DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JUL - 7 2000

TRANSMITTED VIA FACSIMILE

William A. Carter, M.D.
Chief Executive Officer
Hemispherx Biopharma, Inc.
One Penn Center
1617 JFK Boulevard
Philadelphia, PA 19103

RE: AMPLIGEN (POLY I:POLY C12U)
MACMIS #8800

Dear Dr. Carter:

This letter concerns materials disseminated by Hemispherx Biopharma, Inc. (Hemispherx) for its product, Ampligen, which is an unapproved new drug and the subject of an Investigational New Drug Application (IND) with the Food and Drug Administration (FDA). The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed these materials as part of its routine monitoring and surveillance program. From its review, DDMAC has concluded that Hemispherx is promoting Ampligen as safe and effective prior to approval, in violation of the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations.

BACKGROUND

Ampligen is an investigational new drug manufactured by Hemispherx Biopharma, Inc. The generic name of Ampligen is poly I:poly C12U. Hemispherx has indicated that it intends to develop Ampligen for the treatment of individuals with human immunodeficiency virus (HIV) and Chronic Fatigue Syndrome (CFS).

We previously issued an untitled letter, dated October 15, 1998, to Hemispherx for promoting Ampligen as safe or effective while the product was under investigation. In our letter, we informed you that your activities were in violation of the Act and applicable regulations. In your response, dated October 29, 1998, you assured us that Hemispherx would discontinue or revise all materials concerning Ampligen to conform with the Act and regulations.

However, notwithstanding your assurances, you continue to promote Ampligen as safe and effective prior to approval in your press releases and on your Internet website. Such

activities constitute promotion of an investigational new drug as safe or effective in violation of the Act and its implementing regulations. In addition, your promotional materials are false or misleading in that they fail to disclose facts that are material in light of representations made about Ampligen.

PRESS RELEASES

Hemispherx promotes Ampligen as safe and effective in several press releases. In addition, Hemispherx fails to reveal facts that are material in light of representations made about Ampligen.

Safety

In press releases, Hemispherx promotes Ampligen as "generally well tolerated" or "well tolerated" but fails to disclose risk information associated with the use of Ampligen. For example, in your press release dated February 17, 2000, entitled ***"Hemispherx Files for HIV Emergency Treatment IND and Phase II/III Trials,"*** you state, ***"To date, Ampligen has been studied in 126 patients and has been consistently well tolerated in its trials."*** However, toxicities that have been reported in dose-escalating studies of Ampligen in HIV-infected patients include, but are not limited to, flushing, chills, fever, chest tightness, nausea, malaise, shortness of breath, flu-like symptoms, leukopenia, neutropenia, and leukocytosis.

Effectiveness

In your February 22, 2000 press release, you present that, ***"...Ampligen demonstrated synergistic activity with anti-retroviral therapy leading to potential enhanced suppression of replicating HIV virus...."*** Similarly, in your press release of December 16, 1999, entitled ***"Hemispherx Announces New Approach to HIV Multi-Drug Resistance,"*** you state, ***"...multiple HIV genetic mutations that made the 14 anti-HIV drugs approved by the Food and Drug Administration (FDA) ineffective did not diminish the pronounced anti-viral effectiveness of Ampligen."*** These statements make conclusions concerning the effectiveness of Ampligen, an investigational new drug, in violation of the Act and its implementing regulations.

INTERNET WEBSITE

Although some of the materials referenced below were originally issued by third parties, this letter does not concern the third parties or their original communications.

Your website, www.hemispherx.com, contained a direct link to transcripts of Dr. Mazlen's CFS Radio Program, which promote Ampligen as safe or effective. For example, the linked transcript from Dr. Mazlen's CFS Radio Program from February 28, 1999, presents the following conversation between Dr. Mazlen and Dr. Paul Cheney:

- ***First, of all, there's no doubt in my mind as I've seen it in clinical practice that this drug [Ampligen] is bioactive in this syndrome [CFS]...***
- ***Ampligen also has potent antiviral properties as well...***

- ***The other parallel issue for Ampligen is that it appears that the longer that you take it, if you are responding to it, the better the outcome…***

Further, your website is directly linked to a web page containing anecdotal reports of CFS patients who participated in clinical trials. For example, on the ***"Other CSF Links"*** page on your website there is a link entitled, ***"The 'Ampligen 511 Panel' Patients Speak About Their Experiences with Ampligen at the AACFS Conference."*** The link goes directly to the patient testimonials that are located at www.cfids-me.org. These patient testimonials promote Ampligen as safe or effective prior to approval. The following statements are examples of patient testimonials:

- ***…after 10 years of consistent abnormality, a return to normal ranges for the first time, with Ampligen being the only new variable in my life, clearly demonstrates the efficacy of this drug***
- ***Unlike IV gamma globulin, Ampligen is not offering me only symptomatic relief. I am healing from the inside out.***
- ***There has been a dramatic improvement in my quality of life***
- ***Call me Lazarus…the only reason I am here and functioning pretty well today is Ampligen. I have absolutely no doubts about its efficacy in the treatment of my illness***
- ***No Adverse Effects–And Immediate Benefits to Boot-The Ampligen Bounce***

Lastly, your website also contains press releases, including but not limited to those previously described, that promote Ampligen as safe or effective.

REQUESTED ACTIONS

Hemispherx should immediately cease dissemination of materials or activities that contain these and similar claims, representations, and conclusions concerning the safety or effectiveness of Ampligen. In addition, Hemispherx should respond in writing no later than July 21, 2000 describing its plan to comply. Hemispherx should also include a list of materials being discontinued, as well as the date of discontinuation.

We note that the link from your website to Dr. Mazlen's CFS Radio Program has been discontinued since March 10, 2000, however, the link to the patient testimonials is currently active.

Your response should be directed to the undersigned by fax at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-42, 17B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds Hemispherx that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #8800.

Sincerely,

/S/

Ele Ibarra-Pratt, R.N., M.P.H.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

HEMISPHERx BIOPHARMA, INC.

Hemispherx Files for HIV Emergency Treatment IND and Phase II/III Trials

PHILADELPHIA, Feb. 17 /PRNewswire/ -- Hemispherx Biopharma, Inc. (Amex: HEB; HEBws) today announced that it has filed for HIV Emergency Treatment IND and Phase II and Phase III trials with the Food and Drug Administration.

The Company's new HIV Emergency Treatment IND application is intended to be used to study the effects of Ampligen on the growing number of people with AIDS (PWA's) who are developing resistance to their currently approved regimens, some of whom have been left with no other clinical options. Hemispherx's Phase II and Phase III trials are intended to study the effects of Ampligen in combination with several Highly Active Antiretroviral Therapy (HAART) regimens, which have been structured by Anderson Clinical Research.

``This is a very exciting development at a critical time in the epidemic when the promise of Highly Active Antiretroviral Therapy has begun to fade," said Dr. William A. Carter, Chairman and Chief Executive Officer of Hemispherx. ``Clinical trials and Emergency Treatment Protocols need to begin now to target the growing number of patients who are quickly exhausting their therapeutic options."

These new filings follow the lead of other studies, which were presented at the IBT Conference in Boston last December, that showed Ampligen is highly synergistic with 12 of the 14 approved HIV medications. To date, Ampligen has been studied in 126 patients and has been consistently well tolerated in its trials. The new studies will evaluate not only the previous surrogate markers, such as the improvements in Cell Mediated Immunity, but how Ampligen, in Immune Base Therapy, may further reduce viral load in people with AIDS.

HEB's Web Site: http://www.hemispherx.com

Information contained in this news release other than historical information, should be considered forward-looking and is subject to various risk factors and uncertainties. For instance, the strategies and operations of Hemispherx involve risks of competition, changing market conditions, changes in laws and regulations affecting these industries and numerous other factors discussed in this release and in the Company's filings with the Securities and Exchange Commission. Accordingly, actual results may differ materially from those in any forward-looking statements.

HEMISPHERx BIOPHARMA, INC.

Hemispherx Biopharma Clarifies Treatment IND

PHILADELPHIA, Feb. 22 /PRNewswire/ -- In response to inquiries regarding the Hemispherx Biopharma, Inc. (Amex: HEB; HEBws) press release of February 17, 2000, the Company stated that the Emergency Treatment IND application refers to special sections of the Code of Federal Regulations as amended by the FDA Modernization Act (FDAMA) of 1997. Accelerated access to promising investigational drugs is permitted specifically for patients who have potentially life threatening illnesses.

The company also stated that it had previously sponsored and completed an FDA authorized Phase II controlled study with HIV/AIDS patients, which was published in a peer reviewed medical journal.

Based in part on the results of recent laboratory studies presented at the Immune Based Therapy-2 (IBT-2) and Search for a Cure Conferences in Boston, Massachusetts, Ampligen® demonstrated synergistic activity with anti- retroviral therapy leading to potential enhanced suppression of replicating HIV virus. These new data prompted some AIDS activists and clinicians to demand the organization of a Treatment IND and the development of several Phase III trials that may confirm the data seen in earlier clinical studies, including the Phase I/II Federally sponsored AIDS Clinical Trial Group (ACTG) study designated number 038, also previously published in a peer reviewed medical journal.

A Company spokesperson said that it expected, in cooperation with FDA scientists and FDA clinicians, to devise strategies that would accomplish expanded access while collecting additional medical information on efficacy and safety. The company said that the magnitude of side effects of the presently approved anti-retroviral drug regimens was formidable, and that it would work closely with the FDA to evaluate side-effect profiles when Ampligen® is added to these regimens. To date, all published studies have suggested that Ampligen® is generally well tolerated.

Information contained in this news release other than historical information, should be considered forward-looking and is subject to various risk factors and uncertainties. For instance, the strategies and operations of Hemispherx involve risks of competition, changing market conditions, changes in laws and regulations affecting these industries and numerous other factors discussed in this release and in the Company's filings with the Securities and Exchange Commission. Accordingly, actual results may differ materially from those in any forward-looking statements.

HEMISPHERx BIOPHARMA, INC.

Hemispherx Announces New Approach to HIV Multi-Drug Resistance

Test Results Show Potential Advantages of Immune Therapy When HIV Undergoes Massive Genetic Mutation

PHILADELPHIA, Dec. 16 /PRNewswire/ -- Hemispherx Biopharma, Inc. (Amex: HEB; HEBws) today announced that recent independent laboratory test results show potential advantages of its product Ampligen® when virologic failure occurs clinically with the presently available arsenal of anti-HIV drugs.

According to findings presented today at the Search for a Cure Conference in Boston, multiple HIV genetic mutations that made the 14 anti-HIV drugs approved by the Food and Drug Administration (FDA) ineffective did not diminish the pronounced anti-viral effectiveness of Ampligen®. For example, viral resistance to all members of the newest class of powerful HIV inhibitors -- termed protease inhibitors -- were completely overcome by Ampligen®.

Of the nearly 345,000 patients receiving anti-HIV treatment in the U.S., an estimated 60% have failed with their current drug regimen, in part due to the development of drug resistance caused by viral mutations.

These results, developed by independent researchers at the University of California at Irvine, were presented as a companion paper to a new report that found that Ampligen® provided potent antiviral therapeutic synergy against the unmutated form of the virus with 12 of the 14 available FDA-approved anti-HIV drugs.

The new test tube studies examined various concentrations of the different drugs and multiple strains of highly drug-resistant HIV (isolated from HIV-infected individuals in the U.S.) under conditions designed to simulate the clinical situation. In some of the tested cases, HIV resistance to available antiretroviral drugs actually increased more than 20,000 times, such as to the newer protease inhibitors, without altering the anti-viral effectiveness of Ampligen® in any detectable way.

``It is sobering to realize that the so-called highly active antiretroviral therapy (HAART) is actually not always active enough," said William A. Carter, Chairman and Chief Executive Officer of Hemispherx. ``As we strive to induce a remission and to eradicate HIV, we need as physicians to consider why and how a well-documented small fraction of HIV-infected individuals, termed 'clinical non-progressors,' escape the AIDS-defining events indefinitely, sometimes even without the benefit of HAART.

``Recent studies suggest," Dr. Carter added, ``that the immune systems of these protected individuals are really working differently, and they seem to manipulate HIV more like a herpes virus infection, such as cold sores, rather than as a lethal infection. The overarching question is how can immune-

based therapy help drug (HAART) therapy to achieve a similar highly favorable outcome?"

Because double-stranded RNA technology, which includes Ampligen®, represents a new mechanism of immune action distinctly different from that of any of the available 14 FDA-approved drugs, it is a most promising area for further investigation.

Hemispherx Biopharma, Inc. is a biopharmaceutical company specializing in new therapeutic approaches to HIV/AIDS, Chronic Fatigue Syndrome (CFS) and hepatitis B/C utilizing the immune system. It has offices in Philadelphia, Belgium and France and new drug development facilities in the Washington, D.C., area. Hemispherx was recently listed on the ``Russell 2000" Index of small capitalization stocks.

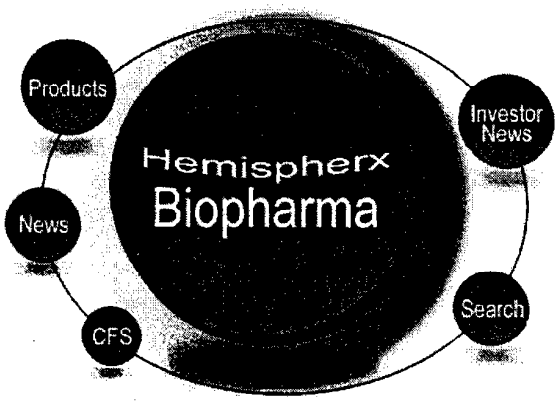
Information contained in this news release other than historical information, should be considered forward-looking and is subject to various risk factors and uncertainties. For instance, the strategies and operations of Hemispherx involve risks of competition, changing market conditions, changes in laws and regulations affecting these industries and numerous other factors discussed in this release and in the Company's filings with the Securities and Exchange Commission. Accordingly, actual results may differ materially from those in any forward-looking statements.

You are visitor number 54995 to Hemispherx's home on the web.

Welcome!

We're so glad you stopped by. Browse around, learn about us, and drop us a line.

On this page you'll find:
Company Profile | Corporate Officers | Contact Information



NEW! Hemispherx Advances New Approach to Correct Damaged Genomic Expression

NEW! Hemispherx Authorizes Repurchase of 200000 Additional Shares of Common Stock

NEW! Hemispherx Biopharma Clarifies Treatment IND

NEW! Hemispherx Files for HIV Emergency Treatment IND and Phase II/III Trials

NEW! Biovail acquires Ampligen marketing rights

Dr. Mazlen's CFS Radio Show

CNBC DOW JONES BUSINESS VIDEO

Click here for an interview with CEO Dr. William Carter.

Employment Opportunities

back to the top

Company Profile

HEMISPHERx BIOPHARMA, INC has devoted nearly three decades to exploring, understanding, and mastering the mechanism of RNA technology. The Company's longevity as a biomedical research and drug development institution, coupled with its record of tremendous enduring scientific achievement is evidence of HEB's long-term commitment to this promising new class of drugs and to bring new therapeutic choices to

CFS Radio Program
February 28th, 1999
Roger G. Mazlen, M.D. Host
with
Dr. Paul Cheney

Dr. Mazlen
We are really honored today to have a very eminent guest with us today, Dr. Paul Cheney. Dr. Cheney is the founder/director of the Cheney Clinic which is located on Bald Head Island in North Carolina. He's also prominent from the early beginning of research into Chronic Fatigue Syndrome or CFIDS. He's a board certified internist. He additionally trained for two years in tumor immunology at the CDC and then became Chief of Medicine at the Mount Home Airforce Base Hospital in Montana. Of course, from there there's a long history of research and involvement and prominence in the field of research into Chronic Fatigue Syndrome, so I'm going ask Paul to tell us a little bit about how that started. Paul, welcome to the show and we'd like to hear from you now.

Dr. Cheney
Yes, thank you, Roger. My introduction to this illness was as a practicing internist on the north shore of Lake Tahoe in 1985 when in the spring of that year we began to see an increasing, actually, an accelerating number of patients, peaking in the summer of '85 and then decelerating quickly by the fall of '85, producing about 200 cases in that small area of the California/Nevada line and the Sierra Nevada Mountains. Initially we thought there was some sort of flu-like illness among our patients who were previously quite healthy but over time they would not resolve the symptomatology and evolved slowly over time a triad of symptoms, characterized by debilitating fatigue, increasing cognitive disturbances affecting their ability to function cognitively, and then incredible pain, particularly muscle pain but also other kinds of accelerated pain. And that was the triad that we saw and these patients would not get well. And so we invited both the CDC and later Dr. Komaroff, then chief of medicine at Harvard who'd been seeing a large number of cases in Boston to come out and help us research this epidemic culminating in a publication in the Annals of Internal Medicine at about 1991 describing what we saw in that time.

Dr. Mazlen
Well, of course, it's history and most of the patients with Chronic Fatigue Syndrome are well aware of your work and Peterson and others in this area and we commend you for those early efforts, but you've gone a long way since. You've been very much involved nationally in the area of research into Chronic Fatigue Syndrome. You had mentioned to me a new concept as to what the disease is as it develops, when we had spoken prior to the show, maybe you would just like to go into that a little bit.

Dr. Cheney
Yes, the syndrome we call Chronic Fatigue Syndrome probably belongs to a larger subset of disorders known as post-infectious or post-viral syndromes, at least in a hefty subset of patients, perhaps 60-70% who were perfectly healthy until one day they come down a flu-like or mono-like illness and aren't the same thereafter. There's a smaller subset that have more insidious onset and they represent a different type of illness, but the majority of patients appear to be a post-infectious or post-viral syndrome. In that regard, there's another syndrome known as Reye's Syndrome, which evolves typically in children, although it can hit adults as well, who come down with a viral illness, sometimes the flu, sometimes chicken pox, and are resolving the acute viral syndrome and then take a dramatic turn for the worse almost at the moment they're getting better from the viral syndrome and the disease we call Reye's is characterized by disturbed liver function in the aftermath of the viral infection, that then produces a severe toxicity that affects the central nervous system and frequently death ensues. And Chronic Fatigue Syndrome might be viewed as a sort of slowly developing Reye's Syndrome in that they come down with a viral syndrome and then they emerge from that with a disorder in liver function and detoxification at the cellular level, we think involving glutathione but also other pathways, and that results in a progressive toxification systemically, particularly from the

portal circulation similar to Reye's and then a hit to the central nervous system, probably a zenobiotic toxicity to the deep brain structures that gives us the emerging picture of debilitating fatigue, cognitive disturbances, hypothalamic-pituitary-adrenal axis disturbances and severe pain. So, it's sort of like a post-infectious slowly developing Reye's Syndrome as an analogy to another more acute illness we call Reye's Syndrome.

Dr. Mazlen
Now, also, there's a connection here which you make me aware of to the 37 kilodalton variant of the RNase L and I want you to do on and talk about that.

Dr. Cheney
Right, well, that's a really intriguing issue because no one really fully understands why liver detoxification fails in Reye's Syndrome, but in Chronic Fatigue Syndrome there was discovered some years ago by Dr. Robert Suhadolnik that a very significant up regulation in an enzymatic pathway known as the 2-5A RNase L pathway was highly activated in Chronic Fatigue Syndrome. This particular pathway, although a potent antiviral pathway inhibiting viral protein synthesis and therefore viral replication, also inhibits human protein synthesis and enzyme production and could easily be the cause of this liver detox and cellular detox failure in this disorder that sets off this compounded set of problems. Dr. Suhadolnik, a few years after discovering this pathway was highly activated then discovered it was aberrantly activated with evidence of a low molecular weight, 37 kDA protein, kDA simply that as kilodalton, the size of the protein. The normal RNase L is 80 kilodaltons. This low molecular weight is only 37, slightly less than half the size. This could particular enzyme is extraordinarily active, over 6 times more active than normal RNase L and it resists proteolytic degradation and therefore lasts longer in the body and it can really cream protein synthesis and enzyme production and cellular function and from that human function.

Dr. Mazlen
Apparently, it also uses up some of the precursors for glutathione production, is that correct?

Dr. Cheney
Well, it certainly is a rapid cycling enzyme system that consumes ATP by the bucket load, kind of a black hole for ATP, as it were. So, it's a consumer of energy, but most importantly, it impairs enzymatic production in virtually every enzyme in the body. It has a huge, huge effect on human function.

Dr. Mazlen
So, this is one of the cornerstones, but on the other hand, it's only been found in about 30-40% of Chronic Fatigue Syndrome cases.

Dr. Cheney
Correct. That was kind of an interesting discovery because we were hopeful that it might be true marker for this disease, but it was not to be present in a large subset, but it was primarily present in the first 5 years of illness and at about 5 years or so, plus or minus, it begins to down regulate, such that by the 8th to 12th year of illness there's virtually no 37 kDA left, yet the patients do not necessarily recover, although we think their illness shifts or changes as this 37 kDa down regulates.

Dr. Mazlen
I want to ask you, Paul, if you can talk a little bit about your current research in Chronic Fatigue Syndrome?

Dr. Cheney
Yes, of course we have a number of projects. One is of course collaborating with Dr. Suhadolnik regarding the 37 kDa protein and it's meaning in this disorder, but a recent effort at this clinic has been--actually it's the culmination of several years of looking at defects in detoxification pathways, in particular the glutathione system which appears to be particularly impaired in this syndrome and we

tried treating this in a variety of ways, first, obviously with oral therapy with reduced l-glutathione and injectable glutathione and in a few cases with precursors to glutathione such as n-acetylcysteine and although we were seeing modest benefits, particularly pressure headaches, with reduced l-glutathione, we were not getting a huge clinical benefit overall and the glutathione system remained impaired as measured by endpoint markers such as liver peroxides in the urine. So we began to look out at other approaches that might work better and we became aware of a weakly hydrolyzed whey protein concentrate, marketed as Immunocal but in fact a whey protein concentrate that's weakly hydrolyzed and that appears to be important in it's effectiveness. We read about this product and were interested in its potential for improving the glutathione system and from there wondering if it would help this disease. So, we launched a program about 6 months ago testing the efficacy of this in CFIDS and we are, at this point, analyzing the data and pleasantly surprised at what we're seeing.

Dr. Mazlen
So, you're getting some positive results then?

Dr. Cheney
Yes, we are and we do think, however, there's a subset of patients that appear not to respond to this product. There's a larger subset that appears to respond clinically. Some interesting and unexpected results were seen in the study but overall I think it was a positive clinical response and other interesting facets of this product making us a lot more interested and perhaps more aggressive in treating this glutathione defect with these kinds of products.

Dr. Mazlen
Now, this is a small study so I presume that you feel at this point it warrant expansion into larger trials. I think so.

Dr. Cheney
We only have 7 patients which isn't a large number, but there was a very consistent response in several areas suggesting that 7 is almost enough to make some observations about it, but I think from a scientific standpoint we'll need more studies and larger numbers.

Dr. Mazlen
Well, it's exciting because anything that's helps this population of people who reign from moderate to severely ill or totally disabled is certainly a welcome advent to the therapeutic armamentarium for us, primary care physicians and researchers. I want to take one quick call on the line from Jeeney, then we'll go on with other things. Jeeney, welcome to the show. Do you have a quick question?

Jeeney
My question today is about ampligen. I've been hearing so many mixed reviews. After you had your study and the people stopped taking the ampligen, what was that result?

Dr. Cheney
Well, there are several things I think that are important to note about ampligen. First, of all, there's no doubt in my mind as I've seen it in clinical practice that this drug is bioactive in this syndrome. That is it can help people sometimes substantially. However, it does not help everyone. And it may be that the reason--there may be a couple of different reasons--one reason may be that no everyone has activation of this RNase L pathway which ampligen appears to be very potent at regulating, in CFIDS at least, downregulating. If that pathway is not activated, then ampligen may not be very rational or even effective. Ampligen also has potent antiviral properties as well and I think some of these patients may not have a significant viral activation state which may be another reason why it doesn't work in everyone. The other parallel issue for ampligen is that it appears that the longer that you take it, if you are responding to it, the better the outcome and in the initial study in 1991-92 we essentially only treated for 6 months in most cases, a year at most and that may have been a relative under treatment and so when you're under treated with ampligen, even if you're a responder you tend to degrade very quickly when you stop and conversely, when the drug is treated for longer periods of time a better

clinical therapeutic plateau is reached, there appears to be some stability at maintaining a plateau once the drug is stopped. So, I think it's kind of uncertain in my own mind exactly what will happen when you stop this drug. My sense is that if it's stopped prematurely, one will end up pretty much back where you were. If it's maintained over a longer period of time, there's a much better chance of stability. If you are a responder, the chances of a response, all comers, appears to be 2 chances in 3 and that might be raised a little bit if one targets a subset of patients, specifically ones that are within the first 5 years of their illness who have abrupt onset and who may have activation of this RNase L pathway.

Dr. Mazlen
You mentioned earlier, briefly to me, not on the show, but privately, that there's a significant incidence of chlamydia pneumoniae found in CFIDS patients. Can you comment further on that?

Dr. Cheney
Yes, of course this syndrome has sort of a long history of viral and, more recently, non-viral microbial activation reported as associated with this disorder. For the listening audience, it's important to distinguish between association of an organism versus causality, and that's a thing critically important in this syndrome. This syndrome may represent an immune activation state and with the disordered glutathione system which can create a sort of biological terrain in which microorganisms that lay dormant in our bodies almost back from childhood can activate and then other organisms that we may catch during our lives, and these organisms are not typically active, but are kept in a dormant state by our immune systems indicates that in CFS the conditions are ripe at times for the reactivation of these dormant and latent organisms. One of these organisms which is ubiquitous in the population but typically not active is chlamydia pneumoniae, which has been reported as active in a large percentage of these cases.

Dr. Mazlen
Well, that's a significant addition because they still have trouble with a lot of infectious disease specialists in dealing with Chronic Fatigue Syndrome. Many of them don't feel it has anything significant if they just show a positive Epstein Barr viral capsid antibody, IgG, etc.

I want you, Paul, to give me your email address for the audience.

Dr. Cheney
Yes, the email address is... we have a website which is pcheney@fnmedcenter.com.

Dr. Mazlen
And also I want to mention that if people are interested in getting research information on Immunocal they can call 212-875-9930 after the show or call my office at 516-352-9483 for some general information. We're going to have the patent holder and discover of the Immunocal process for production, Dr. Gustavo Buonos will be our guest on March 28th along with Dr. Allen Sommersall and others. They'll be here live from Montreal so we can pick up on this at that time. We have a caller on the line, let's go to Caroline. Caroline, do you have a question?

Caroline
I actually have two. One is that College Pharmacy is selling a generic Immunocal and I wanted to know whether Dr. Cheney thinks that is as good or if he's familiar with it and the second is that if you have the test for the RNase L marker for ampligen and you don't have that activated pathway, are you definitely not a good candidate for ampligen?

Dr. Cheney
Very good questions. Regarding generic type products of a whey protein concentrate, we do know from the patent application involving Immunocal that in comparison with the typical whey protein concentrates, the Immunocal product is far superior in it's ability to improve glutathione status. With regard to other generic products that might be available however, I can't comment. I haven't looked at

them. Theoretically, in my view it would be possible to make a generic that would work, I just don't know if a particular generic will work and that would have to be looked at carefully.

With regard to RNase L itself, if it's not activated doesn't exclude, in my opinion, a response to ampligen, but rather reduces the chance somewhat, I don't know how much, but I think there are people that definitely responded to ampligen to did not have activation of this pathway because ampligen may do more than just modulate this enzyme pathway. It has other effects.

Transcribed by

Carolyn Viviani
carolynv@inx.net

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HEMISPHERx BIOPHARMA, INC.

OTHER CFS LINKS

- The True Costs to the Nation of Public Apathy Regarding CFS
- The "Ampligen 511 Panel" Patients Speak About Their Experiences with Ampligen at the AACFS Conference

Home News Products CFS Investors Search

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Last modified: November 01, 1998

AACFS Home Page
The CFIDS Association of America
The CFIDS/M.E. Information Page
CFS Home Page of the U.S. Centers for Disease Control (CDC)

Index to Abstracts from AACFS Conference October 1998

Abstracts of Papers Presented at The Bi-Annual Research Conference of the American Association for Chronic Fatigue Syndrome (AACFS) October 10-11, 1998 -- Cambridge, Massachusetts

Ampligen 511 Participant Panel

October 11, 1998 -- Chair, Dr. Susan Levine
October 12, 1998 -- Chair, Dr. Marsha Wallace

Karen Lang

As we share our experiences with Ampligen with you today, please understand that we are speaking only for ourselves, and describing only our individual experiences with this drug. Following our presentations, we invite your questions and discussion. But please remember, we are patients. Our expertise is limited. Specific scientific and administrative questions should be directed to others at this conference who have expertise in these areas.

I am Karen Lang. I am one of the Incline Village, Nevada, Ampligen 511 study participants. I am in my eleventh month of taking Ampligen. I got sick with CFS in February of 1989, and was diagnosed with it in 1991 by Dr. Daniel Peterson. In 1992, I tested positive for upregulation of the 2'5A' Synthetase Rnase L antiviral pathways. My natural killer cell function has hovered around 5-8%, with abnormally low natural killer cell enumeration. For years I have lived with the knowledge that this early immune defense against cancer and other serious disease has been profoundly damaged.

During the first few years of my illness, as I became more physically and cognitively disabled by CFS, my husband added my bookkeeping and office duties to his farming responsibilities. We have lost a great deal of income over the years because his focus has been diverted away from farming to also doing the office jobs I could no longer do. He and our 3 children took over most of my household and family duties as well. I could not work, I could not manage my household and my growing family.

From 1993 to 1997, I took 5 grams of gamma globulin intravenously every week. It boosted my immune system so that it could fight off infections more effectively. It reduced my headaches and body pain. It improved my energy levels. But it did not fix the problems in my 2'5A' Synthetase RNase L pathways, and it did not improve my natural

killer cell function.

Before being selected as an Ampligen recipient, I was tested for the RNase L enzyme dysfunction that has been identified by Dr. Robert Suhadolnik at Temple University. I was positive for the novel 37 kilodalton enzyme, and negative for the 80 and 42 kilodalton enzymes that have been found in healthy people.

December 15, 1997, I had my first Ampligen infusion. I did not know how, or if, I would respond to the drug. I entered the study with the understanding that no drug is going to work for everyone who tries it, especially within a disease population as diverse as CFS. I knew there were no guarantees for success.

For the first few months, I felt worse than I did before starting the study. I was wiped out, energy levels were low, I had more pain and flu-like symptoms than I'd had before taking Ampligen. It took some time for my body to adjust to the drug.

My first noticeable improvement came about one month after I started. I didn't notice it. The people around me did. My husband and some other friends told me I was tracking better during phone conversations. Then my fellow Ampligen patients began to comment on my clearer thinking, and I found I could visit a little with neighbors, even go out to dinner once in a while, and live to talk about it the next day.

Two months after starting Ampligen, I was able to organize my taxes almost entirely by myself, something I have not been able to do in years.

Three months into the therapy, I went skiing for an hour with my son, something else I have not been able to do in years. I broke a rib, but it was a small price to pay for being able to return for a brief period of time to a quality of life I thought I'd never experience again.

Four months into the study, my natural killer cell function returned to the normal range for the first time since 1991,and my white blood count rose into the low normal range.

Five months into it, I noticed one day that I was able to copy 3 or 4 numbers at a time, (catalog numbers and phone numbers, for example) without having to copy them laboriously, one number at a time.

After six months, treadmill testing showed a 7% increase in my oxygen consumption (V02 max), and a 90% increase in work load (elevation).

From the sixth month on, other lab measurements that have been chronically high or low are returning to the normal ranges. Lab work is done every two months during the study. My labs from September 24 show my white blood count at 8.3, the highest it's been since the early 90s, and RBC, MCV, MCH, and MCHC are all in the normal ranges, also for the first time since the early 90s.

Some clinicians might view these improvements as insignificant changes, but to me, after 10 years of consistent abnormality, a return to normal ranges for the first time, with Ampligen being the only new variable in my life, clearly demonstrates the efficacy of this drug.

These lab results provide objective evidence that my immune system, and other internal systems that have been broken for years, are healing. After years of expensive treatments that have helped my symptoms, but have not addressed the underlying disease, here is a drug therapy in Ampligen that is fixing what is medically wrong, from the inside out.

I am also rediscovering a quality of life I had forgotten about. I had forgotten how good it feels to be a productive member of my family. I can now do the correspondence for the business, and some of the phone communications with vendors and agencies. I had forgotten what simple pleasure there is in remembering what I read. I had forgotten so many of the daily activities that healthy, normal people take for granted, things I used to take for granted but no longer even remembered. I am enjoying the details in life again, the little things that make life worthwhile.

My health is improving, and my ability to think properly. My energy level is increasing. When I overdo, my recovery time is much shorter than it was before Ampligen. I am still recovering, but for the first time since 1989, I am enjoying the sweet taste of feeling good again. I am looking forward to better health, and the promise of leading a normal life again, one that includes family, work and play.

Unlike IV gamma globulin, Ampligen is not offering me only symptomatic relief. I am healing from the inside out. I look forward to the day - soon, I hope - when Ampligen is approved for the treatment of CFS, and is available to other patients who need it. Thank you.

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Linda Barossi

My name is Linda Barossi. I am a participant in the Ampligen 5ll study in Incline Village, Nevada.

I got the "flu" in 1986 and did not recover. Symptoms came and went, I went from doctor to doctor with a variety of strange complaints which were explained away as the product of a stressful job and overwork. Many others worked just as much, just as hard. *They* didn't have these symptoms!

I owned Horizon Aviation in Auburn, CA since 1979, a flight school, aircraft sales, maintenance and rentals. I was a pilot.

From l992 to l995 my symptoms progressed and I was becoming severely disabled, yet forging ahead as much as was possible. My initial visit with Dr. Peterson was in January of 1996. After extensive testing, I was informed that I had a markedly abnormal exercise tolerance test, a very low VO2 max (53% of predicted, which within a year dropped to 43%), an abnormal brain scan, low natural killer cell function, elevated T4:T8 ratio, low IgG Subclass I, and subsequently tested positive on the tilt table for NMH and exhibited the abnormal 37 kDa enzyme in the 2-5A synthetase/Rnase L pathway.

As my health continued to deteriorate, I put my business on the market for sale as well as my home of 17 years. I moved to Reno to be closer to Dr. Peterson and any treatment available. I had my first Ampligen infusion on December 15, l997.

The first three months were difficult. Some of my symptoms - pain, headache, nausea were intensified. Nothing new in symptoms appeared, but I felt worse. I watched as others in the group were showing improvement. One man actually coming alive before our very eyes, another woman able to walk, carry her children, skipping around gleefully. I couldn't help but think, what about me?

My response was slow. I first began to notice that I would have periods of time with *no* pain, truly a miracle for me, the pain I had experienced for so long was intense. I then found myself tackling an accounting nightmare that was previously impossible. I completed all the corporate accounting for my business and related taxes. I had the ability to *walk* through an entire grocery store -- no electric cart needed, I was cooking again with energy left to eat what I prepared. The things that I previously took for granted and that many don't even consider, were slowly coming back to me. What an incredible feeling!

After 6 months on Ampligen my exercise tolerance test revealed significant (l5%) improvement in functional capacity from the pre-Ampligen test. Duration of the exercise increased by two minutes and six seconds. The final elevation of the treadmill, at the same speed, rose from 2.5 to l0.8, a 76% improvement. Oxygen consumption increased 2l%. I did not endure severe pain afterward and actually attended a party that evening.

After 10 months of this drug, I continue to realize slow but steady improvement. Yes, I must still be careful not to "overdo" and that's difficult when you are feeling so much better and see that your life is coming back. The difference now, which is such a dramatic change, is that the penalty is much less severe -- a few hours of rest and I am able to resume activity.

There has been a dramatic improvement in my quality of life. My thoughts are now of the future and what it holds. This is truly an exciting time. I have started to prepare a resumé and with God's help and a continuing supply of Ampligen, a part time job may be close by.

I am so grateful for the return of my life and wish for others the opportunity to experience the same joyful reunion.

Linda Barossi
The Ampligen 511 Trial: Patient Perspectives on Efficacy
Fourth International AACFS Conference, Cambridge, MA
October 10, l998

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Steve Edwards

Steve Edwards -- Brief Bio -- October 4, 1998

I am 50 years old, have a wonderful wife of 29 years, and 3 sons, aging 25, 20, and 19. At this time I am 14 months into the Ampligen 511 program in Charlotte, North Carolina. I am under the supervision and care of Charles W. Lapp; M.D. My family resides in Missouri, our home for the past 15 years.

My onset of CFIDS occurred exactly 7 years ago this month. At that time I had been employed for 212 years as a Turf Agronomist with a midwestern golf course distribution company. I was enjoying my family and life at its fullest. On return from a trip to Michigan I experienced a bad flu "that never went away."

After 2 months of extensive testing, my local M.D. had basically eliminated all probable causes for this extended illness. Having formerly had 2 patients with CFIDS, my doctor

recommended that I see a specialist in this unknown area and determine if this could be the cause of my illness. We located the Cheney Clinic in Charlotte, North Carolina and made the initial appointment to see Dr. Cheney. Dr. Cheney confirmed a diagnosis of CFIDS after a 3-day visit to his clinic. After my initial diagnosis I was introduced to Dr. Lapp and have been under his care and supervision for the past 7 years.

Even with a good CFIDS program I was unable to continue to work and had to take a disability leave from my job in early 1992. The time between then and the summer of 1997 is sometimes a blur. I fought continuously against this illness but was basically confined to a home environment of fatigue and pain. Thanks to the current Ampligen program I can finally start to see the evasive light at the end of the tunnel.

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Stuart Craig Woolman

> The healthy, the feeling well. when they felt that way. couldn't remember feeling any other. couldn't magine it. They were niftily in their bodies. . . Whereas the sick could only think of being otherwise. Their hearts. their every other thought, went out to that well person they hated a little but wanted to be . . . . The feeling well were running the show, which was why the world was such a savage place.
>
> "Real Estate," *Birds of America* , Lorrie Moore

1. Brief Biography: Stuart Craig Woolman

Education:

Columbia University School of Law (J.D. 1991)
(Harlan Fiske Stone Scholar, 1989-90. 1990-91);
Columbia University Graduate School of Arts & Sciences
(Philosophy) (M.A.199l)(President's Fellow. 1987-88);
Wesleyan University
(B.A. w. Honors 1985)
(Phi Beta Kappa. Dept. Honors in Philosophy);

Experience:

University of the Witwatersrand School of Law
Senior Lecturer, 1993-present
Most Promising Lecturer. 1993
Edward Nathan Fellowship, 1994-96
Vice-Chancellor's Prize - Best Researcher in University under 40,1996
Permanent Post 1996
Creator/Coordinator.
Constitutional Law Programme for Advocates & Attorneys, 1993-1996)
Constitutional Law of South Africa
Co-Managing Editor/Co-Author, 1994-present
South African Journal on Human Rights
Editor, 1994-present
Edward Nathan & Friedland
Fellow. 1994-1996
Commission of Inquiry into the Prevention of Public Violence and Intimidation
Research Associate, 1993-94)

Crowell & Moring
Associate, 1991-93
Morningside Heights Legal Services
Law Guardian, 1989-91
Member of the Bar of the State of New York
Mr. Woolman is the author of articles, books, book chapters,
essays. reviews and position papers on a broad range of legal issues.

II. Introduction: Acknowledgments and Caveats

1. Acknowledgments: While tedious to hear, I would be terribly remiss if I did not thank:

A. Karen Lang and the AACFS
for making this panel possible.
B. Drs. Paul Cheney, Susan Levine, Kristina DahI, Ian Hyams
and the entire staff of the Institute for Preventive Medicine for nursing me back to health.
C. Dr. David Strayer, Dr. William Carter and Hemispherx Biopharma
for making my recovery and my participation in this trial possible, helping me fit "niflily" back into my body and for making this world seem a far less savage place.
D. The Food and Drug Administration
for approving this study as well as the Ampligen 516 study and for making provision for my continued participation in the Ampligen 511 study.

2. Caveats:
I have given lectures before hundreds of professional attorneys, presented papers before scores of respected peers and have appeared before Constitutional Court judges. This public speaking engagement is my first before a group of natural scientists, medical researchers and clinicians. And unlike previous speaking engagements where I possessed a genuine command of the material, here I am on terra incognita. On this technical subject matter, I am in your hands -- and I hope for a kindness and solicitude I would have never expected from another audience.

III. My 30th Year: Being before illness

My 30th year, the year before and up until I became ill, was the best year of my life. I worked hard - and was rewarded for it. Teaching, writing. editing, consulting on commercial matters and politics occupied 10 to 12 hours of every day. Weekends were invariably shared by work and play. I loved my work and the autonomy that came with it. If there were a down-side to this idyll, I suffered from a mild case of "cookie jar" syndrome. Anything that I wanted to do - or imagine doing - I could do. I had to be careful not to put my hand in the cookie jar for fear of overextending myself.

I led an active social life. I had a loving partner - who remains my partner still and whose family has treated me as one of their own - and a wide circle of friends. I never wanted for entertainment or meaningful connection.

I was a decent, enthusiastic, if not particularly gifted athlete. I exercised -- playing tennis, cycling or lifting weights -- at least 5 days a week. When playing with my tennis coach, I could hit fifty balls between the lines during a single practice point as he ran me like a dog from side to side. I regularly cycled upwards of an hour at time. I could bench press over 250 lbs.

Yes, my 30th year was the best year of my life. Everything I touched seemed to turn to

gold. And while I occasionally felt the melancholy that goes along with being human, most of the time I felt that I lived a charmed existence.

I may yet still.

IV. Buried Alive at 31: The Chronology and the Character of My Experience with CFS

My illness began in mid-August of 1994. In July, 1 had suffered a severe herpes infection -- contracted from my girlfriend. Although the herpes legions eventually disappeared, I was left somewhat listless by this initial infection. In August, I contracted a pretty severe case of the flu. When it did not resolve itself within a couple of weeks, I went to see a couple of doctors. They suggested that it was post-viral syndrome and that it would run its course after several months.

It did not, of course, run its course after several months. Instead, I got progressively worse. Psychiatric interventions generally exacerbated the situation. While Cypramil - an SSRI and a cleaner version of Prozac - did not have any deleterious effects, it also did nothing to alleviate my symptoms. Further interventions with a Aurorix - an MAOI - and a Effexor were disastrous and hastened precipitously my decline.

When I reached bottom in early 1995 - after treatment with the two aforementioned psychotropics - the bottom looked like the traditional litany of ailments associated with what I then learned to be Chronic Fatigue Syndrome. (By this time, six months had passed and my GP was ready to diagnosis me as having CFS.)

- **Extreme fatigue.** I operated at about 15% of pre-morbid capacity. I worked, poorly, for two, perhaps three hours a day - when I worked. The remainder of the day was spent largely in bed.
- **Devastating sleep disorder.** In bed, but not asleep. At night, I might get 3 to 4 hours of sleep with high doses of soporifics. I never ever felt rested.
- **Severe Cognitive Impairment.** Perhaps the most psychologically devastating of symptoms. I could not work: no writing, no extemporaneous lectures, limited conversation, inability to read or concentrate, no creativity whatsoever. I felt, to play with Descartes, that if I could not think, I might as well not be.
- **Severe Memory Loss.** Accompanying the severe cognitive impairment was severe memory loss. I would make a phone call and then forget, almost immediately, that I had made it. Between the cognitive impairment and the memory loss, I had a strong and forbidding sense of what a moderate case of Alzheimer's disease must be like: to be trapped inside oneself and to know that one has lost the most meaningful aspects of one's personality.
- **Headaches.** They shattered consciousness - my mind was like so many marbles scattered across an alabaster floor.
- **Fibromyalgia and Muscle Weakness.** My neck and back were a road map of painful ropy muscles and knots that would not yield to the most invasive massage or the best acupuncture. Relief was temporary at best.
- **Sensory Impairment.** I was extremely photosensitive and felt better with my glasses off than on. I loved the darkness of the movies - my sole joy.
- **Hypothermia.** I was always cold, my extremities profoundly so, and always overdressed. Winters in South Africa are even worse than winters [in the United States] - not colder outside, but colder inside because they don't know from insulation or central heating.
- **Swollen lymph glands.** The tell-tale glands in neck, under arms, in groin, throughout the legs. The more swollen they were, the worse I generally felt.
- **Persistent herpes infection.** A consistent companion that remained with me for weeks and months at a time. The legions might clear slightly if I refrained from

sexual activity for a week or two or a month. But the dull background burning sensation was always there.

- **Severe Depression and Excessive Irritability.** While an endogenous depression might have contributed to my illness, the conscious depression I experienced always seemed to me to be primarily reactive to the debilitating nature and ever increasing length of my illness. As for my irritability, I had no control over my life, and little over my mood and temper. Again it seemed a rather natural consequence of the entire illness - but I'm not in a professional position to play chicken-egg.
- **Gastrointestinal Dysbiosis.** My stomach and bowel gave me more headaches than I already had.

Tests taken over time seemed consistent with the diagnosis.

- Positive tilt table for Neurally Mediated Hypotension.
- Blunted and inverted dynamic cortisol responses.
- Elevated liver function tests.
- Gastrointestinal dysbiosis that reflected bacterial infections and other irregularities that were off the charts in terms of severity.

My employers have been extraordinarily generous not only in trying to keep me on the staff but also putting me in a position to recuperate. They gave me a semester off; they diminished my work load. They gave me two years of unpaid sick leave to find a treatment that works. And with their help, I have found it.

When I decided to return home in early 1997, 1 was dead to the world. And until I began the treatment with Ampligen in September of 1997, my improvement was minimal to non-existent. But things changed dramatically beginning in September of 1997.

V. Resurfacing at 35: Ampligen is the Real Thing

Call me Lazarus. Call me the Come-Back-Kid. Whatever you call me, the only reason I am here and functioning pretty well today is Ampligen. I have absolutely no doubts about its efficacy in the treatment of my illness. It has brought me back to life. It is the real thing. What I would like to do now is quickly chart the course of my improvement on Ampligen over the past year.

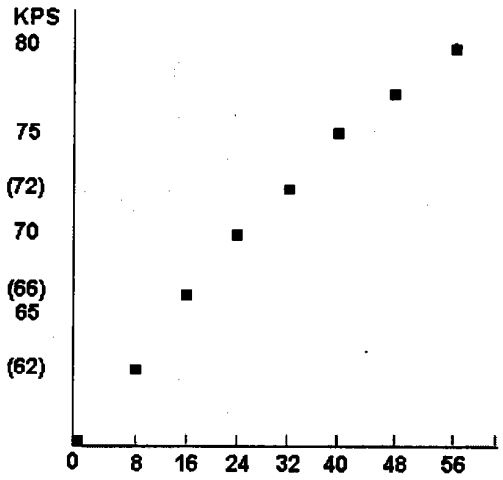
What distinguishes my continued recovery - what consistently astonishes me -- are the weekly, progressive and substantial breakthroughs in cognitive capacity, energy levels and functional capacity. At present, for the better part of each day, I experience cognitive clarity that very closely approximates my pre-morbid state. Put slightly differently, my cognitive deficits, while still present, are not as evident to myself or others. As importantly, I find myself to be fatigue resilient, if not entirely fatigue resistant. Though I may flag somewhat after physical activity like tennis or walking, after sustained social activity, or after a couple of hours at the computer working, I generally feel reinvigorated after a brief rest or a night's sleep. My functional capacity, as reflected by the Karnofsky Performance Scale, would now rate an 80 KPS for scoring purposes. I cannot yet return to my work full-time as a lawyer and academic, or occupy a comparable post. I will, in the near future, start a part-time position as Director of Research for a small not-for-profit political organization, begin doing a limited amount of part-time legal work (if it is available) and may also initiate a new academic project. Given my rate of progress, I fully expect to be a 90 on the KPS and able to work full-time within the next six months or so.

From start to present, my response to Ampligen has been nothing short of amazing: the extraordinary efficacy of the treatment, at least in my case, cannot be seriously questioned. (Indeed, I would reject out of hand any suggestion that my recovery has some other cause or is merely coincidental). The following account captures the efficacy of the treatment by detailing the aforementioned progress in cognition, energy and functionality,

and by noting the vast improvements in sleep, immune function, blood pressure, activity levels, sight, liver enzyme levels, gastrointestinal function, musculoskeletal pain and other markers and symptoms of the illness.

1. KPS Score over Time

The graph on the next page [below] reflects a rough but relatively accurate picture of my improvement since beginning Ampligen treatment in September of 1997.



The first sixteen weeks show in an increase of 8 KPS points: 58 to 66. The secon4 sixteen weeks show an increase of 6 KPS points: 66 to 72. The third sixteen weeks show an increase of 5 KPS points: from 72 to 77. The last eight weeks show an increase of about 3 KPS points. The total KPS increase of the first 56 weeks is 22 points in raw terms. In scored or recorded terms, which involves rounding up and down to the nearest ten, I have gone from a 60 KPS to an 80 KPS. The discrete, incremental scoring simply reflects my best effort to have the number at any given 8-week interval accord with both my objective/functional status and my subjective experience of improvement.)

As the graph shows, my clinical response over this initial 56 weeks of treatment is steady, progressive, incremental improvement. But if one looks at where I started in September of 1997, and where I am in October of 1998, there is just no comparison. I have gone from being flat on my back and out of it to up on my feet and feeling, well. if not groovy, then something close to normal.

The graph also reflects the fact that my functional/objective score and my subjective experience of improvement are no longer 'out of joint'. At various points. I was uncomfortable both rounding up to 60 or to 70 or to 80. At other times, I felt that rounding down to 60 or 70 would be inaccurate. My condition occupied some middle space. At week 56, I feel much of this dissonance has disappeared. I feel far more comfortable now with a score of 80 and the ascription of "normal with symptoms and effort" to my condition.

That said, "normal with symptoms and effort" comes with a couple of important caveats. Full-time work at my chosen profession - academia and the law -- is still at least a few of months beyond me at this juncture: though some academic and legal part-time work is not. Occasional, vigorous physical activity is possible within limits: I still tire very easily. With carefully modulated, moderate exercise, I will fatigue but bounce back after a decent period of rest. I cannot get away with a mere eight or nine hours sleep. Though

sleep is generally restful, I still require some assistance and need almost 11 hours a night.

2. Systemic Responses
This section discusses the extent to which several important markers or symptoms of my illness have improved over the first 56 weeks of treatment.

A. Cognition
Prior to beginning the Ampligen treatment, my overall cognitive function was terrible. I felt retarded. It was an experience akin, perhaps. to a middle stage of Alzheimer's disease - a terrifying awareness of how much has been lost.

At week 16, my mental life was significantly better. Before initiating treatment, I felt as if there were a veil pulled permanently over my consciousness. By week 16,1 had pierced the veil. However, while I was not-too-foggy for a short portion of the day, what clarity I had was contingent. Any moderate activity or a bad night's sleep could cause me to lose whatever clarity I might have had the day before, But at least the lights were on, low but on.

At week 32, my head was near clear for a far better portion of the day and my thought processes began to approximate normal thought processes. I began to recognize myself: my older, pre-illness self. Still, while I was far less susceptible to "fogging up" after minimal exertion, what cognitive clarity I possessed was still very much contingent upon a careful marshaling of my resources.

By week 40, I would say that I had begun to reclaim the better part of my personality and what powers of perception I possessed before falling ill. My memory and my word recall were far better. I found communicating to be far less of a struggle - and I displayed the occasional ability to joke around and speak extemporaneously in a manner that I had not experienced since falling ill four years ago. My cognitive capacity began to be less and less contingent upon my expenditure of energy throughout a day.

At week 56, I am, more and more, my old self. I still think it will be awhile before I can hold rapt the attention of a lecture hall - or even feel in command of an intimate conversation of friends at a dinner table. And although these limitations may appear to be more matters of ego than capacity, they do capture at least part of the difference between my morbid and my pre-morbid states. But while I experience some such cognitive deficits, it is quite astonishing and wondrous to reflect back upon how far I have come. Given my astounding progress, I have every reason to believe that I will continue to gain strength and regain, eventually, all that I have lost.

B. Fatigue
Prior to beginning Ampligen treatment, my energy level was extremely very, very low. It was an effort just to make it through a short day awake. Often I didn't. I was dead on and off my feet.

At week 16, my energy levels were significantly higher. I could run a few errands, drive around, and engage in other low-key activities for a couple of hours without feeling completely overwhelmed or worn out.

At week 32, I generally awoke feeling 'normal': not lively, but awake, clear-headed and possessed of a bit of energy. While my energy level was far higher to begin with and I was able to undertake more intense activities for extended periods of time - a very occasional lecture or memo -- my energy levels remained highly labile. Too much mental or physical activity would leave me "washed out" for the rest of that day and perhaps the next.

At week 40, I found myself somewhat fatigue resilient, if not fatigue resistant. Though I might flag after moderate physical activity like tennis or walking (or even after sustained social activity), I generally felt much better after a brief rest or a night's sleep. If, however, I chose to take it easy all day, I could remain relatively close to fatigue-free for the better part of the day.

At week 56, I'm at the point where I can do a couple hours of work at the keyboard and not feel "washed out". Likewise, I can engage in several hours of social activity or a limited amount of moderate physical exercise without going past my fatigue point. I can end the day, if well-paced and rested, with a not too shabby level of energy. Just plain tired. I certainly have the energy to do significant part-time work under flexible conditions and with plenty of down time. Suffice it to say, however, that I don't yet have the reserves - that regular supply of energy and adrenaline -- to make it through a whole work day.

C. Sleep

Prior to beginning treatment in September, my sleep was poor. I needed soporifics in sizable quantities to get off to sleep. But even medicated sleep brought only the most limited relief. Three hours of light sleep followed by six or seven hours of tossing and turning. I never awoke feeling rested or refreshed.

By sixteen weeks, my sleep had improved immensely: real sleep lasted longer, the overall quality was far better, it was relatively restful. It remained, however, somewhat inconsistent.

At week 32, my sleep was consistently good, consistently restful. I would usually go to sleep between 9:30 p.m. and 10:00 p.m. The first period of sleep would last 4 hours, followed by several shorter periods of sleep. Over 11 to 12 hours in bed would yield 8 to 10 hours of solid sleep.

At week 40, my sleep remained about the same. I still required 11 to 12 hours of sleep a night. However, if I got the requisite hours, I was relatively assured of waking awake -- with relatively few cobwebs. Good sleep began to provide a solid foundation for the next day.

At week 56, I need 11 hours. I prefer more if I can get it. I have gotten away with ten and still awakened and continued to feel quite alert.

I can only hope that over time, and as I continue to improve, I will need less and less sleep and that the quality of sleep will improve. But I can live like this.

D. A Normally Responsive Immune System: Two Experiences

At the end of week 39, 1 came down with a cold. The fact of the cold is interesting in and of itself. I haven't had that many full blown colds over the course of my illness. However, those colds that I did have over the past few years would often lasted several weeks, sometimes over a month. What is, perhaps, most interesting about this cold is the rapid speed at which it resolved. This full-blown cold lasted two days/three nights. I had a Friday night, a Saturday and a Sunday of sneezing, wheezing and feeling even more rotten than usual. By Monday morning the cold was gone. By Tuesday morning, the night after a treatment, I felt as well as I had been feeling prior to the cold.

At week 52, I came down with gastroenteritis. After treatment that night with composine and fluids, the cramping disappeared. After my Ampligen treatment the next day, I felt as I had before the gastroenteritis. (It did, however, take several weeks for my stomach to

straighten itself out completely).

E. Blood Pressure

My blood pressure has been rather low for quite some time: 100/60, sometimes lower. I have also had a positive tilt-table test for neurally-mediated hypotension (December 1996).

Over the past several months, my blood pressure has steadily risen to a point where I now average about 110/70. This moderate rise in blood pressure, constant but not dramatic, is consistent with the improvement in both energy levels and cognition experienced over the same period of time. However, I have continued to improve despite occasional low blood pressure readings and no further upward climb in my BP.

F. Liver Enzyme Levels

For almost four years, and over the course of some 20 tests conducted by internists, liver specialists and by labs for this trial, my liver enzyme levels were consistently, significantly abnormal. At week 48, my liver enzyme tested well within normal parameters - smack dab in the middle of established parameters and significantly below the cutoff point for abnormality.

G. Other Symptoms, Markers and Systems: Eyesight, Sore Throat, Swollen Glands, Gastrointestinal Tract, Musculoskeletal Pain, Persistent Herpes Infection

i. Sight

One of the most interesting changes that I have observed over the past 56 weeks - and one which seems to underscore my general neuro-cognitive renaissance -- has been the improvement in my sight.Prior to initiating treatment, my vision was quite cloudy and I was extremely light sensitive: a condition consistent with my cognitive impairment.

By week 16, I was both less light sensitive and less cloudy, when I did not wear my glasses. Wearing my glasses still elicited both forms of optic discomfort.

At week 32,1 experienced far less photo-sensitivity or cloudiness and was generally able to wear my glasses without discomfort.

At week 40, I could wear my glasses without discomfort and pick up the spin on a tennis ball. (Although when I was tired I sometimes preferred to leave my glasses off.)

At week 56, I would say my eyesight is normal. Still, there are moments, such as when I drive, that I prefer the glasses to be off.

As I noted at week 32. the connection between my improved cognitive function and my improved sight is fairly transparent to me. Occam's razor and existing clinical data -- suggest that both improvements might be traced to the reversal of pre-existing brain injury.

ii. Sore Throats and Swollen glands

Sore throats and large swollen glands were an ever-present feature of this illness: until recently. At week 32, the sore throat - which would fade in-and-out (fading-out after infusions. fading-in a day or two later) - began to diminish in severity. The tell-tale swollen gland in my neck -- which like the sore throat would shade up-and-down in size - took on a more nominal in size.

At week 40, the tell-tale swollen gland was much smaller. It was, however, still present and palpable. When I caught cold at week 39, it flared up, as did two other glands -- one directly below it and the other on the left side of my neck. After getting over the cold - and after several more Ampligen treatments - the single gland alone remained. A tiny reminder.

At week 56, the sore, red throat is gone. And has been gone for some

time. The tell-tale swollen gland remains an ever-constant, tiny reminder - and given to flaring up when provoked.

iii. Gastrointestinal Tract

Prior to beginning treatment in September, my gastrointestinal tract was a mess. Tests taken in June of 1997 showed that on a scale of 0 to 20, with 0 representing optimal digestive and immune function and 20 representing extremely severe dysbiosis - my intestinal tract rated an off the scale 24. By late February of 1998, after 6 months of Ampligen treatment, tests revealed my intestinal tract to be close to optimal function: it rated a mere 5.

At week 40, my gastrointestinal tract appeared to be functioning normally. Although I had not had a GI tract test during that period of time, specific food sensitivities had diminished and bacterial infections were no longer a regular problem.

At week 56, I would say the status quo holds. The gastroenteritis took some getting over, but I would say the GI tract is in pretty good shape.

iv. Musculoskeletal Pain

At week 32,1 was able to report that some of the severely disabling CFS symptoms I had experienced -- including headaches, neck pain and backaches - were largely gone. At week 40, they were still largely absent. At week 56, to the extent I experience such pain, I probably do so no more than the average person.

v. Persistent Herpes Infection

My "persistent herpes infection" became far less persistent as time on the trial has worn on. I have experienced no outbreaks in the last several months nor do I have any background sensation of the infection. At week 56, I can't say that I am herpes free, but I am symptom free.

3. Activities and Activity Levels: From Running on Empty to a Low Battery

At week 0, my primary goal was to stay awake the better part of the day. To achieve this goal, I stayed in bed or in a chair. I didn't do much of anything.

At week 16,1 was able to care for myself. I cooked, cleaned, ran some errands, saw friends every few of weeks.

By week 32, I had begun to engage in the activities associated with a normal life. I gave the very occasional lecture, did a bit of editing, writing and administrative work. I also saw my friends more often and picked up a greater share of the domestic work.

By week 40, my activity rate was far, far higher. I was able to engage in a few different activities over the course of a day: errands, exercise, employment, entertainment (choose two). While I was able to do most of the things normal people do, I was still limited quite significantly in the amount I could do. Generally. I would not do more than one or two things. flexibly arranged to meet my needs.

At week 56, I am far, far less bounded. I can actually undertake a whole gamut of activities - and the pressures that go along with them. I don't relish the experience of running around. I prefer to play it safe. And running around has its costs. But I can turn out 20 substantial c-mails in a day, meet with my publisher for two hours, work on a manuscript. go to the doctor, make my meals, hit the pharmacy and the Post Office, clean up around the house and put away laundry - if I take long rests between stops and if I am willing to be rather flat at the end of the day.

The right metaphor for my condition now is a low battery that I can run down and flat if I do not take care to have it recharged constantly. (Ampligen is an essential part of that re-charging and charging-up process). As long as I take care of the battery, I'm not stuck out on the road stranded. But I can, and have, pushed myself too far.

My hope is that as I continue to improve, my endocrine system heals fully as well. One day in the near future I may have - not a new - but a fully charged battery.

4. Medications and Supplements

At 32 weeks, I noted being able to reduce the concomitant use of other medications and supplements. At 56 weeks, I have winnowed my concomitant medication down to:

Remeron - a very effective anti-depressant and anxyiolitic;
Dormonoct - a soporific; and
Melatonin.

No Adverse Effects - And Immediate Benefits to Boot - The Ampligen Bounce

When I initiated treatment I would experience some flushing, a wheeze, a very palpable increase in the tell-tale lymph node and a point rise in body temperature. Most of these mild adverse effects disappeared with the first 16 weeks of treatment. The temperature rise, which I would hardly call adverse, persisted for almost 40 weeks. With rare exception, my temperature - hypothermic when I started Ampligen therapy - now stays within a relatively normal range. The lymph node continues to respond by increasing in size after the treatment begins. By morning, however, it has subsided to its normal, nominally enlarged size.

What I also continue to experience several hours after an infusion is a lovely, natural tiredness - and a readiness for sleep. I invariably sleep deeper and longer the night after receiving an infusion. I have used this opportunity to cut-back over time on the medication and supplements I have used and still use for sleep.

And then there is the Ampligen bounce. The day after treatment I invariably feel better than I did the day before.

6. Expectations

I hope this presentation gives you a picture of the enormous progress I have made over the first 56 weeks of treatment. Given the significant progress I continued to make during the last 8 week cycle, I have every reason to believe that I will continue to improve the longer I am on this medication. Today, I walk almost "niftily" in my body and believe that given sufficient time -- along with a bit of luck -- that Ampligen will make me whole again. (And with continued access continue to keep me whole). Quite incredible that. Especially when I think of where I was just 56 weeks ago.

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