UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

ROBERT SUTHERS and NIWANA MARTIN,	:	Docket No.: 05 Civ. 4158 (PKC)
Plaintiffs,	:	
v.	:	
AMGEN, INC., a Delaware Corporation,	:	
Defendant.	:	A Civil Action

PLAINTIFFS ROBERT SUTHERS AND NIWANA MARTIN'S REPLY BRIEF IN FURTHER SUPPORT OF THEIR MOTION FOR A PRELIMINARY INJUNCTION

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"<u>The Principal Investigator may ... decide</u> to withdraw you from the study under certain circumstances. Some possible reasons for withdrawing a subject from the study would [include] ... termination or cancellation of the study by the sponsor."
- Informed Consent Document, page 24 (emphasis added)

"Intraputamenal infusion of GDNF is almost certainly effective and at this time appears safe beyond reasonable scientific doubt"
- Principal Investigator Michael Hutchinson, M.D.

INTRODUCTION

Plaintiffs Robert Suthers ("Mr. Suthers") and Niwana Martin ("Ms. Martin") (collectively, "plaintiffs") respectfully submit this Reply Brief in Further Support of Their Motion for a Preliminary Injunction ("Motion").

This case is not at all about whether defendant Amgen, Inc. ("Amgen") must continue to try and bring GDNF to market, whether Amgen must continue to enroll individuals in clinical trials of GDNF, or even whether Amgen was legally or ethically allowed to stop enrolling new individuals in the particular clinical trial at issue here. This case is instead about the fate of the plaintiffs, two individuals that Amgen enrolled in the trial, in the aftermath of Amgen's decision to shut it down. More particularly, it is about whether Amgen must continue to provide GDNF to the plaintiffs, who had holes drilled in their skulls and pumps inserted into their stomachs at Amgen's behest, in view of the fact that Michael Hutchinson, M.D., the trusted, learned physician serving as the Principal Investigator at the trial's New York University location ("Dr. Hutchinson"), has stated unequivocally that GDNF is effective and safe and that he wishes to continue providing GDNF to them.

Amgen's argument in opposition to the Motion reflects its contention that it does not need to provide GDNF to the plaintiffs if the drug is ineffective or dangerous. The plaintiffs agree with this contention; Amgen need not provide GDNF to them if it is ineffective or dangerous. But Amgen's argument hinges on the incorrect hypothesis that GDNF is actually ineffective and dangerous and that it should get to make that decision. Dr. Hutchinson has provided a supplemental Certification containing a comprehensive and definitive refutation of Amgen's concerns about GDNF.[1] Additionally, individuals who served as Principal

[1] See generally Certification of Dr. Hutchinson, attached as Exhibit "A."

Investigators at the trial's University of Kentucky location, Don M. Gash, Ph.D. ("Dr. Gash"), John T. Slevin M.D. ("Dr. Slevin"), and Greg Gerhardt, Ph.D. ("Dr. Gerhardt") (collectively, "Kentucky doctors") have provided a supplemental Certification also refuting Amgen's concerns about GDNF.[2] Furthermore, the Executive Director of the Parkinson's Pipeline Project, Perry D. Cohen, Ph.D. ("Dr. Cohen"), has submitted a compelling Certification concisely setting forth the public policy issues before this Court.[3] These supplemental Certifications do not merely create a factual dispute. Rather, using Amgen's own data, these authors conclusively refute the assertions of Amgen's affiants.

Crucially, Amgen never tells this Court that it did not promise to provide GDNF to the plaintiffs if it is efficacious and safe. Instead, it essentially argues a proposition with which the plaintiffs have no dispute: if GDNF is proven to be neither safe nor effective, Amgen has no obligation to continue supplying the drug to them. On the other hand, if GDNF is safe and effective, at least as demonstrated to date, there can be no question as to the plaintiffs' right to injunctive relief. In the absence of any other curative treatment for Parkinson's either on the market or in the pipeline, the plaintiffs will be irreparably injured if Dr. Hutchinson is not supplied with GDNF at this time. Moreover, they have a likelihood of success on the merits, or, at the very least, have raised sufficiently serious questions about the merits and the balancing of harms tips in their favor.

The extraordinary request that Amgen made of the plaintiffs gave rise to an extraordinary obligation on the part of Amgen. In view of Amgen's abdication of the responsibilities that it clearly undertook, an injunction must issue.

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[2] See generally Certification of Dr. Gash, Dr. Slevin, and Dr. Gerhardt, attached as Exhibit "B."

[3] See generally Certification of Perry D. Cohen, Ph.D., attached as Exhibit "C."

LEGAL ARGUMENT:
AMGEN HAS FAILED TO REBUT THE PLAINTIFFS' COMPELLING ARGUMENT THAT AN INJUNCTION MUST ISSUE

1. Amgen's Own Data Fatally Undercuts Its Argument

(a.) Introduction

The essence of Amgen's opposition papers is that the plaintiffs are not entitled to injunctive relief because GDNF is neither safe nor effective. Amgen posits that, because certain individuals who are associated with it have determined that GDNF does not work and presents a risk of harm to patients enrolled in the study, it could not possibly have an obligation to provide the plaintiffs with GDNF, and it could not have possibly committed a breach of any sort of duty, whether contractual or fiduciary.[4] This argument is predicated on a false calculus: when weighing the risks of harm posed by GDNF against the absence of any benefits, Amgen had no choice but to terminate the trial; that is, if GDNF has no benefits, any risk whatsoever swings the scale in favor of stopping the trial. Dr. Hutchinson, the Kentucky doctors, and Dr. Cohen have carefully reviewed Amgen's submissions and submitted responsive Certifications reflecting the fact that even Amgen's own documents and submissions do not reflect an absence of benefit on the part of GDNF and do not support the conclusion that GDNF is dangerous.

(b.) GDNF Is Efficacious

Amgen commences its argument regarding efficacy[5] by contending that patients who experienced a benefit while GDNF was being delivered to their brains were merely experiencing what is known as a "placebo effect."[6]

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[4] See Memorandum of Defendant Amgen Inc. in Opposition to Plaintiffs' Motion for Preliminary Injunction ("Amgen Mem."), pages 4-16, 19-30.

[5] Of course, a drug that is efficacious when it provides some benefit to the patients not otherwise achievable through other therapies.

[6] See Amgen Mem., page 4.

This is certainly not true of Mr. Suthers, who, as Amgen well knows, received a placebo on October 30, 2003, but did not experience improvement until he crossed over into the GDNF arm of the trial on March 30, 2004.[7] Nor is it true of Ms. Martin, who, as Amgen also knows, received a placebo in November 2003, but did not experience improvement until she crossed over into the GDNF arm of the trial on April 4, 2004.[8]

Nor is it true of anybody receiving GDNF, as Dr. Hutchinson explains:

> There is nothing in the history of medicine where a placebo effect of this magnitude has been witnessed. Nothing, whether surgical or non-surgical, resembles this. To be precise, the fact that fifteen out of fifteen patients have become progressively better, year by year, in a disease where progressive worsening is inevitable, is unheard of in regard to a "placebo effect." Furthermore, there was no statistical evidence from the [double-blind trial] of a significant placebo effect. ... Fifteen our of fifteen patients becoming objectively better over months and years, in a condition where worsening is otherwise inevitable, is not a placebo effect.
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> * * * *
>
> The FDA made a through review of the existing data. They noted that there was signal in both the phase I and phase II studies suggesting that GDNF is efficacious, and they were well aware that efficacy is difficult to prove in small phase II studies. They concluded that it was reasonable for Amgen to refill the pumps with GDNF, and gave Amgen the green light to do so ... .[9]

The Kentucky doctors confirm this, opining "that there is significant evidence for the ... efficacy of ... GDNF. Our preclinical research posits that the efficacy of intraputamenal GDNF therapy is directly related to dose and tissue distribution. These parameters were sufficiently optimized in the two Phase 1 trials where 15 out of 15 treated patients showed significant clinical improvements."[10]

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[7] See Complaint, Exhibit B, ¶¶ 15-18.
[8] See Complaint, Exhibit C, ¶¶ 13-17.
[9] See Exhibit A, ¶¶ 22, 24, 71.
[10] See Exhibit B, ¶ 10.

Supporting the doctors' statements is a recent case study that uncovered incontrovertible biological evidence of GDNF's efficacy:

> Mr. Gill's first patient died recently of a heart attack, four years after starting GDNF infusion, at the age of 75. He had been infused only on one side of the brain. After autopsy a startling finding was made. Tyrosine hydroxylase staining of putamenal tissue (a measure of dopamine function) was five times greater on the infused side than on the other side. Furthermore, the infused side had evidence of marked neuronal resprouting. These results provide direct evidence that GDNF is an effective treatment for Parkinson's Disease. They are incontrovertible and will shortly be published in the world's leading medical journal Nature Medicine.[11]

Supporting the doctors' statements are the Certifications of enrollees Mr. Suthers, Ms. Martin, Edward L. Abney, Delbert Jackson, Roger Thacker, Steven Kaufman, Diana Byrne, James Day, Raymond Hudson, Oliver Plunkett, Thelma Martin, Neil Shadwick, and Daniel Webster.[12] In their respective Certifications, these individuals all state that when they were receiving GDNF, their particular Parkinson's symptoms abated or disappeared, and since GDNF was withdrawn from their systems, their symptoms have returned, bringing with them the misery of Parkinson's disease.[13]

Further supporting both the doctors' statements is a breathtaking "before and after" video demonstrating the marked improvement of Parkinson's sufferers while on GDNF.[14] The "before" shots all depict individuals in the throes of a progressive neurodegenerative disorder exhibiting tremors, shaking, slow movement, and muscle stiffness and rigidity.[15] The "after" shots depict individuals who could pass for completely healthy. The difference is palpable.

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[11] See Exhibit A, ¶¶ 22, 24.

[12] See Certifications, attached as Exhibits "D" through "J," respectively.

[13] See Certifications, attached as Exhibits "D" through "J," respectively.

[14] See Compact Disc, attached as Exhibit "K" (containing a .WMV file of an approximately 4:18 movie produced in England documenting an earlier trial).

[15] See Exhibit K.

Amgen then goes on to point out that according to James Matchum, who works for it as an Associate Director and Biostatistical Scientist, the primary and secondary endpoints of the trial were not achieved, demonstrating GDNF's lack of efficacy.[16] As Dr. Hutchinson explains, however, the success of a Phase II trial like the one conducted here is not dependent on achieving such results for a showing of efficacy:[17]

> Most Phase II studies fail to show any signal suggestive of drug efficacy and are abandoned. Interestingly, of the small minority of Phase II studies which go on to Phase III, most have failed to meet their primary endpoints, but are recommended to go on to phase III because they show a signal suggestive of drug efficacy. This was such a study. ... I therefore respectfully disagree with Drs. Nutt and Wooten. When a study has failed to meet the present endpoints, it is not unscientific to do a post hoc analysis of the data. On that contrary, it is unscientific not to do one. It is of exceptional importance to know if "failure" represents lack of efficacy of a drug, or whether there were problems with the study such that the apparent failure may not have been real (i.e. a Type II error). This was such a study.[18]

While Amgen is correct in stating that the Phase II trial did not reach its endpoints, what Amgen omits to say is that virtually no clinical trial reaches its endpoints. Endpoints are not the measure of efficacy. Rather, the results in every trial thus far conducted on GDNF, including the results of the trial that the plaintiffs participated in, viewed as a whole, demonstrate efficacy.

The Kentucky doctors and Amgen met with the FDA after Amgen reviewed the primate data to discuss whether patients could continue to be supplied with GDNF.[19] If the clinical trials that had been conducted had failed to demonstrate efficacy, the FDA would have had nothing to

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[16] See generally Amgen Mem., pages 5-6.

[17] See generally Exhibit A, ¶¶ 26-32.

[18] See Exhibit A, ¶¶ 28-29. Consistently, the Kentucky doctors have averred that the investigators "were on the bubble of achieving efficacy in the Amgen Phase 2 trial." See Exhibit B, ¶ 10.

[19] See Exhibit A, ¶ 71; see also Exhibit B, ¶¶ 8-9.

consider. Indeed, the risk/benefit calculus is easy when the benefit side is zero because no risk is worth no benefit.

But the FDA was sufficiently impressed with the efficacy data, regardless of whether it met any theoretical endpoints, to sanction continued use of GDNF.[20] For whatever reason, Amgen declined the opportunity.

As Dr. Hutchinson explains:

> Representatives of the investigators (specifically, Dr. Gash and Dr. Penn) met with FDA scientists in Washington D.C. on January 10th 2005. Also present at the meeting were representatives from Amgen. The FDA made a thorough review of the existing data. They noted that there was signal in both the phase I and phase II studies suggesting that GDNF is efficacious, and they were well aware that efficacy is difficult to prove in small phase II studies. They concluded that it was reasonable for Amgen to refill the pumps with GDNF, and gave Amgen the green light to do so, provided the patients were closely monitored.
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> On February 11th 2005, Amgen officially refused.
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> This, despite the full backing of the Food and Drug Administration.
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> This, despite a unanimous decision by a distinguished panel of experts forming the Executive Committee of the Parkinson's Disease Foundation, chaired by the most distinguished clinical expert on Parkinson's Disease alive today, Dr. Stanley Fahn, to recommend reinstatement of GDNF.
>
> This, despite a similar resolution by the Washington-based Parkinson Action Network.
>
> This, despite a public declaration by Dr. Lieberman, head of the Miami-based National Parkinson Foundation, in favor of reinstatement.
>
> This, despite exhortations from the vast majority of patients, many of whom had already had their lives returned to them.[21]

[20] See Exhibit A, ¶ 71; see also Exhibit B, ¶¶ 8-9.
[21] See Exhibit A, ¶¶ 71-77.

Once some benefit to GDNF is assumed, the risk/benefit calculus drastically changes in favor of supplying the drug and granting the relief plaintiffs seek.

(b.) GDNF Is Safe

Amgen commences its argument regarding safety by contending that patients in the Phase II study of GDNF had developed neutralizing antibodies.[22]

As the Kentucky doctors explain, this is completely normal and of no clinical significance:

> Contrary to the statements provided by some other individuals, the situation of neutralizing GDNF antibodies is similar to that of neutralizing antibodies to beta interferon. Up to 45% of the patients treated with beta interferon develop antibodies, without clinical manifestations. One reason is that other related proteins in the body can substitute for beta interferon. GDNF also has closely related proteins that can substitute for it. An example is neurturin, which is found in overlapping brain areas with GDNF. Other proteins related to GDNF are found outside of the brain in the body. It should be stated again that clinical manifestations to GDNF antibodies have not been documented in patients receiving GDNF therapy. The muscle weakness in one patient receiving GDNF has since been reported as being due to other causes.[23]

And, as Dr. Hutchinson explains,

> [r]egarding the antibody issue, "neutralizing antibodies" are almost invariably seen when proteins are injected into the body. This is true of Amgen's leading drug, Epogen. This is true of the interferons used to treat multiple sclerosis, where up to 50% of patients develop them. Despite the pejorative appellation, neutralizing antibodies simply reduce the effectiveness of a drug and very rarely cause life-threatening complications. They are to be expected.
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> It can now be said that about 10% of patients treated with GDNF will develop neutralizing antibodies. Two out of fifteen patients in Bristol and Kentucky have them, and have presumably had them

[22] See generally Amgen Mem., pages 9-10.
[23] See Exhibit B, ¶ 8.

> for years (since they take only about 3 months to develop), yet have suffered no ill effects.[24]

Consistent with Dr. Hutchinson's testimony, Roger Perlmutter, M.D., Ph.D., the Executive Vice President of Research and Development at Amgen ("Dr. Perlmutter"), who now avers that the patients' developing antibodies was "very serious and troubling," actually told Dr. Hutchinson that "he had 'never been bothered' by the antibodies" in February 2005.[25]

Amgen continues its argument regarding safety by setting forth the fact that a certain study on primates "showed that a significant cluster of primates developed unusual and unexpected lesions in the cerebellum."[26]

As Dr. Hutchinson and the Kentucky doctors opine, however, Amgen has completely misinterpreted the data about the primates. As explained by Dr. Hutchinson, whatever lesions occurred were the result of abrupt withdrawal of high doses of GDNF and not exposure to the protein:

> While on vacation in England, on September 1, 2004, I received a telephone call from Mr. Dan Lee at Amgen. He told me that the study was to be stopped because of damage seen in the cerebellum in three of the monkeys. ...
>
> Upon my return to New York, on or about September 8th 2004, I reviewed the pathology slides that had been emailed to us. My first reaction was astonishment. There was indeed some loss of Purkinje cells, but no evidence of inflammation, arguing against hypoxic-ischemic change or direct toxicity.
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> Then I noticed that the three affected monkeys were all in the high-dose recovery group. The animal experiment was as follows: 15 animals received high doses of GDNF. All fifteen animals had their pumps abruptly switched off at six months. Ten were sacrificed immediately and their brains examined for signs of toxicity. None were found. The five remaining monkeys had their pumps switched off but were kept alive for an additional three

[24] See Exhibit B, ¶ 8.
[25] See Exhibit A, ¶ 60; see also Exhibit 1 to Amgen Mem., ¶ 38.
[26] See Amgen Mem., pages 10-13.

> months (the "recovery phase") before being sacrificed. Lesions were seen in the cerebellum in 3/5 of these monkeys.
>
> If Amgen's hypothesis were correct, i.e., that the lesions were due to the direct toxicity of GDNF, then all monkeys would be equally at risk, since they had all been exposed for six months. The math is simple. Assuming Amgen's hypothesis of direct GDNF toxicity is correct, the probability that lesions would only be seen in the five recovery animals can be calculated exactly. It is 2.2%. Therefore Amgen's hypothesis is rejected with 97.8% confidence, i.e. beyond any reasonable scientific doubt.[27]

And as explained by the Kentucky doctors,

> [i]f the cerebellar lesions are not an artifact resulting from the procedural problems (and the lesions seen in the study have not been replicated), a complete and independent assessment of the factors underlying the development of cerebellar lesions in the four monkeys cannot be made until all the data are made public. In our opinion, GDNF withdrawal is the other leading candidate as the mechanism of action producing the lesions and is consistent with confidential information which Amgen has not released. ... Contrary to the statements provided by some other individuals, the cerebellum can be closely monitored for tissue loss by MRI. Techniques are available and used for the patients in the Kentucky study to detect the loss of as little as 0.5% of cerebellar tissue. It is generally considered that tissue loss/injury compromising more than 25% of the cerebellum is required before clinical symptoms emerge. It should be stated again that cerebellar lesions from GDNF therapy have not been found in patients.[28]

The best that Amgen can say is that there is profound disagreement among the experts as to what that data suggest. But even assuming that Amgen's experts are correct that the lesions were caused by exposure and not withdrawal – an assumption that the plaintiffs vigorously oppose – two questions remain: how serious is the risk and how likely is it to occur. As Dr. Hutchinson and the Kentucky doctors opine, the occurrence of the lesions in question is certainly

[27] See Exhibit A, ¶¶ 58-59.
[28] See Exhibit B, ¶¶ 5-6.

not catastrophic and nothing in the data suggests that the probability of such occurrence is significant.[29]

In the end, the choice is for the patients and their physician to decide whether the risks are worth the benefits. Given the seriousness of their disease and its inevitable progression, the patients still choose therapy, even if they believed the risks that Amgen says are posed.

The one party who should not have the unilateral option to make that decision is the one party in the research enterprise whose stake is purely financial. In this regard, Amgen misreads the plaintiffs' argument about conflicts. There can be no question that Amgen's motives in conducting any clinical trial are financial; each time out, it seeks to get its drug approved so that both its stock price and its revenues will increase. The Principal Investigators here, on the other hand, seek what is in the best therapeutic interest of their charges and what is in the best interests of the advancement of medicine in the fight against Parkinson's. Similarly, the plaintiffs seek what is in their best therapeutic interest and what is in the best interests of medicine. At the very least, the plaintiffs and the Principal Investigators should have a vital say in the decision at hand, particularly given the extraordinary physical commitment they gave once they agreed to be a human subject and the flimsy evidence underpinning Amgen's decision to terminate the trial.

2. An Injunction Must Issue

(a.) Introduction

As stated in the plaintiffs' opening papers, "[a] motion for a preliminary injunction should ... be granted [when] the movant demonstrates (1) irreparable harm and (2) either (a)

[29] See Exhibit A, ¶¶ 36-59; see also Exhibit B, ¶¶ 5-7.

likelihood of success on the merits or (b) 'sufficiently serious questions' on the merits and a balance of hardships 'tipping decidedly' in the movant's favor."[30]

Contrary to Amgen's contention,[31] it is far from certain that the plaintiffs are seeking a mandatory injunction, which would require them to demonstrate the existence of "clear" or "substantial" likelihood of success on the merits.[32] As the Second Circuit has observed on more than one occasion, "[c]onfusion in breach of contract cases as to whether an injunction is mandatory or prohibitory may stem from the meaning of 'status quo.' A plaintiff's view of the status quo is the situation that would prevail if its version of the contract were performed. A defendant's view of the status quo is its continued failure to perform as the plaintiff desires. To a breach of contract defendant, any injunction requiring performance may seem mandatory. Here, the plaintiffs seek to maintain what is the true status quo – their continued receipt of GDNF so long as it is safe. Amgen upset the status quo when it ran afoul of its contractual and fiduciary duties to the plaintiffs.

Moreover, contrary to Amgen's contention, an injunction would not provide the plaintiffs with "the entire relief [they] seek in the litigation."[33] The "entire relief" that the plaintiffs seek is the right to receive GDNF indefinitely so long as it is safe and effective. The injunction that the plaintiffs seek would merely provide them with the right to receive GDNF pendente lite. A jury will ultimately have the responsibility of determining whether Amgen acted reasonably in declaring that GDNF was not safe and effective. If a jury somehow determined, after hearing all

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[30] See, e.g., Brooks v. Giuliani, 84 F.3d 1454, 1462 (2d Cir. 1996) (citing Jackson Dairy, Inc. v. H.P. Hood & Sons, Inc., 596 F.2d 70, 72 (2d Cir. 1979)).

[31] See Amgen Mem., page 17-19.

[32] See, e.g., Tom Doherty Assoc's, Inc. v. Saban Entertainment, Inc., 60 F.3d 27 (2d Cir. 1995)

[33] See Amgen Mem., page 18.

of the evidence, that Amgen appropriately terminated the trial because GDNF is unsafe or inefficacious, the plaintiffs would obviously not be entitled to continue to receive it indefinitely.

Regardless of the semantic distinctions that run through the jurisprudence of injunctive relief, it is clear that the plaintiffs have demonstrated the existence of irreparable harm in the absence of an injunction and the existence of a likelihood of success on the merits.

(b.) The Plaintiffs Have Clearly Demonstrated Irreparable Harm

Predictably, Amgen argues that plaintiffs have failed to demonstrate the existence of irreparable harm in the absence of an injunction because GDNF provides no benefit.[34] It posits that the "plaintiffs cannot demonstrate irreparable harm from being denied a drug that has been clinically shown to be of no benefit to them" and posits that the plaintiffs "are more likely to be harmed by continued GDNF therapy than helped."[35] This position is without merit because, as set forth at great length in § 1 of this Memorandum, GDNF is both efficacious and safe.

Moreover, in all of the cases that Amgen cites in support of its argument, patients sought treatment that they believed was beneficial but the scientific community believed was not. In Graham, a case in which an assured under a policy of health insurance sued for coverage for an experimental treatment known as High Dose Chemotherapy with Stem Cell Rescue ("HDC/SCR"), her own expert conceded "that the effectiveness of HDC/SCR could not be established ... ."[36] In Glauser-Nagy, a case in which an assured sought coverage for a similar experimental drug, "[t]he witnesses for both sides agreed" that efficacy could not be proven.[37] In Elsroth, another such case, there was "simply no evidence" of the drug's efficacy.[38] Finally, in

[34] See Amgen Mem., pages 29-32.
[35] See Amgen Mem., page 29.
[36] See Graham v. Medical Mut. of Ohio, 130 F.3d 293, 296-97 (7th Cir. 1997).
[37] See Glauser-Nagy v. Medical Mut. of Ohio, 987 F. Supp. 1002 (N.D.Ohio 1997).
[38] See Elsroth v. Consol. Edison Co., 10 F. Supp. 2d 427, 432 (S.D.N.Y. 1998).

Hassan, a case in which a prisoner sought interferon treatment for his hepatitis, his own doctor conceded that "interferon treatment is effective in only a small number of hepatitis patients, and that even for those patients who respond well to such treatment, there is a high rate of relapse."[39]

In this litigation, by contrast to all of the cases discussed above, the plaintiffs' physician, the Principal Investigator designated by Amgen to be its only representative to have contact with the plaintiffs, to protect them as human subjects and to provide them care, opines that it is in their best therapeutic interest to be resupplied GDNF and that, without it, they will continue to deteriorate as their disease progresses.

As has already been stated, the issue of irreparable harm could not be clearer. Plaintiffs are sick now and getting worse. The issuance of an injunction will mean they will receive therapy that will halt this continuous state of deterioration and drastically improve their lives on a day-to-day basis.

(c.) The Plaintiffs Have a Likelihood of Succeeding on the Merits Of Their Claims

The essence of Amgen's argument on the merits of the plaintiffs' claims is that the Informed Consent Document does not contain an express promise to supply the drug even if it is safe and effective.[40] The fatal flaw in this argument is that plaintiffs do not contend that the Informed Consent Document is the entire contract between the parties or the sole source of Amgen's promises. As Amgen is well aware, in the context of human subject research, an informed consent document is merely evidence of a process that is supposed to take place between the principal investigator and the subject.[41] It is within that process that promises are made and the agreement is formed. Here, both parties to that process acknowledge that the

[39] See Hassan v. Khanyile, 1998 WL 264834 at * 1 (S.D.N.Y. May 21, 1998).
[40] See Amgen Mem., pages 19-39.
[41] See 45 C.F.R. 46.116.

plaintiffs had reason to believe that they would continue to receive GDNF so long as it was in their therapeutic best interest.

In this regard, Dr. Hutchinson's Certification provides that

> I forcefully reject Amgen's suggestion that I made promises to my patients that they would receive GDNF no matter what the results of the study. This makes no sense whatsoever and would be entirely out of character. For example, one of my patients asked me if he would continue to receive GDNF after the study was completed, and I told him that if the study was successful, Amgen would of course keep him on the drug. He asked me to confirm this with Amgen, and I telephoned the director of the project, Michael Traub, who confirmed this.
>
> The patients certainly had every reason to believe that if the drug were safe and effective, Amgen would continue to supply it.

Amgen's argument also fails to acknowledge that, to the extent that the Informed Consent Document did not expressly promise the plaintiffs the right to receive GDNF indefinitely so long as it was deemed safe and effective, the plaintiffs were laboring under what researchers commonly term the "therapeutic misconception," the phenomenon whereby participants in a clinical trial form "a belief that the purpose of a clinical trial is to benefit individual subjects, rather than to generate data for the purpose of advancing scientific knowledge."[42] Surely no individual would agree to have a hole drilled in his or her skull, a pump implanted in his or her stomach, and a catheter placed between the two, with the concomitant risk of significant medical complications, if that individual thought that he or she was a mere guinea pig subject to the whims of the company providing the pharmaceutical traveling between the pump and his or her skull.

The plaintiffs were not mere guinea pigs. Rather, their trusted doctor was treating them with GDNF. Recognizing this, the very informed consent document that Amgen claims gives

[42] See, e.g., Alice K. Page, Ethical Issues In International Biomedical Research: An Overview, 37 Journal of Health Law 629, 649 (Fall 2004).

the plaintiffs no rights whatsoever expressly gave them a very important right – the right to let the Principal Investigator, Dr. Hutchinson, make the choice as to whether or not they would be withdrawn from the study.[43]

It is clear that the plaintiffs have demonstrated a clear likelihood of success on the merits or, at the very least, sufficient questions going to the merits and an absence of harm on the part of Amgen in the event that an injunction issues.[44]

(d.) The Plaintiffs Have Made a Valid Public Policy Claim

This is not a case about desperate patients seeking drugs that science, medicine, and the government say do not work. To the contrary, here, both plaintiffs' physician and the FDA believe that GDNF is safe and effective. The public policy argument is, thus, not whether patients should run the hospital, as Amgen frames it. The issue is whether the physicians should determine whether life saving therapy should cease or whether decision should be unilaterally in the hands of the drug company.

The various public organizations devoted to Parkinson's research have expressed their opinion on this public policy issue. According to Dr. Cohen, who, as previously stated, is the Executive Director of the Parkinson's Pipeline Project,

> The Parkinson Pipeline Project ... unanimously supports the [plaintiffs'] request for reinstatement of their GDNF treatments. ... By halting the GDNF trials, Amgen is denying the Parkinson's community potentially valuable information on GDNF therapy.
>
> * * * *

[43] See Amgen Mem., Exhibit 21 thereto (providing that "[t]he Principal Investigator may ... decide to withdraw you from the study under certain circumstances. Some possible reasons for withdrawing a subject from the study would [include] ... termination or cancellation of the study by the sponsor").

[44] See Amgen Mem., Exhibit 1 thereto, ¶ 68 (Affidavit of Dr. Perlmutter providing that "the costs associated with continuing patients on the GDNF study would have been relatively low").

New treatments average nearly 15 years to move from scientific discovery to the drugstore. People with Parkinson's do not have years to wait for a cure or better therapy; for us, time is simply not neutral. ...

* * *

What Amgen sees as the "failure" of its phase II, placebo control study to reach primary endpoints is not considered conclusive by many of the study doctors. They point to important differences between this study and the successful Phase I studies in the methods for applying the medication to the affected parts of the mid-brain and the doses administered (1/3), as well as flaws in the measurement and analysis methods. ...

Since Amgen ceased their treatments, many trial participants have been forced back into the prison of advanced Parkinson's disease, for which there are currently no other treatment options, since Parkinson's medications no longer work for them. ...

* * * *

Reinstatement of GDNF treatment is important not only to today's patients but to our prospects of being able to recruit sufficient numbers of people for future trials. If pharmaceutical companies do not treat human research participants with respect, if they ignore patients' viewpoints of the trial process and the evaluation of treatments, and cause participants unnecessary suffering, patients will become less inclined to volunteer for future clinical trials. All of us – people with Parkinson's, researchers and the pharmaceutical companies, such as Amgen – will lose.[45]

[45] See generally Exhibit C.

CONCLUSION

It is respectfully concluded that, for the foregoing reasons, a preliminary injunction directing Amgen to provide Dr. Hutchinson with GDNF and allow him to administer it to the plaintiffs, within seven days, must issue.

Dated: Tuesday, May 24, 2005

/s/
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