UNITED STATES DISTRICT COURT FOR THE
SOUTHERN DISTRICT OF OHIO
EASTERN DIVISION

CARETOLIVE,
a not-for-profit corp.,
Plaintiff,

Civil No. 2:08-CV-00005

JUDGE FROST

v.

MAGISTRATE JUDGE KING

U.S. FOOD and DRUG
ADMINISTRATION,
Defendant.

PLAINTIFF'S MEMORANDUM IN OPPOSITION TO FOOD AND DRUG ADMINISTRATION'S MOTION TO STAY PROCEEDINGS

Ours is a government of laws, laws duly promulgated and laws duly observed. No one is above the law: not the executive, not the Congress, and not the judiciary. One of our laws is the Freedom of Information Act (FOIA). That law, no less than any other, must be duly observed." *American Civil Liberties Union v. Dep't of Defense*, 339 F. Supp. 2d 501, 502 (S.D.N.Y. 2004) (internal citations omitted). The FDA needs constant reminding of this fact.

Defendant has failed to fully respond to the Freedom of Information Act (FOIA) requests made by Plaintiff, CareToLive, on August 15, 2008. FDA claims the request was sent to the wrong address but the name and address used were exactly as set forth by the FDA itself on its website, at the time the FOIA request was made. Regardless, the FDA confirmed receipt by no later than September 11, 2007. That alone makes the FOIA response significantly overdue.

Plaintiff did receive a response from the CBER division of the FDA on November 6, 2007. Plaintiff then received a response from the Commissioner in January 2008. In the January response, Commissioner Andrew von Eschenbach claimed he had no responsive documents. On February 26, 2008, that response changed and the Commissioner did admit that his office possessed documents relative to the request and did produce some documents. Those documents provided proof of the post AC lobbying of the commissioner by special government employee Howard Scher. Neither of these responses was fully responsive to the FOIA request because the most damning documents reside with Richard Pazdur of CDER.

At the FDA, the FOIA request was divided and sent to three separate divisions of the FDA. The documents believed to be the most likely to expose the unlawful and improper actions of the FDA relative to Provenge, are possessed by Richard Pazdur at the FDA. These responsive documents, either possessed or

possibly destroyed during pending litigation by Dr. Richard Pazdur, have thus far been purposely withheld by the FDA's CDER division. Dr. Pazdur is certainly aware of the CareToLive request but refuses to provide the documents, due to the fact that they will be demonstrative of his improper involvement in the conspiracy to sabotage Provenge. This Court will recall that Plaintiff expressed fear soon after litigation was filed in case number 07-729, that important documents might be destroyed.

In an effort to avoid the filing of this litigation, Counsel for Plaintiff made several calls to the CDER FOIA office. In the last call Counsel asked whether the documents could be expected soon (if the answer was yes this litigation may not have been filed). Instead the response was that Counsel would not receive them any time soon, and thus this litigation commenced. A previous call in early December was responded to with a voice mail that said that they were "working on the request" and that "many of the documents would be the same as those that were already provided by CBER". The tone of the responses changed from early to late December. The tone in early December, versus the tone in late December/early January, went from being "informative and helpful" to more like a "your not getting them" tone. If CDER knew in early December that many of the documents would be the *similar* to those already produced by other divisions of the FDA, then it logically follows that they had already located documents, some the same, and

some different, and should have provided what they had to Plaintiff as required by law. If there is a certain order they take the requests in, why did they look at all, as was indicated by the FOIA representative. Without some knowledge as to the results of the search, the FOIA employee would not have known what was to be included in part of the response, as far back as early December. It can be surmised that she knew this because she had been working on the request which was now three months ago. Indeed it begs the question: how did they even have time to see what CBERS responsive documents were and why did they need to.

The statutory deadline imposed upon CDER by the Freedom of Information Act has not been complied with. All of the responses were received after the FOIA mandated deadline. To date, the CDER response has still not been received, although it has been approximately 7 months from when it was requested.

Despite the *very simple* nature of the request, and despite the ability of both CBER and the Commissioner's office to respond, the CDER division, and in particular Richard Pazdur, has not responded. The request was responded to by both other divisions and that response was less than a total of 50 pages combined, which is certainly not voluminous. Now Defendants seek a stay under, 5 U.S.C. § 552(a)(6)(C).

While 80 men die every day without having had the ability to access Provenge, the FDA continues to refuse to act in a reasonable and humanitarian

manner. While 90,000 AIPC patients suffer daily, the therapy that will help them, sits on a shelf unable to be accessed, because of the ambitions of Richard Pazdur. The FDA knows darn well exactly where the documents are, and, has the ability to provide them quickly. It is not the *inability* to respond that keeps the documents from Plaintiff. It is their *unwillingness to respond*. The FDA even now refuses to act in a reasonable and humane manner. Most likely CDER has the documents that have been requested but chooses not to provide them because of the embarrassment and increased scrutiny that the agency will incur when they release the documents. The agency has not exercised due diligence, and has acted in bad faith, *both* in the underlying matter, and in the refusal to provide the documents requested, in a timely manner. These documents will help to uncover the improper actions of the FDA, but the agency is compounding its wrong doing, by now refusing to provide the documents. The documents requested are not voluminous, and no specific reason has been set forth by Defendants as to why the FOIA request to CDER has not been responded to. Contrary to other cases cited by Defendants, the request by Plaintiff is a very simple, straightforward, and an easily complied with request. This is a high profile matter and the whereabouts of these documents has likely been discussed, ascertained and even reviewed by general counsel and/or by top officials at the FDA.

If the Court is insistent on staying this matter, then prior to or during the stay, the Court should allow Plaintiff to take the deposition of Richard Pazdur and the CDER FOIA representative, so that the Plaintiff can present evidence as to the absolute simplicity of the response to the FOIA request, and show that it is the agency's unwillingness, rather than its inability to respond, that is causing the non compliance. The CTL request is a very simple, basic, and easy request. It does not seek voluminous amounts of documents. It is very specific and very easy to respond to, as demonstrated by the two other FDA divisions who did in fact respond. In fact two other departments were able to respond in November and January (revised response in February). The Defendants have failed to demonstrate a reason why it would be more difficult for CDER to comply, versus the Commissioner's office or the CBER division. The CDER division has not responded at all to the Plaintiff's FOIA request other than to take several phone calls from Plaintiff seeking compliance. The fact that the most culpable of divisions is the one that has failed to respond, is not coincidental.

The importance of the request is that the response if full and complete will show that Richard Pazdur, an employee in the CDER division of the FDA, that had no reason to be involved in the CBER decision whether or not to approve Provenge, conspired with others to sabotage Provenge.

> **(6)(A)** Each agency, upon any request for records made under paragraph (1), (2), or (3) of this subsection, shall--

(i) determine within 20 days (excepting Saturdays, Sundays, and legal public holidays) after the receipt of any such request whether to comply with such request and shall immediately notify the person making such request of such determination and the reasons therefor, and of the right of such person to appeal to the head of the agency any adverse determination; and

……..

(B)(i) In unusual circumstances as specified in this subparagraph, the time limits prescribed in either clause (i) or clause (ii) of subparagraph (A) may be extended by written notice to the person making such request setting forth the unusual circumstances for such extension and the date on which a determination is expected to be dispatched. No such notice shall specify a date that would result in an extension for more than ten working days, except as provided in clause (ii) of this subparagraph.

(ii) With respect to a request for which a written notice under clause (i) extends the time limits prescribed under clause (i) of subparagraph (A), the agency shall notify the person making the request if the request cannot be processed within the time limit specified in that clause and shall provide the person an opportunity to limit the scope of the request so that it may be processed within that time limit or an opportunity to arrange with the agency an alternative time frame for processing the request or a modified request. Refusal by the person to reasonably modify the request or arrange such an alternative time frame shall be considered as a factor in determining whether exceptional circumstances exist for purposes of subparagraph (C).

(iii) As used in this subparagraph, “unusual circumstances” means, but only to the extent reasonably necessary to the proper processing of the particular requests--

(I) the need to search for and collect the requested records from field facilities or other establishments that are separate from the office processing the request;

(II) the need to search for, collect, and appropriately examine a voluminous amount of separate and distinct records which are demanded in a single request; or

(III) the need for consultation, which shall be conducted with all practicable speed, with another agency having a substantial interest in the determination

of the request or among two or more components of the agency having substantial subject-matter interest therein.

(iv) Each agency may promulgate regulations, pursuant to notice and receipt of public comment, providing for the aggregation of certain requests by the same requestor, or by a group of requestors acting in concert, if the agency reasonably believes that such requests actually constitute a single request, which would otherwise satisfy the unusual circumstances specified in this subparagraph, and the requests involve clearly related matters. Multiple requests involving unrelated matters shall not be aggregated.

(C)(i) Any person making a request to any agency for records under paragraph (1), (2), or (3) of this subsection shall be deemed to have exhausted his administrative remedies with respect to such request if the agency fails to comply with the applicable time limit provisions of this paragraph. If the Government can show exceptional circumstances exist and that the agency is exercising due diligence in responding to the request, the court may retain jurisdiction and allow the agency additional time to complete its review of the records. Upon any determination by an agency to comply with a request for records, the records shall be made promptly available to such person making such request. Any notification of denial of any request for records under this subsection shall set forth the names and titles or positions of each person responsible for the denial of such request.

(ii) For purposes of this subparagraph, the term “exceptional circumstances” does not include a delay that results from a predictable agency workload of requests under this section, unless the agency demonstrates reasonable progress in reducing its backlog of pending requests.

(iii) Refusal by a person to reasonably modify the scope of a request or arrange an alternative time frame for processing a request (or a modified request) under clause (ii) after being given an opportunity to do so by the agency to whom the person made the request shall be considered as a factor in determining whether exceptional circumstances exist for purposes of this subparagraph.

(iii) This subparagraph shall not be considered to affect the requirement under subparagraph (C) to exercise due diligence.

There are no special circumstances that justify the agencies lack of due diligence in this very important matter. Plaintiff would go so far as to assert that the documents are at least partially in hand but are being intentionally withheld by the agency to avoid embarrassment in the face of heightened public and congressional scrutiny of the FDA's mishandling of this matter.

The procedural provisions of the Act in particular, reflect the nature of the obligation which Congress intended to impose on agencies in the production of agency records. First, Congress has provided that agencies normally must decide within 10 days whether to comply with an FOIA request unless they can establish "unusual circumstances" as defined in the Act. 5 U.S.C. §§ 552(a)(6)(A), (B). The "unusual circumstances" specified by the Act include "the need to search for and collect the requested records from field facilities and other establishments that are separate from the office processing the request." Only general and hypothetical reasons have been given by the FDA for non compliance to date. In order to avoid having to outright lie to this Court, Defendants couch everything in terms of generalities. To be specific is to have to be truthful, in other words, they would have to make misrepresentations to the Court. The truth is that these documents have already been found, (at least in part) identified, and policed, but are being withheld in bad faith. At a deposition, the FDA employees would have to admit after being placed under oath, that these documents have been or can be easily and

readily produced, and in fact have been identified and reviewed by the legal department, yet are being withheld.

The FOIA generally provides that every federal agency shall promptly make available upon request records reasonably described. 5 U.S.C. § 552(a)(3)(A). *Rugiero v. U.S. Dept. of Justice*, 257 F.3d 534, *543 (C.A.6 (Mich.),2001). In general, the courts are established to declare rights, and they should not take into account the resources of the defendant as an excuse for not declaring a right. Otherwise, the courts will have to go beyond examining the relationship of the parties, generally a sufficiently difficult task, and go into the relationship of the defendant to all other persons having a claim upon him, an essentially unmanageable task,*Open America v. Watergate Special Prosecution Force ,* 547 F.2d 605, 620 (D.C.Cir.1976) (Leventhal, J., concurring); *Caswell v. Califano,* 583 F.2d 9, 17 (1st Cir.1978) ("the vindication of almost every legal right has an impact on the allocation of scarce resources. And the courts ... can hardly permit the legal rights of litigants to turn upon the alleged inability of the defendant fully to meet his obligations to others."); *cf. Maggio v. Zeitz,* 333 U.S. 56, 68 S.Ct. 401, 92 L.Ed. 476 (1948) (limited circumstances in which court should stay enforcing declared right because of impossibility of compliance); *United States v. Rylander,* 460 U.S. 752, 103 S.Ct. 1548, 1552, 75 L.Ed.2d 521 (1983) (defendant has burden

of proving impossibility of compliance). Holden v. Heckler 584 F.Supp. 463, *492 (D.C.Ohio,1984).

These “administrative deadlines” of Section 552(a)(6)(A) are modified by the following subparagraph (B), which provides that in “unusual circumstances,” for example, where the request involves *voluminous records, or records must be obtained from field office or storage*, the total time limits may be extended for an additional ten working days. Thereafter, an applicant who has not received either the information requested or denial of his request will be deemed to have exhausted his administrative remedies (subparagraph (C)), and may then bring suit in the appropriate district court pursuant to Section 552(a)(4)(B). The specific language of the 1974 amendments on which the Government relies appears in 5 U.S.C. s 552(a)(6)(C): “If the Government can show exceptional circumstances exist and that the agency is exercising due diligence in responding to the request, the court may retain jurisdiction and allow the agency additional time to complete its review of the records.” *Open America v. Watergate Special Prosecution Force* 547 F.2d 605, *609-610, 178 U.S.App.D.C. 308,**312 - 313 (C.A.D.C. 1976).

The assertion of the agency that they cannot comply with the request because of unusual circumstances is made in bad faith. The FDA merely seeks to avoid or delay further scrutiny by the public and Congress while this matter remains in the spotlight. The FDA is under intense pressure by numerous

Congressmen over their inept actions in the Provenge matter, and the last thing they want is the documents proving the improper involvement of the co-conspirators with Richard Pazdur, to be displayed to the public.

As stated in Open America v. Watergate Special Prosecution Force

> The "exceptional circumstances" of subparagraph (C) are something different. "If the Government can show exceptional circumstances exist and that the agency is exercising *due diligence in responding to the request*, the court may retain jurisdiction and allow the agency additional time to complete its review of the records." This was put in as a safety valve after the protests of the administration that the rigid limits of subparagraphs (A) and (B) might prove unworkable.[FN11] Subparagraph (C) obviously contemplates (1) that the agency *611**314will have found it impossible to respond to a request within the time limits specified, even with all due diligence, and for reasons not confined to those listed in subparagraph (B); [FN12] (2) that the requesting party will have gone to court; and (3) that the court *612**315will hear evidence (a) as to what "exceptional circumstances" may excuse the Government from the rigid time limits of subparagraphs (A) and (B), and (b) as to the "due diligence" of the agency, if that is challenged by plaintiff.
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> Open America v. Watergate Special Prosecution Force 547 F.2d 605, *610-612, 178 U.S.App.D.C. 308,**313 - 315 (C.A.D.C. 1976)(emphasis added)

The Court went on to say "We do not see, either on the face of the statute or on any sane analysis of the situation confronting the FBI and all other Government agencies in regard to Freedom of Information Act requests, why we should order such a reallocation of resources. *Plaintiffs have alleged no urgency, have alleged no exceptional need, for the information they seek*" Open America v. Watergate Special Prosecution Force 547 F.2d 605, *614, 178 U.S.App.D.C. 308,

**317 (C.A.D.C. 1976)(emphasis added).This case is different because 90,000 men that currently suffer from late stage prostate cancer (AIPC) will die from their cancer (unless something else kills them first) without any reasonable hope for remission. Each day of delay these men get sicker and thus less likely to benefit from Provenge. Each day of delay causes the whole field of immunotherapies for cancer treatment to be further delayed. For these 90,000 men, each day their immune systems get weaker, and Provenge is less likely to help them. These men will benefit from a therapy voted by a panel of 17 experts to be safe and for which there has been established substantial evidence of efficacy. The documents will shed light on the corrupt process within the FDA that led to the improper, inhumane and unreasonable action of the FDA in denying approval to Provenge. Urgency and exceptional need make this case different than the Open America case.

Attached hereto as “Appendix A”, is the Science and extent of harm arguments made by Plaintiff in the 6th Circuit Court of Appeals. The appendix sets forth in clarity, the arguments relative to the urgency and need of access to Provenge. The documents requested support the arguments made by CareToLive and will allow the public and Congress to exercise proper oversight over an FDA that has become dysfunctional. Once the public is aware of all the facts that transpired in the FDA when they capriciously denied approval to Provenge, and the

lack of due process afforded the dying men by the FDA, public outrage will force the FDA or Congress to fix the terrible mistake that has been made, even if the Courts will not act on the underlying merits of the arguments made by Plaintiff in CTL vs. FDA, case number 07-729. As stated in Open America v. Watergate: “We believe that Congress intended for a district court to require an agency to give priority to a request for information if some exceptional need or urgency attached to the request justified putting it ahead of all other requests received by the same agency prior thereto”. We believe also that Congress wished to reserve the role of the courts for two occasions, (1) when the agency was *not showing due diligence in processing plaintiff's individual request* or was lax overall in meeting its obligations under the Act with all available resources, and (2) when plaintiff can show a *genuine need* and *reason for urgency* in gaining access to Government records ahead of prior applicants for information. Open *America v. Watergate Special Prosecution Force* 547 F.2d 605, *615, 178 U.S.App.D.C. 308, **318 (C.A.D.C. 1976). The urgency and need for this treatment for an unmet medical need, is set forth in Appendix A. This is unprecedented in that the FDA has never overruled an expert panel that voted overwhelmingly for approval of a therapy for a life threatening condition for which no viable alternative treatments exist. The decision occurred because of the wrongful conspiracy that will become clearer upon production of the documents requested by CTL under FOIA.

The public has an interest in accountability, along with a properly functioning FDA that does not allow the will of a single, misguided individual, who recruited others to assist him, to thwart advancement in the fight against cancer.

CONCLUSION

The Plaintiffs FOIA request from the CDER division of the FDA was neither complex not did it request voluminous or confidential documents. It was a simple, straightforward request which was seemingly easily complied with by two other agency divisions. This is a matter of great public importance and these documents are required to demonstrate the capricious nature of the actions taken by the FDA and the improper manipulation of the process by Richard Pazdur who conspired with others to block the approval of Provenge. The reply from both CBER and the Commissioner's office was a few pages of easily accessible information. The Plaintiff, accompanied by an IT expert, and with access to Richard Pazdur’s computer, (even if done in camera), could obtain the information in less than one hour. The documents could have been provided in less than 10 % of the time spent by the FDA in defending against this complaint.

Respectfully submitted,

S/Kerry M. Donahue

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Kerry M. Donahue
6295 Emerald Parkway
Dublin, Ohio 43016

CERTIFICATE OF SERVICE

This motion for leave has been e-filed and thus sent to all parties of record by the Clerk's e-filing system.

Kerry M. Donahue

APPENDIX A

THE SCIENCE

Its is against the manifest weight of the evidence to say that the AIPC patients awaiting Provenge suffered no harm because they have merely been denied a speculative future benefit because Provenge has been proven beyond a reasonable doubt to be both safe and effective. Never before has the FDA not followed the overwhelming recommendation of its Advisory Committee when considering a treatment for a serious life threatening condition. It is only because of the clearly capricious conduct by the FDA that these men continue to be denied Provenge.

The agency attempts to underwhelm the Court by stressing a 4.5 month “average” extension in survival to Provenge patients. That understates the effectiveness. Average is different from median. It’s an important distinction because misuse of the term "median survival" is one of the deceptive arguments used by those who are against Provenge approval (FDA). When anti-Provenge forces use the "average" terminology and attribute it to the median, they are undercutting the total Provenge beneficial effect. At the time of the committee meeting it is estimated that the actual average survival benefit in the 9901 trial

was in the 10-12 month range, judging from the likely survival through Feb/Mar 2007 of 20 out of the 28 three-year survivors from 10/04. These 20 Provenge arm survivors would have lived anywhere from 5.5 to 7 years after their randomization between 1/00 and 10/01.

All trials show that Provenge is efficacious by extending survival (D9901 and D9902a). Triple the survival after 3 years. All six clinical studies following PC patients after Provenge treatment have all demonstrated the effectiveness of Provenge. The Provenge arm had a *median* survival advantage of 4.5 months vs. the control arm. The *median* survival is calculated from each arm by taking the survival time of the person in each arm *at the 50th percentile*. It does not reflect the true long term benefit of a treatment. The Appellee stresses that result because the layman tends to misinterpret it. Numerous patients are doing well on an ongoing basis at 5, 6 and even 7 years since receiving Provenge, whereupon the men who were randomized to placebo in these trials are nearly all dead. For example, say for two treatments, “a” and “b”, the median is a month. After a year all patients in group “a” are dead yet all remain alive in group “b”. The median stays the same in spite of the fact that many patients are still alive in “b”.

The more stunning figure is the 34% survival after three years in the Provenge arm, vs 11% in the control arm. This is a disease stage where the typical survival was 16-19 months, so a 34% three-year survival is very impressive. Also, we knew that in March 2007, only 8 of the 28 three-year survivors in the 9901 trial had died (the calculations for the trial ended in Sept 2004). Therefore, this means that as of 3/07, 20 out of 82 men survived between 5.5 and 7.1 years (the enrollment period for 9901 was 1/00 to 9/01).

The agency also stresses that Provenge missed the no longer favored primary endpoint, Time to Progression (TTP). When the trial began nearly 10 years ago the FDA suggested this TTP endpoint, which has since been determined by the FDA, including Drs. Scher and Hussain, *to be less important than survival*, which is an endpoint that cannot be faked or manipulated. What is meant when the FDA says "it missed its primary endpoint" is that it did not slow selected symptoms of disease progression to an *extremely statistically significant level*. The p value, as calculated by the study investigators, was 0.052, meaning that it barely missed being "stat sig" to the arbitrarily high level of 0.05. It is not as if the results show that the treatment "failed to slow progression." The results do show that the treatment slowed progression of symptoms of the disease. *Most*

biostatisticians would call a p=0.052 level of significance “nominally statistically significant.” Why the FDA did not think so in this case is unknown.

Unfortunately the FDA forced clerical errors to be counted in the final analysis, which meant that the FDA-calculated p value was 0.085. This still means that the slower progression seen in the Provenge arm was 91.5%-94.8% due to the Provenge, and not due to random chance. Therefore, combined with the 0.01 survival p value (99% due to the Provenge), you have a pretty strong correlation. So, should a correlation of 91.5% (low end of ttp) and 99% be thrown completely out, as the Appellee suggests by omission? Not when, in the real world, you are talking about people's lives. Not when the FDA hasn’t believed since at least 2005 that TTP is not an appropriate endpoint.

Fundamentally, the FDA denied Provenge because it did not meet an endpoint the FDA has already said is unacceptable. Provenge met the survival endpoint, *the only endpoint the FDA has accepted for approval since 2005*, at the p=0.01 threshold of significance. There is no defensible, real-world reason (as opposed to biostatistical mathematical abstractions) why the data on survival is less accurate simply because it was not listed as a “primary” endpoint. People die

when they die, and whether that death is counted first or second on a piece of paper makes no difference as to whether the person is dead or alive.

Importantly the FDA knew full well that Provenge had missed on the inappropriate FDA advised endpoint of TTP *when it accepted the BLA submission.* The later proclamation that more data were needed because Provenge missed on TTP was therefore post ad hoc contrived. This was completely understood and accepted by the FDA and was not supposed to be a barrier to approval. The scientific community has changed its thinking on TTP and determined along with the FDA that TTP is a chemotherapy evaluation technique that does not translate to evaluation of the efficacy of an immunotherapy like Provenge. The FDA's Oncologic Drugs Advisory Committee (ODAC) determined in 2005 that *survival was the only acceptable endpoint for prostate cancer*. Every pivotal trial for AIPC since then has been advised by the FDA to make survival as a primary endpoint. The FDA has, to the Appellant's knowledge, never agreed to a Special Protocol Assessment for an AIPC trial with any primary endpoint but survival.

Now, take Provenge's negligible side effects when compared to the only currently approved treatment for late stage prostate cancer, a Chemotherapy treatment called Taxotere. Taxotere kills 52% of its advanced PC patients outright

according to published data, not to mention its other severe and debilitating side. Despite the severe side effects, Taxotere extends life on average by only 2.5 months. Compared to Provenge, which has occasional side effects of mild flu like symptoms for a few days after treatment (6-9 days total for the entire course of treatment), the current approved treatment is *less* safe and *less* effective. What the antiquated FDA has done is to evaluate new therapies, like Provenge, the same way it has evaluated chemotherapy treatments through the years. The FDA, by virtue of its own revised trial design guidance, has demoted the importance of traditional markers such as TTP, subordinating them to overall survival. Nonetheless, Appellees continue to trot out TTP like a champion mare when it suits them in this case, while telling anyone else designing a trial that it is an unacceptable endpoint for making an approval decision.. The 9902a study was terminated early because the applicant, prior to the FDA arriving at the same conclusion, determined that survival *should* be the endpoint rather then TTP, and *not* because TTP would be missed as suggested by Appellee.

This begs the question to Appellees: "Which is it?" Your guidance since 2005 has been that TTP is not a suitable endpoint for an approval decision in AIPC, only survival. Yet in the situation with Provenge, TTP was *supposedly* the driver

for the decision and the FDA said the survival benefit was insufficient for approval.

The safety profile of Provenge was never really an issue, until Howard Scher (the FDA special employee, who according to newly established guidelines implemented right after the Provenge AC, would not have been eligible to participate in the process, *even* if just only his disclosed conflicts were considered) *after voting with all other AC members that Provenge was safe*, improperly implied in a post AC letter that there may be a safety issues. Appellees seek to use it again now as a second red herring to try to justify the non-approval decision. Appellees talk of concern of cerebral vascular accident ("CVA") events (strokes) but the CVA's were not statistically significant as, in this older patient population, small numbers of CVA events are normal. The risk of CVA's of U.S. men older than 65 is anecdotally estimated to be 2-3% per year. For the 147 patients in the 9901/9902A treated group, there were 8 CVA's. If one estimates that the average survival of this group for the three-year study period was ~26 months, this data would be consistent with the expected risk of CVAs. The Provenge *AC voted unanimously positive on the safety question,* a vote which occurred after the AC discussion of the issue, and members were informed that the FDA and Dendreon have planned to subsequently monitor 3000 Provenge patients for CVAs and any

other identified safety issues, in a post approval follow up study. Provenge is considered to have very minimal side effects, in stark contrast to chemotherapy treatments.

Importantly, the FDA statistician himself said that the chance that the survival data were in error was 1 in 40. Yet the FDA, at the urging of a few employees with their own agenda, delayed approval, with a request that rings hollow; "for more data". At the three year measuring point, 27% of high grade Gleason grade patients (the sickest to begin with) were alive vs 0% for placebo.

Plaintiff is not asking the FDA for any special treatment regarding the rigorous scientific license requirements. Provenge has met each and every Congressional statutory requirement as the submitted BLA data proves. It has also met the endpoint guidance the FDA put in place beginning in 2005. Only the FDA appears to be ignoring its own licensing requirements and guidance. Plaintiff merely seeks review of the Agency actions that appear to have been capricious.

EXTENT OF HARM

The error of the Court in accepting Defendants statement that, in not having access to Provenge the patients suffer a harm no different than when they wait for approval of other innovative treatments, misses the point that the FDA

acted capriciously in making the decision not to approve (CR). It's the capriciousness of the action that has caused the harm. A factual determination that the patients are only missing out on a merely speculative benefit is difficult to comprehend in the face of the scientific facts coupled with the overwhelming opinion of the 17 member expert committee, hand selected by the FDA to provide their opinions. The FDA's refusal to accept the decision of the experts in this matter is akin to this Court having the luxury of selecting a jury of 17 experts of its choice, from throughout the country, then having those experts review and listen to the evidence, and then ignore their verdict.

Approximately 27,000 men a year are dying from late stage prostate cancer. There are no good treatment options. Unlike other medications evaluated by the Courts, for the first time ever in any Court of Law, this discussion concerns a treatment for an absolutely terminal disease (AIPC) that has no chance of remission, and involves a treatment that was voted overwhelmingly to be safe and to have demonstrated substantial evidence of efficacy by the expert committee. AIPC is different from earlier stage prostate cancer, where 70% of men die of something other than their prostate cancer, or any other cancer that is in earlier stages. In those situations the patient could be treated by other medicines and could have their cancer go into remission. Dendreon sought access

to Provenge ONLY for late stage prostate cancer patients who are AIPC (androgen independent prostate cancer that has later returned after failure of hormone therapy, surgery, and radiation therapy). This is not a class of patients that has other reasonable treatments available or that has hope for remission. This is a first ever, absolutely unprecedented case whereby such circumstances exist, yet the patients are being denied access. The result (harm) is not some minor malady, it is death. Provenge is undeniably safe, so what possible harm could have resulted from conditional approval, enabling men to access it now while additional "data" are accumulated.

The harm done to persons who are already very sick, as late stage prostate cancer patients are, and who are allowed to get sicker by the day awaiting treatment, is irreparable. Sickness and chance of wellness in the case of late stage prostate cancer patients is compounded by an already weakened immune system, which becomes more damaged as the illness progresses and makes the chance of recovery more and more remote as the compromised immune system has less and less chance to repair itself to attack the cancer. Delay, non approval, and denial, all add up to the same thing, a rapidly approaching, painful death with no viable treatments. Unlike the patient class in *Rutherford*, unless something else kills them first AIPC patients will die from the cancer.

It is not only the harm to the individuals involved that we must consider in assessing the public interest. Our society as a whole suffers when we neglect the poor, the hungry, the disabled, the sick, or when we deprive them of their rights or privileges. Society's interest lies on the side of affording fair procedures to all persons, even though the expenditure of governmental funds is required. It would be tragic, not only from the standpoint of the individuals involved but also from the standpoint of society, were poor, elderly, disabled and sick people to be wrongfully deprived of essential benefits for any period of time.