FOIA Number: 2007-1550-F

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AIDS ACTION NOW!
317 College Street, Suite 420, Toronto, Ontario, M6G 4A2
Tel: 416-928-2206 Fax: 416-928-2185

7 May 1997

Glaxo Wellcome Inc.
7333 Mississauga Road North
Mississauga, Ontario
Canada
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Fax: 905-819-3356
Attention: David Krakovsky
Clinical Research

Dear Ladies and Gentlemen:

Re: Compassionate Access to 1592U89

We are writing to express our concerns about the compassionate use program for 1592 as described by you in our meeting of May 1, 1997.

The Numbers

First of all, we are shocked by the paltry 2000 spots in the adult program for Europe, Australia, Canada and the United States. As you will know, the number of AIDS cases in these countries is well over 700,000. Glaxo Wellcome has been a model of generosity with the 3TC open label program which was relatively unrestricted and, in total, provided 3TC to approximately 50,000 individuals. Why is there such a difference in these programs?

You indicated that your reasons for limiting the compassionate access are as follows:

1) supply problems as a result of the change in formulation.

This is obviously something that is difficult for the community to judge and is a common reason put forward to limit compassionate access. To alleviate the community's suspicions that this is not a valid reason, and in keeping with your stated intention to have a "transparent" relationship with the community, would you allow an independent production analyst to inspect your production capacities? Merck agreed to such an independent review and this was beneficial to both the company and the community which were at loggerheads over a similar supply issue.

We appreciate that drug supply may be a rate-limiting factor in the development of the compassionate use/open label program, however we would ask you to undertake to scale up production to meet the need.

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2) you must ensure adequate supply for the conduct of clinical trials.

We understand that you have approximately 33 trials either ongoing or in development. Would it be possible to prioritize the trials required for regulatory approval and then review the relative urgency of the conduct of some of the planned additional or supportive trials vis-à-vis the needs of the compassionate use program, in consultation with the community? This might allow you to better "balance a limited supply of drug with the competing needs of an extensive clinical development program and the compassionate use/open label study" keeping in mind that "[t]he ultimate goal is to meet the needs of individuals... (your letter to the Canadian HIV/AIDS Community dated April 29, 1997)

3) there are more treatment options now than when 3TC entered into Phase III trials in June of 1993 and, therefore, you do not perceive that there is as much of a need; that there is not as much of a "drought" now as there was when you began the 3TC open label program in December 1993.

We find this argument hard to follow for two reasons: if you do not think that there is a real need for 1592 at this time, why have you imposed more limiting entry criteria than with 3TC and why have you capped the number of spots available? Secondly, we would suggest that for the individuals who have either exhausted all available options, or for whom their only option right now is to add one drug to a failing regimen, there is a real drought.

4) you have safety concerns about 1592; approximately 250 trial participants have taken 1592, and none for more than six months.

We are not advocating that everyone should abandon therapies which are working for a product which is just now beginning Phase III trials; however, a practice has evolved over the course of this epidemic to allow for compassionate access to a drug once Phase I and II trials are complete and the gross toxicities and adverse events are known. At this point, the acute safety concerns have been met and we acknowledge that there will, of course, be chronic safety concerns. However, this will be a staggered process of risk assessment - by the time that those who receive 1592 on a compassionate basis have been on the drug for six months, those trial participants will have had a further six months of exposure, and so on.

The Entry Criteria

We recognize that it is probably impossible to design a *limited* compassionate access program which will please everyone. Certainly, we feel that the entry criteria may need to be further "tiered" according to severity of the situation in order to most fairly ration the supply on the basis of need. This will probably depend, in part, on the size of the initial demand and would probably be best determined separately by each of Australia, Europe, Canada and the United States. Also, as supply increases we would expect to see the criteria made more liberal.

However, we do feel that your "salvage" program must be amended to adequately provide for mild to moderate AIDS Dementia Complex (ADC). Although we understand that you do have a clinical

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trial for mild to moderate ADC, there are only 90 spots worldwide, and we do not consider it ethical to force people into a placebo-controlled clinical trial as their only hope of obtaining the drug. We recommend that the entry criteria be amended to add a category for those with mild to moderate ADC who have failed on or are intolerant of AZT and d4T. Even if the supply cannot meet the demand, we would prefer to encourage these individuals to apply so that we can assess the need and allow for a tiered system of access based on severity of need, as supply increases over time.

The Registration Process

You have indicated that the adult program will take place at geographically dispersed centres. We are vehemently opposed to this suggestion. There are numerous potential problems with such a system whereby an investigator for an area would hand pick individuals from his/her practice. When Merck Frosst initiated a program such as this in Canada it created a great deal of ill feelings toward the company. A practice has evolved in Canada in the last few years of compassionate access programs to utilize a centralized application and registration centre run by an arm of the Canadian HIV Trials Network. This has worked, is respected by the community, and is seen as the only fair and equitable way to allocate the limited supply of the drug. This would also allow us to better assess the real demand for compassionate access to 1592. We would, therefore, recommend that Canada be allowed to develop its own registration process in consultation with the community and that you utilize the Canadian HIV Trials Network as the registration centre and also as the Canadian contract research organization (CRO).

We understand that you would prefer to limit the Canadian sites for distribution to two or three which will be involved in the Phase III studies of 1592 and will, therefore, have some experience of 1592. We believe it is possible to have more sites with HIV-experienced physicians involved in the distribution of 1592 as was possible with 3TC. It is preferable that patients are able to stay with their own physicians and clinics for the continuity of their care, and that more physicians develop some experience of 1592. Clear guidelines in the protocol should ensure that the drug is appropriately used and monitored. At the very least, we will need more sites for distribution to reflect the geographical reality of AIDS incidence in Canada.

Possible Inter-Company Collaborative Compassionate Use Salvage Program

We are all aware that it will not be the best use of 1592 to take it as monotherapy, or to add it to a failing regimen; however, individuals who have exhausted all other options will have no choice. We are pleased that there are no restrictions on using 1592 *with* other experimental therapies; however, this does not ensure or facilitate that someone in need will be able to access other experimental therapies at the same time. For this reason, we query whether you would look at the possibility of an inter-company collaborative compassionate use salvage program, with companies such as Dupont Merck and Gilead, for individuals who have exhausted *all* options, so that such individuals could be offered two or three experimental therapies at once and a real hope of sustained benefit. Perhaps such a pilot program could be coordinated by a branch of the ICC.

AIDS Action Fund
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Future Communications

We would appreciate seeing your draft protocol including the informed consent form so that we may provide you with input. We would also be interested in seeing the Case Report Forms. We trust that you will continue to consult with us in a meaningful way through the development of this program.

Benefits of Compassionate Access

Lastly, we would ask you to consider the following possible advantages of a liberal compassionate access program:

- avoids negative publicity
- creates goodwill
- marketing - physician experience
  - word of mouth
- creates a market which will pressure third-party payers such as government drug plans and insurance companies - In Canada the widespread compassionate access to 3TC resulted in a great deal of pressure on the government drug plans to cover the drug for those on social assistance.
- creates an ultimate market - keeping someone alive until the drug is licensed.

The consequences of an inadequate program are obvious:

- some may die irreversible or untreatable and, possibly preventable, opportunistic infections;
- some may die unnecessarily before access to 1592 is expanded.

It seems ironic that we are faced now with responding to such a limited compassionate use program, of less than 100 spots for Canada, while on May 15, 1997 Glaxo Wellcome representatives will be attending the Prix Galien ceremonies in Montreal nominated for their innovative new product, 3TC, and that in the media package for the launch of 3TC, GW prides itself on the fact that "[t]hrough the open-label program close to 2800 people living with HIV/AIDS were able to access 3TC in Canada prior to its approval".

We look forward to your early response.

Yours very truly,

Maggie Atkinson
Co-Chair

GlaxoWellcome

CLINICAL RESEARCH DEPARTMENT

May 22, 1997

Maggie Atkinson
CTAC Advisory Team
AIDS Action Now Co-Chair
517 College Street, Suite 420
Toronto, Ontario,
M6G 4A2

Dear Maggie:

Thank you very much for sending us your comments about the 1592U89 compassionate access programme discussed at our May 1st meeting. We have given much thought to your concerns and have discussed these issues with our international colleagues in the US and UK.

Comparing the 3TC programme to the proposed 1592U89 programme at this point in time is difficult. At the comparable point in 3TC's clinical development, the compassionate use programme that we are proposing for 1592U89 did not exist. In fact, the 3TC programme commenced after the majority of the patients had been enrolled into the pivotal phase III studies, and the efficacy/safety profile was better established.

We are initiating the 1592U89 compassionate use programme earlier, as we prepare to start enrollment into the phase III clinical studies. This is an "interim" programme designed to provide some drug to those people who need it, while still obtaining important information in this anti-retroviral experienced population, prior to initiating an expanded access programme. The numbers for this programme (2,500) are greater than those planned for the clinical trial programme during the same period. Towards the end of the year, as more supplies and data become available, we can then initiate the larger expanded access programme. The size of that program will be decided based on safety and efficacy data when it is available from the pivotal clinical studies.

In order to address your concerns we have taken each into consideration as follows:

1) Supply:

The following is a detailed review of the development of 1592U89, which we hope will address your concerns over the supply issues as a result of the change in formulation.

In the summer of 1995 following the merger of the two companies Glaxo Wellcome had a number of compounds in development for the treatment of HIV including: 3TC, 1592U89, 141W94, 1263W94, 935 and tucaresol. Resource was distributed amongst the projects according to the potential of each compound as demonstrated in the early stages of development - those compounds that showed the greatest potential had the greatest resource allocated. Limited resource was applied to 1592U89, which, with post laboratory data appeared the least promising of the HIV drugs in development at that time. However, by November 1995, the situation had changed dramatically when 1592U89 demonstrated marked efficacy in the clinic. These contradictory results were unexpected. It is very unusual for a compound to perform poorly in the laboratory and then go on to show significant

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promise in the clinic, as was the case with 1592U89. Manufacturing scale-up plans, usually initiated on the basis of promising laboratory results were, therefore not in place when these first results with 1592U89 emerged. Chemical resource had been fully assigned to other more promising compounds anticipating that they would be the preferred compound for further development. Fewer chemists worked on 1592U89 and consequently a robust manufacturing process had not been established.

Glaxo Wellcome has a history of working together with communities affected by HIV and was aware of, and very sensitive to the needs of people with HIV and the compassionate requirements for drug outside of the clinical development programme. Consequently, full human and financial resource was put behind the 1592U89 development programme and in particular the number of manufacturing staff was increased by over 300%. Although the manufacturing process was not robust, the chemists persevered and eventually scaled it up to produce greater quantities of 1592U89. It was clear, however, that this process would not support the anticipated huge drug substance requirements of the clinical programme. It also became obvious that supply of drug could not be met from the pilot plant facilities (pilot plant is the intermediate step between the laboratory and full-scale manufacturing). Therefore as well as having to identify a new process, our chemists would have to transfer it rapidly into full scale manufacturing facilities. In addition to these challenges, it was also necessary to move the manufacturing project to the UK.

By the end of November a seemingly viable process was identified; one batch was made in the pilot plant during January 1996 and within 2 months the process was transferred to full production.

By March 1996 the new process was being operated at full scale production, eventually producing large quantities of 1592U89 powder ready for the next stage in manufacture. Due to the need to move 1592U89 through clinical development at a rapid pace and the future need for access on a compassionate basis for those people with no other treatment options, considerable risks were taken in transferring the process to production. Normally before transfer occurs several pilot plant campaigns would be carried out providing experience of often up to 20 batches at each stage of the process. On this occasion only a single pilot plant campaign was carried out producing only ONE batch at each stage. Glaxo Wellcome's manufacturing staff were requested to prepare for full scale production prior to the feasibility of the chemistry being established in the pilot plant. Scale-up from laboratory to full production can often take as long as 2 years or more, but with 1592U89 this was achieved in less than 6 months. All the effort, expertise and risk taking seemed to be paying off.

Everything was going well in primary manufacture until the first batch of 1592U89 was produced in June 1996. A problem was encountered, not with the actual chemistry, but with the physical form of the drug substance itself. The compound was proving difficult to filter and dry, furthermore the pharmacy department were experiencing difficulty in formulating it into capsules. Instead of the substance presenting as a fine powder ready to encapsulate, it was presenting as a large, very hard, solid mass. By this time 1592U89 was at late Phase II clinical development and although significant effort was made to try and resolve the problem, it soon became clear that the salt part of the molecule needed to be changed. This would have been a large undertaking at the very early stage of primary manufacture, but with a considerable amount of unusable drug substance already manufactured, it was a very serious problem, threatening the whole clinical programme. In the past, pharmaceutical drug development programmes have sometimes been discontinued with problems such as these, due to the potential long delays in clinical development programmes. Once again resource was stepped up and the problem was resolved. This problem may have been identified earlier had more time been taken for pilot plant testing, highlighting the risks that are involved in fast-track development. After extensive tests on several different salt forms a suitable alternative salt was identified.

Within four months a new alternative salt had been identified, scaled up into the pilot plant and transferred into full scale production to produce the new version of 1592U89.

At the end of December 1996 and during early 1997 the new 1592U89 had to undergo strict bioequivalence tests enforced by regulatory authorities, as well as further toxicology studies. By the end of March 1997 the new version 1592U89 had passed all these tests and further primary scale-up is now planned. As a comparison, the quantity of 1592U89 planned at this stage of development is 10 to 20 times greater than that produced for other drugs.

1592U89 Development
Calendar of Events

January	
February	
March	New process for 1592U89 scale-up in operation.
April	
May	1592U89 in full scale manufacture.
June	Problem with salt identified.
July	
August	
September	
October	New salt identified and in full scale production.
November	
December	1592U89 undergoes regulatory tests.
January	
February	
March	1592U89 passes regulatory tests.
April	Full scale production.
May	Full scale production.
June	Full scale production.
July	Full scale production.

2) Prioritizing clinical trials:

At this point in the development of 1592U89, we are obligated to learn as much as we can about the utility of this drug in well-controlled clinical trials. We are attempting to balance this work with an early compassionate use programme to provide 1592U89 to those patients with immediate medical need for the drug. Indeed, in this effort we are already prioritizing clinical trials in order to accomplish both of these objectives.

3) Need:

Many treatment options exist now and we cannot encourage patients to forego currently marketed drugs with proven efficacy in favor of a new treatment about which very little is known at this

time. Who best will benefit from 1592U89 remains to be determined from the Phase III clinical trial programme.

4) Safety concerns:

We acknowledge that safety issues are an ongoing concern and may have less impact on people with very few options. This is why we are committed to compassionate access for 1592U89 and why the programme is starting so early in the clinical development programme.

5) Entry criteria:

At this early stage in development, the treating physicians need to determine who best qualifies for the drug based on their clinical judgment. We are open to applying a system designed in conjunction with physicians, yourselves and the Canadian HIV Trials Network (CTN). Your input into any additional criteria for selection will be considered.

6) Mild to moderate dementia patients:

Since no data is available to prove that 1592U89 is effective against dementia, the ongoing clinical trial (CNAB3004) needs to be completed as soon as possible to address this point. Patients in this trial are adding either 1592U89 or placebo to their existing treatment regimen, and are not subject to receive a substandard of care. We understand your concerns and as such we have agreed to broaden the entry criteria to include people with MSK stage 2 disease once recruitment into the clinical trial is complete. We believe the company would be considered irresponsible by allowing treating physicians to release an unproven drug at an earlier stage of the disease than this, as quite often early stage dementia can be confused with other conditions.

7) Registration Process:

As discussed at our meeting on May 1, we agree that there is a need to provide access to the drug across the country in the most equitable manner possible, and that the CTN could play a role in the registration and selection of applicants. After our meeting we held discussions with the CTN, and they have agreed in principle to assist us with the programme. The CTN will issue information to all physicians about the program, accept applications, and review and approve applicants for entry into the programme, very similar to their involvement with the saquinavir compassionate use programme.

The logistics of CTN's role need to be worked out once more information about the programme is available. Access will be based on geographic need as determined by the prevalence of HIV/AIDS in each region across the country. The above will ensure that participating centres will not be able to hand pick individuals from their own practice, and that all who apply will have an opportunity to access the drug. The overall programme will be conducted by a contract research organization (CRO).

Due to Canada's size, we did not want to limit Canadian centres to only two or three, and put forward a proposal for eight centres across the country, as discussed at our meeting on May 1. As a result of this week's compassionate use teleconference, we are able to implement this programme at approximately 12 centres across the country. The number of participants for each country should be finalized within the next week, and we will communicate this information to you as soon

as it is available. Individuals outside of these centres can apply for the programme through their physician. If they are approved, individuals will have to go to a participating centre for access to drug, and attend all study-related visits for assessment and data collection. Required visits will likely be every two months, and individuals can continue to see their own physician during this time. As we are collecting important safety and efficacy data, which will help shape the expanded access programme, consistency must be maintained by involving a limited number of centres/physicians world-wide.

8) Intercompany collaborative programme:

A 1592U89 collaborative studies review team has been organized to review all external study proposals for scientific and clinical merit and strategic importance. This team has reviewed over 40 proposals to date, and a number of them have been accepted. Glaxo Wellcome is working with a number of collaborative groups including the ICC, ACTG, etc., to establish and conduct collaborative studies with 1592U89, as well as our other products. We remain open to collaboration. We hope that our colleagues in the industry will also feel the need to furnish drugs to those most in need at the earliest possible time in their development.

9) Future considerations:

We truly believe that opening this "interim" programme ahead of the expanded access programme is a way to provide early access to 1592U89. This will allow more information to be obtained, in order to use this drug in the best way possible for the expanded access programme, while trying to meet the varying needs of communities internationally.

We hope that this information helps to explain the rationale behind the programme more clearly. If in the future you would like to discuss any subject with us, we would be more than happy to meet with you.

Sincerely,

David Krakowsky, B.Sc. Phm., Pharm. D.
Clinical Research Manager,
Infectious Diseases

cc: T. McAuley
L. Blinder
R. Guerin
C. Lafleur
R. Kort
C. McClure

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CLINICAL RESEARCH DEPARTMENT

May 22, 1997

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promise in the clinic, as was the case with 1592U89. Manufacturing scale-up plans, usually initiated on the basis of promising laboratory results were, therefore not in place when these first results with 1592U89 emerged. Chemical resources had been fully assigned to other more promising compounds anticipating that they would be the preferred compound for further development. Fewer chemists worked on 1592U89 and consequently a robust manufacturing process had not been established.

Glaxo Wellcome has a history of working together with communities affected by HIV and was aware of, and very sensitive to the needs of people with HIV and the compassionate requirements for drug outside of the clinical development programme. Consequently, full human and financial resource was put behind the 1592U89 development programme and in particular the number of manufacturing staff was increased by over 300%. Although the manufacturing process was not robust, the chemists persevered and eventually scaled it up to produce greater quantities of 1592U89. It was clear, however, that this process would not support the anticipated huge drug substance requirements of the clinical programme. It also became obvious that supply of drug could not be met from the pilot plant facilities (pilot plant is the intermediate step between the laboratory and full-scale manufacturing). Therefore as well as having to identify a new process, our chemists would have to transfer it rapidly into full scale manufacturing facilities. In addition to these challenges, it was also necessary to move the manufacturing project to the UK.

By the end of November a seemingly viable process was identified; one batch was made in the pilot plant during January 1996 and within 2 months the process was transferred to full production.

By March 1996 the new process was being operated at full scale production, eventually producing large quantities of 1592U89 powder ready for the next stage in manufacture. Due to the need to move 1592U89 through clinical development at a rapid pace and the future need for access on a compassionate basis for those people with no other treatment options, considerable risks were taken in transferring the process to production. Normally before transfer occurs several pilot plant campaigns would be carried out providing experience of often up to 20 batches at each stage of the process. On this occasion only a single pilot plant campaign was carried out producing only ONE batch at each stage. Glaxo Wellcome's manufacturing staff were requested to prepare for full scale production prior to the feasibility of the chemistry being established in the pilot plant. Scale-up from laboratory to full production can often take as long as 2 years or more, but with 1592U89 this was achieved in less than 6 months. All the effort, expertise and risk taking seemed to be paying off.

Everything was going well in primary manufacture until the first batch of 1592U89 was produced in June 1996. A problem was encountered, not with the actual chemistry, but with the physical form of the drug substance itself. The compound was proving difficult to filter and dry, furthermore the pharmacy department were experiencing difficulty in formulating it into capsules. Instead of the substance presenting as a fine powder ready to encapsulate, it was presenting as a large, very hard, solid mass. By this time 1592U89 was at late Phase II clinical development and although significant effort was made to try and resolve the problem, it soon became clear that the salt part of the molecule needed to be changed. This would have been a large undertaking at the very early stage of primary manufacture, but with a considerable amount of unusable drug substance already manufactured, it was a very serious problem, threatening the whole clinical programme. In the past, pharmaceutical drug development programmes have sometimes been discontinued with problems such as these, due to the potential long delays in clinical development programmes. Once again resources was stepped up and the problem was resolved. This problem may have been identified earlier had more time been taken for pilot plant testing, highlighting the risks that are involved in fast-track development. After extensive tests on several different salt forms a suitable alternative salt was identified.

Within four months a new alternative salt had been identified, scaled up into the pilot plant and transferred into full scale production to produce the new version of 1592U89.

At the end of December 1996 and during early 1997 the new 1592U89 had to undergo strict bioequivalence tests enforced by regulatory authorities, as well as further toxicology studies. By the end of March 1997 the new version 1592U89 had passed all these tests and further primary scale-up is now planned. As a comparison, the quantity of 1592U89 planned at this stage of development is 10 to 20 times greater than that produced for other drugs.

1592U89 Development
Calendar of Events

January	
February	
March	New process for 1592U89 scale-up in operation.
April	
May	1592U89 in full scale manufacture.
June	Problem with salt identified.
July	
August	
September	
October	New salt identified and in full scale production.
November	
December	1592U89 undergoes regulatory tests.
January	
February	
March	1592U89 passes regulatory tests.
April	Full scale production.
May	Full scale production.
June	Full scale production.
July	Full scale production.

2) Prioritizing clinical trials:

At this point in the development of 1592U89, we are obligated to learn as much as we can about the utility of this drug in well-controlled clinical trials. We are attempting to balance this work with an early compassionate use programme to provide 1592U89 to those patients with immediate medical need for the drug. Indeed, in this effort we are already prioritizing clinical trials in order to accomplish both of these objectives.

3) Need:

Many treatment options exist now and we cannot encourage patients to forego currently marketed drugs with proven efficacy in favor of a new treatment about which very little is known at this

time. Who best will benefit from 1592U89 remains to be determined from the Phase III clinical trial programme.

4) Safety concerns:

We acknowledge that safety issues are an ongoing concern and may have less impact on people with very few options. This is why we are committed to compassionate access for 1592U89 and why the programme is starting so early in the clinical development programme.

5) Entry criteria:

At this early stage in development, the treating physicians need to determine who best qualifies for the drug based on their clinical judgment. We are open to applying a system designed in conjunction with physicians, yourselves and the Canadian HIV Trials Network (CTN). Your input into any additional criteria for selection will be considered.

6) Mild to moderate dementia patients:

Since no data is available to prove that 1592U89 is effective against dementia, the ongoing clinical trial (CNAB3004) needs to be completed as soon as possible to address this point. Patients in this trial are adding either 1592U89 or placebo to their existing treatment regimen, and are not subject to receive a substandard of care. We understand your concerns and as such we have agreed to broaden the entry criteria to include people with MSK stage 2 disease once recruitment into the clinical trial is complete. We believe the company would be considered irresponsible by allowing treating physicians to release an unproven drug at an earlier stage of the disease than this, as quite often early stage dementia can be confused with other conditions.

7) Registration Process:

As discussed at our meeting on May 1, we agree that there is a need to provide access to the drug across the country in the most equitable manner possible, and that the CTN could play a role in the registration and selection of applicants. After our meeting we held discussions with the CTN, and they have agreed in principle to assist us with the programme. The CTN will issue information to all physicians about the program, accept applications, and review and approve applicants for entry into the programme, very similar to their involvement with the saquinavir compassionate use programme.

The logistics of CTN's role need to be worked out once more information about the programme is available. Access will be based on geographic need as determined by the prevalence of HIV/AIDS in each region across the country. The above will ensure that participating centres will not be able to hand pick individuals from their own practice, and that all who apply will have an opportunity to access the drug. The overall programme will be conducted by a contract research organization (CRO).

Due to Canada's size, we did not want to limit Canadian centres to only two or three, and put forward a proposal for eight centres across the country, as discussed at our meeting on May 1. As a result of this week's compassionate use teleconference, we are able to implement this programme at approximately 12 centres across the country. The number of participants for each country should be finalized within the next week, and we will communicate this information to you as soon

as it is available. Individuals outside of these centres can apply for the programme through their physician. If they are approved, individuals will have to go to a participating centre for access to drug, and attend all study-related visits for assessment and data collection. Required visits will likely be every two months, and individuals can continue to see their own physician during this time. As we are collecting important safety and efficacy data, which will help shape the expanded access programme, consistency must be maintained by involving a limited number of centres/physicians world-wide.

8) Intercompany collaboration programme:

A 1592U89 collaborative studies review team has been organized to review all external study proposals for scientific and clinical merit and strategic importance. This team has reviewed over 40 proposals to date, and a number of them have been accepted. Glaxo Wellcome is working with a number of collaborative groups including the ICC, ACTG, etc., to establish and conduct collaborative studies with 1592U89, as well as our other products. We remain open to collaboration. We hope that our colleagues in the industry will also find the need to furnish drugs to those most in need at the earliest possible time in their development.

9) Future considerations:

We truly believe that opening this "interim" programme ahead of the expanded access programme is a way to provide early access to 1592U89. This will allow more information to be obtained, in order to use the drug in the best way possible for the expanded access programme, while trying to meet the varying needs of communities internationally.

We hope that this information helps to explain the rationale behind the programme more clearly. If in the future you would like to discuss any subject with us, we would be more than happy to meet with you.

Sincerely,

David Krakowsky, B.Sc. Phm., Pharm. D.
Clinical Research Manager,
Infectious Diseases

cc: T. McAuley
L. Binder
R. Guerin
C. Lafeuille
R. Kort
C. McClure

1592 ACCESS COALITION

To: Sandy Thurmond	From : Linda Grinberg	
Company: White House-AIDS Office	Telephone: 310-471-6565	
Fax Number: 1-202-632-1096	Fax Number: 310-471-4565	
Subject : Conf. Call	Date: 6/18/97	Pages: 1 2

Please see attached list of participants in today's conference call scheduled at 6:00 EST/3:00 PST.

Reminder: The phone number to call in to is (800) 360-0565. Please ask for the 1592 Access Coalition call with Jeff Getty & Linda Grinberg, moderators.

If there is any problem in accessing the call, please call (800) 825-2125 and tell operator the conf. call # is 811-~~8888~~. 48

We look forward to speaking with you later today.

1592 ACCESS COALITION

Name	Affiliation	Phone	Fax
1. Meg Atkinson	AIDS Action Now!/Toronto	416-487-8065	416-533-2127
2. Ron Baker	S.F. AIDS Foundation	415-487-8065	415-487-8069
3. Bill Bahlman	Treatment & Data Committee	212-929-4952	212-929-4952
4. Peter Cashman	ACT UP Los Angeles	213-669-7301	213-669-7302
5. Sally Cooper	PWA Health Group	212-255-0520	212-255-2080
6. Leigh Paidolfino-Danas	U.K.	44-171-793-7444	
7. Paul Davis	ACT UP Philadelphia	215-731-1844	215-731-1845
8. Martin Delaney	Project Inform	415-331-0184	415-331-2114
9. Jeff Getty	ACT UP Golden Gate	510-653-6278	510-653-6099
10. David Gilden	Gay Men's Health Crisis	718-624-6578-h 212-367-1452-o	918-624-8399
11. Linda Grinberg	Project Inform/F.A.I.R.	310-471-6565	310-471-4565
12. John Iverson	ACT UP East Bay	510-568-1680	
13. Cleve Jones	Names Project	707-865-9047	707-865--0541
14. Kiyoshi Kiromiya	Critical Path	215-545-2212	215-545-2212
15. Kate Krauss	ACT UP Philadelphia	215-731-1844	215-731-1845
16. James Learned	PWA Health Group	212-255-0520	212-255-2080
17. Jules Levin	N.A.T.A.P.	718-624-8541	718-624-8399
18. Andy Lipschitz, MD		516-935-6359	516-938-5470
19. L. Joel Martinez	Center for AIDS	713-527-8219	713-521-3679
20. Eileen Mitzman	Mother's Voices	212-737-3335	212-737-1092
21. Lili Rundback	Mother's Voices	212-730-2777	212-730-4378
22. Matthew Sharp	ACT UP Golden Gate	415-626-4053	415-626-0451
23. Theo Smart	Treatment Action Group	212-260-2607	212-673-8921

Revised 6/18/97

Fax from Linda Grinberg

To: Sandy Thurmond	From : Linda Grinberg	
Company: The White House, AIDS Czar	Telephone: 310-471-6565	
Fax Number: 1-202-632-1096	Fax Number: 310-471-4565	
Subject : 1592 Cons. Stmt. Update & News Clips	Date: 6/4/97	Pages: 12

Sandy: I must tell you that you boosted our morale enormously with your enthusiasm and commitment to go to bat for us with Glaxo on this important issue. I spoke with a number of folks on the call afterwards and they were excited and encouraged by you -- your "can do" attitude, the astute questions you asked and the issues you zeroed in on. We're all keeping our fingers crossed, hoping and praying you can make a difference. As you know, based on recent statistics, it is estimated that approx. 50,000 in the U.S. alone will probably die this year, and this drug could be the difference between life and death to many of these people.

I just wanted to copy you on the signatures collected to date on the 1592 Consensus Statement, which I finally had time to update. I must point out to you that this drive really took on a life of its own, as there hasn't been press publicizing the Consensus Statement since several articles appeared in November and December of last year, and approx. 150 additional signatures have come in since then, unsolicited, simply by word of mouth.

One item we neglected to mention to you, which may possibly be another factor in this inadequate compassionate use program (or lack thereof) may be a perception that if the drug is more widely available through expanded access they fear they may have difficulty enrolling patients in the trials program, and filing the NDA is top priority. We met with Glaxo reps last summer in DC, pressing them to begin planning for expanded access, as it was clear back then that late-stage patients would not qualify for their trials program. They finally responded in a very heated conf. call with 20-30 community reps in November, at which time they declared they wouldn't even begin to consider expanded access until Phase III trials were fully accrued, as they were afraid this would interfere with their ability to recruit patients. The response was quite angry, across the board, as not only was this precedent setting, they were just beginning Phase II/III trials and nowhere even close to beginning Phase III trials, thus precipitating the Cons. Statement. Phase III trials are only just beginning now, I might add, with unexplained delays and little progress since Vancouver last July ...

Evidently, I believe we were mistaken about the expiration on the patent on Zantac, as when I did some checking I found some recent articles, attached, indicating that the patent runs out this July, at which time there will be generic competition. Haven't located the exact date on the expiration of AZT yet, but we'll keep you informed.

It's a pleasure to work with you on this. Having someone in the White House who seems to genuinely care, after so many years of silence and seeming complacency, is such a breath of fresh air and the sense of renewed faith and hope yesterday was truly palpable.

We look forward to our followup call on the 11th. Thanks!!! Good luck on the 10th!

Best, Linda

cc: Jeff, Ron, Cleve, and Marty

Consensus Statement on 1592 Expanded Access and Accelerated Approval

- **Overview**

Access to Glaxo Wellcome's 1592U89 ("1592") now in development, potentially represents the only viable option for delaying disease progression for many people living with HIV and AIDS who have exhausted the benefit from currently approved antiviral therapies. In early clinical studies, 1592 has demonstrated a more potent level of antiviral activity than other RT inhibitors, with minimal side effects. It's most important property, however, is that people have not previously been exposed to it and it therefore offers the hope of renewed antiviral activity. This renders the drug critically important to two patient populations: (1) those who have already lost sensitivity to the other drugs of this type, and (2) those who need to use at least one "fresh" or new nucleoside analogue RT inhibitor to make reasonable use of combination therapy with protease inhibitors or non-nucleoside RT inhibitors. Existing evidence clearly suggests that combining such drugs with previously used therapies diminishes their effectiveness and leads to more rapid development of resistance.

The benefit of this drug may be limited due to the development of resistance, a problem common to all currently approved antiviral compounds. While it may take years of additional study to determine its optimal use, this should not delay prompt access to this therapy by people in immediate need. Delaying the availability of this drug until Phase III trials are fully accrued is unacceptable and represents a significant change from past practices. For example, the ddI, d4T, and AZT expanded access programs all took place while trials were still recruiting. We are very concerned that the recent activities of several pharmaceutical companies represents a broad effort to minimize the number of patients served by expanded access programs. Any such effort around 1592 would be a moral affront to the rights and needs of people with HIV/AIDS and their healthcare providers.

We hereby propose the following 1592 expanded access program, to be phased in in stages, with immediate access to those in urgent need.

- **First Phase - Compassionate Use/Salvage Therapy**

Glaxo Wellcome and the Food and Drug Administration must cooperate and take a more compassionate stance to make this promising compound immediately available in a "salvage program" once a recommended dosing schedule has been established. This compassionate access/salvage program should make drug available as soon as possible for those people who have failed existing therapies and risk near-term danger of death or life-threatening infections.

The development of this drug must take into consideration its unique potential to provide benefit to the acutely compromised segment of the HIV-infected population. Availability of salvage strategies is of the highest priority for people living with HIV. There is no logical or moral reason to withhold this drug from people with advanced illness, people whose lives hang in the balance. Currently, this compound qualifies, by any humane standard, for compassionate use.

This first phase of Compassionate Use/Salvage Therapy should provide 1592 without delay to patients who meet any one of the following two requirements:

1. ***CD4+ Cell Count <50 OR Viral Load >40,000 copies/ml***
   AND Treatment Failure to approved RT Inhibitors AND at least one Protease Inhibitor;
2. ***Diagnosis of AIDS Dementia Complex (ADC), unresponsive to existing therapies.***

We believe evidence of the above conditions can be accomplished with a minimal amount of paperwork. A physician's letter accompanied by one lab report should be sufficient to establish any of the above criteria.

- **Second Phase - Expanded Access**

This second phase of Expanded Access should provide 1592 during recruitment and conduct of Phase II/III clinical trials, but no later than ninety (90) days from the start-up of the First Phase, to patients who meet any of the following criteria:

1. ***Patients who do not qualify for or are denied entry in a 1592 clinical trial and have a medical need for 1592, or***

2. *Patients who do not live within a radius of 15 miles of an active clinical trial site, or*
3. *Patients whose lives would be immediately jeopardized by randomization to an ineffective treatment regimen, or*
4. *Patients with a CD4+ Cell count below entry requirements of clinical trials, or*
5. *Viral Load greater than 20,000 copies/mL, despite use of currently approved therapies, or*
6. *Treatment Failure or demonstrated genotypic or phenotypic resistance to approved RT inhibitors.*

- **Accelerated Approval**

This compound should be licensed for accelerated approval as soon as possible. FDA approval of this compound should be based on existing regulations governing accelerated approval of new drugs for life-threatening illnesses:

1. *Clear evidence of benefit on surrogate markers have been demonstrated;*
2. *Principal toxicities and drug interactions have been defined;*
3. *Longer-term development plans have been initiated designed to determine the drug's usefulness in promoting clinical and survival improvements and durability of response, as part of a medical strategy for coping with HIV infection.*

**We urge the sponsor to file applications for accelerated approval as soon as possible.*

- **Resistance, Pharmacokinetics and Drug Interactions**

As with all antivirals, the development of drug-resistant strains of virus, drug interactions and pharmocokinetic variances while using this compound may warrant additional considerations. To address this concern, sponsors should also be required, prior to accelerated approval, to present meaningful data on:

1. *the speed and levels of resistance encountered;*
2. *the degree of cross-resistance found with other nucleoside analogues;*
3. *the interaction of the compound with other commonly used anti-HIV medications;*
4. *bioavailability in men, women, and children and determination of the degree which blood levels vary depending on body weight.*

- **Summation**

Any effort to withhold access to promising compounds is contrary to the interests of HIV-infected people, inconsistent with the Accelerated Approval regulations, and scientifically unwarranted. The long history of the development of the earlier generation of antiviral drugs clearly demonstrates that it is possible to accrue patients and continue conducting clinical trials of compounds, long after their marketing approval. Because of the issues of drug resistance and drug failure over time, new therapies for HIV disease will continue to play a critical role no matter how many drugs become available on the market. New therapies, like 1592, must continue to be made available as rapidly as possible to patients with immediate needs for changed or improved treatment.

* *Revised as of 11/27/96*

ORGANIZATIONS: **SIGN-ONS AS OF MAY 30, 1997**

1. **ACTUP BOSTON, Boston, MA**
2. **ACTUP EAST BAY, Oakland, CA**
3. **ACTUP GOLDEN GATE, San Francisco, CA**
4. **ACTUP LOS ANGELES, Los Angeles, CA**
5. **ACTUP MINNESOTA, Minneapolis, MN**
6. **ACTUP NEW YORK, New York, NY**
7. **ACTUP PARIS, Paris, FRANCE**
8. **ACTUP PHILADELPHIA, Philadelphia, PA**
9. **AIDS ACTION COMMITTEE OF MASSACHUSETT,Boston, MA**
10. **AIDS ACTION COUNCIL, Washington, DC**
11. **AIDS HEALTHCARE FOUNDATION, Pasadena, CA**
12. **AIDS PROJECT LOS ANGELES /APLA, Los Angeles, CA**

13. **AIDS RESEARCH ALLIANCE, Los Angeles, CA**
14. **AIDS RESEARCH INFORMATION CENTER, INC/ARIC, Baltimore, MD**
15. **AIDS SERVICE CENTER, Pasadena, CA**
16. **AIDS SURVIVAL PROJECT, Atlanta, GA**
17. **AIDS TREATMENT INITIATIVES, Atlanta, GA**
18. **AIDS TREATMENT NEWS, San Francisco, CA**
19. **BEING ALIVE, Los Angeles, CA**
20. **BRITISH COLUMBIA PERSONS WITH AIDS SOCIETY, Canada**
21. **CENTER FOR AIDS, THE, Houston, Texas**
22. **COUNSELING CENTER, THE dba GULF COAST MENTAL HEALTH, MI**
23. **FACE- L.A., Pasadena, CA**
24. **FLORIDA AIDS ACTION COUNCIL, Florida**
25. **GAY LIBERATION FRONT, Minneapolis, MN**
26. **GAY MEN'S HEALTH CRISIS/GMHC, New York, NY**
27. **LINDA GRINBERG FOUNDATION, Los Angeles, CA**
28. **HAITIAN AMERICAN COMMUNITY COUNCIL, Delray Beach, Florida**
29. **HOMESTEAD HOSPICE & THE "DALLAS HOUSE", Los Angeles, CA**
30. **IHS AT HANOVER**
31. **ISRAEL AIDS TASK FORCE, Tel Aviv, Israel**
32. **KRAUS MEDICAL PARTNERS, Los Angeles, CA**
33. **LAMBDA COUNSELING CENTER, Miami, Miami Beach, Ft. Lauderdale & Palm Beach, FL**
34. **LIVING WELL PROJECT/ASIAN PACIFIC ISLANDERS AIDS SERVICES, San Francisco, CA**
35. **LOG CABIN REBUBLICANS, Washington, D.C.**
36. **MOTHER'S VOICES, New York, NY**
37. **MULTICULTURAL AIDS COALITION, INC., Boston, MA**
38. **NATIONAL AIDS TREATMENT ADVOCACY PROJECT/NATAP, New York, NY**
39. **NATIONAL ASSOCIATION OF PEOPLE WITH AIDS/NAPWA, Washington, DC**
40. **NATIONAL MINORITY AIDS COUNCIL, Washington, DC**
41. **OPEN DOORS**
42. **PARAGON MEDICAL RESEARCH, Los Angeles, CA**
43. **POZ MAGAZINE, New York, NY**
44. **PROJECT INFORM, San Francisco, CA**
45. **PROJEKT INFORMATION, Munich, Germany**
46. **PWA HEALTH GROUP, New York, NY**
47. **PWAlive/MINNESOTA, Minneapolis, MN**
48. **REACH OF SOUTHERN ARIZONA, AZ**
49. **RESEARCH SANCTUARY, Los Angeles, CA**
50. **SAN FRANCISCO AIDS FOUNDATION/BETA, San Francisco, CA**
51. **SAN LUIS OBISPO HIV CARE CONSORTIUM, CA**
52. **SEARCH FOR A CURE, Boston, MA**
53. **SONOMA COUNTY COMMISSION ON AIDS, CA**
54. **SO. MISSISSIPPI AIDS TASK FORCE, MI**
55. **TAMPA AIDS NETWORK, Tampa, FL**
56. **TEST POSITIVE AWARE, Chicago, IL**
57. **TREASURE COAST COMMUNITY AIDS NETWORK, Florida**
58. **TREATMENT ACTION GROUP/TAG, New York, NY**
59. **TREATMENT & DATA COMMITTEE, New York, NY**
60. **UNITED FOUNDATION FOR AIDS, Miami, FL**
61. **VALLEY AIDS INFORMATION NETWORK, Corvallis, Oregon**
62. **WOMEN ALIVE, Los Angeles, CA**

INDIVIDUALS: **SIGN-ONS AS OF MAY 30, 1997**

1. George H. Adams, Atlanta, Georgia
2. Moises Agosto, National Minority AIDS Council, Washington, DC
3. Linda R. Allen
4. Harlan Annheuser, Marietta, Georgia
5. Alberto Avendano, MD, Florida AIDS Action Council, Florida
6. Bill Bahlman, Treatment & Data Committee, New York
7. A. Cornelius Baker, National Association of People with AIDS/NAPWA, Washington, DC

8. Ron Baker, SF AIDS Foundation/BETA, San Francisco, California
9. David Barr, Gay Men's Health Crisis/GMHC, New York, New York
10. Dirk Belau, Geneva, Switzerland
11. Carol Bennett
12. Jessica C. Bigg, So. Mississippi AIDS Task Force, Mississippi
13. Voa Bigg, So. Mississippi AIDS Task Force, Mississippi
14. Ron A. Braun, Pacific Oaks Medical Group, Van Nuys, California
15. G'dali Braverman, Living Well Project, San Francisco, California
16. William K. Brent, Jr., So. Mississippi AIDS Task Force, Mississippi
17. Larry Bressiour, Search for a Cure, Boston, Massachusetts
18. Gregory Britt, AIDS Research Alliance, Los Angeles, California
19. Sara J. Brookins, So. Mississippi AIDS Task Force, Biloxi, Mississippi
20. Nicholas F. Brookins, So. Mississippi AIDS Task Force, Biloxi, Mississippi
21. Jean Haspel Brooks, RJNPC, Infectious Disease Associates, Atlantic City Medical Center, , Atlantic City, New Jersey
22. Carl Brown, Treasure Coast Community AIDS Network, Florida
23. Glenn Brown, ACTUP Philadelphia, Pennsylvania
24. Randall Brown, Atlanta, Georgia
25. William D. Bryant, Boulder Creek, California
26. Todd Burger, Chicago, Illinois
27. John J. Caringi, W. Virginia
28. Deborah A. Carriveau, W. Virginia
29. Jan Casey
30. Jeffrey B. Cason, New York, New York
31. Peter Cashman, ACTUP Los Angeles, California
32. Rhonda Chambers, HIV Study Group, Austin, Texas
33. Henry E. Chang, AIDS Healthcare Foundation, California
34. James Clark, Laguna Beach, California
35. Keith L. Cobb, Georgia Public Health Lab, Tucker, Georgia
36. Winifred Cochran, Marietta, Georgia
37. C. Trustran Coffin, Atlanta, Georgia
38. Mark Cohen, United Foundation for AIDS, So. Miami, Florida
39. Judith Colbs, Atlanta, Georgia
40. Marvin Colbs, Atlanta, Georgia
41. Christopher Collins
42. Richard Cooper, M.D., Kraus Medical Partners, Los Angeles, California
43. Sarah ("Sally") C. Cooper, PWA Health Group, New York, New York
44. Drew Cornutt, Atlanta, Georgia
45. Susan Cornutt, Atlanta, Georgia
46. Jim Corti, Research Sanctuary & Linda Grinberg Foundation, Los Angeles, California
47. Gary E. Costa, Being Alive, California
48. John Curtis Cottingham, Alabama
49. Linda F. Cottingham, State of Alabama, Dept. of Human Resources, Alabama
50. Spencer Cox, Treatment Action Group/TAG, New York, New York
51. Myron C. Crider, Morrow, Georgia
52. Michael J. Cross, PWA, San Francisco, California
53. Harold W. Cummings, Atlantic City, New Jersey
54. Denise Dagrosa, Infectious Disease Associates, Atlantic City Medical Center, Atlantic City, New Jersey
55. Richard T. Dalton, Flowery Branch, Georgia
56. Donald T. Daniels, PAC, AIDS Healthcare Foundation, Los Angeles, California
57. Tony Davis, Mother's Voices, New York, New York
58. Robert Dal Porto, PWA with Being Alive, Los Angeles, California
59. Kenneth De Haan
60. Martin Delaney, Project Inform, California
61. Margo Denison, Valley AIDS Information Network, Inc., Corvallis, Oregon
62. Rebecca Dennison, W.O.R.L.D., Oakland, California
63. John Deshane, Los Angeles, California
64. Scott Dewees, W. Hollywood, California
65. John Dolan, Raleigh, North Carolina
66. Jim Driscoll, Log Cabin Republicans, San Francisco, California
67. Marianne DuBose, So. Mississippi AIDS Task Force, Mississippi
68. Ferd Eggan, AIDS Coordinator, City of Los Angeles, California
69. Peter Engelhard, D.O., Fisher Medical Group, Miami, Florida
70. Michael England, San Francisco, California

71. Amy Erlich, Atlanta, Georgia
72. Donna Eschulz-Wilkinson, FACE-L.A., Pasadena, California
73. Charles Farthing, M.D., AIDS Healthcare Foundation, Los Angeles, California
74. Tracy Fennell
75. Gil Ferguson, British Columbia Persons with AIDS Society, Canada
76. Gary Foret, Atlanta, Georgia
77. Frances Frazetta
78. Brenda Freiberg, Board of Directors, Project Inform & AIDS Service Center, California
79. Ruben Gamundi, AIDS Project Los Angeles, California
80. David Garner, Atlanta, Georgia
81. Ramon M. Garcia, REACH of So. Arizona, Bisbee, Arizona
82. Aileen Getty, Homestead House & The "Dallas House", Los Angeles, California
83. Jeff Getty, ACT UP Golden Gate, San Francisco, CA
84. Greg Gilliam, Chicago, Illinois
85. Marc Gilbert, Atlantic City Medical Center patient, Atlantic City. New Jersey
86. Joseph L. Goebelt, Santa Clara, California
87. Michael Gottlieb, M.D., Gottlieb Medical Group, Los Angeles, California
88. Garrison J. Grace, Ft. Lauderdale, Florida
89. Jeff Graham, AIDS Survival Project, Atlanta, Georgia
90. Linda Grinberg, Linda Grinberg Foundation & Project Inform, California
91. Jeffrey S. Gunnoe, West Virginia
92. John Haiduck, Test Positive Aware, Chicago, Illinois
93. Robert Halfhial, Minneapolis, Minnesota
94. Lee Hardy, ARIC, Inc., Baltimore, Maryland
95. Larry Harman, Ph.D., Lambda Counseling Center, Miami, Ft. Lauderdale & Palm Beach, Florida
96. Zaida Harrington, Biloxi, Mississippi
97. Mark Harris, Atlanta, Georgia
98. Robert E. Hart, Atlanta, Georgia
99. John F. Haskell, Chicago, Illinois
100. Roberta Luskin-Hawk, M.D., St. Joseph Hospital, Chicago, Illinois
101. Rene Milet Hernandez, Multicultural AIDS Coalition, Inc., Boston, Massachusetts
102. Rachael Hincey
103. Gideon Hirsch, Israel AIDS Task Force, Tel Aviv, Israel
104. Peter M. Hoffmann, Treasure Coast Community AIDS Network, Florida
105. Stephanie Hoffman, Lithonia, Georgia
106. Carlton Hogan, PWAlive, Minneapolis, Minnesota
107. Ernest Hopkins, National Association of People with AIDS/NAPWA, Washington, DC
108. Dennis Hughes, Treasure Coast Community AIDS Network, Florida
109. Terrence L. Ibbs, D.O., N. Miami Beach, Florida
110. Crystal Iondan, Treasure Coast Community AIDS Network, Florida
111. John Iverson, ACTUP/East Bay, Oakland, California
112. John S. James, AIDS Treatment News, San Francisco, California
113. Michael James, Atlanta, Georgia
114. Joseph J. Johnson, Treasure Coast Community AIDS Network, Florida
115. Lewis E. Johnson, Chicago, Illinois
116. Robert Folan Johnson, ACTUP Boston, Boston, Massachusetts
117. Andrew Johnston, M.D., Chicago, Illinois
118. Cleve Jones, Founder/AIDS Memorial Quilt, Villa Grande, California
119. Mary Jones, Fan Free Clinic, Richmond, VA
120. Leslie Kaliades, PWA, Jamaica, New York
121. Linda Kaplan, Syracuse, New York
122. Larry Kessler, AIDS Action Committee - Boston, Boston, Massachusetts
123. Chai Khoo, San Jose, California
124. David E. Kilburn, San Luis Obispo HIV Care Consortium, California
125. Barry Krost, Board of Directors, Project Inform, San Francisco, California
126. Ann Kurth, Mother's Voices, New York, New York
127. Irma Lamberty, Infectious Disease Associates, Atlantic City Medical Center, , Atlantic City, New Jersey
128. Terry Laug, San Jose, California
129. Michael J. Lavery, Niskayuna, New York
130. James Learned, PWA Health Group, New York, New York
131. Gina Lee, Gahanna, Ohio
132. Sheryl A. Leon, The Counseling Center dba Gulf Coast Mental Health, Biloxi, Mississippi
133. Jules Levin, National AIDS Treatment Advocacy Project/NATAP, New York, New York

134. Darrell Limbocker, Tennessee Colony, Texas
135. Dennis Littrell, Raleigh, North Carolina
136. Mary Lucey, AIDS Policy Analyst, City of Los Angeles, California
137. Peter E. Mace-Myers, Atlanta, Georgia
138. Nancy MacNeil, Project Director, Women Alive, Los Angeles, California
139. James V. Madaras, Treasure Coast Community AIDS Network, Florida
140. Thomas L. Magee, M.D., Medical Offices, Los Angeles, California
141. Rachelle Mark, Los Angeles, California
142. L. Joel Martinez, The Center for AIDS, Houston, Texas
143. Kevin McCaffery, W. Virginia
144. Andrea McCardell, Infectious Disease Associates, Atlantic City Medical Center, Atlantic City, New Jersey
145. James McKee
146. Paul McLaughlin, Treasure Coast Community AIDS Network, Florida
147. Michael G. Meatyard, Atlanta, Georgia
148. Lee Mitchell
149. Edward Mohilef, Ph.D., EGM Associates, Flagstaff, Arizona
150. Kelley P. Moore, Tampa AIDS Network, Tampa, Florida
151. Robin Capps Munger
152. Alfredo Munoz, Oakland, California
153. Kelley P. Moore, Tampa, Florida
154. Kenneth Noonan, Everett, Washington
155. Christopher B. O'Hare, Treasure Coast Community AIDS Network, Florida
156. John Ortado, Jr., Treasure Coast Community AIDS Network, Florida
157. Paula L. Osborn
158. Robin R. Pabon, So. Mississippi AIDS Task Force, Mississippi
159. Allison Peterson, Marietta, Georgia
160. Eddie Lee Pitts, Atlanta, Georgia
161. Tony Poleto, Treasure Coast Community AIDS Network, Florida
162. Wallace Potts, self-employed film archivist, Los Angeles, California
163. Shirley Pough, Treasure Coast Community AIDS Network, Florida
164. Martin J. Powers, Chicago, Illinois
165. Chris Presley
166. William D. Prevatt, Tampa AIDS Network, Tampa, Florida
167. Robert Curt Raposa, Pelham, Georgia
168. Barton Rarick, Chicago, Illinois
169. Jonathan David Reed, Atlanta, Georgia
170. Robert Rivera, So. Mississippi AIDS Task Force, Mississippi
171. Nicholas Roche, ACTUP Paris, Paris, FRANCE
172. Gary R. Rose, AIDS Action Council, Washington, DC
173. James Rousey, Exec. Director, AIDS Treatment Initiatives, Atlanta, Georgia
174. Maria L. Samies, So. Mississippi AIDS Task Force, Mississippi
175. Scott Sanders, Oakland, CA
176. Norma Santos, Atlantic City Medical Center, , Atlantic City, New Jersey
177. John B. Schulz, Oakland, California
178. Sue W. Scott, AIDS Service Center, Pasadena, California
179. Matthew Sharp, ACTUP Golden Gate, San Francisco, California
180. Jennifer A. Sinclair, Oakland, California
181. B. Scott Shaw, Atlanta, Georgia
182. Michael Sheehan, AIDS Foundation San Diego, San Diego, California
183. Michael Shriver, NAPWA, Washington, D.C.
184. John E. Smith, Treasure Coast Community AIDS Network, Florida
185. William L. Snedden, Treasure Coast Community AIDS Network, Florida
186. Andrea Springsteen, Los Angeles, California
187. David Springsteen, Los Angeles, California
188. Judy Springsteen, Los Angeles, California
189. Lois Springsteen, Boulder Creek, California
190. Wayne P. Springsteen, Los Angeles, California
191. Roy Standifer, Jr. Dallas, Georgia
192. Joe M. Stewart
193. William P. Stewart, Jr., Haitian Amerian Community Council, Delray Beach, Florida
194. Norm Stuart, Research Sanctuary, Los Angeles, California
195. Sean Strub, Poz Magazine, New York, New York
196. Richard Tafel, Log Cabin Republicans, Washington, DC

197. Rob Tan, Rob Tan & Associates, San Francisco, California
198. Susanna Calvin Thomas, Open Doors
199. Michael Tolentino, Chicago, Illinois
200. Rachel Tolmachoff, Chair, Treatment & Care Committee, Sonoma County Commission on AIDS, Sonoma, California
201. Wilton Towe, Jr., Adairsville, Georgia
202. Amy Valenzuela, AIDS Project Long Beach, Long Beach, California
203. Jack Ryerson Varney, Atlanta, Georgia
204. Delia A. Viator, The Counseling Center dba Gulf Coast Mental Health, Biloxi, Mississippi
205. Gerald S. Viator, Biloxi, Mississippi
206. Oswald T. Weber, Founding Director, Projekt Information, Munich, Germany
207. Leland J. Wersal, Treasure Coast Community AIDS Network, Florida
208. Robert C. White, St. Louis, Missouri
209. Terri L. Wieder, Smyrna, Georgia
210. Scobel Wiggins, Georgia
211. Ken Wilkinson, FACE-L.A., Pasadena, CA
212. Lynie Williams, Tecumseh, Missouri
213. Mark Williams, PWA, New Jersey
214. Lee Winchell, Los Angeles, California
215. Phillip Winchell, APLA client, Los Angeles, California
216. Yvonne Wind, PA-C, N. Miami Beach, Florida
217. Thomas S. Woodward, Atlanta, Georgia
218. Vicki Worley, IHS, Hanover

A Hepatitis Drug That May Cure Glaxo
Business Week (05/12/97) No. 3526, P. 104; Flynn, Julie; Symonds, William C.; O'Hamilton, Joan C.; et al.

In 1990, Glaxo Wellcome acquired the marketing rights to the AIDS drug 3TC, which it sells under the brand name Epivir. Epivir produced $315 million in revenues in its first year of availability and analysts estimate that the drug could reach sales of up to $840 million by the year 2000. Now, it seems the chemical compound, renamed lamivudine, could be the most effective treatment available against hepatitis B, a disease that kills some 2 million people each year. Data from a trial in Hong Kong,Taiwan, and Singapore show that 96 percent of patients who received a 100mg dose of lamivudine reported significant suppression of the hepatitis B virus (HBV) with few side effects. About two-thirds of the subjects also had decreased liver inflammation. The discovery of lamivudine's hepatitis-suppressing potential will likely provide Glaxo with a needed boost, since the patent for the anti-ulcer drug Zantac, its No. 1 product, will soon expire. Lamivudine "will be the gold standard" for treatment of hepatitis B, predicts Timothy M. Block, chief scientific advisor of the Hepatitis B Foundation. However, others argue that the drug's marketing potential is being overestimated, because the drug is not a "cure" and only 16 percent of patients taking the drug showing no sign of HBV in their blood.

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5/19/97 +Glaxo Wellcome: Sales 2.75B Pounds In 4 Mos To April >GLX
(MORE) DOW JONES NEWS 05-19-97

5/19/97 Glaxo Wellcome - Sales -2: Up 10% Excluding Currency >GLX
LONDON (Dow Jones)--Drug giant Glaxo Wellcome PLC (GLX) said Monday its total sales in the four months to April 30 were 2.75 billion GBP, 10% higher than year-earlier levels in constant exchange-rate terms.

However, the continuing strength of the pound meant sales in sterling terms were unchanged, the group's Chairman Sir Colin Corness told shareholders.
(MORE) DOW JONES NEWS 05-19-97

5/19/97 Glaxo Wellcome - Sales -3: Zantac Sales Down 7% >GLX
Corness said sales in Glaxo's largest product, anti-ulcerant Zantac, continued to decline, as expected.

The first U.S. patent on the drug - which was the world's top-selling prescription pharmaceutical until the end of 1996 - expires in July, opening the company to generic competition in the ulcer-treatment market from companies such as Novopharm Inc.

Zantac's sales in the four months to April 30 were 7% lower at constant exchange rates. On the same basis, sales of all the

group's other products rose 15%.

"Respiratory products have now become the group's largest therapy area, with sales of antiviral and central nervous system products showing strong growth," the chairman told shareholders.

(END) DOW JONES NEWS 05-19-97

5/19/97 Glaxo Wellcome - Sales -4: Sykes Succeeds Corness As Chmn

Glaxo Wellcome PLC Chairman Sir Colin Corness said Glaxo's trading profit growth is in excess of total sales growth. However, the adverse impact on Glaxo's 1997 sales would be around 5% if sterling stays at its current levels.

Corness said he remains 'confident' that the group will meet the three-year sales targets it set out earlier in the year. **In March, Glaxo said the expiry of Zantac means its sales will grow in low single digits in 1997 and 1998, with double-digit sales growth resuming in 1999. The projections exclude the impact of currency moves, 'which clearly could have a significant effect.'**

In his review of business progress, Sir Richard Sykes, deputy chairman and chief executive, said Zantac now only compares with 20% of Glaxo's total sales, compared with 43% as recently as 1994. The key factor in reducing the significance of Zantac was Glaxo PLC's takeover of Wellcome PLC on May 1, 1995 to form the new group.

Sykes said the company could lose up to 90% of its U.S. sales of Zantac from generic competition after July.

'So, the much-heralded cataclysm is finally upon us,' said Sykes. 'Only we do not see it quite that way.'

He said the reason for his confidence is the breadth and depth of Glaxo's portfolio and product pipeline. 'We now have major businesses - with potential for good growth bolstered by new products - in therapeutic areas such as respiratory diseases, the central nervous system, antivirals and anti-infectives,' Sykes said, adding that the company is expanding into areas such as influenza, diabetes and stroke.

'The quality, depth and diversity of our pipeline is without question,' said Sykes, who will succeed Corness as chairman after the shareholder meeting.

(END) DOW JONES NEWS 05-19-97

5/15/97 Glaxo Drugs Reduce Risk Of AIDS From HIV - Report >GLX

LONDON (Dow Jones)--Two Glaxo Wellcome PLC (GLX) products, Epivir and Retrovir, are "highly effective" in reducing the progression of HIV-I to AIDS when taken together, a news release from Britain's leading medical journal, The Lancet, confirmed Friday.

In clinical trials in Canada, Australia, Europe and South Africa, the Lancet said the addition of Epivir to Retrovir resulted in "a significant reduction in progression to AIDS or death."

Both products are already marketed as AIDS treatments and are often used together. **Last year, Retrovir had sales of 283 million GBP and Epivir had sales of 196 million GBP.**

In a commentary in the Lancet, Dr. Mark Feinburg urged caution, saying this combination 'alone cannot achieve durable

suppression of HIV replication in most treated patients.'

Glaxo is currently developing the compound used in Epivir, called Lamivudine, for use as a treatment for Hepatitis B.

(END) DOW JONES NEWS 05-15-97

5/15/97 Glaxo Nonnicotine Pill Cleared As Smoking-Cessation Program
By Elyse Tanouye
Staff Reporter of The Wall Street Journal

A nonnicotine prescription pill will soon give smokers a new way to attack their addiction.

Glaxo Wellcome PLC's Zyban received Food and Drug Administration approval as the first nonnicotine prescription treatment for smoking addiction. The drug, which is also sold as the antidepressant Wellbutrin SR, helps people stop smoking by boosting dopamine and norepinephrine, two brain chemicals that give a person a sense of well-being and energy. Nicotine boosts the same chemicals, leading to addiction. But using Zyban allows patients to get the same feeling while weaning themselves off nicotine.

Physicians who treat smokers say they welcome a new tool to help their patients quit. An estimated 33 million smokers in the U.S. want to quit smoking, and 16 million try each year, but only 1.2 million smokers succeed. The only medications previously approved to help smokers quit are nicotine-based, such as patches, gum, nasal sprays and inhalers, but these fail in most patients.

Besides giving a second chance to patients who fail nicotine-based therapies, said John Hughes, a nicotine researcher and professor of psychiatry at the University of Vermont, Zyban will be particularly helpful for patients who object to using nicotine products, or patients who might become depressed after quitting.

Zyban will be entering a $500 million U.S. market for smoking-cessation drugs, currently dominated by over-the-counter nicotine-based patches and gum. The drug is one of Glaxo's top marketing priorities and could reach annual sales of between $200 million and $300 million in a couple of years, estimated Robert Ingram, head of Glaxo's U.S. operations.

The company began priming the market with an advertisement in last month's Reader's Digest magazine. The ad urged readers to return a postcard requesting information on smoking cessation. Glaxo is expected to do more direct-to-consumer advertising in addition to traditional marketing to physicians.

Glaxo plans to package the product with a support program, which includes brochures containing tips to quit smoking, and a toll-free telephone number to sign up for more personalized help. Patients who seek the additional help will receive a more individualized cessation program, and they will receive periodic phone calls from a counselor to check on their progress and to offer advice.

Smokers who want to quit these days are much tougher cases than those in the past, said Dr. Hughes. "We've gotten all the easy quits and now gotten down to the hard-core group," he said. Those patients tend to be severely nicotine-dependent or have a psychiatric problem, such as depression, he said.

Smokers are likely to be attracted to Zyban because it is new, predicted John Pinney, a health and smoking-cessation consultant in Bethesda, Md. But he worried that managed-care plans would erect barriers to patients getting the drug, as they have for nicotine-based products. A survey his firm conducted two years ago found that many managed-care plans either didn't cover the nicotine-based smoking-cessation products or placed tough restrictions on them.

Smokers "have to be very motivated, but if you put up too many barriers, the motivation may go away, and we've just lost the chance to get a person to quit smoking," he said.

In clinical trials, 49% of patients who took Zyban quit smoking after four weeks, compared with 36% who took a patch and 23% who used a placebo. Patients who used both Zyban and a nicotine patch had the best results, with 58% quitting.

(END) DOW JONES NEWS 05-15-97

5/15/97 +Glaxo Gets FDA Clearance On Zyban >GLX

(MORE) DOW JONES NEWS 05-15-97

5/15/97 Glaxo/FDA - Zyban -2: Available In U.S. In 6-8 Weeks >GLX

LONDON (Dow Jones)--Glaxo Wellcome PLC (GLX) said Thursday the U.S. Food & Drug Administration has approved Zyban, the first nicotine-free prescription medicine to help people stop smoking.

Zyban will be available on prescription to U.S. smokers within the next six to eight weeks, together with a patient-support program, Glaxo said in a statement.

(END) DOW JONES NEWS 05-15-97

5/15/97 Glaxo/FDA - Zyban -3: Stk Up; Sales Seen $300M In 5 Years

Glaxo's shares rallied immediately on the news. At 10 a.m. EDT (1400 GMT) they are at 1270 pence, up 18.5 pence on the day, on provisional volume of 2.04 million shares.

One pharmaceuticals analyst, speaking on condition of anonymity, said there have been plenty of indications that Zyban would be approved. 'It should already have been discounted in the share price,' he said.

The analyst said Zyban's annual sales will probably go as high as $300 million within the next five years.

Zyban is the tradename of bupropion hydrochloride. It will be marketed in a sustained-release tablet.

(END) DOW JONES NEWS 05-15-97

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Company: Office of AIDS Policy
Phone:
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From: William Schuyler
Company: Glaxo Wellcome Inc.
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Date: 5/30/97
Pages including this cover page: 3

Comments:

Daniel –

I hope this helps. I'm sorry it took all day. As for the sites where the compassionate use program will be available, those will be determined at the June 3rd meeting. Please call me if you need anything else.

William

GlaxoWellcome

April 28, 1997

Community Update: Glaxo Wellcome 1592 Compassionate Use

We are pleased to provide you with more details about our first steps to broaden access to Glaxo Wellcome's investigational drug, 1592, for the treatment of HIV disease. This letter and attachment outline three Glaxo Wellcome programs. These initiatives will run concurrently with controlled clinical studies, which are now underway for both treatment naive and experienced patients.

As you know, a considerable amount of discussion has taken place involving the company, the HIV community and treaters concerning the best way to provide early access to 1592, while also making best use of limited drug supplies until a larger expanded access program begins in early 1998. The importance of learning more about the appropriate role of 1592 has been raised many times, so we have designed a program for adults that encompasses an open label study which allows for collection of safety and efficacy data. We feel it is important to gather data on a broad population of people in addition to that which is being collected through our clinical trials. These data (viral load and safety) will also provide important information that can be used to help shape the expanded access initiative.

We will be providing access to 1592 initially via three programs: a pediatric program, a program for people with severe AIDS Dementia Complex (ADC) and an adult program. The entry criteria for each program are listed on the attached sheet. The ADC and the pediatric programs will be conducted via a centralized registration procedure, whereby doctors phone to register new participants. The adult program will take place at geographically dispersed centers. We plan to initiate the pediatric program in June. The dementia and the adult programs will begin in July.

The entry criteria for the adult program have been established to allow participants to combine 1592 with other anti-HIV therapies. Specifically, to be eligible to participate individuals must have failed at least two nucleoside reverse transcriptase inhibitors and one protease inhibitor. The adult program will be run through geographically dispersed centers across North America, Europe and Australia. We will provide a list of centers as soon as it is finalized.

To date, there have been approximately 250 people treated with 1592 in the phase II clinical trials. The new initiatives will involve approximately 2,500 people in the three compassionate use/open label studies. This is in addition to the more than 2,000 people in some 20 studies in the ongoing clinical trial program. Through this program, we are attempting to allocate limited supply of drug between the competing needs of extensive clinical trials and this compassionate use/open label program. We view this as the first steps in a broad effort to provide 1592 to the people who need it prior to its approval and until a larger expanded access program can be put in place.

If you have any questions on this program, please contact me or Michael Joyner at 919-483-2987.

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1592
Compassionate Use/Open Label Program
Entry Criteria

Pediatrics

- Viral load > 100,000 copies/ml
- CD4 count < 15%
- Failed at least one NRTI

AIDS Dementia Complex

- Severe dementia (to be defined)
- Diagnosed by a neurologist
- Prior treatment with AZT

ADULTS

- Viral load > 50,000 copies/ml (where measured)
- CD4 count < 100/mm3
- Failed at least two NRTI and one PI

MEMO

To: Sandra L. Thurman

From: Daniel C. Montoya and Sheldon E. Gilbert

Subject: GlaxoWellcome-FDA-1592 Access Coalition Conference Call

Date: July 11, 1997

Attached are the minutes from the teleconference call held between all parties enumerated above held yesterday, July 9, 1997 from 1:00-2:30 pm EDT. The conference convened to address a letter that had been sent out by Jennifer McMillan, Director of Health Care Coalitions and Advocacy Relations at Glaxo Wellcome in a response to a letter that had been sent to her on June 16, 1997.

In their letter, Glaxo Wellcome restated its commitment to provide 1592 to "as many people as possible through compassionate use and expanded access protocols." Before beginning to address their definitive plans to establish such programs and policies of compassionate use and expanded protocols, GW gave a brief explanation of the 1592 delay in development claiming that it was due to problem with the physical form of the drug that had been discovered last summer.

Compassionate Use. GW plans to develop a "pace" enrollment into the Compassionate Use Program in order to provide "a limited supply of drug to as many people as possible". Plans to provide 1592 to approximately 2,400 patients in U.S. (apparently twice as many people as was previously intended considering how the original plan was for a non-paced program which would provide 1592 to 2,000 patients worldwide, with drug for 1200 in US). This "pace" program would allow for 100 patient per week enrollment. In addition, GW stated its commitment to sustaining supply of 1592 in each patient who is enrolled in program as long the person is responding and tolerating drug.

Are intent of collecting data from numerous physicians who have extensive experience with the experimental drug from all of their 65 sites for compassionate use programs in the US. But GW claimed that they could not extend themselves by providing 1592 outside of their designated sites.

Expanded Access. GW claimed that if all goes well with production scale-up and there are no safety and efficacy concerns that begin to emerge, then they will be able to move into " a more traditional expanded access program in March of 1998". Although criteria for expanded access have yet to be finalized, GW anticipates being able to accommodate a "cumulative total of over 13,000 people worldwide on an expanded access basis." This however, would include nearly 4,000 people who will receive 1592 on the open label programs for this year and the one following.

Protocols and Clinical Trial Sites. GW has apparently distributed a number of protocol outlines and site lists that it will continue to provide.

Accelerated Approval. GW made clear that active discussion with FDA about the approval of 1592 are still on-going and that it will provide the community with updates on the drug's development and approval process.

The conference call that was held soon after the distribution of GlaxoWellcome's letter was a highly contentious and often times emotional discussion that centered around much of what the Coalition considered to be often inconsistent and duplicitous information or misinformation rather. There was much debate of the original figures of 20,000 - 30,000 patients that the Coalition felt GW had firsts agreed to in their proposed Compassionate Use and Expanded Access programs. Many of the Coalition members felt that they simply were not being told the full story about 1592. For if it had received FDA approval in such early stages in its development then there should be little cause for the delay in its distribution.

1592 Access Coalition

Conference Call: Wednesday, July 9, 1997

Jeff Getty moderated this conference call between GlaxoWellcome (GW), the FDA and the 1592 Access Coalition.

I. FDA

As a preface to any discussion of the drug, 1592, between the Coalition and GW, the FDA, when asked by the Coalition whether they needed more reassurance that the drug met federal safety guidelines, they quicklymade it quite clear that to their knowledge the drug had been approved.

Representatives of the FDA then began commenting on some of the logistics of the expansion of Compassionate Use Programs and Expanded Access Programs, addressing some of the problems that many companies may encounter in their attempt to increase treatment programs with particular focus on how management relates to standard access. The FDA commented that often times supplies that are needed for standard access are taken from those that are designated to clinical trials. Secondly, small companies that are on the verge of marketing encounter distributing problems (i.e. small batches).

Note: *Although 15 minutes had been allotted for discussion with the FDA, all matters were succinctly addressed in only the first 5 minutes of the conference.*

II. Compassionate Use Program

A. *GlaxoWellcome Commitment:*

When asked by one of the Coalition members to state their commitment before all those present to use their "best efforts" to increase the size of treatment programs if additional drug becomes available, representatives of GW refused to make such promises or commitments. They claimed that limitations based on production costs in addition to inadequate data on 1592 (as it is still in early stages of production) would make the expansion of such programs "unjustifiable". As they put it, they "simply are not ready to make such a commitment".

B. *Triage*

A triage, established by one of the members of the Coalition had been described and was met with little discussion afterwards. Apparently it had already been discussed and approved by the Coalition prior to the conference, and it was being presented to GW for the first time. The stipulations for the Triage were as follows:

1. If the patient's health is rapidly declining
2. If the patient's health is undergoing slow/moderate decline but is still able to wait
3. If the patient's health is stable and is still able to wait a couple of months

C. Distribution Off-site/On-site

There was some concern on the behalf of the Coalition on the accessibility to the 65 sites for Compassionate Use Programs that GW has apparently develope to mant of its patients. One Coalition member who has just learned that in order to facilitate site accessibility in Canada, GW reimburses the travel expenses of patients who either live in rural areas or are too ill to travel and require special services, wanted to know if similar steps will be taken in the United States.

Representatives of the pharmaceutical company stated that they intended to have in place a similar program once there was enough data to support the expansion of larger programs in 1998. They then closed by saying that they will have to determine the ability to fund such a travel reimbursement program in the United States at some later date----but no definitive answer was given, in fact one of the representatives of GW claimed that he never knew of the existence of such a program in Canada.

D. Pediatric and Dementia Allocation

One coalition member concerned about the 2,000 patient figure reported in a letter from GW on July 8, wanted to know whether pediatric and demented patients were accounted for in such a figure or any of their other figures for that matter.

One representative of GW stated that the patients that are being referred to, have in no way been forgotten as insinuated by the coalition member who had raised the point. They were simply not included in the 2,000 patient figure because it was believed that it had already been understood. "There are 2,000 patients world-wide for the Adult Program (of which 1200 will be in the U.S.), 200 pediatric patients and 200 demented patients."

There seemed to be a great deal of uncertainty over these figures and was a great source of contention throughout a large part of the conference. One representative from GW claimed instead that there would be 250 and not 200 pediatric and demented patients respectively.

E. Equity of Access

There were some concerns on the part of the Coalition on the extent to which preferential treatment would preclude the equitable distribution of medicine in many of these planned sites. Thus feeling that such concern warrants strict regulation, the Coalition asked GW to commit itself to seeing that such mechanisms are placed to ensure the equal patient access to 1592.

GW responded by ensuring the Coalition that they will do their utmost to have in place such a community-based corrective mechanism by communicating with investigators, but doing so may prove difficult due to patient anonymity.

One Coalition member stated his complete dissatisfaction for GW's efforts and contended that a more aggressive approach would be needed and was willing todiscuss the placement of a more

austere program with GW at some later date.

III. Expanded Access Program

A. Unresolved Patient Figures

The greatest source of contention between the Coalition and GW was over some of the patient figures that, according to nearly all of the members of the Coalition, were always changing. The discussion over the inconsistency of GW's patient figures first began with a recommendation by one Coalition member that the GW provide regular weekly/monthly progress reports on such programs (i.e. the number of patients that apply and are approved/disapproved).

One representative of GW questioned the necessity of such regular progress reports.

This was quickly met by a response from one of the Coalition members who argued that such reports are intrinsic components that are put in place to safeguard the rights of patients and ensure the maintenance of their needs.

This soon led to a heated debate on the ethical nature of much of GW's marketing policies of 1592 over the past few months. Many of the Coalition members felt that GW simply "was not being honest". They expected patient figures to range from 20,000-30,000 and not, as they felt, the wholly unacceptable figure of 8,000-9,000 patients. Some members of the Coalition voiced great concern over GlaxoWellcome's apparent breach of the original agreement to have 5,000 patients worldwide enrolled in the Compassionate Use program to what is now 4,000 patients worldwide. As a result, the "pacing" procedure would now only allow for only 100 patients enrolled in the Compassionate Use program every week as opposed to the the original 200 patients per week.

In trying to understand what may have possibly led GW to come up with such figures, members of the Coalition were quite skepticalabout the claims made by GW that product capacity played a large part in limiting these numbers

GW maintained that they came up with such figures based on a number of factors, among them data from the CDC and estimated costs for clinical trials.

One member of the Coalition contended however that it was quite possible to sustain Expanded Access programs while still running clinical trials.

One representative of GW then proceeded to passionately restate her company's commitment to eradicating this disease and felt that GW had been nothing less than "honest" throughout this entire process with members of the community. But her statements were soon met with a great deal of vitriol and critique that was fully played out at the end of the conference with the personal statements made from each of the Coalition members to GW.

B. Availability

Although the Coalition remonstrated the March deadline for the availability of 1592, GW maintained that they can not do anything earlier than the first quarter of 1998.

One member of the Coalition strongly advised GW to take heed of the proposed Triage to ensure that those patients who really deserve the drug will receive it.

GW then added that they plan on changing the Compassionate Use Program from a center-based program in 1997 to a non-center-based program in 1998.

IV. Follow-up Meeting

A. The date for the next meeting was not able to be set and will be taken up at some later time with individual parties.

B. Established that the developments of 141 will need to be on the agenda for the next meeting.

C. Established that the size of and inclusion/exclusion criteria of expanded access programs needed to be readdressed.

V. Personal Statements/Summations by Coalition Members

Eileen Mitzman: *"I do not understand why a company of this size feels so limited. I want GW to understand that my daughter died of this disease because she wasted. I want GW to know that everyday they wait another person dies of this disease!"*

Andy Lipshick: *"When is GW going to enroll its first patient in its Compassionate Use Program?"*

GW: "We do not know as of yet. Sometime in July."

Andy Lipshick: *"When in July?! We are already in July!"*

Paul: *"Of the 65 sites how many have received approval for IRBs?*

GW: "We do not know."

Steve: *"How will GW ensure that non- preferential treatment will not occur?"*

John James: *"To what extent do small batches have to become approved?"*

Teo: *"I am convinced that GW doesn't have the drug to expand the program. If they really had the drug then they would have had approval sooner! Perhaps the drug is not working*

and they don't want to admit it! They want to control any possible negative buzz! But this doesn't resolve GW of its responsibilities of getting the drug to those who still desperately need it and have no other options."

Lee Jones: *" I am a member of a small support group in Northern California and I just want GW to know that four of our members (children) will not make it to your March 1998 deadline."*

_____: *"I feel that GW is making a mockery of Compassionate Use Programs!"*

Peter Cashman: *"GW has to do its best to ensure that there is equity in access and equity in treatment."*

_____: *"GW needs to take heed of some of the lessons learned by some of its biggest competitors. Bristol Meyer is still benefitting from its generosity while LaRoche is still suffering from its standard access policies. GW needs to go back to the drawing board."*

Marty: *"I am less enamored with 1592 than others. GW has changed for the worst over the past few years. It has new people that are grossly mismanaging the company. So many of its best scientists have already left the company."*

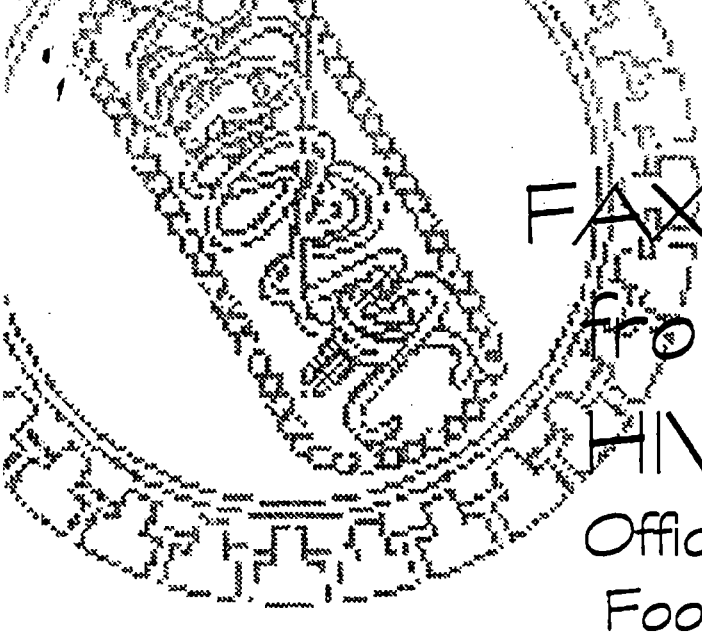
_____: *" I am very discouraged with GW. Seven members of my own group were even arrested in their New York corporate offices."*

_____: *"Likewise I am also disappointed about the extent to which GW has done little to address the issue of pediatric patients and as well as patients with dementia. Secondly, either this company underestimates the intelligence of the people with whom they are dealing with or they have crafted a very clever marketing plan---I would venture to say the latter--just admit it GW!"*

David Gillman: *"Certainly the development of 1592 and 141 has been an extremely slow process when compared to saquinavir. GW also needs to realize that enrollment problems (i.e. over-saturation) do not always occur. It didn't happen with 3TC. GW should have an unlimited access program."*

Mrs. Greenberg: *"I think that we all need to keep in mind that we are here to stay in touch with our humanity. GW's ability to eliminate nearly 11,000 people from Expanded Access programs with the arbitrary stroke of a pen is a travesty!"*

NOTE: Some of the statements above made by some of the members of the Coalition are not direct quotes. They were in large part paraphrased with the intent of making them as close to the original statements as possible.



FAX Message from Richard Klein HIV/AIDS Program

Office of Special Health Issues
Food and Drug Administration

Date: 9. July - WED
To: DANIEL MONTOYA. ONAP
FAX No. 202 632 1096

Message:

In case you have not seen this, I am attaching a copy of a letter from Glaxo to the Coalition from yesterday, outlining their proposed plans.

I'll let you know how the meeting goes

Best
Richard

cover sheet plus 2 pages

Office of Special Health Issues, Food and Drug Administration,
5600 Fishers Lane, HF-12, Rockville, MD 20857
Voice - 301.827.4460 FAX - 301.443.4555 e-mail: Rklein@bangate.fda.gov

GlaxoWellcome

July 8, 1997

TO: 1592 Access Coalition
FROM: Jennifer McMillan
Director, Health Care Coalitions and Advocacy Relations
Glaxo Wellcome Inc.

CC: R. Ingram, P. Young, S. Lafon

Thank you for your letter of June 16.

We wish to reiterate our commitment to provide 1592 to as many people as possible through compassionate use and expanded access protocols. Your letter called for three stages of access: compassionate use, expanded access and accelerated approval. As you know, our plans have long included this tiered approach to access.

As we have discussed, we encountered a problem with the physical form of the drug substance last summer, which resulted in some delays while a new alternative salt was identified, scaled up into the pilot plant and transferred into full scale production. We will have additional quantities of 1592 early in 1998, but in the meantime, the drug supply we currently have available is limited.

We have addressed the concerns outlined in your letter below. In addition, we will convene a teleconference to address your questions from 1 p.m. to 2 p.m. EDT on July 9. If you have not received information about the call, please contact Michael Joyner at (919) 483-2987.

Compassionate Use

In order to provide a limited supply of drug to as many people as possible, we have developed a plan to "pace" enrollment into the compassionate use program in the United States. This will allow us to provide 1592 to approximately 2,400 patients in the US, which is twice as many people as was previously projected. (Our initial proposal was for a non-paced program which would provide 1592 to 2,000 patients worldwide, with drug for 1,200 patients allocated to the US.) We believe that this measured approach of enrollment will also allow us to provide the participating sites with emerging data on this therapy, which will help physicians evaluate which patients are likely to benefit from 1592. As a result, the sites should be able to effectively triage their patients.

Glaxo Wellcome is committed to sustaining supply of 1592 to each person who enters the compassionate use program as long as the person is responding and tolerating the drug (until accelerated approval is achieved.)

We will review the responsibilities of the regional sites with the study coordinators. The participating sites are aware of their role to accept referrals from other practices. We will periodically query sites for that information.

Glaxo Wellcome Inc.
Five Moore Drive
PO Box 13398
Research Triangle Park
North Carolina 27709

Telephone
919 248 2100

There are now more than 65 US sites for the compassionate use program. We believe it is important that patients receive 1592 from physicians who have some experience with this experimental drug, and it is essential that we collect safety data on patients in this program. As a result, we cannot commit to providing access outside of the regional sites. The use of regional centers will be re-assessed prior to initiating the expanded access program in 1998.

Expanded Access

Assuming that the production scale-up continues without unexpected delay and that no safety and efficacy concerns from the controlled studies or the compassionate use programs emerge, we will be able to move into a more traditional expanded access program in March of 1998. Although the criteria for our expanded access program are not yet finalized, we anticipate being able to accommodate a cumulative total of over 13,000 people worldwide on an expanded access basis. This figure includes approximately 4,000 people who will receive 1592 on the open label programs this year and for whom 1592 will continue to be available through expanded access next year.

Protocols and Clinical Trial Sites

A number of protocol outlines and site lists have already been distributed, and we will continue to provide these as the studies and site lists are finalized.

Accelerated Approval

We are in active discussion with the FDA regarding the development of 1592 and we will provide the community with updates on that process when significant new information is available. We are pleased to be able to expand the use of 1592 at such an early stage in the drug's development. As you know, these initiatives are significantly earlier in the development process than the access programs for any other HIV treatment.

Finally, we believe it is important to re-emphasize our commitment to the development of 1592. Glaxo Wellcome has every incentive (medical, ethical, economic) to diligently pursue development of 1592 and we are working hard to do this in a manner that can clearly demonstrate the safety and efficacy of the drug.

We look forward to answering any questions you may have regarding these initiatives.

1592 ACCESS COALITION

To: Daniel Montoya	From : Linda Grinberg	
Company: White House - AIDS Office	Telephone: 310-471-6565	
Fax Number: 1-202-632-1096	Fax Number: 310-471-4565	
Subject : Microsoft Word - AGENDA.DOC	Date: 7/8/97	Pages: 2

Please see attached agenda.

If there are any items which you would like to specifically address for which your name is not assigned, please contact either Jeff or me prior to the scheduled call tomorrow.

We will all have the opportunity to make a statement at the conclusion of the call.

1592 ACCESS COALITION

CONFERENCE CALL AGENDA

GW has agreed to allow Jeff Getty to moderate the conference call scheduled for tomorrow, Wednesday, July 9, 1997. Jeff will be assigning various coalition members the task of presenting the following issues. We need to try and stick to the agenda, the time limitations, and be as concise and to the point as possible, due to the time constraints. Each coalition member will be called upon to make a statement at the conclusion of the call.

I. FDA (15 minutes)

- A. Flexibility regarding increasing size of Compassionate Use Program
  1. GMP issues? [Theo, Ron or Linda?]
  2. Safety issues? [ditto]
- B. Flexibility regarding increasing size of Expanded Access Program
  1. GMP issues? [Theo, Ron or Linda?]
  2. Safety issues? [ditto]

II. Compassionate Use Program (15 minutes)

- A. Good faith promise to use "best efforts" increase size of program if additional drug becomes available [Sandy Thurman or Linda?];
- B. Triage [Marty];
- C. Off site distribution of drug to patients unable or too sick to travel [Theo];
- D. Travel Expenses to Sites (offered to Canadians) [Peter Cashman];
- E. Pediatric and Dementia allocation? (1,000 patients apparently missing from staggered rollout number, 500 from original proposal per GW letter) [James Learned];
- F. Equity of Access [Kiyoshi?]

III. Expanded Access Program (30 minutes)

- A. 8,000-9,000 size unacceptable/20,000 minimum per previous conversations; [David Gold or Marty or Ron?]
- B. March '98 date unacceptable; [Kate or Paul Davis?]
- C. Traditional distribution channels via healthcare providers [Dave Gilden];

IV. Followup Meeting (5 minutes) [Linda]

- A. Date certain & set before call concludes
- B. readdress size of and inclusion/exclusion criteria of expanded access program
- C. 141 development plans
- D. In person, travel reimbursement

V. Statements/Summation by Coalition Members (25 minutes):

Jeff will call upon members of coalition to speak for no more than 1 minute each.

FAX from: LINDA GRINBERG

From FAX #: (310) 471-4565 No. of pages: 3
To: Daniel Montoya FAX # 202-632-109
Company Sally Duncan
Remarks White House - AIDS Office Date: 7/8/97

GlaxoWellcome Fax

Health Care Coalitions

To	Distribution	Fax	
From	Jennifer McMillan	Date	07/08/97
Telephone	919/483-2392	Total Pages	3
Fax	919/483-0571		

DISTRIBUTION:

Ron Baker	Kiyoshi Kiromiya
Bill Bahlman	Jules Levin
Cornelius Baker	Andy Lipschitz, MD
Peter Cashman	L. Joel Martinez
Sally Cooper	Theo Smart
Paul Davis	Henry Chang
Martin Delaney	Moises Agosto
Jeff Getty	John James
David Gilden	Amy Valenzuela
David Gold	Cleve Jones
Eileen Mitzman	John Iverson
Uli Rundback	Linda Grinberg

Mission

Glaxo Wellcome is a research-based company whose people are committed to fighting disease by bringing innovative medicines and services to patients throughout the world and to the healthcare providers who serve them.

Values

High Standards
Valuing Customers
Valuing People
Teamwork
Embracing Change
Achievement
Corporate Citizenship

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Glaxo Wellcome Inc.

Five Moore Drive
PO Box 13398
Research Triangle Park, NC
27709-3398

Telephone
919/483-2392

Fax
919/483-0571

GlaxoWellcome

July 8, 1997

TO: 1592 Access Coalition
FROM: Jennifer McMillan
Director, Health Care Coalitions and Advocacy Relations
Glaxo Wellcome Inc.

CC: R. Ingram, P. Young, S. Lafon

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Finally, we believe it is important to re-emphasize our commitment to the development of 1592. Glaxo Wellcome has every incentive (medical, ethical, economic) to diligently pursue development of 1592 and we are working hard to do this in a manner that can clearly demonstrate the safety and efficacy of the drug.

We look forward to answering any questions you may have regarding these initiatives.

1592 ACCESS COALITION

June 13, 1997

Mr. Robert Ingram
Chief Executive Officer
Glaxo Wellcome, Inc.
5 Moore Drive
Research Triangle, NC 27709

Re: Development of Abacavir (1592)

Dear Mr. Ingram:

Community treatment advocacy groups and activists watch with growing concern as the major pharmaceutical companies continue to reduce the size of compassionate use and expanded access programs for promising new AIDS drugs. The limited 1592 compassionate use program proposed by Glaxo Wellcome provides the most recent example of the industry's misguided policy on early access.

The individuals and organizations listed below call on Glaxo Wellcome to take the following actions regarding 1592:

I. **Compassionate Use Program**
   - A. Commit to significantly increase the size of the compassionate use program scheduled to begin in July 1997. (It is anticipated that more than 10,000 patients worldwide may need 1592);
   - B. Triage patients to ensure those in most critical need are given highest priority;
   - C. Provide monthly progress reports to designated community representative(s) regarding production capacity and patient enrollment;
   - D. Describe procedures to ensure equity of access and avoidance of preferential treatment to patients at selected sites;
   - E. Provide the drug to patients who cannot access the medical sites designated by Glaxo. (Traditionally, compassionate use programs reach patients through their healthcare providers.)

II. **Expanded Access Program**
   - A. Initiate an expanded access program at the earliest possible date in 1997;
   - B. Provide details regarding inclusion/exclusion criteria, size and scope of program, distribution plans, and other pertinent information as soon as possible.

III. **Protocols and Clinical Trial Sites** - Provide information on 1592 protocols and identify clinical study sites, as promised, immediately.

IV. **Accelerated Approval**
   - A. File for accelerated approval of 1592 no later than March 1998;
   - B. Initiate rolling data submissions to FDA as soon as possible.

Promising new therapies such as 1592 must become available as soon as possible to people without treatment options who face disease progression or death. Community advocates and

activists call upon Glaxo Wellcome and all AIDS drug manufacturers to recognize that people with advanced disease have a basic right to speedy access to new experimental therapies when all other treatment options have failed.

We look forward to receiving your response to our concerns regarding 1592.

Sincerely,

1592 ACCESS COALITION

Ron Baker	David Gilden	Andrew Lipschitz, M.D.
Bill Bahlman	Linda Grinberg	Joel Martinez
Peter Cashman	John Iverson	Eileen Mitzman
Sally Cooper	Cleve Jones	Leigh Paidolfino-Danas
Paul Davis	Kate Krauss	Lili Rundback
Martin Delaney	James Learned	Matthew Sharp
Jeff Getty	Jules Levin	Theo Smart

Endorsements of AIDS Organizations:

ACT UP Golden Gate, Oakland, CA
AIDS Service Center, Pasadena, CA
Community Research Initiative on AIDS (CRIA), N.Y., N.Y.
F.A.I.R./Foundation for AIDS and Immune Research, Los Angeles, CA
Healing Alternatives Foundation, San Francisco, CA
N.A.T.A.P./National AIDS Treatment Advocacy Project, N.Y., N.Y.
Project Inform, San Francisco, CA
PWA Health Group, N.Y., N.Y.
San Francisco AIDS Foundation, San Francisco, CA
Treatment Action Group, N.Y., N.Y.

AGREED and ACCEPTED this ___ day of June, 1997:

By:_____ **Of:**_____
(Signature) (Organization)

Print Name:_____ **Phone:**_____ **Fax:**_____

592 ACCESS COALITION

:	From : Linda Grinberg	
mpany:	Telephone: 310-471-6565	
x Number:	Fax Number: 310-471-4565	
bject : Abacavir/1592	Date: 6/16/97	Pages: 4

axo Wellcome has announced that it will shortly launch a compassionate use program for its new ug, commonly known as "1592". Activists throughout the nation who have worked with the company to velop this program feel it is inadequate to meet the need. The program offered thus far is severely nited in both size and compassion and will initially reach 2500 people worldwide. Plans for a larger panded access program, also promised by Glaxo, have been delayed until the beginning of 1998, at the rli st.

any standard, this is not good enough. The number of people with an immediate need for this drug ntinues to grow each week.

e need your support – and that of your organization – to improve upon this program.

hile many people have shown clinical improvement with protease inhibitors, increasing numbers have w failed on all available combinations. Others have never been in a position to benefit because they ck the other "new" unused companion drugs needed to make an effective combination therapy. eople have simply run out of drug options. 1592 is the only new drug likely to become available in the ar future to help those in the most desperate need. In preliminary testing, 1592 appears to be asonably safe and highly potent – perhaps 10 times more potent than AZT. It will make a critically eeded addition to the arsenal of drugs needed to combat HIV.

e are asking you to join and support our efforts by adding the endorsement of your organization to the owing list of groups who have already signed on. We also ask that you circulate this fax and letter to l organizations as soon as possible. Every name adds to its strength.

you have any questions or need more information about 1592 or the proposed program and why ment activists find it inadequate, please contact Ron Baker at 415-543-4440. If you want to get ore involved, please contact Jeff Getty at 510-653-6099. Please fax back your signed endorsements to 10-471-4565.

ime is of the essence. Thanking you in advance for your ongoing support and your prompt attention to is matter.

Memorandum

TO: Sandra L. Thurman and Daniel C. Montoya

FROM: Michael Diz

DATE: June 25, 1997

RE: Conference call with Jeff Getty and other activists- June 25, 1997

COMMENTS:

*Glaxo has reportedly verbally agreed with a Canadian activist to set up a triage drug assistance program and to pay for those in the compassionate use program to travel to the drug distribution sites.

*In the Expanded Access Program, which will begin in the first quarter of 1998, the drugs will be available through local physicians.

*No such agreements are known to have been reached with US activists.

*Those on the call requested that the ONAP set up a meeting this week between Glaxo and the community.

*Those on the call also requested that the ONAP insist that Glaxo produce a written response to the "demand letter" which was sent to them several days ago.

GlaxoWellcome Fax

Federal Government Relations and Public Policy

To	Daniel Montoya	Fax	(202) 632-1096
From	William J. Schuyler	Date	June 24, 1997
Telephone	(202) 783-1277	Total Pages	4
Fax	(202) 783-1740		

Daniel:

I promised to get you some updated information about industry's commitment to assuring access to HIV treatments. I've enclosed a couple of new documents describing what Glaxo Wellcome is doing on its own to help people with HIV and AIDS, and describing some federal programs we participate in that help assure access to medications. I hope these help.

William

Mission

Glaxo Wellcome is a research-based company whose people are committed to fighting disease by bringing innovative medicines and services to patients throughout the world and to the healthcare providers who serve them.

Values

High Standards
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Corporate Citizenship

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GlaxoWellcome

GLAXO WELLCOME HIV MEDICATION ACCESS EFFORTS

Rapidly emerging data concerning the beneficial effects of multi-drug combinations in the management of HIV disease have increasingly focused attention on the health care resources needed to ensure that people living with HIV disease receive state-of-the-art medical care. As the leader in the discovery and development of medications for the management of HIV disease, Glaxo Wellcome has worked with government, academia and the HIV community for many years to enhance knowledge and education about the effective use of HIV medications. In addition to its significant ongoing research and development programs, Glaxo Wellcome has undertaken a number of initiatives to work with those involved in the delivery of care to address the issue of medication access and reimbursement for people living with HIV disease.

National

Since 1987, the company has contributed more than $13 million to grass roots, state and national AIDS community programs. Access to care initiatives are a key focus of contributions efforts.

More than 30,000 individuals with HIV disease in the United States received Epivir® (lamivudine, 3TC) at no cost through an open label compassionate use program in place from October 1993 through December 1995. The Glaxo Wellcome program was the largest expanded access program ever conducted for an HIV therapy. Plans are currently underway for open label and expanded access programs in children and adults for 1592, a compound in development for the treatment of HIV infection.

Substantial medication discounts have been provided to health care facilities, including those serving individuals with HIV disease, which are under Federal Contract.

The company is an active participant in the Inter-Company Collaboration for AIDS Drug Development, a group of pharmaceutical companies formed in 1993 to facilitate early combination and comparative studies of antiviral agents for the treatment of HIV disease. This group, although not focused on funding, shares preclinical and clinical data, drug supplies and assays to facilitate the study of combination therapies.

The company is also an active participant in the Forum for Collaborative HIV Research, a partnership of public and private organizations including research-based pharmaceutical companies, government agencies and patient advocates to oversee clinical research into therapeutic strategies to treat and manage HIV infection and AIDS. The forum was formed in early 1997 when Vice President Al Gore met with pharmaceutical executives and government officials to discuss drug development efforts.

Glaxo Wellcome is actively involved in the AIDS Drug Assistance Program Future Funding Working Group, a coalition of industry and community representatives working to increase Ryan White funds. Activities have included visits with key Administration and Congressional leaders as well as ongoing efforts to quantify the need for increased funding and the economic benefits of HIV therapy.

Glaxo Wellcome Inc.

1500 K Street NW
Suite 650
Washington DC 20005

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202 783 1777

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202 783 1740

State

Glaxo Wellcome provided rebates to Medicaid and state entitlement programs of more than $20 million on its HIV medications during the 12-month period of April 1996 through March 1997.

The company has voluntarily extended rebates in excess of $6 million to 20 states that did not have distribution mechanisms in place to take advantage of Federal rebate programs.

Glaxo Wellcome state field managers are actively working with states that are experiencing fiscal difficulties on an individual basis to identify and assess various legislative and programmatic initiatives to help them meet their patients' health care needs.

Glaxo Wellcome has funded numerous initiatives at the state and local level to improve access to medications and quality of health care for people with HIV disease. Examples include a training program for case managers in California, a New Jersey program that provides support to women parolees, and many contributions to improve case management and medical services at AIDS service agencies and community-based organizations throughout the country. These contributions often provide a needed boost to programs faced with a decline in government funding and increasing demands for services.

Glaxo Wellcome has developed the Ryan White Title II AIDS Drug Assistance Budget Model, a pharmacoeconomic model that assists in determining costs and demonstrates benefits including patient outcomes of HIV therapies. At the request of state ADAP directors, we work in conjunction with these programs to estimate the budget and funding necessary to support a given formulary or to compare the health and economic outcomes associated with multiple, alternative formularies.

Patient Assistance

Glaxo Wellcome has its own Patient Assistance Program to make its prescription medications, including all HIV medications, available to patients who do not have or qualify for private insurance or government-funded programs. Last year, the company made available products valued at more than $18 million through this program to qualified participants.

The company is dedicated to providing patients with information and guidance in finding alternative reimbursement sources for needed medicines. The Patient Assistance Program has an active case management program and the ability to work with individuals on a case-by-case basis. Last year we actively assisted more than 550 HIV patients through our reimbursement case management services.

Although the company recognizes that many states are experiencing fiscal difficulties, the Patient Assistance Program is not intended to supplement or replace government-sponsored programs. Rather, it is a philanthropic activity to help individuals who simply are not eligible for any other program.

FEDERALLY MANDATED DISCOUNTS FOR HIV AND AIDS TREATMENTS

Public Health Service Drug Pricing Program

Under the PHS Drug Pricing Program, a large number of health care providers that provide care to people with HIV or AIDS are eligible to receive mandatory discounts from pharmaceutical companies. These discounts are available to health care providers identified as eligible by the Public Health Service. These providers are given discounts comparable to those available to state Medicaid programs, equal to the lowest price available in the private marketplace less any inflation (CPI) reduction.

Many public hospitals participate in a number of these PHS programs and, thus, have access to these discounts. Entities meeting the requirements of the following programs may receive PHS discounted drug prices.

- *Federally Qualified Health Center Program*: these programs include Migrant Health Centers, Community Health Centers, Health Services for the Homeless, and Health Services for Residents of Public Housing.

- *Health Care Services Program*: AIDS medications are available under Titles I, II, and III of the Ryan White CARE Act which provides funds to state AIDS Drug Assistance Programs (ADAP).

- *Comprehensive Hemophilia Diagnostic Treatment Centers.*

- *Projects and Programs for the Prevention and Control of Sexually Transmitted Diseases.*

- *Family Planning Programs.*

- *Native American Health Care Clinics.*

- *Tuberculosis Clinics.*

- *Disproportionate share hospitals:* these hospitals serve a larger than average number of poor or uninsured people.

Medicaid

OBRA '90 requires pharmaceutical manufacturers to pay rebates to state Medicaid programs for all drugs they purchase. These Medicaid discounts are either the larger of 15.1 percent of the average wholesale price of a drug or the highest discount given to any private purchaser of a drug. Both these discounts are further reduced by any price increases greater than inflation.

GlaxoWellcome Fax

CORPORATE AFFAIRS

To	Daniel Montoya	**Fax**	202-632-1096
Office of National AIDS Policy			
From	Jennifer McMillan		
Telephone	919-483-2392	**Date**	6/18/97
Fax	919-483-0571	**Total Page**	5

Mission

Glaxo Wellcome is a research-based company whose people are committed to fighting disease by bringing innovative medicines and services to patients throughout the world and to the healthcare providers who serve them.

Values

High Standards

Valuing Customers

Valuing People

Teamwork

Embracing Change

Achievement

Corporate Citizenship

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Glaxo Wellcome Inc.

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Glaxo Wellcome Memo

To: *Daniel Montoya, White House Office of National AIDS Policy*
From: *Jennifer McMillan*
Date: *06/18/97*
Subject: *Follow-up Information*

Daniel,

I have attached some information in response to the issues that we discussed briefly in our telephone conversation earlier this week.

The entry criteria for the open label/compassionate use program is outlined in the "Community Update" and its attachment.

In addition, you asked if we could provide you with some idea about what the company has done in response to community concerns thus far. The second attachment is a consensus letter we received from the community that outlines a program of compassionate use, expanded access and accelerated approval. Overall, we are progressing along this track in our development and access plans for 1592.

Our criteria for compassionate use reflects the community's concerns that patients not be required to fail *all* available therapy before they can access 1592. Instead, we have allowed patients to participate in compassionate use if they still have a drug option to combine with 1592, which reflects the current thinking regarding adding more than one new drug to a regimen.

We built on the community's suggestion by adding a separate compassionate use program for children. And we responded to the community's request to develop a program for patients with AIDS dementia.

We are thoroughly evaluating the development of drug-resistant virus in relation to 1592 use. This is an area of great concern to both the community and Glaxo Wellcome.

Finally, we clearly both agree that moving this product through development to the filing for accelerated approval as quickly as possible is in everyone's best interest.

I hope this information and the attached materials are helpful. Please call me if I can provide more.

Regards,

CC: William Schuyler

GlaxoWellcome

April 28, 1997

Community Update: Glaxo Wellcome 1592 Compassionate Use

We are pleased to provide you with more details about our first steps to broaden access to Glaxo Wellcome's investigational drug, 1592, for the treatment of HIV disease. This letter and attachment outline three Glaxo Wellcome programs. These initiatives will run concurrently with controlled clinical studies, which are now underway for both treatment naive and experienced patients.

As you know, a considerable amount of discussion has taken place involving the company, the HIV community and treaters concerning the best way to provide early access to 1592, while also making best use of limited drug supplies until a larger expanded access program begins in early 1998. The importance of learning more about the appropriate role of 1592 has been raised many times, so we have designed a program for adults that encompasses an open label study which allows for collection of safety and efficacy data. We feel it is important to gather data on a broad population of people in addition to that which is being collected through our clinical trials. These data (viral load and safety) will also provide important information that can be used to help shape the expanded access initiative.

We will be providing access to 1592 initially via three programs: a pediatric program, a program for people with severe AIDS Dementia Complex (ADC) and an adult program. The entry criteria for each program are listed on the attached sheet. The ADC and the pediatric programs will be conducted via a centralized registration procedure, whereby doctors phone to register new participants. The adult program will take place at geographically dispersed centers. We plan to initiate the pediatric program in June. The dementia and the adult programs will begin in July.

The entry criteria for the adult program have been established to allow participants to combine 1592 with other anti-HIV therapies. Specifically, to be eligible to participate individuals must have failed at least two nucleoside reverse transcriptase inhibitors and one protease inhibitor. The adult program will be run through geographically dispersed centers across North America, Europe and Australia. We will provide a list of centers as soon as it is finalized.

To date, there have been approximately 250 people treated with 1592 in the phase II clinical trials. The new initiatives will involve approximately 2,500 people in the three compassionate use/open label studies. This is in addition to the more than 2,000 people in some 20 studies in the ongoing clinical trial program. Through this program, we are attempting to allocate limited supply of drug between the competing needs of extensive clinical trials and this compassionate use/open label program. We view this as the first steps in a broad effort to provide 1592 to the people who need it prior to its approval and until a larger expanded access program can be put in place.

If you have any questions on this program, please contact me or Michael Joyner at 919-483-2987.

Jennifer McMillan
Director, Health Care Coalitions and Advocacy Relations

Glaxo Wellcome Inc.
Five Moore Drive
PO Box 13398
Research Triangle Park
North Carolina 27709

Telephone
919 248 2100

1592
Compassionate Use/Open Label Program
Entry Criteria

Pediatrics

- Viral load > 100,000 copies/ml
- CD4 count < 15%
- Failed at least one NRTI

AIDS Dementia Complex

- Severe dementia (to be defined)
- Diagnosed by a neurologist
- Prior treatment with AZT

ADULTS

- Viral load > 50,000 copies/ml (where measured)
- CD4 count < 100/mm3
- Failed at least two NRTI and one PI

Consensus Statement on 1592 Expanded Access and Accelerated Approval

- **Overview**

Access to Glaxo Wellcome's 1592U89 ("1592") now in development, potentially represents the only viable option for delaying disease progression for many people living with HIV and AIDS who have exhausted the benefit from currently approved antiviral therapies. In early clinical studies, 1592 has demonstrated a more potent level of antiviral activity than other RT inhibitors, with minimal side effects. It's most important property, however, is that people have not previously been exposed to it and it therefore offers the hope of renewed antiviral activity. This renders the drug critically important to two patient populations: (1) those who have already lost sensitivity to the other drugs of this type, and (2) those who need to use at least one "fresh" or new nucleoside analogue RT inhibitor to make reasonable use of combination therapy with protease inhibitors or non-nucleoside RT inhibitors. Existing evidence clearly suggests that combining such drugs with previously used therapies diminishes their effectiveness and leads to more rapid development of resistance.

The benefit of this drug may be limited due to the development of resistance, a problem common to all currently approved antiviral compounds. While it may take years of additional study to determine its optimal use, this should not delay prompt access to this therapy by people in immediate need. Delaying the availability of this drug until Phase III trials are fully accrued is unacceptable and represents a significant change from past practices. For example, the ddI, d4T, and AZT expanded access programs all took place while trials were still recruiting. We are very concerned that the recent activities of several pharmaceutical companies represents a broad effort to minimize the number of patients served by expanded access programs. Any such effort around 1592 would be a moral affront to the rights and needs of people with HIV/AIDS and their healthcare providers.

We hereby propose the following 1592 expanded access program, to be phased in in stages, with immediate access to those in urgent need.

- **First Phase - Compassionate Use/Salvage Therapy**

Glaxo Wellcome and the Food and Drug Administration must cooperate and take a more compassionate stance to make this promising compound immediately available in a "salvage program" once a recommended dosing schedule has been established. This compassionate access/salvage program should make drug available as soon as possible for those people who have failed existing therapies and risk near-term danger of death or life-threatening infections.

The development of this drug must take into consideration its unique potential to provide benefit to the acutely compromised segment of the HIV-infected population. Availability of salvage strategies is of the highest priority for people living with HIV. There is no logical or moral reason to withhold this drug from people with advanced illness, people whose lives hang in the balance. Currently, this compound qualifies, by any humane standard, for compassionate use.

This first phase of Compassionate Use/Salvage Therapy should provide 1592 without delay to patients who meet any one of the following two requirements:

1. ***CD4+ Cell Count <50 OR Viral Load >40,000 copies/ml***
   AND Treatment Failure to approved RT Inhibitors AND at least one Protease Inhibitor;
2. ***Diagnosis of AIDS Dementia Complex (ADC), unresponsive to existing therapies.***

We believe evidence of the above conditions can be accomplished with a minimal amount of paperwork. A physician's letter accompanied by one lab report should be sufficient to establish any of the above criteria.

- **Second Phase - Expanded Access**

This second phase of Expanded Access should provide 1592 during recruitment and conduct of Phase II/III

clinical trials, but no later than ninety (90) days from the start-up of the First Phase, to patients who meet any of the following criteria:

1. ***Patients who do not qualify for or are denied entry in a 1592 clinical trial and have a medical need for 1592, or***
2. ***Patients who do not live within a radius of 15 miles of an active clinical trial site, or***
3. ***Patients whose lives would be immediately jeopardized by randomization to an ineffective treatment regimen, or***
4. ***Patients with a CD4+ Cell count below entry requirements of clinical trials, or***
5. ***Viral Load greater than 20,000 copies/ml., despite use of currently approved therapies, or***
6. ***Treatment Failure or demonstrated genotypic or phenotypic resistance to approved RT inhibitors.***

- **Accelerated Approval**

This compound should be licensed for accelerated approval as soon as possible. FDA approval of this compound should be based on existing regulations governing accelerated approval of new drugs for life-threatening illnesses:

1. ***Clear evidence of benefit on surrogate markers have been demonstrated;***
2. ***Principal toxicities and drug interactions have been defined;***
3. ***Longer-term development plans have been initiated designed to determine the drug's usefulness in promoting clinical and survival improvements and durability of response, as part of a medical strategy for coping with HIV infection.***

****We urge the sponsor to file applications for accelerated approval as soon as possible.***

- **Resistance, Pharmacokinetics and Drug Interactions**

As with all antivirals, the development of drug-resistant strains of virus, drug interactions and pharmocokinetic variances while using this compound may warrant additional considerations. To address this concern, sponsors should also be required, prior to accelerated approval, to present meaningful data on:

1. ***the speed and levels of resistance encountered;***
2. ***the degree of cross-resistance found with other nucleoside analogues;***
3. ***the interaction of the compound with other commonly used anti-HIV medications;***
4. ***bioavailability in men, women, and children and determination of the degree which blood levels vary depending on body weight.***

- **Summation**

Any effort to withhold access to promising compounds is contrary to the interests of HIV-infected people, inconsistent with the Accelerated Approval regulations, and scientifically unwarranted. The long history of the development of the earlier generation of antiviral drugs clearly demonstrates that it is possible to accrue patients and continue conducting clinical trials of compounds, long after their marketing approval. Because of the issues of drug resistance and drug failure over time, new therapies for HIV disease will continue to play a critical role no matter how many drugs become available on the market. New therapies, like 1592, must continue to be made available as rapidly as possible to patients with immediate needs for changed or improved treatment.

AGREED and ACCEPTED this ____ day of _____, 1996:
**** Revised as of 11/27/96***

By: _____ **Of:** _____

Signature **Organization**

Print Name: _____ **Please fax to: 310-471-4565**

1592 ACCESS COALITION

To: Daniel Montoya	From : Linda Grinberg	
Company: White House - AIDS Office	Telephone: 310-471-6565	
Fax Number: 1-202-632-1096	Fax Number: 310-471-4565	
Subject : Conf. Call	Date: 6/18/97	Pages: 1 2

Please see attached list of participants in today's conference call scheduled at 6:00 EST/3:00 PST.

Reminder: The phone number to call in to is (800) 360-0565. Please ask for the 1592 Access Coalition call with Jeff Getty & Linda Grinberg, moderators.

If there is any problem in accessing the call, please call (800) 825-2125 and tell operator the conf. call # is 811-~~6888~~ 48

We look forward to speaking with you later today.

1592 ACCESS COALITION

Name	Affiliation	Phone	Fax
1. Meg Atkinson	AIDS Action Now!/Toronto	416-487-8065	416-533-2127
✓2. Ron Baker	S.F. AIDS Foundation	415-487-8065	415-487-8069
✓3. Bill Bahlman	Treatment & Data Committee	212-929-4952	212-929-4952
✓4. Peter Cashman	ACT UP Los Angeles	213-669-7301	213-669-7302
✓5. Sally Cooper/James	PWA Health Group	212-255-0520	212-255-2080
6. Leigh Paldolfino-Danas	U.K.	44-171-793-7444	
✓7. Paul Davis	ACT UP Philadelphia	215-731-1844	215-731-1845
8. Martin Delaney	Project Inform	415-331-0184	415-331-2114
✓9. Jeff Getty	ACT UP Golden Gate	510-653-6278	510-653-6099
10. David Gilden	Gay Men's Health Crisis	718-624-6578-h 212-367-1452-o	918-624-8399
✓11. Linda Grinberg	Project Inform/F.A.I.R.	310-471-6565	310-471-4565
✓12. John Iverson	ACT UP East Bay	510-588-1680	
✓13. Cleve Jones	Names Project	707-865-9047	707-865--0541
14. Kiyoshi Kiromiya	Critical Path	215-545-2212	215-545-2212
✓15. Kate Krauss	ACT UP Philadelphia	215-731-1844	215-731-1845
16. James Learned	PWA Health Group	212-255-0520	212-255-2080
17. Jules Levin	N.A.T.A.P.	718-624-8541	718-624-8399
✓18. Andy Lipschitz, MD		516-935-6359	516-938-5470
19. L. Joel Martinez	Center for AIDS	713-527-8219	713-521-3679
✓20. Eileen Mitzman	Mother's Voices	212-737-3335	212-737-1092
21. Lili Rundback	Mother's Voices	212-730-2777	212-730-4378
22. Matthew Sharp	ACT UP Golden Gate	415-626-4053	415-626-0451
✓23. Theo Smart	Treatment Action Group	212-260-2607	212-673-8921

Revised 6/18/97

AIDS ACTION NOW!
517 College Street, Suite 420, Toronto, Ontario, M6G 4A2
Tel: 416-928-2206 Fax: 416-928-2185

7 May 1997

Glaxo Wellcome Inc.
7333 Mississauga Road North
Mississauga, Ontario
Canada
L5N 6L4
Fax: 905-819-3396
Attention: David Krakovsky
Clinical Research

Dear Ladies and Gentlemen:

Re: Compassionate Access to 1592U89

We are writing to express our concerns about the compassionate use program for 1592 as described by you in our meeting of May 1, 1997.

The Numbers

First of all, we are shocked by the paltry 2000 spots in the adult program for Europe, Australia, Canada and the United States. As you will know, the number of AIDS cases in these countries is well over 700,000. Glaxo Wellcome has been a model of generosity with the 3TC open label program which was relatively unrestricted and, in total, provided 3TC to approximately 50,000 individuals. Why is there such a difference in these programs?

You indicated that your reasons for limiting the compassionate access are as follows:

1) supply problems as a result of the change in formulation.

This is obviously something that is difficult for the community to judge and is a common reason put forward to limit compassionate access. To alleviate the community's suspicions that this is not a valid reason, and in keeping with your stated intention to have a "transparent" relationship with the community, would you allow an independent production analyst to inspect your production capacities? Merck agreed to such an independent review and this was beneficial to both the company and the community which were at loggerheads over a similar supply issue.

We appreciate that drug supply may be a rate-limiting factor in the development of the compassionate use/open label program, however we would ask you to undertake to scale up production to meet the need.

AIDS Action Now!
7 May 1997

2) you must ensure adequate supply for the conduct of clinical trials...

We understand that you have approximately 33 trials either ongoing or in development. Would it be possible to prioritize the trials required for regulatory approval and then review the relative urgency of the conduct of some of the planned additional or supportive trials vis-à-vis the needs of the compassionate use program, in consultation with the community? This might allow you to better "balance a limited supply of drug with the competing needs of an extensive clinical development program and this compassionate use/open label study" keeping in mind that "[t]he ultimate goal is to meet the needs of individuals... (your letter to the Canadian HIV/AIDS Community dated April 29, 1997)

3) there are more treatment options now than when 3TC entered into Phase III trials in June of 1993 and, therefore, you do not perceive that there is as much of a need; that there is not as much of a "drought" now as there was when you began the 3TC open label program in December 1993.

We find this argument hard to follow for two reasons: if you do not think that there is a real need for 1592 at this time, why have you imposed more limiting entry criteria than with 3TC and why have you capped the numbers of spots available? Secondly, we would suggest that for the individuals who have either exhausted all available options, or for whom their only option right now is to add one drug to a failing regimen, there is a real drought.

4) you have safety concerns about 1592; approximately 250 trial participants have taken 1592, and none for more than six months.

We are not advocating that everyone should abandon therapies which are working for a product which is just now beginning Phase III trials; however, a practice has evolved over the course of this epidemic to allow for compassionate access to a drug once Phase I and II trials are complete and the gross toxicities and adverse events are known. At this point, the acute safety concerns have been met and we acknowledge that there will, of course, be chronic safety concerns. However, this will be a staggered process of risk assessment - by the time that those who receive 1592 on a compassionate basis have been on the drug for six months, those trial participants will have had a further six months of exposure, and so on.

The Entry Criteria

We recognize that it is probably impossible to design a *limited* compassionate access program which will please everyone. Certainly, we feel that the entry criteria may need to be further "tiered" according to severity of the situation in order to most fairly ration the supply on the basis of need. This will probably depend, in part, on the size of the initial demand and would probably be best determined separately by each of Australia, Europe, Canada and the United States. Also, as supply increases we would expect to see the criteria made more liberal.

However, we do feel that your "salvage" program must be amended to adequately provide for mild to moderate AIDS Dementia Complex (ADC). Although we understand that you do have a clinical

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7 May 1997

trial for mild to moderate ADC, there are only 90 spots worldwide, and we do not consider it ethical to force people into a placebo-controlled clinical trial as their only hope of obtaining the drug. We recommend that the entry criteria be amended to add a category for those with mild to moderate ADC who have failed on or are intolerant of AZT and d4T. Even if the supply cannot meet the demand, we would prefer to encourage these individuals to apply so that we can assess the need and allow for a tiered system of access based on severity of need, as supply increases over time.

The Registration Process

You have indicated that the adult program will take place at geographically dispersed centres. We are vehemently opposed to this suggestion. There are numerous potential problems with such a system whereby an investigator for an area would hand pick individuals from his/her practise. When Merck Frosst initiated a program such as this in Canada it created a great deal of ill feelings toward the company. A practice has evolved in Canada in the last few years of compassionate access programs to utilize a centralized application and registration centre run by an arm of the Canadian HIV Trials Network. This has worked, is respected by the community, and is seen as the only fair and equitable way to allocate the limited supply of the drug. This would also allow us to better assess the real demand for compassionate access to 1592. We would, therefore, recommend that Canada be allowed to develop its own registration process in consultation with the community and that you utilize the Canadian HIV Trials Network as the registration centre and also as the Canadian contract research organization (CRO).

We understand that you would prefer to limit the Canadian sites for distribution to two or three which will be involved in the Phase III studies of 1592 and will, therefore, have some experience of 1592. We believe it is possible to have more sites with HIV-experienced physicians involved in the distribution of 1592 as was possible with 3TC. It is preferable that patients are able to stay with their own physicians and clinics for the continuity of their care, and that more physicians develop some experience of 1592. Clear guidelines in the protocol should ensure that the drug is appropriately used and monitored. At the very least, we will need more sites for distribution to reflect the geographical reality of AIDS incidence in Canada.

Possible Inter-Company Collaborative Compassionate Use Salvage Program

We are all aware that it will not be the best use of 1592 to take it as monotherapy, or to add it to a failing regimen; however, individuals who have exhausted all other options will have no choice. We are pleased that there are no restrictions on using 1592 with other experimental therapies; however, this does not ensure or facilitate that someone in need will be able to access other experimental therapies at the same time. For this reason, we query whether you would look at the possibility of an inter-company collaborative compassionate use *salvage* program, with companies such as Dupont Merck and Gilead, for individuals who have exhausted *all* options, so that such individuals could be offered two or three experimental therapies at once and a real hope of sustained benefit. Perhaps such a pilot program could be coordinated by a branch of the ICC.

Future Consultation

We would appreciate seeing your draft protocol including the informed consent form so that we may provide you with some input. We would also be interested in seeing the Case Report Forms. We trust that you will continue to consult with us in a meaningful way through the development of this program.

Benefits of Compassionate Access

Lastly, we would ask you to consider the following possible advantages of a liberal compassionate access program:

- avoids negative publicity
- creates goodwill
- marketing - physician experience
  - word of mouth
- creates a market which will pressure third-party payers such as government drug plans and insurance companies - In Canada the widespread compassionate access to 3TC resulted in a great deal of pressure on the government drug plans to cover the drug for those on social assistance.
- creates an ultimate market - keeping someone alive until the drug is licensed.

The consequences of an inadequate program are obvious:

- some may die irreversible or untreatable and, possibly preventable, opportunistic infections;
- some may die unnecessarily before access to 1592 is expanded.

It seems ironic that we are faced now with responding to such a limited compassionate use program, of less than 100 spots for Canada, while on May 15, 1997 Glaxo Wellcome representatives will be attending the Prix Galien ceremonies in Montreal nominated for their innovative new product, 3TC, and that in the media package for the launch of 3TC, GW prides itself on the fact that "[t]hrough the open-label program close to 2800 people living with HIV/AIDS were able to access 3TC in Canada prior to its approval".

We look forward to your early response.

Yours very truly,

Maggie Atkinson
Co-Chair

GlaxoWellcome

CLINICAL RESEARCH DEPARTMENT

May 22, 1997

Maggie Atkinson
CTAC Advisory Team
AIDS Action Now Co-Chair
517 College Street, Suite 420
Toronto, Ontario,
M6G 4A2

Dear Maggie:

Thank you very much for sending us your comments about the 1592U89 compassionate access programme discussed at our May 1st meeting. We have given much thought to your concerns and have discussed these issues with our international colleagues in the US and UK.

Comparing the 3TC programme to the proposed 1592U89 programme at this point in time is difficult. At the comparable point in 3TC's clinical development, the compassionate use programme that we are proposing for 1592U89 did not exist. In fact, the 3TC programme commenced after the majority of the patients had been enrolled into the pivotal phase III studies, and the efficacy/safety profile was better established.

We are initiating the 1592U89 compassionate use programme earlier, as we prepare to start enrollment into the phase III clinical studies. This is an "interim" programme designed to provide some drug to those people who need it, while still obtaining important information in this anti-retroviral experienced population, prior to initiating an expanded access programme. The numbers for this programme (2,500) are greater than those planned for the clinical trial programme during the same period. Towards the end of the year, as more supplies and data become available, we can then initiate the larger expanded access programme. The size of that program will be decided based on safety and efficacy data when it is available from the pivotal clinical studies.

In order to address your concerns we have taken each into consideration as follows:

1) Supply:

The following is a detailed review of the development of 1592U89, which we hope will address your concerns over the supply issues as a result of the change in formulation.

In the summer of 1995 following the merger of the two companies Glaxo Wellcome had a number of compounds in development for the treatment of HIV including: 3TC, 1592U89, 141W94, 1263W94, 935 and tucaresol. Resource was distributed amongst the projects according to the potential of each compound as demonstrated in the early stages of development - those compounds that showed the greatest potential had the greatest resource allocated. Limited resource was applied to 1592U89, which, with poor laboratory data appeared the least promising of the HIV drugs in development at that time. However, by November 1995, the situation had changed dramatically when 1592U89 demonstrated marked efficacy in the clinic. These contradictory results were unexpected. It is very unusual for a compound to perform poorly in the laboratory and then go on to show significant

promise in the clinic, as was the case with 1592U89. Manufacturing scale-up plans, usually initiated on the basis of promising laboratory results were, therefore not in place when these first results with 1592U89 emerged. Chemical resources had been fully assigned to other more promising compounds anticipating that they would be the preferred compound for further development. Fewer chemists worked on 1592U89 and consequently a robust manufacturing process had not been established.

Glaxo Wellcome has a history of working together with communities affected by HIV and was aware of, and very sensitive to the needs of people with HIV and the compassionate requirements for drug outside of the clinical development programme. Consequently, full human and financial resource was put behind the 1592U89 development programme and in particular the number of manufacturing staff was increased by over 300%. Although the manufacturing process was not robust, the chemists persevered and eventually scaled it up to produce greater quantities of 1592U89. It was clear, however, that this process would not support the anticipated huge drug substance requirements of the clinical programme. It also became obvious that supply of drug could not be met from the pilot plant facilities (pilot plant is the intermediate step between the laboratory and full-scale manufacturing). Therefore as well as having to identify a new process, our chemists would have to transfer it rapidly into full scale manufacturing facilities. In addition to these challenges, it was also necessary to move the manufacturing project to the UK.

By the end of November a seemingly viable process was identified; one batch was made in the pilot plant during January 1996 and within 2 months the process was transferred to full production.

By March 1996 the new process was being operated at full scale production, eventually producing large quantities of 1592U89 powder ready for the next stage in manufacture. Due to the need to move 1592U89 through clinical development at a rapid pace and the future need for access on a compassionate basis for those people with no other treatment options, considerable risks were taken in transferring the process to production. Normally before transfer occurs several pilot plant campaigns would be carried out providing experience of often up to 20 batches at each stage of the process. On this occasion only a single pilot plant campaign was carried out producing only ONE batch at each stage. Glaxo Wellcome's manufacturing staff were requested to prepare for full scale production prior to the feasibility of the chemistry being established in the pilot plant. Scale-up from laboratory to full production can often take as long as 2 years or more, but with 1592U89 this was achieved in less than 6 months. All the effort, expertise and risk taking seemed to be paying off.

Everything was going well in primary manufacture until the first batch of 1592U89 was produced in June 1995. A problem was encountered, not with the actual chemistry, but with the physical form of the drug substance itself. The compound was proving difficult to filter and dry, furthermore the pharmacy department were experiencing difficulty in formulating it into capsules. Instead of the substance presenting as a fine powder ready to encapsulate, it was presenting as a large, very hard, solid mass. By this time 1592U89 was at late Phase II clinical development and although significant effort was made to try and resolve the problem, it soon became clear that the salt part of the molecule needed to be changed. This would have been a large undertaking at the very early stage of primary manufacture, but with a considerable amount of unusable drug substance already manufactured, it was a very serious problem, threatening the whole clinical programme. In the past, pharmaceutical drug development programmes have sometimes been discontinued with problems such as these, due to the potential long delays in clinical development programme. Once again resource was stepped up and the problem was resolved. This problem may have been identified earlier had more time been taken for pilot plant testing, highlighting the risks that are involved in fast-track development. After extensive tests on several different salt forms a suitable alternative salt was identified.

Within four months a new alternative salt had been identified, scaled up into the pilot plant and transferred into full scale production to produce the new version of 1592U89.

At the end of December 1996 and during early 1997 the new 1592U89 had to undergo strict bioequivalence tests enforced by regulatory authorities, as well as further toxicology studies. By the end of March 1997 the new version 1592U89 had passed all these tests and further primary scale-up is now planned. As a comparison, the quantity of 1592U89 planned at this stage of development is 10 to 20 times greater than that produced for other drugs.

1592U89 Development
Calendar of Events

January	
February	
March	New process for 1592U89 scale-up in operation.
April	
May	1592U89 in full scale manufacture.
June	Problem with salt identified.
July	
August	
September	
October	New salt identified and in full scale production.
November	
December	1592U89 undergoes regulatory tests.
January	
February	
March	1592U89 passes regulatory tests.
April	Full scale production.
May	Full scale production.
June	Full scale production.
July	Full scale production.

2) Prioritizing clinical trials:

At this point in the development of 1592U89, we are obligated to learn as much as we can about the utility of this drug in well-controlled clinical trials. We are attempting to balance this work with an early compassionate use programme to provide 1592U89 to those patients with immediate medical need for the drug. Indeed, in this effort we are already prioritizing clinical trials in order to accomplish both of these objectives.

3) Need:

Many treatment options exist now and we cannot encourage patients to forgo currently marketed drugs with proven efficacy in favor of a new treatment about which very little is known at this

time. Who best will benefit from 1592U89 remains to be determined from the Phase III clinical trial programme.

4) Safety concerns:

We acknowledge that safety issues are an ongoing concern and may have less impact on people with very few options. This is why we are committed to compassionate access for 1592U89 and why the programme is starting so early in the clinical development programme.

5) Entry criteria:

At this early stage in development, the treating physicians need to determine who best qualifies for the drug based on their clinical judgment. We are open to applying a system designed in conjunction with physicians, yourselves and the Canadian HIV Trials Network (CTN). Your input into any additional criteria for selection will be considered.

6) Mild to moderate dementia patients:

Since no data is available to prove that 1592U89 is effective against dementia, the ongoing clinical trial (CNA23004) needs to be completed as soon as possible to address this point. Patients in this trial are adding either 1592U89 or placebo to their existing treatment regimen, and are not subject to receive a substandard of care. We understand your concerns and as such we have agreed to broaden the entry criteria to include people with MSK stage 2 disease once recruitment into the clinical trial is complete. We believe the company would be considered irresponsible by allowing treating physicians to release an unproven drug at an earlier stage of the disease than this, as quite often early stage dementia can be confused with other conditions.

7) Registration Process:

As discussed at our meeting on May 1, we agree that there is a need to provide access to the drug across the country in the most equitable manner possible, and that the CTN could play a role in the registration and selection of applicants. After our meeting we held discussions with the CTN, and they have agreed in principle to assist us with the programme. The CTN will issue information to all physicians about the program, accept applications, and review and approve applicants for entry into the programme, very similar to their involvement with the saquinavir compassionate use programme.

The logistics of CTN's role need to be worked out once more information about the programme is available. Access will be based on geographic need as determined by the prevalence of HIV/AIDS in each region across the country. The above will ensure that participating centres will not be able to hand pick individuals from their own practice, and that all who apply will have an opportunity to access the drug. The overall programme will be conducted by a contract research organization (CRO).

Due to Canada's size, we did not want to limit Canadian centres to only two or three, and put forward a proposal for eight centres across the country, as discussed at our meeting on May 1. As a result of this week's compassionate use teleconference, we are able to implement this programme at approximately 12 centres across the country. The number of participants for each country should be finalized within the next week, and we will communicate this information to you as soon

as it is available. Individuals outside of these centres can apply for the programme through their physician. If they are approved, individuals will have to go to a participating centre for access to drug, and attend all study-related visits for assessment and data collection. Required visits will likely be every two months, and individuals can continue to see their own physician during this time. As we are collecting important safety and efficacy data, which will help shape the expanded access programme, consistency must be maintained by involving a limited number of centres/physicians world-wide.

8) Intercompany collaborative programme:

A 1592U89 collaborative studies review team has been organized to review all external study proposals for scientific and clinical merit and strategic importance. This team has reviewed over 40 proposals to date, and a number of them have been accepted. Glaxo Wellcome is working with a number of collaborative groups including the ICC, ACTG, etc., to establish and conduct collaborative studies with 1592U89, as well as our other products. We remain open to collaboration. We hope that our colleagues in the industry will also find the need to furnish drugs to those most in need at the earliest possible time in their development.

9) Future communications:

We truly believe that opening this "interim" programme ahead of the expanded access programme is a way to provide early access to 1592U89. This will allow more information to be obtained, in order to use the drug in the best way possible for the expanded access programme, while trying to meet the varying needs of communities internationally.

We hope that this information helps to explain the rationale behind the programme more clearly. If in the future you would like to discuss any subject with us, we would be more than happy to meet with you.

Sincerely,

David Krakovsky, B.Sc. Phm., Pharm. D.
Clinical Research Manager,
Infectious Diseases

cc: T. McAuley
L. Binder
R. Guerin
C. Laforce
R. Kort
C. McClure

GlaxoWellcome

GLAXO WELLCOME HIV MEDICATION ACCESS EFFORTS

Rapidly emerging data concerning the beneficial effects of multi-drug combinations in the management of HIV disease have focused attention once again on the health care resources needed to ensure that people living with HIV disease receive state-of-the art medical care. As the leader in the discovery and development of medications for the management of HIV disease, Glaxo Wellcome has worked with government, academia and the HIV community for many years to enhance knowledge and education about the effective use of HIV medications. In addition to its significant ongoing research and development programs, Glaxo Wellcome has undertaken a number of initiatives to work with those involved in the delivery of care to address the issue of medication access and reimbursement for people living with HIV disease.

National

- Glaxo Wellcome is actively involved in the AIDS Drug Assistance Program Future Funding Working Group, a coalition of industry and community representatives working to increase Ryan White funds in 1997 as well as free up current funds caught up in reauthorization delays. Activities have included visits with key Administration and Congressional leaders as well as ongoing efforts to quantify the need for increased funding and the economic benefits of HIV therapy.

- Substantial medication discounts have been provided to health care facilities, including those serving individuals with HIV disease, which are under Federal Contract.

- Since 1987, the company has contributed more than $12 million to state and national AIDS community programs. Access to care initiatives are a key focus of contributions efforts. An additional $1 million has been provided to support conferences that offer AIDS service organizations the opportunity to network and collaborate on common issues.

- More than 30,000 individuals with HIV disease in the United States received Epivir® (lamivudine, 3TC) at no cost through an open label compassionate use program in place from October 1993 through December 1995. The Glaxo Wellcome program was the largest expanded access program ever conducted.

- Glaxo Wellcome recently participated in a meeting with Vice President Al Gore concerning AIDS medication issues and attended President Clinton's White House Conference on HIV and AIDS in December 1995.

- The company is an active participant in the Inter-Company Collaboration for AIDS Drug Development, a group of pharmaceutical companies formed in 1993 to facilitate early combination and comparative studies of antiviral agents for the treatment of HIV disease. This group, although not focused on funding, shares preclinical and clinical data, drug supplies and assays to facilitate the study of combination therapies.

(over)

Glaxo Wellcome Inc.

Five Moore Drive
Research Triangle Park
North Carolina 27709

Telephone
919 248 2100

State

- Glaxo Wellcome provided rebates to Medicaid and state entitlement programs of more than $10 million on its HIV medications during a recent 12-month period.

- The company has voluntarily extended rebates in excess of $5 million to 22 states that did not have distribution mechanisms in place to take advantage of Federal rebate programs.

- Glaxo Wellcome state government managers are actively working with states that are experiencing fiscal difficulties on an individual basis to identify and assess various legislative and programmatic initiatives to help them meet their patients' health care needs.

- Glaxo Wellcome has funded a number of initiatives at the state and local level to improve access to medications and quality of health care for people with HIV disease. Examples include a training program for case managers in California, a N.J. program which provides support to women parolees, and many contributions to improve case management and medical services at AIDS service agencies and community-based organizations throughout the country. These contributions often provide a needed boost to programs faced with a decline in government funding and increasing demands for services.

- The company is in active discussion with Ryan White administrators in several states about development of a study to identify and assess successful programs to assist states in improving their drug access and reimbursement programs.

Patient Assistance

- Glaxo Wellcome has its own Patient Assistance Program to make its prescription medications, including all HIV medications, available to patients who do not have or qualify for private insurance or government-funded programs. Last year, the company made available products valued at more than $22 million through this program to qualified participants.

- The company is dedicated to providing patients with information and guidance in finding alternative reimbursement sources for needed medicines. The Patient Assistance Program has an active case management program and the ability to work with individuals on a case-by-case basis.

- Although the company recognizes that many states are experiencing fiscal difficulties, the Patient Assistance Program is not intended to supplement or replace government sponsored programs. Rather, it is a philanthropic activity to help individuals who simply are not eligible for any other program.

3/4/96

Fax from Linda Grinberg

To: Sandy Thurmond	From : Linda Grinberg	
Company: The White House, AIDS Czar	Telephone: 310-471-6565	
Fax Number: 1-202-632-1096	Fax Number: 310-471-4565	
Subject : 1592 Cons. Stmt. Update & News Clips	Date: 6/4/97	Pages: 12

Sandy: I must tell you that you boosted our morale enormously with your enthusiasm and commitment to go to bat for us with Glaxo on this important issue. I spoke with a number of folks on the call afterwards and they were excited and encouraged by you -- your "can do" attitude, the astute questions you asked and the issues you zeroed in on. We're all keeping our fingers crossed, hoping and praying you can make a difference. As you know, based on recent statistics, it is estimated that approx. 50,000 in the U.S. alone will probably die this year, and this drug could be the difference between life and death to many of these people.

I just wanted to copy you on the signatures collected to date on the 1592 Consensus Statement, which I finally had time to update. I must point out to you that this drive really took on a life of its own, as there hasn't been press publicizing the Consensus Statement since several articles appeared in November and December of last year, and approx. 150 additional signatures have come in since then, unsolicited, simply by word of mouth.

One item we neglected to mention to you, which may possibly be another factor in this inadequate compassionate use program (or lack thereof) may be a perception that if the drug is more widely available through expanded access they fear they may have difficulty enrolling patients in the trials program, and filing the NDA is top priority. We met with Glaxo reps last summer in DC, pressing them to begin planning for expanded access, as it was clear back then that late-stage patients would not qualify for their trials program. They finally responded in a very heated conf. call with 20-30 community reps in November, at which time they declared they wouldn't even begin to consider expanded access until Phase III trials were fully accrued, as they were afraid this would interfere with their ability to recruit patients. The response was quite angry, across the board, as not only was this precedent setting, they were just beginning Phase II/III trials and nowhere even close to beginning Phase III trials, thus precipitating the Cons. Statement. Phase III trials are only just beginning now, I might add, with unexplained delays and little progress since Vancouver last July ...

Evidently, I believe we were mistaken about the expiration on the patent on Zantac, as when I did some checking I found some recent articles, attached, indicating that the patent runs out this July, at which time there will be generic competition. Haven't located the exact date on the expiration of AZT yet, but we'll keep you informed.

It's a pleasure to work with you on this. Having someone in the White House who seems to genuinely care, after so many years of silence and seeming complacency, is such a breath of fresh air and the sense of renewed faith and hope yesterday was truly palpable.

We look forward to our followup call on the 11th. Thanks!!! Good luck on the 10th!

Best, Linda

cc: , If, Ron, Cleve, and Marty

Consensus Statement on 1592 Expanded Access and Accelerated Approval

- **Overview**

Access to Glaxo Wellcome's 1592U89 ("1592") now in development, potentially represents the only viable option for delaying disease progression for many people living with HIV and AIDS who have exhausted the benefit from currently approved antiviral therapies. In early clinical studies, 1592 has demonstrated a more potent level of antiviral activity than other RT inhibitors, with minimal side effects. It's most important property, however, is that people have not previously been exposed to it and it therefore offers the hope of renewed antiviral activity. This renders the drug critically important to two patient populations: (1) those who have already lost sensitivity to the other drugs of this type, and (2) those who need to use at least one "fresh" or new nucleoside analogue RT inhibitor to make reasonable use of combination therapy with protease inhibitors or non-nucleoside RT inhibitors. Existing evidence clearly suggests that combining such drugs with previously used therapies diminishes their effectiveness and leads to more rapid development of resistance.

The benefit of this drug may be limited due to the development of resistance, a problem common to all currently approved antiviral compounds. While it may take years of additional study to determine its optimal use, this should not delay prompt access to this therapy by people in immediate need. Delaying the availability of this drug until Phase III trials are fully accrued is unacceptable and represents a significant change from past practices. For example, the ddI, d4T, and AZT expanded access programs all took place while trials were still recruiting. We are very concerned that the recent activities of several pharmaceutical companies represents a broad effort to minimize the number of patients served by expanded access programs. Any such effort around 1592 would be a moral affront to the rights and needs of people with HIV/AIDS and their healthcare providers.

We hereby propose the following 1592 expanded access program, to be phased in in stages, with immediate access to those in urgent need.

- **First Phase - Compassionate Use/Salvage Therapy**

Glaxo Wellcome and the Food and Drug Administration must cooperate and take a more compassionate stance to make this promising compound immediately available in a "salvage program" once a recommended dosing schedule has been established. This compassionate access/salvage program should make drug available as soon as possible for those people who have failed existing therapies and risk near-term danger of death or life-threatening infections.

The development of this drug must take *into consideration* its unique potential to provide benefit to the acutely compromised segment of the HIV-infected population. Availability of salvage strategies is of the highest priority for people living with HIV. There is no logical or moral reason to withhold this drug from people with advanced illness, people whose lives hang in the balance. Currently, this compound qualifies, by any humane standard, for compassionate use.

This first phase of Compassionate Use/Salvage Therapy should provide 1592 without delay to patients who meet any one of the following two requirements:

1. ***CD4+ Cell Count <50 OR Viral Load >40,000 copies/ml***
   AND Treatment Failure to approved RT Inhibitors AND at least one Protease Inhibitor;
2. ***Diagnosis of AIDS Dementia Complex (ADC), unresponsive to existing therapies.***

We believe evidence of the above conditions can be accomplished with a minimal amount of paperwork. A physician's letter accompanied by one lab report should be sufficient to establish any of the above criteria.

- **Second Phase - Expanded Access**

This second phase of Expanded Access should provide 1592 during recruitment and conduct of Phase II/III clinical trials, but no later than ninety (90) days from the start-up of the First Phase, to patients who meet any of the following criteria:

1. ***Patients who do not qualify for or are denied entry in a 1592 clinical trial and have a medical need for 1592, or***

2. ***Patients who do not live within a radius of 15 miles of an active clinical trial site, or***
3. ***Patients whose lives would be immediately jeopardized by randomization to an ineffective treatment regimen, or***
4. ***Patients with a CD4+ Cell count below entry requirements of clinical trials, or***
5. ***Viral Load greater than 20,000 copies/mL, despite use of currently approved therapies, or***
6. ***Treatment Failure or demonstrated genotypic or phenotypic resistance to approved RT inhibitors.***

- **Accelerated Approval**

This compound should be licensed for accelerated approval as soon as possible. FDA approval of this compound should be based on existing regulations governing accelerated approval of new drugs for life-threatening illnesses:

1. ***Clear evidence of benefit on surrogate markers have been demonstrated;***
2. ***Principal toxicities and drug interactions have been defined;***
3. ***Longer-term development plans have been initiated designed to determine the drug's usefulness in promoting clinical and survival improvements and durability of response, as part of a medical strategy for coping with HIV infection.***

**We urge the sponsor to file applications for accelerated approval as soon as possible.*

- **Resistance, Pharmacokinetics and Drug Interactions**

As with all antivirals, the development of drug-resistant strains of virus, drug interactions and pharmocokinetic variances while using this compound may warrant additional considerations. To address this concern, sponsors should also be required, prior to accelerated approval, to present meaningful data on:

1. ***the speed and levels of resistance encountered;***
2. ***the degree of cross-resistance found with other nucleoside analogues;***
3. ***the interaction of the compound with other commonly used anti-HIV medications;***
4. ***bioavailability in men, women, and children and determination of the degree which blood levels vary depending on body weight.***

- **Summation**

Any effort to withhold access to promising compounds is contrary to the interests of HIV-infected people, inconsistent with the Accelerated Approval regulations, and scientifically unwarranted. The long history of the development of the earlier generation of antiviral drugs clearly demonstrates that it is possible to accrue patients and continue conducting clinical trials of compounds, long after their marketing approval. Because of the issues of drug resistance and drug failure over time, new therapies for HIV disease will continue to play a critical role no matter how many drugs become available on the market. New therapies, like 1592, must continue to be made available as rapidly as possible to patients with immediate needs for changed or improved treatment.

* *Revised as of 11/27/96*

ORGANIZATIONS: **SIGN-ONS AS OF MAY 30, 1997**

1. **ACTUP BOSTON, Boston, MA**
2. **ACTUP EAST BAY, Oakland, CA**
3. **ACTUP GOLDEN GATE, San Francisco, CA**
4. **ACTUP LOS ANGELES, Los Angeles, CA**
5. **ACTUP MINNESOTA, Minneapolis, MN**
6. **ACTUP NEW YORK, New York, NY**
7. **ACTUP PARIS, Paris, FRANCE**
8. **ACTUP PHILADELPHIA, Philadelphia, PA**
9. **AIDS ACTION COMMITTEE OF MASSACHUSETT,Boston, MA**
10. **AIDS ACTION COUNCIL, Washington, DC**
11. **AIDS HEALTHCARE FOUNDATION, Pasadena, CA**
12. **AIDS PROJECT LOS ANGELES /APLA, Los Angeles, CA**

13. **AIDS RESEARCH ALLIANCE, Los Angeles, CA**
14. **AIDS RESEARCH INFORMATION CENTER, INC./ARIC, Baltimore, MD**
15. **AIDS SERVICE CENTER, Pasadena, CA**
16. **AIDS SURVIVAL PROJECT, Atlanta, GA**
17. **AIDS TREATMENT INITIATIVES, Atlanta, GA**
18. **AIDS TREATMENT NEWS, San Francisco, CA**
19. **BEING ALIVE, Los Angeles, CA**
20. **BRITISH COLUMBIA PERSONS WITH AIDS SOCIETY, Canada**
21. **CENTER FOR AIDS, THE, Houston, Texas**
22. **COUNSELING CENTER, THE dba GULF COAST MENTAL HEALTH, MI**
23. **FACE- L.A., Pasadena, CA**
24. **FLORIDA AIDS ACTION COUNCIL, Florida**
25. **GAY LIBERATION FRONT, Minneapolis, MN**
26. **GAY MEN'S HEALTH CRISIS/GMHC, New York, NY**
27. **LINDA GRINBERG FOUNDATION, Los Angeles, CA**
28. **HAITIAN AMERICAN COMMUNITY COUNCIL, Delray Beach, Florida**
29. **HOMESTEAD HOSPICE & THE "DALLAS HOUSE", Los Angeles, CA**
30. **IHS AT HANOVER**
31. **ISRAEL AIDS TASK FORCE, Tel Aviv, Israel**
32. **KRAUS MEDICAL PARTNERS, Los Angeles, CA**
33. **LAMBDA COUNSELING CENTER, Miami, Miami Beach, Ft. Lauderdale & Palm Beach, FL**
34. **LIVING WELL PROJECT/ASIAN PACIFIC ISLANDERS AIDS SERVICES, San Francisco, CA**
35. **LOG CABIN REBUBLICANS, Washington, D.C.**
36. **MOTHER'S VOICES, New York, NY**
37. **MULTICULTURAL AIDS COALITION, INC., Boston, MA**
38. **NATIONAL AIDS TREATMENT ADVOCACY PROJECT/NATAP, New York, NY**
39. **NATIONAL ASSOCIATION OF PEOPLE WITH AIDS/NAPWA, Washington, DC**
40. **NATIONAL MINORITY AIDS COUNCIL, Washington, DC**
41. **OPEN DOORS**
42. **PARAGON MEDICAL RESEARCH, Los Angeles, CA**
43. **POZ MAGAZINE, New York, NY**
44. **PROJECT INFORM, San Francisco, CA**
45. **PROJEKT INFORMATION, Munich, Germany**
46. **PWA HEALTH GROUP, New York, NY**
47. **PWAlive/MINNESOTA, Minneapolis, MN**
    REACH OF SOUTHERN ARIZONA, AZ
49. **RESEARCH SANCTUARY, Los Angeles, CA**
50. **SAN FRANCISCO AIDS FOUNDATION/BETA, San Francisco, CA**
51. **SAN LUIS OBISPO HIV CARE CONSORTIUM, CA**
52. **SEARCH FOR A CURE, Boston, MA**
53. **SONOMA COUNTY COMMISSION ON AIDS, CA**
54. **SO. MISSISSIPPI AIDS TASK FORCE, MI**
55. **TAMPA AIDS NETWORK, Tampa, FL**
56. **TEST POSITIVE AWARE, Chicago, IL**
57. **TREASURE COAST COMMUNITY AIDS NETWORK, Florida**
58. **TREATMENT ACTION GROUP/TAG, New York, NY**
59. **TREATMENT & DATA COMMITTEE, New York, NY**
60. **UNITED FOUNDATION FOR AIDS, Miami, FL**
61. **VALLEY AIDS INFORMATION NETWORK, Corvallis, Oregon**
62. **WOMEN ALIVE, Los Angeles, CA**

INDIVIDUALS: **SIGN-ONS AS OF MAY 30, 1997**

1. George H. Adams, Atlanta, Georgia
2. Moises Agosto, National Minority AIDS Council, Washington, DC
3. Linda R. Allen
4. Harlan Annheuser, Marietta, Georgia
5. Alberto Avendano, MD, Florida AIDS Action Council, Florida
6. Bill Bahlman, Treatment & Data Committee, New York
7. A. Cornelius Baker, National Association of People with AIDS/NAPWA, Washington, DC

8. Ron Baker, SF AIDS Foundation/BETA, San Francisco, California
9. David Barr, Gay Men's Health Crisis/GMHC, New York, New York
10. Dirk Belau, Geneva, Switzerland
11. Carol Bennett
12. Jessica C. Bigg, So. Mississippi AIDS Task Force, Mississippi
13. Voa Bigg, So. Mississippi AIDS Task Force, Mississippi
14. Ron A. Braun, Pacific Oaks Medical Group, Van Nuys, California
15. G'dali Braverman, Living Well Project, San Francisco, California
16. William K. Brent, Jr., So. Mississippi AIDS Task Force, Mississippi
17. Larry Bresslour, Search for a Cure, Boston, Massachusetts
18. Gregory Britt, AIDS Research Alliance, Los Angeles, California
19. Sara J. Brookins, So. Mississippi AIDS Task Force, Biloxi, Mississippi
20. Nicholas F. Brookins, So. Mississippi AIDS Task Force, Biloxi, Mississippi
21. Jean Haspel Brooks, RJNPC, Infectious Disease Associates, Atlantic City Medical Center, , Atlantic City, New Jersey
22. Carl Brown, Treasure Coast Community AIDS Network, Florida
23. Glenn Brown, ACTUP Philadelphia, Pennsylvania
24. Randall Brown, Atlanta, Georgia
25. William D. Bryant, Boulder Creek, California
26. Todd Burger, Chicago, Illinois
27. John J. Caringi, W. Virginia
28. Deborah A. Carriveau, W. Virginia
29. Jan Casey
30. Jeffrey B. Cason, New York, New York
31. Peter Cashman, ACTUP Los Angeles, California
32. Rhonda Chambers, HIV Study Group, Austin, Texas
33. Henry E. Chang, AIDS Healthcare Foundation, California
34. James Clark, Laguna Beach, California
35. Keith L. Cobb, Georgia Public Health Lab, Tucker, Georgia
36. Winifred Cochran, Marietta, Georgia
37. C. Trustran Coffin, Atlanta, Georgia
38. Mark Cohen, United Foundation for AIDS, So. Miami, Florida
39. Judith Colbs, Atlanta, Georgia
40. Marvin Colbs, Atlanta, Georgia
41. Christopher Collins
42. Richard Cooper, M.D., Kraus Medical Partners, Los Angeles, California
43. Sarah ("Sally") C. Cooper, PWA Health Group, New York, New York
44. Drew Cornutt, Atlanta, Georgia
45. Susan Cornutt, Atlanta, Georgia
46. Jim Corti, Research Sanctuary & Linda Grinberg Foundation, Los Angeles, California
47. Gary E. Costa, Being Alive, California
48. John Curtis Cottingham, Alabama
49. Linda F. Cottingham, State of Alabama, Dept. of Human Resources, Alabama
50. Spencer Cox, Treatment Action Group/TAG, New York, New York
51. Myron C. Crider, Morrow, Georgia
52. Michael J. Cross, PWA, San Francisco, California
53. Harold W. Cummings, Atlantic City, New Jersey
54. Denise Dagrosa, Infectious Disease Associates, Atlantic City Medical Center, Atlantic City, New Jersey
55. Richard T. Dalton, Flowery Branch, Georgia
56. Donald T. Daniels, PAC, AIDS Healthcare Foundation, Los Angeles, California
57. Tony Davis, Mother's Voices, New York, New York
58. Robert Dal Porto, PWA with Being Alive, Los Angeles, California
59. Kenneth De Haan
60. Martin Delaney, Project Inform, California
61. Margo Denison, Valley AIDS Information Network, Inc., Corvallis, Oregon
62. Rebecca Dennison, W.O.R.L.D., Oakland, California
63. John Deshane, Los Angeles, California
64. Scott Dewees, W. Hollywood, California
65. John Dolan, Raleigh, North Carolina
66. Jim Driscoll, Log Cabin Republicans, San Francisco, California
67. Marianne DuBose, So. Mississippi AIDS Task Force, Mississippi
68. Ferd Eggan, AIDS Coordinator, City of Los Angeles, California
69. Peter Engelhard, D.O., Fisher Medical Group, Miami, Florida
70. Michael England, San Francisco, California

71. Amy Erlich, Atlanta, Georgia
72. Donna Eschulz-Wilkinson, FACE-L.A., Pasadena, California
73. Charles Farthing, M.D., AIDS Healthcare Foundation, Los Angeles, California
74. Tracy Fennell
75. Gil Ferguson, British Columbia Persons with AIDS Society, Canada
76. Gary Foret, Atlanta, Georgia
77. Frances Frazetta
78. Brenda Freiberg, Board of Directors, Project Inform & AIDS Service Center, California
79. Ruben Gamundi, AIDS Project Los Angeles, California
80. David Garner, Atlanta, Georgia
81. Ramon M. Garcia, REACH of So. Arizona, Bisbee, Arizona
82. Aileen Getty, Homestead House & The "Dallas House", Los Angeles, California
83. Jeff Getty, ACT UP Golden Gate, San Francisco, CA
84. Greg Gilliam, Chicago, Illinois
85. Marc Gilbert, Atlantic City Medical Center patient, Atlantic City. New Jersey
86. Joseph L. Goebelt, Santa Clara, California
87. Michael Gottlieb, M.D., Gottlieb Medical Group, Los Angeles, California
88. Garrison J. Grace, Ft. Lauderdale, Florida
89. Jeff Graham, AIDS Survival Project, Atlanta, Georgia
90. Linda Grinberg, Linda Grinberg Foundation & Project Inform, California
91. Jeffrey S. Gunnoe, West Virginia
92. John Haiduck, Test Positive Aware, Chicago, Illinois
93. Robert Halfhial, Minneapolis, Minnesota
94. Lee Hardy, ARIC, Inc., Baltimore, Maryland
95. Larry Harman, Ph.D., Lambda Counseling Center, Miami, Ft. Lauderdale & Palm Beach, Florida
96. Zaida Harrington, Biloxi, Mississippi
97. Mark Harris, Atlanta, Georgia
98. Robert E. Hart, Atlanta, Georgia
99. John F. Haskell, Chicago, Illinois
100. Roberta Luskin-Hawk, M.D., St. Joseph Hospital, Chicago, Illinois
101. Rene Milet Hernandez, Multicultural AIDS Coalition, Inc., Boston, Massachusetts
102. Rachael Hincey
103. Gideon Hirsch, Israel AIDS Task Force, Tel Aviv, Israel
104. Peter M. Hoffmann, Treasure Coast Community AIDS Network, Florida
105. Stephanie Hoffman, Lithonia, Georgia
106. Carlton Hogan, PWAlive, Minneapolis, Minnesota
107. Ernest Hopkins, National Association of People with AIDS/NAPWA, Washington, DC
108. Dennis Hughes, Treasure Coast Community AIDS Network, Florida
109. Terrence L. Ibbs, D.O., N. Miami Beach, Florida
110. Crystal Iondan, Treasure Coast Community AIDS Network, Florida
111. John Iverson, ACTUP/East Bay, Oakland, California
112. John S. James, AIDS Treatment News, San Francisco, California
113. Michael James, Atlanta, Georgia
114. Joseph J. Johnson, Treasure Coast Community AIDS Network, Florida
115. Lewis E. Johnson, Chicago, Illinois
116. Robert Folan Johnson, ACTUP Boston, Boston, Massachusetts
117. Andrew Johnston, M.D., Chicago, Illinois
118. Cleve Jones, Founder/AIDS Memorial Quilt, Villa Grande, California
119. Mary Jones, Fan Free Clinic, Richmond, VA
120. Leslie Kaliades, PWA, Jamaica, New York
121. Linda Kaplan, Syracuse, New York
122. Larry Kessler, AIDS Action Committee - Boston, Boston, Massachusetts
123. Chai Khoo, San Jose, California
124. David E. Kilburn, San Luis Obispo HIV Care Consortium, California
125. Barry Krost, Board of Directors, Project Inform, San Francisco, California
126. Ann Kurth, Mother's Voices, New York, New York
127. Irma Lamberty, Infectious Disease Associates, Atlantic City Medical Center, , Atlantic City, New Jersey
128. Terry Laug, San Jose, California
129. Michael J. Lavery, Niskayuna, New York
130. James Learned, PWA Health Group, New York, New York
131. Gina Lee, Gahanna, Ohio
132. Sheryl A. Leon, The Counseling Center dba Gulf Coast Mental Health, Biloxi, Mississippi
133. Jules Levin, National AIDS Treatment Advocacy Project/NATAP, New York, New York

134. Darrell Limbocker, Tennessee Colony, Texas
135. Dennis Littrell, Raleigh, North Carolina
136. Mary Lucey, AIDS Policy Analyst, City of Los Angeles, California
137. Peter E. Mace-Myers, Atlanta, Georgia
138. Nancy MacNeil, Project Director, Women Alive, Los Angeles, California
139. James V. Madaras, Treasure Coast Community AIDS Network, Florida
140. Thomas L. Magee, M.D., Medical Offices, Los Angeles, California
141. Rachelle Mark, Los Angeles, California
142. L. Joel Martinez, The Center for AIDS, Houston, Texas
143. Kevin McCaffery, W. Virginia
144. Andrea McCardell, Infectious Disease Associates, Atlantic City Medical Center, Atlantic City, New Jersey
145. James McKee
146. Paul McLaughlin, Treasure Coast Community AIDS Network, Florida
147. Michael G. Meatyard, Atlanta, Georgia
148. Lee Mitchell
149. Edward Mohilef, Ph.D., EGM Associates, Flagstaff, Arizona
150. Kelley P. Moore, Tampa AIDS Network, Tampa, Florida
151. Robin Capps Munger
152. Alfredo Munoz, Oakland, California
153. Kelley P. Moore, Tampa, Florida
154. Kenneth Noonan, Everett, Washington
155. Christopher B. O'Hare, Treasure Coast Community AIDS Network, Florida
156. John Ortado, Jr., Treasure Coast Community AIDS Network, Florida
157. Paula L. Osborn
158. Robin R. Pabon, So. Mississippi AIDS Task Force, Mississippi
159. Allison Peterson, Marietta, Georgia
160. Eddie Lee Pitts, Atlanta, Georgia
161. Tony Poleto, Treasure Coast Community AIDS Network, Florida
162. Wallace Potts, self-employed film archivist, Los Angeles, California
163. Shirley Pough, Treasure Coast Community AIDS Network, Florida
164. Martin J. Powers, Chicago, Illinois
165. Chris Presley
166. William D. Prevatt, Tampa AIDS Network, Tampa, Florida
167. Robert Curt Raposa, Pelham, Georgia
168. Barton Rarick, Chicago, Illinois
169. Jonathan David Reed, Atlanta, Georgia
170. Robert Rivera, So. Mississippi AIDS Task Force, Mississippi
171. Nicholas Roche, ACTUP Paris, Paris, FRANCE
172. Gary R. Rose, AIDS Action Council, Washington, DC
173. James Rousey, Exec. Director, AIDS Treatment Initiatives, Atlanta, Georgia
174. Maria L. Samies, So. Mississippi AIDS Task Force, Mississippi
175. Scott Sanders, Oakland, CA
176. Norma Santos, Atlantic City Medical Center, , Atlantic City, New Jersey
177. John B. Schulz, Oakland, California
178. Sue W. Scott, AIDS Service Center, Pasadena, California
179. Matthew Sharp, ACTUP Golden Gate, San Francisco, California
180. Jennifer A. Sinclair, Oakland, California
181. B. Scott Shaw, Atlanta, Georgia
182. Michael Sheehan, AIDS Foundation San Diego, San Diego, California
183. Michael Shriver, NAPWA, Washington, D.C.
184. John E. Smith, Treasure Coast Community AIDS Network, Florida
185. William L. Snedden, Treasure Coast Community AIDS Network, Florida
186. Andrea Springsteen, Los Angeles, California
187. David Springsteen, Los Angeles, California
188. Judy Springsteen, Los Angeles, California
189. Lois Springsteen, Boulder Creek, California
190. Wayne P. Springsteen, Los Angeles, California
191. Roy Standifer, Jr. Dallas, Georgia
192. Joe M. Stewart
193. William P. Stewart, Jr., Haitian Amerian Community Council, Delray Beach, Florida
194. Norm Stuart, Research Sanctuary, Los Angeles, California
195. Sean Strub, Poz Magazine, New York, New York
196. Richard Tafel, Log Cabin Republicans, Washington, DC

197. Rob Tan, Rob Tan & Associates, San Francisco, California
198. Susanna Calvin Thomas, Open Doors
199. Michael Tolentino, Chicago, Illinois
200. Rachel Tolmachoff, Chair, Treatment & Care Committee, Sonoma County Commission on AIDS, Sonoma, California
201. Wilton Towe, Jr., Adairsville, Georgia
202. Amy Valenzuela, AIDS Project Long Beach, Long Beach, California
203. Jack Ryerson Varney, Atlanta, Georgia
204. Delia A. Viator, The Counseling Center dba Gulf Coast Mental Health, Biloxi, Mississippi
205. Gerald S. Viator, Biloxi, Mississippi
206. Oswald T. Weber, Founding Director, Projekt Information, Munich, Germany
207. Leland J. Wersal, Treasure Coast Community AIDS Network, Florida
208. Robert C. White, St. Louis, Missouri
209. Terri L. Wieder, Smyrna, Georgia
210. Scobel Wiggins, Georgia
211. Ken Wilkinson, FACE-L.A., Pasadena, CA
212. Lynie Williams, Tecumseh, Missouri
213. Mark Williams, PWA, New Jersey
214. Lee Winchell, Los Angeles, California
215. Phillip Winchell, APLA client, Los Angeles, California
216. Yvonne Wind, PA-C, N. Miami Beach, Florida
217. Thomas S. Woodward, Atlanta, Georgia
218. Vicki Worley, IHS, Hanover

A Hepatitis Drug That May Cure Glaxo
Business Week (05/12/97) No. 3526, P. 104; Flynn, Julie; Symonds, William C.; O'Hamilton, Joan C.; et al.

In 1990, Glaxo Wellcome acquired the marketing rights to the AIDS drug 3TC, which it sells under the brand name Epivir. Epivir produced $315 million in revenues in its first year of availability and analysts estimate that the drug could reach sales of up to $840 million by the year 2000. Now, it seems the chemical compound, renamed lamivudine, could be the most effective treatment available against hepatitis B, a disease that kills some 2 million people each year. Data from a trial in Hong Kong,Taiwan, and Singapore show that 96 percent of patients who received a 100mg dose of lamivudine reported significant suppression of the hepatitis B virus (HBV) with few side effects. About two-thirds of the subjects also had decreased liver inflammation. The discovery of lamivudine's hepatitis-suppressing potential will likely provide Glaxo with a needed boost, since the patent for the anti-ulcer drug Zantac, its No. 1 product, will soon expire. Lamivudine "will be the gold standard" for treatment of hepatitis B, predicts Timothy M. Block, chief scientific advisor of the Hepatitis B Foundation. However, others argue that the drug's marketing potential is being overestimated, because the drug is not a "cure" and only 16 percent of patients taking the drug showing no sign of HBV in their blood.

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Symbol Searched: GLX

5/19/97 +Glaxo Wellcome: Sales 2.75B Pounds In 4 Mos To April >GLX
(MORE) DOW JONES NEWS 05-19-97

5/19/97 Glaxo Wellcome - Sales -2: Up 10% Excluding Currency >GLX
LONDON (Dow Jones)--Drug giant Glaxo Wellcome PLC (GLX) said Monday its total sales in the four months to April 30 were 2.75 billion GBP, 10% higher than year-earlier levels in constant exchange-rate terms.

However, the continuing strength of the pound meant sales in sterling terms were unchanged, the group's Chairman Sir Colin Corness told shareholders.
(MORE) DOW JONES NEWS 05-19-97

5/19/97 Glaxo Wellcome - Sales -3: Zantac Sales Down 7% >GLX
Corness said sales in Glaxo's largest product, anti-ulcerant Zantac, continued to decline, as expected.

The first U.S. patent on the drug - which was the world's top-selling prescription pharmaceutical until the end of 1996 - expires in July, opening the company to generic competition in the ulcer-treatment market from companies such as Novopharm Inc.

Zantac's sales in the four months to April 30 were 7% lower at constant exchange rates. On the same basis, sales of all the

group's other products rose 15%.

"Respiratory products have now become the group's largest therapy area, with sales of antiviral and central nervous system products showing strong growth," the chairman told shareholders.

(END) DOW JONES NEWS 05-19-97

5/19/97 Glaxo Wellcome - Sales -4: Sykes Succeeds Corness As Chmn

Glaxo Wellcome PLC Chairman Sir Colin Corness said Glaxo's trading profit growth is in excess of total sales growth. However, the adverse impact on Glaxo's 1997 sales would be around 5% if sterling stays at its current levels.

Corness said he remains 'confident' that the group will meet the three-year sales targets it set out earlier in the year. **In March, Glaxo said the expiry of Zantac means its sales will grow in low single digits in 1997 and 1998, with double-digit sales growth resuming in 1999. The projections exclude the impact of currency moves, 'which clearly could have a significant effect.'**

In his review of business progress, Sir Richard Sykes, deputy chairman and chief executive, said Zantac now only compares with 20% of Glaxo's total sales, compared with 43% as recently as 1994. The key factor in reducing the significance of Zantac was Glaxo PLC's takeover of Wellcome PLC on May 1, 1995 to form the new group.

Sykes said the company could lose up to 90% of its U.S. sales of Zantac from generic competition after July.

'So, the much-heralded cataclysm is finally upon us,' said Sykes. 'Only we do not see it quite that way.'

He said the reason for his confidence is the breadth and depth of Glaxo's portfolio and product pipeline. "We now have major businesses - with potential for good growth bolstered by new products - in therapeutic areas such as respiratory diseases, the central nervous system, antivirals and anti-infectives,' Sykes said, adding that the company is expanding into areas such as influenza, diabetes and stroke.

'The quality, depth and diversity of our pipeline is without question,' said Sykes, who will succeed Corness as chairman after the shareholder meeting.

(END) DOW JONES NEWS 05-19-97

5/15/97 Glaxo Drugs Reduce Risk Of AIDS From HIV - Report >GLX

LONDON (Dow Jones)--Two Glaxo Wellcome PLC (GLX) products, Epivir and Retrovir, are "highly effective" in reducing the progression of HIV-I to AIDS when taken together, a news release from Britain's leading medical journal, The Lancet, confirmed Friday.

In clinical trials in Canada, Australia, Europe and South Africa, the Lancet said the addition of Epivir to Retrovir resulted in "a significant reduction in progression to AIDS or death."

Both products are already marketed as AIDS treatments and are often used together. **Last year, Retrovir had sales of 283 million GBP and Epivir had sales of 196 million GBP.**

In a commentary in the Lancet, Dr. Mark Feinburg urged caution, saying this combination 'alone cannot achieve durable

suppression of HIV replication in most treated patients.'

Glaxo is currently developing the compound used in Epivir, called Lamivudine, for use as a treatment for Hepatitis B.

(END) DOW JONES NEWS 05-15-97

5/15/97 Glaxo Nonnicotine Pill Cleared As Smoking-Cessation Program
By Elyse Tanouye
Staff Reporter of The Wall Street Journal

A nonnicotine prescription pill will soon give smokers a new way to attack their addiction.

Glaxo Wellcome PLC's Zyban received Food and Drug Administration approval as the first nonnicotine prescription treatment for smoking addiction. The drug, which is also sold as the antidepressant Wellbutrin SR, helps people stop smoking by boosting dopamine and norepinephrine, two brain chemicals that give a person a sense of well-being and energy. Nicotine boosts the same chemicals, leading to addiction. But using Zyban allows patients to get the same feeling while weaning themselves off nicotine.

Physicians who treat smokers say they welcome a new tool to help their patients quit. An estimated 33 million smokers in the U.S. want to quit smoking, and 16 million try each year, but only 1.2 million smokers succeed. The only medications previously approved to help smokers quit are nicotine-based, such as patches, gum, nasal sprays and inhalers, but these fail in most patients.

Besides giving a second chance to patients who fail nicotine-based therapies, said John Hughes, a nicotine researcher and professor of psychiatry at the University of Vermont, Zyban will be particularly helpful for patients who object to using nicotine products, or patients who might become depressed after quitting.

Zyban will be entering a $500 million U.S. market for smoking-cessation drugs, currently dominated by over-the-counter nicotine-based patches and gum. The drug is one of Glaxo's top marketing priorities and could reach annual sales of between $200 million and $300 million in a couple of years, estimated Robert Ingram, head of Glaxo's U.S. operations.

The company began priming the market with an advertisement in last month's Reader's Digest magazine. The ad urged readers to return a postcard requesting information on smoking cessation. Glaxo is expected to do more direct-to-consumer advertising in addition to traditional marketing to physicians.

Glaxo plans to package the product with a support program, which includes brochures containing tips to quit smoking, and a toll-free telephone number to sign up for more personalized help. Patients who seek the additional help will receive a more individualized cessation program, and they will receive periodic phone calls from a counselor to check on their progress and to offer advice.

Smokers who want to quit these days are much tougher cases than those in the past, said Dr. Hughes. "We've gotten all the easy quits and now gotten down to the hard-core group," he said. Those patients tend to be severely nicotine-dependent or have a psychiatric problem, such as depression, he said.

Smokers are likely to be attracted to Zyban because it is new, predicted John Pinney, a health and smoking-cessation consultant in Bethesda, Md. But he worried that managed-care plans would erect barriers to patients getting the drug, as they have for nicotine-based products. A survey his firm conducted two years ago found that many managed-care plans either didn't cover the nicotine-based smoking-cessation products or placed tough restrictions on them.

Smokers "have to be very motivated, but if you put up too many barriers, the motivation may go away, and we've just lost the chance to get a person to quit smoking," he said.

In clinical trials, 49% of patients who took Zyban quit smoking after four weeks, compared with 36% who took a patch and 23% who used a placebo. Patients who used both Zyban and a nicotine patch had the best results, with 58% quitting.

(END) DOW JONES NEWS 05-15-97

5/15/97 +Glaxo Gets FDA Clearance On Zyban >GLX

(MORE) DOW JONES NEWS 05-15-97

5/15/97 Glaxo/FDA - Zyban -2: Available In U.S. In 6-8 Weeks >GLX

LONDON (Dow Jones)--Glaxo Wellcome PLC (GLX) said Thursday the U.S. Food & Drug Administration has approved Zyban, the first nicotine-free prescription medicine to help people stop smoking.

Zyban will be available on prescription to U.S. smokers within the next six to eight weeks, together with a patient-support program, Glaxo said in a statement.

(END) DOW JONES NEWS 05-15-97

5/15/97 Glaxo/FDA - Zyban -3: Stk Up; Sales Seen $300M In 5 Years

Glaxo's shares rallied immediately on the news. At 10 a.m. EDT (1400 GMT) they are at 1270 pence, up 18.5 pence on the day, on provisional volume of 2.04 million shares.

One pharmaceuticals analyst, speaking on condition of anonymity, said there have been plenty of indications that Zyban would be approved. 'It should already have been discounted in the share price,' he said.

The analyst said Zyban's annual sales will probably go as high as $300 million within the next five years.

Zyban is the tradename of bupropion hydrochloride. It will be marketed in a sustained-release tablet.

(END) DOW JONES NEWS 05-15-97

Fax from Linda Grinberg

To: Sandy Thurmond	From : Linda Grinberg	
Company: The White House, AIDS Czar	Telephone: 310-471-6565	
Fax Number: 1-202-632-1096	Fax Number: 310-471-4565	
Subject : 1592	Date: 6/4/97	Pages: 4

Sandy:

Attached is an editorial and article on 1592 in the June issue of APLA's newsletter, "Positive Living", which also may be of interest.

Linda

A monthly publication of AIDS Project Los Angeles for people with HIV/AIDS

POSITIVE

AIDS PROJECT LOS ANGELES

JUNE 1997

State ADAP formulary expands

By EDDY R. GARCÍA FERNÁNDEZ

Three more HIV-related drugs have been added to the formulary for AIDS Drugs Assistance Program (ADAP), the state- federal-funded program that provides HIV-related medication at low or no cost to people without medical insur-

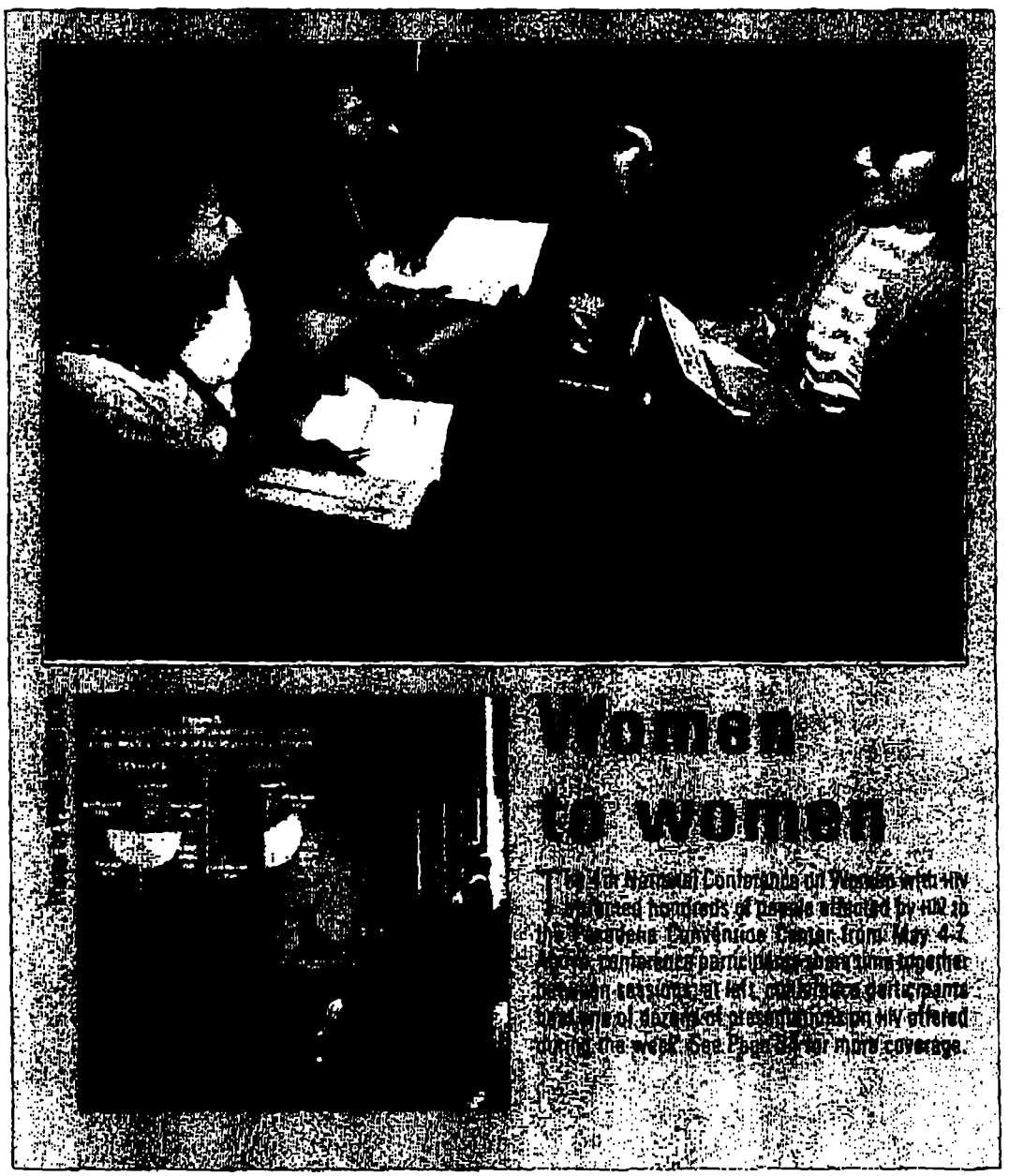
➤ 19

Access program for GW1592 announced

By WILLIAM STRAIN

Following months of prodding by activists in the HIV community, Glaxo Wellcome announced on April 29 that it will initiate three compassion-

➤ 15



Women to Women

The 7th National Conference on Women with HIV [illegible] hundreds of people affected by HIV to [illegible] Convention Center from May 4-7. [illegible] participated in [illegible] sessions at left, and [illegible] panel discussions at right, one of dozens of presentations on HIV offered during the week. See Page 37 for more coverage.

6 A visit with Charles Farthing

24 Birth of an AIDS activist

37 Help fund ADAP

EDITORIAL

Not enough

This summer will see the launch of a limited compassionate-use program for the experimental nucleoside analog, 1592U89.

The use of the adjective "limited" above is especially apt. By opening access to 1592 to only 2,500 people with AIDS beyond those who are already using the drug in clinical trials, the compassionate program that was announced by Glaxo Wellcome Inc. for its drug seems limited in size *and* compassion.

Eight years and counting

1592, which began its long road to development in 1989, is said to pack a punch that is 10 times more powerful than AZT, another Glaxo Wellcome drug of the same class.

According to a consensus statement on the experimental antiretroviral that was released in late 1996, "in early clinical studies, 1592 has demonstrated a more potent level of antiviral activity than other RT inhibitors, with minimal side effects. Its most important property, however, is that people have not been previously exposed to it and it therefore offers the hope of renewed antiviral activity."

At the time that the consensus statement was issued, 48 AIDS-service organizations and 100 individuals had added their support to the call for broader access to 1592.

Glaxo Wellcome's response to that call was the compassionate-use program announced in April: a program will begin with pediatric access in June, and continue in July with programs for adults and people with dementia. The 2,500 available slots in the compassionate-use program will be spread among three continents, including the United States.

Questions to ask

In a *Wall Street Journal* article published last November, many activists express frustration about Glaxo Wellcome's position on 1592. Some wonder if the company may be holding back on 1592 in order to protect its older product, AZT.

Others note that other drugs developed after 1989—Crixivan, Norvir and Viracept— have all leapfrogged past 1592 in being approved by the Food and Drug Administration.

Other drugs have leapfrogged past 1592 in being approved by the FDA.

The sense of impatience surrounding 1592 is nearly palpable. According to Linda Grinberg, a Project Inform Board member and member of the coalition that created the 1996 consensus statement, "a lot of people will not be able to hang on. For some people [1592] may be a Band-Aid, but they may need that Band-Aid." Bill Bahlman, another activist involved in the struggle to achieve broad access to 1592, says that there are surely more than 2,500 people worldwide who are in need of access to 1592. "We're talking about people with AIDS who don't have options," says Bahlman.

In a community update that described Glaxo Wellcome's plans for 1592, Jennifer McMillan, the company's director of Health Care Coalitions and Advocacy Relations, calls the compassionate-use program "the first steps in a broad effort to provide 1592 to the people who need it prior to its approval and until a larger expanded access program can be put in place."

The pace of those steps toward expanded access must quicken. As it stands now, the program for 1592 announced by Glaxo Wellcome is simply not large enough to satisfy the need. ✚

POSITIVE LIVING
Vol. 6, No. 6
Published monthly by AIDS Project Los Angeles' Communications Department
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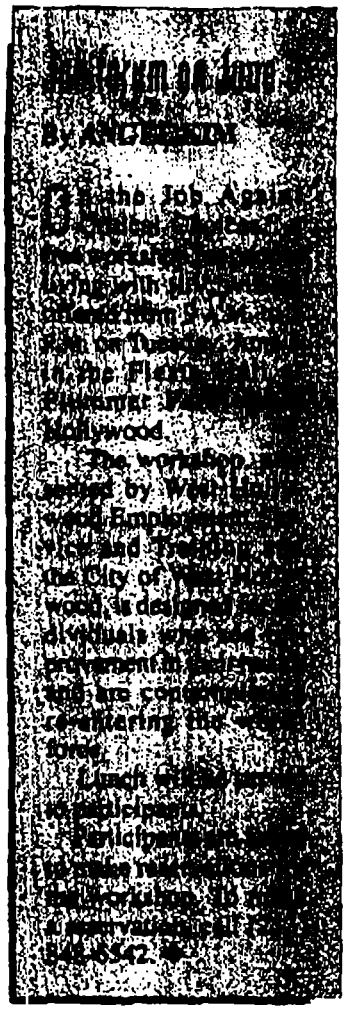

GW 1592

From Page 1

ate use programs for its reverse transcriptase inhibitor, GW1592 (also known as abacavir).

Three compassionate-use programs are in development: a pediatric program, a program for people with severe dementia, and a program for adults with advanced HIV disease. These programs will enroll 2,500 people from 30 to 50 sites in the U.S., Canada, Europe and Australia.

Community activists are urging Glaxo to expand the compassionate use program. Creating more than 2,500 slots could benefit a large number of people who have become resistant to other drugs or can not tolerate them and are relying on access to GW1592 in the very near future.

Although specific sites for the compassionate-use program have not been determined, plans are to locate the sites geographically according to the inci : of HIV-infection. Enrollment in programs will be severely restricted.

The pediatric program, which is expected to open in June, will enroll children and infants who have tried on nucleoside reverse transcriptase inhibitor (like AZT) and have a viral load greater than 100,000 and a T-cell-to-lymphocyte ratio of less than 15 percent.

The dementia and adult programs should be open by July. Enrollment for the pediatric and dementia programs will total 500, leaving the remaining 2,000 slots for the adult program.

Entry criteria for the adult program will include people with viral loads above 50,000 and T-cell counts below 50 who have already tried two nucleoside drugs such as AZT or d4T and one protease inhibitor.

The dementia program will include people diagnosed by a neurologist as having severe dementia who have had treatment with AZT.

Although GW1592 is still in a very early stage of its clinical development, it has already shown promising results in some small studies involving approximately 250 people.

In one recent study, 29 people who had previously been on AZT for less than 12 weeks received GW1592 and AZT. After eight weeks, this group had a reduction in viral load of 1.9 to 2.70 log. Sixty percent of people on this combination had undetectable levels of HIV. This is a very small number of people, but these data suggest that GW1592 is safe and may be as powerful as some protease inhibitors.

Side effects to GW1592 that have been seen in the studies include nausea, headaches, abdominal pain, weakness and sleep disturbance.

Glaxo attributes the small size of the compassionate use program to the lack of safety data on GW1592. A larger expanded access program is expected to begin in early 1998. ✚

William Strain is a treatment advocate in AIDS Project Los Angeles' Treatment Education Program.

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POSITIVE LIVING urges readers to consult their medical practitioners about any therapies or treatment strategies described in this publication.

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to Dan

from JEFF Getty

510-653-6278.

Dan - here is a summary sheet Linda did on GLAXO- welcome.

I am involving Nancy Pelosi's office as well now.

Next week we are forming a national protest + arrest coalition.

please keep me advised as to what calls you folks have made.

Thanks

Jeff Getty

RAG SHEET/GLAXO WELLCOME DRAFT 5/20/97

- Insufficient, inhumane compassionate use program for 1592 (2500 worldwide/2000 adults)
- Not forthcoming on details or timeframe for wider expanded access program ("sometime in '98")
- Inordinate delays in development of Vertex 141 – holding back other companies' drugs.
- Approx. 4-6 month delays in initiation of 1592 trials
- Minimal safety and efficacy data for 1592 on RT-experienced patient population due to primarily focusing on naive patients in trials program to date
- 9 year timeline in development of 1592 – usual time 3 to 5 years
- Refusal to develop time-release formulation of AZT, though feasible
- Demands for expanded access of 1592 date back over a year, necessary supply should've been anticipated and planned
- Deliberate delays in development of 1592 and 141 to maximize profits on AZT and 3TC?
- Lack of coordination with other pharmaceutical companies to offer potent expanded access combinations (141+1592, DMP-266+1592+Adefovir, etc.)
- Refusal to provide protocol lists and trial sites to community on timely basis for 1592 and 141 after numerous requests
- Inherent problems re equity of access at "geophraphic dispersed centers" (preferential treatment of site's own patients, etc.)
- Glaxo is asserting that they have only obtained safety data to date on 250 subjects. Why so little data and so few trials initiated since last summer?
- 1592 Background:
    - 1/96 Retroviral Conf., Saag, et. al. presented 12 weeks of safety, efficacy and PK data on 19 adult subjects;
    - 1/96 Retroviral Conf., Hughes, et. al. presented preliminary data on ongoing safety and PK pediatric study for 24 children
    - 7/96 Itn'l. Conf. in Vancouver, Saag, et. al. presented 16 weeks of safety and antiviral data and reported on 20 patients in 2 arms of a 4 arm study (total number of subjects not listed in abstract TH.b.294);
    - 7/96 Int'l. Conf. in Vancouver, Glaxo presented 12 weeks of PK data on 20 patients on 1592 on dose-escalating regimens.

Fax from Linda Grinberg

To: Sandy Thurmond	From : Linda Grinberg	
Company: The White House, AIDS Czar	Telephone: 310-471-6565	
Fax Number: 1-202-632-1096	Fax Number: 310-471-4565	
Subject :	Date: 5/16/97	Pages: 1

The address and phone number for Jennifer McMillan is as follows:

Glaxo Wellcome
5 Moore Drive
Research Triangle Park, NC 27709
(919) 483-2392

Good luck! Hope you make some headway....

Thanks, again.

Linda

Fax from Linda Grinberg

To: Sandy Thurmond	From : Linda Grinberg	
Company: The White House, AIDS Czar	Telephone: 310-471-6565	
Fax Number: 1-202-632-1096	Fax Number: 310-471-4565	
Subject : 1592 Consensus Statement, etc.	Date: 5/16/97	Pages: 9

Thank you for getting back to me promptly on this urgent matter and your enthusiastic response. As I stated, we've been meeting with various representatives of Glaxo since last Summer, but the chief liason to the community is Jennifer McMillan. Others in attendance at the various meetings and on the conference calls over the past year were Steve LeFon, who I believe is heading up the 1592 development program and Jim Rooney, head of clinical trials. The initial excitement regarding this drug dates back to January 1996, when their initial data was presented by Michael Saag, MD at the Retroviral Conference. Additional data was presented in Vancouver last July, which also created an even bigger buzz. The preliminary data presented at those conferences showed unprecedented antiviral activity for a drug of this class, a nucleoside drug or reverse trancriptase inhibitor (in the same class as AZT, 3TC, ddI, ddC, etc.) Glaxo had led everyone to believe until just recently they'd be filing for accelerated approval by the end of the year, but there have been unexplained delays...

I am quite literally being inundated with desperate phone calls and faxes now on a daily basis, and the frequency and utter desperation seem to be increasing. Many of these phone calls are gut wrenching and heartbreaking -- patients who have failed all the approved drugs with no other options on the horizon, with t-cells crashing and viral load soaring. Clearly many of these folks will not survive if they must wait until this drug is approved in Summer '98.

A program for 2,500 people worldwide (2,000 adults, 250 pediatric, 250 AIDS Dementia Complex) is just plain insulting and immoral, considering this is the largest pharmaceutical company in the world, which currently corners approximately 60-70% of the AIDS drug market (with AZT and 3TC). The "excuse" we are hearing is that there is a lack of safety data (only 250 patients studied thus far), however, any potential side effect of this drug cannot possibly outweigh the side effect of death for this late-stage population. Further, all the data presented thus far indicates that this is an extremely well-tolerated and safe drug.

I am faxing herewith the original consensus statement that I began distributing in November, with the sign-ons as of 1/97. Hundreds of faxes have been received since January, so I need to spend a day updating that list of sign-ons. Additionally, the Wall St. Journal article will provide a bit more background info. Please feel free to call me if you have any questions or comments, anytime... It is so refreshing to see such an enthusiastic response. We sure need you in our corner... Thank you and I look forward to speaking with you next week.

Linda

(Retyped due to skitzie margins & pagination)

Consensus Statement on 1592 Expanded Access and Accelerated Approval

- **Overview**

Access to Glaxo Wellcome's 1592U89 ("1592") now in development, potentially represents the only viable option for delaying disease progression for many people living with HIV and AIDS who have exhausted the benefit from currently approved antiviral therapies. In early clinical studies, 1592 has demonstrated a more potent level of antiviral activity than other RT inhibitors, with minimal side effects. It's most important property, however, is that people have not previously been exposed to it and it therefore offers the hope of renewed antiviral activity. This renders the drug critically important to two patient populations: (1) those who have already lost sensitivity to the other drugs of this type, and (2) those who need to use at least one "fresh" or new nucleoside analogue RT inhibitor to make reasonable use of combination therapy with protease inhibitors or non-nucleoside RT inhibitors. Existing evidence clearly suggests that combining such drugs with previously used therapies diminishes their effectiveness and leads to more rapid development of resistance.

The benefit of this drug may be limited due to the development of resistance, a problem common to all currently approved antiviral compounds. While it may take years of additional study to determine its optimal use, this should not delay prompt access to this therapy by people in immediate need. Delaying the availability of this drug until Phase III trials are fully accrued is unacceptable and represents a significant change from past practices. For example, the ddI, d4T, and AZT expanded access programs all took place while trials were still recruiting. We are very concerned that the recent activities of several pharmaceutical companies represents a broad effort to minimize the number of patients served by expanded access programs. Any such effort around 1592 would be a moral affront to the rights and needs of people with HIV/AIDS and their healthcare providers.

We hereby propose the following 1592 expanded access program, to be phased in in stages, with immediate access to those in urgent need.

- **First Phase - Compassionate Use/Salvage Therapy**

Glaxo Wellcome and the Food and Drug Administration must cooperate and take a more compassionate stance to make this promising compound immediately available in a "salvage program" once a recommended dosing schedule has been established. This compassionate access salvage program should make drug available as soon as possible for those people who have failed existing therapies and risk near-term danger of death or life-threatening infections.

The development of this drug must take into consideration its unique potential to provide benefit to the acutely compromised segment of the HIV-infected population. Availability of salvage strategies is of the highest priority for people living with HIV. There is no logical or moral reason to withhold this drug from people with advanced illness, people whose lives hang in the balance. Currently, this compound qualifies, by any humane standard, for compassionate use.

This first phase of Compassionate Use/Salvage Therapy should provide 1592 without delay to patients who meet any one of the following two requirements:

1. ***CD4+ Cell Count <50 OR Viral Load >40,000 copies/ml***
   AND Treatment Failure to approved RT Inhibitors AND at least one Protease Inhibitor;
2. ***Diagnosis of AIDS Dementia Complex (ADC), unresponsive to existing therapies.***

We believe evidence of the above conditions can be accomplished with a minimal amount of paperwork. A physician's letter accompanied by one lab report should be sufficient to establish any of the above criteria.

- **Second Phase - Expanded Access**

This second phase of Expanded Access should provide 1592 during recruitment and conduct of Phase II/III

clinical trials, but no later than ninety (90) days from the start-up of the First Phase, to patients who meet any of the following criteria:

1. ***Patients who do not qualify for or are denied entry in a 1592 clinical trial and have a medical need for 1592, or***
2. ***Patients who do not live within a radius of 15 miles of an active clinical trial site, or***
3. ***Patients whose lives would be immediately jeopardized by randomization to an ineffective treatment regimen, or***
4. ***Patients with a CD4+ Cell count below entry requirements of clinical trials, or***
5. ***Viral Load greater than 20,000 copies/mL, despite use of currently approved therapies, or***
6. ***Treatment Failure or demonstrated genotypic or phenotypic resistance to approved RT inhibitors.***

- **Accelerated Approval**

This compound should be licensed for accelerated approval as soon as possible. FDA approval of this compound should be based on existing regulations governing accelerated approval of new drugs for life-threatening illnesses:

1. ***Clear evidence of benefit on surrogate markers have been demonstrated;***
2. ***Principal toxicities and drug interactions have been defined;***
3. ***Longer-term development plans have been initiated designed to determine the drug's usefulness in promoting clinical and survival improvements and durability of response, as part of a medical strategy for coping with HIV infection.***

****We urge the sponsor to file applications for accelerated approval as soon as possible.***

- **Resistance, Pharmacokinetics and Drug Interactions**

As with all antivirals, the development of drug-resistant strains of virus, drug interactions and pharmocokinetic variances while using this compound may warrant additional considerations. To address this concern, sponsors should also be required, prior to accelerated approval, to present meaningful data on:

1. ***the speed and levels of resistance encountered;***
2. ***the degree of cross-resistance found with other nucleoside analogues;***
3. ***the interaction of the compound with other commonly used anti-HIV medications;***
4. ***bioavailability in men, women, and children and determination of the degree which blood levels vary depending on body weight.***

- **Summation**

Any effort to withhold access to promising compounds is contrary to the interests of HIV-infected people, inconsistent with the Accelerated Approval regulations, and scientifically unwarranted. The long history of the development of the earlier generation of antiviral drugs clearly demonstrates that it is possible to accrue patients and continue conducting clinical trials of compounds, long after their marketing approval. Because of the issues of drug resistance and drug failure over time, new therapies for HIV disease will continue to play a critical role no matter how many drugs become available on the market. New therapies, like 1592, must continue to be made available as rapidly as possible to patients with immediate needs for changed or improved treatment.

AGREED and ACCEPTED this ____ day of _____, 1996:
**** Revised as of 11/27/96***

By: _____ **Of:** _____

Signature **Organization**

Print Name: _____ **Please fax to: 310-471-4565**

ORGANIZATIONS: SIGN-ONS AS OF JANUARY 25, 1997

1. ACTUP BOSTON, Boston, MA
2. ACTUP EAST BAY, Oakland, CA
3. ACTUP GOLDEN GATE, San Francisco, CA
4. ACTUP LOS ANGELES, Los Angeles, CA
5. ACTUP NEW YORK, New York, NY
6. ACTUP PARIS, Paris, FRANCE
7. ACTUP PHILADELPHIA, Philadelphia, PA
8. AIDS ACTION COMMITTEE - BOSTON, Boston, MA
9. AIDS ACTION COUNCIL, Washington, DC
10. AIDS HEALTHCARE FOUNDATION, Pasadena, CA
11. AIDS PROJECT LOS ANGELES /APLA, Los Angeles, CA
12. AIDS RESEARCH ALLIANCE, Los Angeles, CA
13. AIDS RESEARCH INFORMATION CENTER, INC./ARIC, Baltimore, MD
14. AIDS SERVICE CENTER, Pasadena, CA
15. AIDS SURVIVAL PROJECT, Atlanta, GA
16. AIDS TREATMENT INITIATIVES, Atlanta, GA
17. AIDS TREATMENT NEWS, San Francisco, CA
18. BEING ALIVE, Los Angeles, CA
19. BRITISH COLUMBIA PERSONS WITH AIDS SOCIETY, Canada
20. CENTER FOR AIDS, THE, Houston, Texas
21. COUNSELING CENTER, THE dba GULF COAST MENTAL HEALTH, MI
22. FLORIDA AIDS ACTION COUNCIL, Florida
23. GAY MEN'S HEALTH CRISIS/GMHC, New York, NY
24. LINDA GRINBERG FOUNDATION, Los Angeles, CA
25. HOMESTEAD HOSPICE & THE "DALLAS HOUSE", Los Angeles, CA
26. IHS AT HANOVER
27. ISRAEL AIDS TASK FORCE, Tel Aviv, Israel
28. KRAUS MEDICAL PARTNERS, Los Angeles, CA
29. LAMBDA COUNSELING CENTER, Miami, Miami Beach, Ft. Lauderdale & Palm Beach, FL
30. LIVING WELL PROJECT/ASIAN PACIFIC ISLANDERS AIDS SERVICES, San Francisco, CA
31. LOG CABIN REBUBLICANS, Washington, D.C.
32. MOTHER'S VOICES, New York, NY
33. MULTICULTURAL AIDS COALITION, INC., Boston, MA
34. NATIONAL AIDS TREATMENT ADVOCACY PROJECT/NATAP, New York, NY
35. NATIONAL ASSOCIATION OF PEOPLE WITH AIDS/NAPWA, Washington, DC
36. NATIONAL MINORITY AIDS COUNCIL, Washingto, DC
37. OPEN DOORS
38. PARAGON MEDICAL RESEARCH, Los Angeles, CA
39. POZ MAGAZINE, New York, NY
40. PROJECT INFORM, San Francisco, CA
41. PROJEKT INFORMATION, Munich, Germany
42. PWA HEALTH GROUP, New York, NY
43. PWAlive/MINNESOTA, Minneapolis, MN
44. REACH OF SOUTHERN ARIZONA, AZ
45. RESEARCH SANCTUARY, Los Angeles, CA
46. SAN FRANCISCO AIDS FOUNDATION/BETA, San Francisco, CA
47. SAN LUIS OBISPO HIV CARE CONSORTIUM, CA
48. SEARCH FOR A CURE, Boston, MA
49. SO. MISSISSIPPI AIDS TASK FORCE, MI
50. TEST POSITIVE AWARE, Chicago, IL
51. TREASURE COAST COMMUNITY AIDS NETWORK, Florida
52. TREATMENT ACTION GROUP/TAG, New York, NY
53. TREATMENT & DATA COMMITTEE, New York, NY
54. UNITED FOUNDATION FOR AIDS, Miami, FL
55. WOMEN ALIVE, Los Angeles, CA

INDIVIDUALS: **SIGN-ONS AS OF JANUARY 16, 1997**

1. Linda R. Allen
2. Moises Agosto, National Minority AIDS Council, Washington, DC
3. Alberto Avendano, MD, Florida AIDS Action Council, FL
4. Bill Bahlman, Treatment & Data Committee, NY
5. Cornelius Baker, National Association of People with AIDS/NAPWA, Washington, DC
6. Ron Baker, SF AIDS Foundation/BETA, San Francisco, CA
7. David Barr, Gay Men's Health Crisis/GMHC, New York, NY
8. Dirk Belau, Geneva, Switzerland
9. Carol Bennett
10. Jessica C. Bigg, So. Mississippi AIDS Task Force
11. Voa Bigg, So. Mississippi AIDS Task Force
12. G'dali Braverman, Living Well Project, San Francisco, CA
13. William K. Brent, Jr., So. Mississippi AIDS Task Force
14. Larry Bressiour, Search for a Cure, Boston, MA
15. Gregory Britt, AIDS Research Alliance, Los Angeles, CA
16. Sara J. Brookins, So. Mississippi AIDS Task Force. Biloxi. MI
17. Nicholas F. Brookins, So. Mississippi AIDS Task Force, Biloxi, MI
18. Carl Brown, Treasure Coast Community AIDS Network, FL
19. Glenn Brown, ACTUP Philadelphia, PA
20. William D. Bryant, Boulder Creek, CA
21. Todd Burger, Chicago, IL
22. Jan Casey
23. Jeffrey B. Cason, New York, NY
24. Peter Cashman, ACTUP Los Angeles, CA
25. Henry E. Chang, AIDS Healthcare Foundation, CA
26. James Clark, Laguna Beach, CA
27. Mark Cohen, United Foundation for AIDS, So. Miami, FL
28. Richard Cooper, M.D., Kraus Medical Partners, Los Angeles, CA
29. Sarah ("Sally") C. Cooper, PWA Health Group, New York, NY
30. Jim Corti, Research Sanctuary & Linda Grinberg Foundation, Los Angeles, CA
31. Mark Cohen, United Foundation for AIDS, Miami, FL
32. Gary E. Costa, Being Alive, CA
33. John Curtis Cottingham, AL
34. Linda F. Cottingham, State of Alabama, Dept. of Human Resources
35. Spencer Cox, Treatment Action Group/TAG, New York, NY
36. Myron C. Crider, Morrow, GA
37. Donald T. Daniels, PAC, AIDS Healthcare Foundation, Los Angeles, CA
38. Robert Dal Porto, PWA with Being Alive, Los Angeles, CA
39. Kenneth De Haan
40. Martin Delaney, Project Inform, CA
41. Rebecca Dennison, W.O.R.L.D., Oakland, CA
42. John Deshane, Los Angeles, CA
43. Scott Dewees, W. Hollywood, CA
44. John Dolan, Raleigh, N.C.
45. Jim Driscoll, Log Cabin Republicans, San Francisco, CA
46. Marianne DuBose, So. Mississippi AIDS Task Force
47. Ferd Eggan, AIDS Coordinator, City of Los Angeles, CA
48. Peter Engelhard, D.O., Fisher Medical Group, Miami, FL
49. Charles Farthing, M.D., AIDS Healthcare Foundation, Los Angeles, CA
50. Tracy Fennell
51. Gil Ferguson, British Columbia Persons with AIDS Society, Canada
52. Brenda Freiberg, Board of Directors, Project Inform & AIDS Service Center, CA
53. Ruben Gamundi, AIDS Project Los Angeles, CA
54. Ramon M. Garcia, REACH of So. Arizona, Bisbee, Arizona
55. Aileen Getty, Homestead House & The "Dallas House", Los Angeles, CA
56. Jeff Getty, ACT UP Golden Gate, San Francisco, CA
57. Joseph L. Goebelt, Santa Clara, CA
58. Michael Gottlieb, M.D., Gottlieb Medical Group, Los Angeles, CA
59. Jeff Graham, AIDS Survival Project, Atlanta, GA
60. Linda Grinberg, Linda Grinberg Foundation & Project Inform, CA

61. John Haiduck, Test Positive Aware, Chicago, IL
62. Lee Hardy, ARIC, Inc., Baltimore, MD
63. Larry Harman, Ph.D., Lambda Counseling Center, Miami, Ft. Lauderdale & Palm Beach, FL
64. Zaida Harrington, Biloxi, MI
65. Rene Milet Hernandez, Multicultural AIDS Coalition, Inc., Boston
66. Rachel Hincey
67. Gideon Hirsch, Israel AIDS Task Force, Tel Aviv, Israel
68. Peter M. Hoffman, Treasure Coast Community AIDS Network, FL
69. Carlton Hogan, PWAlive, Minneapolis, Minnesota
70. Ernest Hopkins, National Association of People with AIDS/NAPWA, Washington, DC
71. Dennis Hughes, Treasure Coast Community AIDS Network, FL
72. Terrence L. Ibbs, D.O., N. Miami Beach, FL
73. Crystal Iondan, Treasure Coast Community AIDS Network, FL
74. John Iverson, ACTUP/East Bay, Oakland, CA
75. John S. James, AIDS Treatment News, San Francisco, CA
76. Joseph J. Johnson, Treasure Coast Community AIDS Network, FL
77. Robert Folan Johnson, ACTUP Boston, Boston, MA
78. Cleve Jones, Founder/AIDS Memorial Quilt
79. Larry Kessler, AIDS Action Committee - Boston, Boston, MA
80. Chai Khoo, San Jose, CA
81. David E. Kilburn, San Luis Obispo HIV Care Consortium, CA
82. Barry Krost, Board of Directors, Project Inform, San Francisco, CA
83. Ann Kurth, Mother's Voices, NY
84. Terry Laug, San Jose, CA
85. James Learned, PWA Health Group, New York, NY
86. Gina Lee, Gahanna, Ohio
87. Sheryl A. Leon, The Counseling Center dba Gulf Coast Mental Health, Mississippi
88. Jules Levin, National AIDS Treatment Advocacy Project/NATAP, NY
89. Dennis Littrell, Raleigh, N.C.
90. Mary Lucey, AIDS Policy Analyst, City of Los Angeles
91. Nancy MacNeil, Project Director, Women Alive, Los Angeles, CA
92. James V. Madaras, Treasure Coast Community AIDS Network, FL
93. Thomas L. Magee, M.D., Medical Offices, Los Angeles, CA
94. Rachelle Mark, Los Angeles, CA
95. Joel Martinez, The Center for AIDS, Houston, Texas
96. James McKee
97. Paul McLaughlin, Treasure Coast Community AIDS Network, FL
98. Robin Capps Munger
99. Christopher B. O'Hare, Treasure Coast Community AIDS Network, FL
100. John Ortado, Jr., Treasure Coast Community AIDS Network, FL
101. Paula L. Osborn
102. Robin R. Pabon, So. Mississippi AIDS Task Force
103. Shirley Paugh, Treasure Coast Community AIDS Network, FL
104. Tony Poleto, Treasure Coast Community AIDS Network, FL
105. Wallace Potts, self-employed film archivist, Los Angeles, CA
106. Chris Presley
107. Robert Rivera, So. Mississippi AIDS Task Force
108. Nicholas Roche, ACTUP Paris, Paris, FRANCE
109. Gary R. Rose, AIDS Action Council, Washington, DC
110. James Rousey, Exec. Director, AIDS Treatment Initiatives, Atlanta, CA
111. Maria L. Samles, So. Mississippi AIDS Task Force
112. John B. Schulz, Los Angeles, CA
113. Sue W. Scott, AIDS Service Center, Pasadena, CA
114. Matthew Sharp, ACTUP Golden Gate, San Francisco, CA
115. Michael Shriver, NAPWA, Washington, D.C.
116. John E. Smith, Treasure Coast Community AIDS Network, FL
117. William L. Snedden, Treasure Coast Community AIDS Network, FL
118. Andrea Springsteen, Los Angeles, CA
119. David Springsteen, Los Angeles, CA
120. Judy Springsteen, Los Angeles, CA
121. Lois Springsteen, Boulder Creek, CA
122. Wayne P. Springsteen, Los Angeles, CA

123. Joe M. Stewart
124. Norm Stuart, Research Sanctuary, Los Angeles, CA
125. Sean Strub. Poz Magazine, New York, N.Y.
126. Richard Tafel. Log Cabin Republicans, Washington, DC
127. Rob Tan, Rob Tan & Associates, San Francisco, CA
128. Susanna Calvin Thomas, Open Doors
129. Delia A. Viator, The Counseling Center dba Gulf Coast Mental Health, Biloxi, Mississippi
130. Gerald S. Viator, Biloxi, Mississippi
131. Oswald T. Weber, Founding Director, Projekt Information, Munich, Germany
132. Leland J. Weseal, Treasure Coast Community AIDS Network, FL
133. Robert C. White, St. Louis, Missouri
134. Mark Williams, PWA, New Jersey
135. Lee Winchell, Los Angeles, CA
136. Phillip Winchell, APLA client, Los Angeles, CA
137. Yvonne Wind, PA-C, N. Miami Beach, FL
138. Vicki Worley, IHS, Hanover

11/12/96 Why Isn't Glaxo's New AIDS Drug Ready Yet?
By Michael Waldholz
Staff Reporter of The Wall Street Journal

Stephen Gendin is falling behind in his race against AIDS. He has staved off illness for more than a decade by aggressively cycling through a battery of medications, turning to a new drug each time the virus mutated and overcame an earlier one. "I've taken AZT, DDC, DDI, D4T, 3TC, Saquinavir, Norvir," says Mr. Gendin, the 30-year-old co-founder of a New York mail-order drug company.

"Now I need what's next," he says. "1592 is next." But the potent drug 1592 has been stuck in Glaxo Wellcome PLC's research pipeline for seven years. It now seems unlikely that it will hit the market before mid-1998.

What's taking so long? Glaxo says it didn't recognize the drug's power until recently and now is moving as quickly as it can to complete necessary safety trials and make the drug available. But some critics believe the company is dragging out the development of 1592. After all, development of the powerful AIDS drugs known as protease inhibitors began less than five years ago, and those drugs have been available for almost a year now, extending the lives of thousands of people. The controversy reflects the tremendous demand for new AIDS drugs now that it appears the disease responds, at least temporarily, to treatment.

AIDS activists charge that Glaxo is trying to protect the sales of its two older AIDS drugs, AZT and 3TC. Their combined revenue is expected to hit $600 million this year, double the total in 1995, and could exceed $1 billion in two years. Sales are booming as patients adopt a "cocktail" regimen that combines the two older drugs with one of the new protease inhibitors.

But 1592 is 10 times more powerful than AZT, its chemical and corporate cousin, and it avoids AZT's dangerous side-effects. "Who's going to take AZT if 1592 is available?" asks Martin Delaney, founding director at Project Inform, an AIDS advocacy group.

At the very least, Mr. Delaney and many other AIDS activists contend, Glaxo should make 1592 available immediately to thousands of desperately ill patients under a "compassionate access" program while the drug winds through the long approval process. Virtually every other new AIDS drug has taken that route.

Glaxo officials, saying they haven't gathered enough safety data to do that, deny that they have put commercial considerations before compassion. They concede that work on 1592 and other drugs languished amid the distractions of Glaxo's $14.8 billion acquisition of Wellcome PLC last year. Except for 3TC, all the AIDS drugs in the works were from the Wellcome side. Once Glaxo took over, it didn't offer comparable jobs to most of the top Wellcome research managers who had shepherded
1592 through initial studies. As a result, most of the managers left.

"There were a lot of distractions," says James Rooney, who ran a clinical-studies department at Wellcome before the merger and is now a vice president at Gilead Sciences Inc., Foster City,
Calif. "There was a lot of wrestling over new procedures, switching jobs and locations, and uncertainty over which projects would go forward," he says.

The drug 1592 was one of a batch of new chemicals developed in the labs at Wellcome in the late 1980s, when scientists were looking for better versions of AZT. Both drugs, as well as 3TC, belong to a class called nucleosides, which work by blocking an enzyme that is critical to an early phase in the replication of HIV, the virus that causes AIDS.

11/12/96 Why Isn't Glaxo's -2-: In Second Clinical Trial Phase

Wellcome researchers spent several years testing other compounds first. "We had no reason to expect 1592 to be so much more powerful than the others," says Lynn Smiley, director of the
company's AIDS clinical trials. Scientists uncovered 1592's antiviral muscle about a year ago, after another experimental drug failed and they began human testing of 1592.

The drug is now in the second of three phases of clinical trials. Glaxo officials say they need another year or more before seeking Food and Drug Administration approval. Because 1592 will be combined with so many other medicines as part of the "cocktail" therapy -- about nine other AIDS drugs are
approved or soon will be -- the company must conduct a wider range of safety trials than its earlier drugs required.

"We are very sensitive to the desperation out there from patients who need new drugs," says Stephen LaFon, a Glaxo researcher who helps run tests of the drug. "But we have to balance speed of getting the drug to these few patients and the need to get the best kind of clinical information we can."

That doesn't help patients who have already developed resistance to AZT and other nucleosides. The cocktail approach, by combining three or more drugs that attack different parts of the virus, has been able to reduce HIV to undetectable levels in many patients, allowing the immune system to rebound and fight off deadly infections. But if a patient's HIV has already developed resistance to the AZT-like component, the cocktail will ultimately fail. 1592 could be the new ingredient that would make the cocktail work again.

"You can't just pile a protease drug atop a failing regimen. It won't work," says Martin Markowitz, a research physician at the Aaron Diamond AIDS Research Center in New York.

Demands for the release of 1592 have been growing steadily since this past summer, when Glaxo scientists revealed results of a three-month-long, 80-person study that showed that combining 1592 and AZT was as effective at reducing HIV levels as some three-drug cocktails that included a protease inhibitor. Patient advocates argue that several drugs were released for "compassionate access" based on even fewer test patients than Glaxo has used in studying 1592. But Glaxo officials say the manufacturing process isn't geared up enough to support widespread distribution right now. Jennifer McMillan, a Glaxo executive who works with AIDS activists, also cites more serious concerns: If 1592 were released now, patients might be less willing to participate in clinical trials because they could, instead, get easy access to free doses of the drug.

Glaxo, surprised by surging demand for 3TC after studies underscored its power, had let 30,000 patients get that drug in a similar program from 1993 to 1995, but it was unable to collect much useful data. "We want to be careful and not repeat that mistake," Ms. McMillan says.

That distresses some people struggling against infection. Spencer Cox, who helps run Treatment Action Group, a New York advocacy group, has watched the HIV levels in his blood rise sharply in recent months as older drugs stopped working and new protease drugs couldn't plug the gap. "I fully understand Glaxo Wellcome's desire for caution," he says. "But I also know I could benefit from 1592 right now. I don't see any reason not to make it available today."

11/12/96 Why Isn't Glaxo's -3-: Only 175 Patients Have Taken Drug

For now, only 175 patients have taken 1592, and only several hundred more will get it when final-stage trials begin sometime next year. That leaves out patients like Mr. Gendin, the 30-year-old New Yorker. He can't take part in Glaxo's expanded trials because such experiments typically use subjects who haven't already developed resistance to earlier drugs. His virus levels have more than doubled in recent months, and Mr. Gendin worries more about HIV outracing his immune system than about any safety problems of Glaxo's experimental drug.

"I have to have" 1592, Mr. Gendin says simply. "I've got nothing to lose."

From Discovery to Approval

Glaxo Wellcome's new AIDS drug is taking longer to become available than some recently developed AIDS drugs

DRUG	*COMPANY*	*DISCOVERED*	*TIME TO APPROVAL*
1592	**Glaxo Wellcome**	**1989**	**About nine years***
Invirase	Hoffmann-La Roche	1989	Six years
Crixivan	Merck	1992	Four years
Norvir	Abbott Labs	1993	Three years
141	Glaxo Wellcome (Vertex)	1993	Five years*
Viracept	Agouron Pharmaceuticals	1994	Three years*

*Anticipated

1592 ACCESS COALITION

To: Daniel Montoya	From : Linda Grinberg	
Company: White House - AIDS Office	Telephone: 310-471-6565	
Fax Number: 1-202-632-1096	Fax Number: 310-471-4565	
Subject : Conf. Call	Date: 6/18/97	Pages: 2

Please see attached list of participants in today's conference call scheduled at 6:00 EST/3:00 PST.

Reminder: The phone number to call in to is (800) 360-0565. Please ask for the 1592 Access Coalition call with Jeff Getty & Linda Grinberg, moderators.

If there is any problem in accessing the call, please call (800) 825-2125 and tell operator the conf. call # is 811-8888.

We look forward to speaking with you later today.

1592 ACCESS COALITION

Name	Affiliation	Phone	Fax
1. Meg Atkinson	AIDS Action Now!/Toronto	416-487-8065	416-533-2127
2. Ron Baker	S.F. AIDS Foundation	415-487-8065	415-487-8069
3. Bill Bahlman	Treatment & Data Committee	212-929-4952	212-929-4952
4. Peter Cashman	ACT UP Los Angeles	213-669-7301	213-669-7302
5. Sally Cooper	PWA Health Group	212-255-0520	212-255-2080
6. Leigh Paldolfino-Danas	U.K.	44-171-793-7444	
7. Paul Davis	ACT UP Philadelphia	215-731-1844	215-731-1845
8. Martin Delaney	Project Inform	415-331-0184	415-331-2114
9. Jeff Getty	ACT UP Golden Gate	510-653-6278	510-653-6099
10. David Gilden	Gay Men's Health Crisis	718-624-6578-h 212-367-1452-o	918-624-8399
11. Linda Grinberg	Project Inform/F.A.I.R.	310-471-6565	310-471-4565
12. John Iverson	ACT UP East Bay	510-568-1680	
13. Cleve Jones	Names Project	707-865-9047	707-865--0541
14. Kate Krauss	ACT UP Philadelphia	215-731-1844	215-731-1845
15. James Learned	PWA Health Group	212-255-0520	212-255-2080
16. Jules Levin	N.A.T.A.P.	718-624-8541	718-624-8399
17. Andy Lipschitz, MD		516-935-6359	516-938-5470
18. L. Joel Martinez	Center for AIDS	713-527-8219	713-521-3679
19. Eileen Mitzman	Mother's Voices	212-737-3335	212-737-1092
20. Lili Rundback	Mother's Voices	212-730-2777	212-730-4378
21. Matthew Sharp	ACT UP Golden Gate	415-626-4053	415-626-0451
22. Theo Smart	Treatment Action Group	212-260-2607	212-673-8921