trial. Enrollment in this trial began in January 2008 and on April 23, 2008, PTC announced it had begun. (Id.) Phase IIb is an international trial, taking place at more than 35 sites in 11 different countries. (Id.; Parkin Decl. Exh. D; Hatch Decl. Exh. 8.) Despite this, PTC is **still recruiting** some of the 165 participants the study seeks. (Id.) Jacob does not fulfill the Phase IIb study protocol because he can no longer walk. (Id.)

Possible Alternatives for Jacob. Although Jacob was not enrolled in the initial Phase IIa trial, 21 C.F.R. §312.34 would allow him to be treated alongside trial members as a protocol exception. Of note, Jacob's treatment would not influence any data resulting from the Phase IIa extension protocol. (Id. Exh. L).

Prior to receiving PTC124, each child must undergo a thorough examination by one of the physicians running the study. (Id. ¶ 42.) Included in this examination is an invasive muscle biopsy to determine a child's dystrophin levels. (Id.) There is a six-month waiting list for an appointment with Dr. Brenda Wong, the lead researcher of the Phase IIa study at Cincinnati Children's Hospital. (Id. ¶

43.) Jacob has an appointment with Dr. Wong on August 6, 2008, and a muscle biopsy could be performed at that time. (Id.) The Gunvalsons are more than willing to subject Jacob to this invasive procedure if PTC agrees to provide PTC124 for Jacob's treatment, even though FDA approval would still be necessary. (Id.) On August 6, therefore, Jacob can complete the medical prerequisites for beginning treatment with PTC124. (Id.)

There appears to be less than a dozen American children – Jacob is perhaps the only one – that are not eligible for inclusion into either the Phase IIa extension or Phase IIb study. (Id. ¶ 44.) Only one in more than 46,000 children has DMD due to the nonsense mutation (the only form of DMD that PTC124 treats). (Id. ¶ 5 & Exhs. E-F.) Boys with DMD usually die by age 25 and some die as young as 13. (Id. ¶ 44.) Most DMD children in their early teens are still ambulatory and thus are eligible for the Phase IIb study. (Id.) At the other end, due to DMD's debilitating effects, many patients over 18 are on a ventilator and therefore would not participate in PTC's clinical studies. (Id.) Further, to take part in the studies, a child must not only have DMD, but also have the nonsense mutation confirmed by gene sequencing. (Id. ¶ 44 & Exh. G.) Consequently, most, if not all, of those children who meet these criteria are already eligible to participate in either the Phase IIa extension or the Phase IIb study. (Id. ¶ 44.) As PTC is still recruiting candidates for the Phase IIb trial, Jacob may be the only child with DMD who

could be helped with PTC124 but is not being allowed to participate in a clinical trial with the drug. (Id.)

Alternatively, Jacob could be treated in a single-patient IND. Dr. Parkin, Jacob's physician, has already requested that PTC give him permission to do so. (Id. ¶¶ 20, 45.) As part of the conditions of Jacob's treatment (under any compassionate use method) with PTC124, the Gunvalsons are prepared to sign a full release concerning liability and any necessary "informed consent" document, pay for PTC124 and its administration, undertake the necessary applications to secure approval from the FDA for a "compassionate use" exception, and complete any other task necessary to secure Jacob access to PTC124. (Id. ¶ 46.)

Despite PTC's repeated promises that Jacob would get PTC124, the success of the earlier clinical trials, and the availability of compassionate use exceptions to provide Jacob the drug, PTC has expressly rejected Jacob's requests to receive PTC124 either as a protocol exception or through a single-use IND. (Id. ¶ 47.)

At best, PTC has stated that it is willing to consider Jacob's participation in some "future" clinical trial, assuming he qualifies under that trial's protocols. (Id.) However, PTC has admitted that it has not asked the FDA for approval of any such trials, and that no such trials are currently being planned. (Id.) Given the time necessary to plan and approve a clinical trial and the anticipated completion dates of the Phase IIb study of PTC124 (August 2010) and the Phase IIa study extension

(96 weeks, meaning around the same time), Jacob will probably die before he is eligible to receive PTC124 on the schedule proposed by PTC Therapeutics.[7] (Id.)

Jacob needs PTC124. Jacob could walk until March 2007, when he fell and probably suffered a compression spinal fracture. (Gunvalson Decl. ¶48) Jacob was then fitted with Kafo braces which permitted him to stand up and walk. (Id.) In March 2007, Jacob could pick up a glass of water and drink it. (Id.) He could use the toilet by himself. (Id.) He could sit up in bed without help and transfer himself to a chair. (Id.) Throughout 2007, Jacob could utilize a scooter. (Id.)

By March of 2008 – just one year later – Jacob could no longer utilize his Kafo braces in an efficient manner, as his muscles continued to weaken. (Id. ¶ 49.) Jacob now has to use a power chair, needs assistance to transfer from the power chair to the toilet and can no longer lift a glass of water. (Id.)

Jacob's condition will continue to deteriorate, and, without intervention, he will die within the foreseeable future. (Id.) Therefore, unless he has prompt access to PTC124, Jacob will not be alive, or will be so incapacitated that he will not be able to participate, by the time any future clinical trial begins. (Id.) Further, the longer Jacob deteriorates, the less likely he is to benefit from the drug, and the less

[7] Clinical investigations of new drugs require at least three phases. 21 C.F.R. §312.21. PTC is unlikely to begin Phase III trials until after the current ones finish, and Jacob may not qualify to receive PTC124 under any Phase III protocol.

benefit he will derive from it. (Id. ¶ 54.) PTC124 is Jacob's last, best and only chance to slow, stop or even reverse the effects of his condition.

ARGUMENT

POINT I

THE GUNVALSONS ARE ENTITLED TO A PRELIMINARY INJUNCTION REQUIRING PTC TO PROVIDE JACOB PTC124

In ruling on a motion for a preliminary injunction, the Court should consider, and balance, four factors: 1) plaintiffs' likelihood of success; 2) whether plaintiffs will suffer irreparable harm; 3) whether the irreparable harm to plaintiff outweighs the harm to defendants; and 4) the public interest. See Sypniewski v. Warren Hills Reg'l Bd. of Educ., 307 F.3d 243, 252 (3d Cir. 2002), cert. denied, 538 U.S. 1033 (2003). As set forth below, Plaintiffs easily meet all four factors, and therefore request that the Court order PTC to make PTC124 available to Jacob for either a "protocol exception" in the Phase IIa extension clinical study or a single patient IND supervised by Dr. John Parkin, if authorized by the FDA.

POINT II

PLAINTIFFS HAVE A STRONG LIKELIHOOD OF SUCCESS ON THE MERITS OF THEIR CLAIMS

A. PTC's Conduct is Barred by Promissory Estoppel

Under the equitable principle of promissory estoppel, a promise that, by reasonable reliance, induces a definite and substantial detriment is binding if

injustice can be avoided only by enforcement of the promise. See Pop's Cones, Inc. v. Resorts Int'l Hotel, Inc., 307 N.J. Super. 461, 469 (App. Div. 1998) (citation omitted).[8] Promissory estoppel eliminates the plaintiff's need to establish the formal elements of a contract. R.J. Longo Const. Co., Inc. v. Transit Am., Inc., 921 F. Supp. 1295, 1305 (D.N.J. 1996).

There are four elements to such a claim: (1) a clear and definite promise (2) made with the expectation that the promise will rely upon it, and (3) reasonable reliance upon the promise (4) which results in definite and substantial detriment. See Lobiondo v. O'Callaghan, 357 N.J. Super. 488, 499 (App. Div.), certif. denied, 177 N.J. 224 (2003). Significantly it applies to future promises where they are made to influence others who then are induced to act or forbear based upon the promise. Royal Assocs. v. Concannon, 200 N.J. Super. 84, 91 (App. Div. 1985) (defendant estopped from taking adverse action against plaintiff based upon his promises). The elements of promissory estoppel are readily satisfied here.

First, PTC made multiple clear and definite promises to plaintiffs. Prior to each of the 28-day studies, PTC told Cheri not to discontinue Jacob's Gentamicin treatment for such a short trial, and more importantly, that there would be no future detriment to Jacob by not participating in them. Now, of course, Jacob is foreclosed from receiving PTC124 under the Phase IIa extension study specifically

[8] Minnesota and New Jersey law are consistent on this matter's substantive issues.

because he did not participate in the 28-day trials. Additionally, on a number of occasions PTC promised that Jacob would get access to PTC124:

- On July 14, 2006, following the annual PPMD conference, Dr. Miller, PTC's Chief Medical Officer, told Cheri that Jacob would get PTC124 once results were back from the Phase IIa trial and the results were positive;
- On September 27, 2006, at the National Generic Alliance's Annual Gala, Claudia Hirawat, PTC's Senior Vice President, told Cheri that Jacob would get access to PTC124;
- On September 28, 2006, at a PPMD conference, Dr. Stuart Peltz, PTC's President and CEO, promised Cheri that Jacob would get PTC124;
- In October 2006, Hirawat again told Cheri and Dr. John Parkin that Jacob would have access to PTC124 during a telephone conference;
- After a July 2007 PPMD conference, while Cheri and Jacob visited her home, Hirawat promised PTC would put Jacob in a PTC124 clinical trial;
- On November 26, 2007, Diane Goetz, a PTC patient liaison, told Cheri that Jacob will be able to get access to PTC124 (although not under an expanded use protocol).

As PTC knows, for these promises to be meaningful, Jacob must have access to PTC124 while it can still provide some benefit for him, not after he dies.

Further, these promises were made with the expectation that Jacob, Cheri and John would rely upon them. Due to Cheri's extensive work with and on behalf of PTC, Dr. Miller, Hirawat, Dr. Peltz and Goetz were well aware of Jacob's medical condition and treatment, and his need for PTC124. Furthermore, throughout this time period, PTC Therapeutics continued to benefit from Cheri's involvement with PPMD, her fundraising efforts, her discussions with the media,

and her discussions with government agencies and elected officials, all of which helped bring in research dollars for PTC. In fact, many of PTC's promises were made hand-in-hand with thanks from it for all the benefits resulting from Cheri's work. How ironic that PTC continued to benefit from Cheri's advocacy while Jacob continued to suffer from DMD, the very illness PTC124 fights.

Similarly, the Gunvalsons detrimentally and reasonably relied on PTC's promises. Jacob specifically did not participate in the earlier PTC124 clinical trials due to PTC's representations and assurances. The Gunvalsons had no reason to doubt PTC. The close working relationship between Cheri and certain PTC executives further led Cheri to have confidence in the company and to believe its promises. PTC's executives socialized with Cheri, with one executive even hosting Cheri and Jacob for an overnight stay in her home, and Cheri received emails from PTC that Jacob was in their thoughts.

Additionally, reliance on PTC's promises has resulted in a substantial detriment to the Gunvalsons. Jacob is foreclosed from receiving PTC124 in the Phase IIa extension only because he did not participate in the previous study, even though PTC promised that Jacob would not be harmed by doing so. Also, the Gunvalsons discontinued Jacob's Gentamicin in part due to PTC's promises that Jacob would be enrolled in a PTC124 trial after being off it for 90 days. Further,

Cheri continued to work on PTC's behalf through her advocacy of funding for DMD research, believing it would help Jacob when he received PTC124.

Finally, PTC should not be permitted to hide behind its proffered excuse – that PTC124 is still undergoing clinical trials – to refuse Jacob access to it. In Dahl v. Hem Pharmaceuticals Corp., 7 F.3d 1399, 1401 (9th Cir. 1993), patients affected with chronic fatigue syndrome participated in a clinical trial to determine whether an experimental medication was both safe and effective. Plaintiffs claimed that the defendant had promised to continue providing them the drug after the study's completion at no charge for a full year, if statistical analysis confirmed efficacy, yet defendant refused to follow through after the study ended. Id. The Court of Appeals affirmed the district court's grant of a preliminary injunction requiring the defendant to provide the drug to these patients, confirming that a promise by a company to provide an experimental drug still in clinical trials is enforceable. Id. at 1403-04.

Dahl relied upon the first-year law school case, Hamer v. Sidway, 124 N.Y. 538 (1891), wherein an uncle promised his nephew a windfall if he refrained from drinking, using tobacco and playing cards or billiards until age 21. 7 F.3d at 1405. That court held consideration had been given and a unilateral contract entered into because the nephew refrained from the prohibited activities based on the promise, completing performance. Id. Jacob's situation is even closer than Dahl, as he

actually refrained from participating in the 28-day PTC124 studies because PTC told him it would not affect his ability to receive it later. Now it has. Given Jacob's prognosis, it is hard to imagine a case of clearer detrimental reliance.

In fact, Jacob's claim is stronger than that in Dahl because the FDA noted that drug, unlike PTC124, had induced several "serious and potentially life-threatening reactions that were observed during the study." Id. at 1402. The court, however, permitted the plaintiffs to get the drug, reasoning that they were getting it "with their eyes open to its experimental status." Id. at 1404. By stark contrast, PTC has admitted that PTC124 has raised no safety concerns to date, and Genzyme has entered into a $437 million deal with PTC to develop and commercialize PTC124. Surely, Genzyme would not commit almost half a billion dollars to PTC if there were real concerns about PTC124's safety. Further, the Gunvalsons are clearly aware of the drug's experimental status and will provide PTC with a full release. If the patients in Dahl could receive access to an experimental drug with serious safety concerns, then *a fortiori* Jacob should receive PTC124. Accordingly, PTC should be estopped from refusing to provide PTC124 to Jacob.

B. PTC Fraudulently Misrepresented that Jacob Would Receive PTC124

PTC intentionally misrepresented to the Gunvalsons that Jacob would receive PTC124. This egregious conduct has caused Jacob to forego helpful

treatment and, if PTC's representations are not fulfilled, threatens to extinguish his hope to survive much longer.

"Every fraud in its most general and fundamental conception consists of the obtaining of an undue advantage by means of some act or omission that is unconscientious or a violation of good faith." Jewish Ctr. of Sussex County v. Whale, 86 N.J. 619, 624 (1981) (citation omitted). A false representation of existing intention with respect to a future event constitutes a misrepresentation. See California Natural, Inc. v. Nestle Holdings, Inc., 631 F. Supp. 465, 473 (D.N.J. 1986). A fraudulent misrepresentation may occur by silence or omission rather than an affirmative statement, and the relationship of the parties may create a duty to disclose. Berman v. Gurwicz, 189 N.J. Super. 89, 93 (Ch. Div. 1981).

Where, as with this motion, plaintiffs seek only equitable remedies, they need not prove scienter (knowledge of the misrepresentation's falsity and an intention to obtain an undue advantage therefrom). Whale, 86 N.J. at 625. (citations omitted). In other words, an innocent misrepresentation may constitute equitable fraud; there need not be proof that the maker made the statement with knowledge that it was false. Liebling v. Garden State Indem., 337 N.J. Super. 447, 453 (App. Div. 2001). Therefore, to receive equitable relief, Plaintiffs need only prove that (1) PTC made a material misrepresentation; (2) PTC intended the

misrepresentation be relied upon; (3) Plaintiffs relied on the misrepresentation, and (4) Plaintiffs were damaged thereby. Whale, 86 N.J. at 624-25.

Here, PTC made multiple material misrepresentations to the Gunvalson family. First, it twice told the Gunvalsons that Jacob would suffer no negative ramifications if he refrained from participating in the PTC124 28-day studies. Obviously, this was not true – Jacob is now precluded from participating in the Phase IIa extension by the terms of its protocol. Second, on multiple occasions PTC told the Gunvalsons that Jacob would get access to PTC124. PTC's current resistance to Jacob's access to the drug and its failure to suggest any future access to it – notwithstanding the FDA regulation to the contrary – means that Jacob likely will have no meaningful future access to PTC124.

Second, PTC intended that these statements be relied upon. When Hirawat told Jacob to refrain from participating in the earlier PTC124 studies, she did so in response to specific inquiries by the Gunvalson family which made clear the family was relying on her response. Similarly, PTC's assurances that Jacob would receive PTC124 were made in the context of close personal relationships between PTC executives and the Gunvalsons. Often they were made contemporaneously with events recognizing Cheri's work in securing funding for DMD research which inured to PTC's benefit, and in response to specific, pointed queries whether Jacob

would ever get PTC124. They were also made in connection with instructions that Jacob's would need to be off Gentamicin for 90 days to get PTC124.

Third, the Gunvalsons relied upon the above misrepresentations. As explained above, they did not place Jacob in the PTC124 28-day trials based on assurances that foregoing those trials would not prejudice his chances to receive PTC124 in the future. Further, Cheri was told multiple times that Jacob would receive PTC124, and, among other things, Jacob's discontinued taking Gentamicin because he would need to be off it for at least 90 days prior to beginning PTC124.

Finally, the Gunvalsons have been damaged by PTC's misrepresentations. By the terms of the Phase IIa extension, Jacob is now foreclosed from receiving PTC124, and Jacob continues to deteriorate each day he lacks effective treatment despite PTC's clear and unequivocal promises that he would receive PTC124, knowing that he will ultimately die without it. Accordingly, Plaintiffs are entitled to an injunction that would (1) put Jacob where he would otherwise be but for PTC's misrepresentations concerning participation in the earlier studies and/or (2) allow Jacob access to PTC124, as he has been promised by PTC multiple times.

C. PTC Negligently Misrepresented that Jacob Would Receive PTC124

Similarly, Plaintiffs have a strong likelihood of prevailing on their negligent misrepresentation claim. To prove a negligent misrepresentation claim, a plaintiff must demonstration that (1) the defendant negligently provided false information;

(2) the plaintiff was a reasonably foreseeable recipient of that information; (3) the plaintiff justifiably relied on the information; and (4) the false statements were a proximate cause of the plaintiff's damages. McCall v. Metropolitan Life Ins. Co., 956 F. Supp. 1172, 1186 (D.N.J. 1996); Singer v. Beach Trading Co., Inc., 379 N.J. Super. 63, 74 (App. Div. 2005). The failure to provide correct information at a time when it might affect future actions constitutes negligent misrepresentation. Karu v. Feldman, 119 N.J. 135, 148 (1990). Again, silence or omission may give rise to misrepresentation claim. See Berman, 189 N.J. Super. at 93.

As set forth above, on multiple instances PTC, through its employees and executives, communicated false information to the Gunvalsons. If not fraudulent, at the least these statements were negligently provided. "In order to determine whether any statements by defendants were negligently made, it is necessary to determine whether defendants owed plaintiff a duty to exercise reasonable care in communicating facts . . . and, if so, whether communication of false information was a breach of that duty." Singer, 379 N.J. Super. at 74. PTC has publicly touted its development of PTC124 to treat children with Jacob's rare form of DMD. Moreover, PTC has specifically told the Gunvalsons that Jacob would receive access to PTC124, and therefore, has a duty to Jacob and his family. Id. at 76-77. This is especially so when PTC's relationship with the Gunvalsons is scrutinized. Cheri has been thanked by PTC for her role in securing millions in public grants

for the company. And Cheri, sometimes with Jacob, has attended events alongside PTC representatives, even staying at a Vice President's home.

Just as clearly, PTC breached that duty by making the false statements to the Gunvalsons. PTC ultimately controls who receives PTC124. It helps plan clinical studies and sets protocols. Therefore, PTC by definition breached its duty to the Gunvalsons by providing them false information about the effect of nonparticipation in a PTC124 clinical trial, the protocol for inclusion in PTC124 clinical trials, or Jacob's ability to access PTC124 in general.

Second, although these misrepresentations were generally made to Cheri, it was reasonably foreseeable that she would share such statements with Jacob and his father as well. Therefore, all three plaintiffs in this matter were reasonably foreseeable recipients of this information. H. Rosenblum, Inc. v. Adler, 93 N.J. 324, 352 (1983) (liability extends to "reasonably foresee[able] recipients" of statement); Singer, 379 N.J. Super. at 76 (third party who did not rely on the misstatement, but was injured as a result of another's reliance on such statement, can sustain a cause of action for negligent misrepresentation).

Finally, as explained *supra*, the Gunvalsons justifiably relied on PTC's false statements, which proximately caused their damages. For these reasons, Plaintiffs are likely to prevail on their negligent misrepresentation claim, and an injunction should issue to prevent further harm based upon PTC's negligent mispresentations.

POINT III

PLAINTIFFS WILL SUFFER IRREPARABLE HARM THAT FAR OUTWEIGHS ANY POSSIBLE HARM TO PTC THERAPEUTICS

Jacob will undeniably suffer irreparable harm without a preliminary injunction. PTC124 is the only promising drug for Jacob's form of DMD, and one which has, after several clinical studies, raised no significant safety concerns. Jacob's condition has rapidly deteriorated, and each day he is denied access to PTC124 it gets worse. Without it, he will ultimately die. This is surely irreparable.

Moreover, the irreparable harm to the Gunvalsons that would occur if an injunction is not issued outweighs PTC's if it is. Here, the contrast is stark. Simply put, PTC will not sustain any harm if it allows the drug to be utilized by Jacob. In fact, PTC has never articulated any possible harm it might suffer when rejecting the Gunvalsons' recent entreaties for PTC124. Furthermore, the Gunvalsons have already agreed that, if they receive PTC124 through a compassionate use exception, they will compensate PTC Therapeutics for the medication, pay for the administration of any single-patient IND trial if one is undertaken, and provide any releases or waiver of liability concerning use of PTC124. See Kopicki v. Fitzgerald Automotive Family Employment Benefits Plan, 121 F. Supp. 2d 467, 472 (D. Md. 2000) (balance of hardships typically favor a terminally-ill patient seeking "the best procedures available to extend his life").

The Gunvalsons' dilemma was made clear in Dozsa v. Crum & Forster Ins. Co., 716 F. Supp. 131 (D.N.J. 1989). There, plaintiff's insurer denied coverage for a cutting-edge cancer treatment. Id. at 132. The court granted relief, observing:

> If a preliminary injunction is not granted, ultimate relief for plaintiff will come too late. The procedure must be administered promptly or his physical condition will deteriorate to a point where treatment will be impossible. Failure to provide treatment will probably result in death in a matter of months. If he receives treatment it is likely that his life span will be substantially extended.

Id. at 140. The Court also held that any monetary damage to defendants would be minimal because plaintiff's condition was "a rare one," and therefore, the public interest was to see "that plaintiff receives the benefits to which he is entitled," and "the equities weigh[ed] heavily in favor of granting a preliminary injunction." Id.

Here, the equities weigh only heavier in Jacob's favor. There are very few boys in Jacob's position. Indeed, PTC has not yet been able to obtain 165 volunteers for its Phase IIb study, even though trial spans 11 different countries, and is open to anyone who qualifies. When the minor inconvenience, if any, to PTC is contrasted with the devastation DMD continues to wreak on Jacob, a preliminary injunction should clearly ensue.

POINT IV

THE PUBLIC INTEREST STRONGLY FAVORS INJUNCTIVE RELIEF

It is undisputed that Jacob becomes weaker by the day, and will soon die without PTC124. There cannot be a greater public interest than that of preserving

life. See, e.g., N.J. Const. Art. I ¶ 1 ("enjoying and defending life" is a "natural and unalienable right"); Kopicki, 121 F. Supp. 2d at 480 (the public interest "clearly favors the preservation of life and a patient receiving medical benefits to which he is entitled"); In re Conroy, 98 N.J. 321, 349 (1985) (state interest in preserving life is "most significant").

Second, clear expressions of governmental policy support the use of compassionate use exemptions. The plain language of 21 C.F.R. §312.34(a) makes its clear that its purpose is "to facilitate the availability of promising new drugs to desperately ill patients as early in the drug development process as possible." Similar governmental expression may be gleaned from the "fast track" and "orphan drug" status accorded to PTC124. See 21 U.S.C. §§356, 360dd. See also 21 U.S.C. §360bbb. Regulations and statutes such as these are a clear expression of public policy or interest, Gulf Coast Indus. Workers Union v. Exxon Co., U.S.A., 991 F.2d 244, 250-53 (3d Cir. 1993); Mallerdino v. Pfizer, Inc., 2006 WL 2050701, at *7 (E.D. Wis. July 19, 2006) (concerning FDA regulations); Home for Crippled Children v. Prudential Ins. Co. of Am., 590 F. Supp. 1490, 1498 (W.D. Pa. 1984); Pierce v. Ortho Pharm. Corp., 84 N.J. 58, 72 (1980), and it is difficult to imagine a more strongly worded governmental expression than 21 C.F.R. §312.34(a).

Furthermore, the FDA has continued to make strong public statements in support of "compassionate use" exceptions. Given that Jacob qualifies for such an

exception under 21 C.F.R. §312.34 and the FDA, through Dr. Katz, has already indicated that Jacob should pursue such an exception, the only impediment to Jacob's treatment with PTC124 appears to be PTC's refusal to provide it. The public interest strongly favors the use of drugs that have demonstrated both safety and efficacy, while still undergoing clinical trials. PTC124 is such a drug. Therefore, the public interest favors the issuance of the requested injunctive relief.

CONCLUSION

For the foregoing reasons, plaintiffs respectfully request that the Court grant a preliminary injunction enjoining PTC from refusing to (1) provide PTC124 so that Jacob could apply for a protocol exception under Phase IIa study of PTC124; or (2) allow a single patient IND to be administered by Dr. Parkin.

Respectfully submitted,

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APPENDIX

The following timeline is provided for the Court's reference and corresponds to information included in Plaintiffs' Statement of Facts:

Date	Event	Reference
1999	Jacob diagnosed with Muscular Dystrophy	Gunvalson Decl. ¶ 2
2000	PTC receives no federal grant money	Hatch Decl. Exh. 7
2001	Cheri joins PPMD	Gunvalson Decl. ¶ 10
2001	NIH Funding for DMD research is $14.3 Million	Gunvalson Decl. Exh. J
2001	PTC receives $140,000 in federal grants	Hatch Decl. Exh. 7
2001	Cheri gets Sen. Wellstone and Rep. Peterson to sponsor MD CARE Act, to increase MD research funding; proceeds to call and get 235 Congressmen and 49 Senators to author the only disease specific bill to pass Congress that year	Gunvalson Decl. ¶ 11 & Exh. J
December 18, 2001	MD CARE Act signed and DMD research funding increased to $54 million	Gunvalson Decl. ¶ 12 & Exh. J
December 2001	Gunvalson appointed to NIH Review Board to designate Centers of Excellence for DMD Research	Gunvalson Decl. ¶ 13
2002	PTC receives $126,500 in federal grants	Hatch Decl. Exh. 7

Date	Event	Reference
January 2003	Jacob begins Gentamicin treatment	Gunvalson Decl. ¶ 6 & Exh. O
2003	Project Catalyst – a joint venture of PPMD and PTC Therapeutics – is formed	Gunvalson Decl. ¶¶ 8-9 & Exh. H
2003	PTC receives $1,370,936 in federal grants	Hatch Decl. Exh. 7
2004	PTC receives $1,130,779 in federal grants	Hatch Decl. Exh. 7
2005	PTC receives $1,471,417 in federal grants	Hatch Decl. Exh. 7
2005	Cheri convinces PTC to apply for more federal grants from NIH	Gunvalson Decl. ¶ 15
Late 2005	Phase II clinical study announced; Cheri told by Dr. Richard Finkel and PTC's Claudia Hirawat (1) not to enroll Jacob, and (2) there would be no negative effects on Jacob for not participating	Gunvalson Decl. ¶ 17 & Exh. E
Late 2005	Phase II clinical study for PTC124 begins; Jacob is not enrolled	Gunvalson Decl. ¶ 17
2006	PTC receives $4,081,856 in federal grants	Hatch Decl. Exh. 7
March 1, 2006	PTC files (and soon withdraws) Securities Offering with SEC	Hatch Decl. Exh. 6
March 30, 2006	PTC announces that FDA gives PTC124 fast-track status.	Gunvalson Decl. ¶ 18 & Exh. E

Date	Event	Reference
March or April 2006	Dr. Parkin asks PTC if he can undertake single patient IND and have access to drug	Gunvalson Decl. ¶ 20; Parkin Decl. ¶ 5 & Exh. B
April 14, 2006	PTC's CMO, Langdon Miller, advises Dr. Parkin that only a 28-day trial has been completed and wants to complete further studies showing efficacy and safety before single patient IND warranted	Gunvalson Decl. ¶ 20; Parkin Decl. ¶ 6 & Exh. C
April 24, 2006	Dr. Russell Katz, director of the FDA's Division of Neuro-Pharmacological Drug Products, suggests to Cheri that Jacob apply for compassionate use exception	Gunvalson Decl. ¶ 21 & Exh. L
July 13, 2006	Dr. Miller assures Gunvalsons that Jacob will get PTC124 at annual PPMD conference	Gunvalson Decl. ¶ 24
July 13, 2006	Claudia Hirawat, PTC's Vice President, instructs Cheri not to enroll Jacob in Phase IIa trial, again telling her he will not be negatively effected by decision	Gunvalson Decl. ¶ 25
September 27, 2006	While at National Genetic Alliance meeting where Cheri is recognized for her advocacy work, Vice President Hirawat of PTC assures Cheri that Jacob will get access to the drug	Gunvalson Decl. ¶ 26
September 28, 2006	Dr. Peltz, CEO of PTC, assures Cheri that Jacob will have access to PTC124	Gunvalson Decl. ¶ 28
October 21, 2006	News release announces success of Phase IIa trial based on preliminary data	Gunvalson Decl. Exh. M

Date	Event	Reference
October 2006	Hirawat assures Cheri and Dr. Parkin that Jacob would get access to PTC124 during telephone conference call	Gunvalson Decl. ¶ 29; Parkin Decl. ¶ 7
March 2007	Jacob loses ambulation (the ability to walk)	Gunvalson Decl. ¶ 30 & Exh. N
May 2007	PTC announces that preliminary data for Phase IIa study is positive, with effectiveness and no serious side effects	Gunvalson Decl. Exh. G
May 30, 2007	Jacob examined by Dr. Brenda Wong, primary investigator of PTC124 studies at Cincinnati Children's Hospital	Gunvalson Decl. ¶ 30 & Exh. N
June 2007	In reliance on PTC's statements, Jacob taken off Gentamicin	Gunvalson Decl. ¶ 30
July 11, 2007	PTC announces NIH award of $15.4 million to PTC and U-Penn	Gunvalson Decl. Exh. I
July 14, 2007	At annual PPMD conference, Dr. Peltz reiterates that Jacob will get access to PTC124	Gunvalson Decl. ¶ 31
July 2007	Hirawat tells Cheri and Jacob that PTC is working to put Jacob in a clinical trial	Gunvalson Decl. ¶ 32
October 10, 2007	PTC's Vice President Hirawat e-mails Cheri that she was thinking about Jacob	Gunvalson Decl. Exh. O
October 18, 2007	PTC announces results of Phase IIa trial, with PTC124 reported to be successful and without serious side effects	Gunvalson Decl. ¶ 34

Date	Event	Reference
October 25, 2007	Hirawat writes she was deeply touched by Jacob's visit and considers Gunvalsons family; says new round of studies being discussed with FDA and opines on what next steps mean for Jacob	Gunvalson Decl. Exh. P
November 26, 2007	PTC employee Diane Goetz advises the Gunvalsons that Jacob will get PTC124, but not through "expanded access"	Gunvalson Decl. ¶ 35
December 30, 2007	Goetz emails Cheri that Jacob does not qualify for Phase IIb trial, PTC is "philosophically opposed" to single patient IND, and she does not understand the term "protocol exception," but PTC is looking for another trial for Jacob	Gunvalson Decl. ¶ 36 & Exh. R
January 1, 2008	Cheri sends Goetz email indicating Dr. Katz had suggested Jacob receive PTC124 through protocol exception	Gunvalson Decl. ¶ 38 & Exh. S
January 4, 2008	Without explanation, Goetz denies Cheri's request for a protocol exception	Gunvalson Decl. ¶ 39 & Exh. T
January 14, 2008	Bettilou Taylor, staff director at Senate Labor, Health and Human Services Appropriations Committee, emails Goetz to ask why PTC "won't grant a protocol exception"	Gunvalson Decl. ¶ 40 & Exh. U
January 25, 2008	Goetz replies to Taylor, without explanation, that PTC would not provide PTC124 to Jacob	Gunvalson Decl. ¶ 40 & Exh. U

Date	Event	Reference
April 23, 2008	PTC announces commencement of Phase IIb study, which requires that patients be ambulatory so that physician can measure success by distance walked in 6 minutes	Gunvalson Decl. Exh. V
July 17, 2008	Genzyme enters into a $437 million deal with PTC to develop and commercialize PTC124	Halpern Decl. Exh. A
July-August 2008	Patients will begin to receive PTC124 as part of Phase IIa study extension	Gunvalson Decl. ¶ 42
August 6, 2008	Jacob has appointment to be examined by Dr. Brenda Wong, primary investigator for the Phase IIa extension at Cincinnati Children's Hospital	Gunvalson Decl. ¶ 43
June 2010	Expected completion date for the first patients to begin the 96-week Phase IIa study extension	Gunvalson Decl. ¶ 42
August 2010	Expected completion date for Phase IIb study	Hatch Decl. Exh. 8