January 21, 2002

Dockets Management Branch
Food and Drug Administration
Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

Re: Docket Number 02P-0435 (Petition for Stay) - Submission of Comments by Alpha Therapeutic Corporation

Dear Sir or Madam:

These comments are submitted on behalf of Alpha Therapeutic Corporation (Alpha) in response to the Petition for Stay filed by Aventis Behring L.L.C. (Aventis Behring) on October 2, 2002 (Aventis Petition). The petition requests that the Commissioner stay effective approval of Alphanate® Antihemophilic Factor (Human) (Alphanate) for the treatment of von Willebrand Disease (vWD) pending final resolution of the issues in Aventis Behring October 2, 2002, Citizen Petition.

As set forth below, petition must be denied based on the following grounds:

1. Aventis Behring has not demonstrated that it will suffer irreparable harm;

2. Aventis Behring's petition is frivolous and is not being pursued in good faith;

3. Aventis Behring has failed to demonstrate sound public policy grounds supporting the stay; and

4. The delay resulting from the requested stay is outweighed by public health and other public issues.

## DISCUSSION

### I. Aventis Behring Has Not Demonstrated that It Will Suffer Irreparable Harm.

Aventis Behring argues, as it must, that it will suffer irreparable harm as a result of FDA's approval of Alphanate for any indication related to vWD. The harm Aventis Behring alleges, however -- economic injury due to competition and breach of a monopoly position -- falls far short of meeting the very high burden of proof for demonstrating irreparable injury in support of the drastic relief sought here.

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Irreparability of injury is a high standard, *Bristol-Myers Squibb Co. v. Shalala*, 923 F. Supp. 212, 220 (D.D.C. 1996) (citations omitted), and Aventis Behring must demonstrate that the harm it will suffer is "neither remote nor speculative, but actual and imminent." *Direx Israel, Ltd.*, 952 F.2d at 812 (citations omitted). "Mere injuries, however substantial, in terms of money, time and energy necessarily expended in the absence of a stay, are not enough." *Hughes Network Systems, Inc. v. Interdigital Communications Corporation*, 17 F.3d 691, 694 (4th Cir. 1994) (citations omitted). *See also Bristol-Myers Squibb v. Shalala*, 923 F. Supp. 212, 220 (D.C. 1996)(quoting *Wisconsin Gas Co. v. FERC*, 758 F.2d 669, 674 (D.C. Cir. 1985) ("It is well settled that economic loss does not, in and of itself, constitute irreparable harm."). *Cf. Gulf Oil Corp. v. DOE*, 514 F. Supp. 1019, 1025 (D.D.C. 1981) (monetary injury is only properly considered in support of a preliminary injunction where the injury is sufficiently large in proportion to the moving party's business that the loss of the amount of money involved would cause extreme hardship, or even threaten destruction of the business). Aventis Behring fails to demonstrate its projected losses from competition from Alphanate and, in fact, fails to provide any evidence whatsoever of irreparable harm.

It is also important to note that, although Aventis Behring cites *Bracco Diagnostics, Inc. v. FDA*, 963 F. Supp. 20 (D. D.C. 1997), in support of its claim of irreparable injury, that case stands against Aventis Behring. In *Bracco*, the court based its finding of irreparable injury on two factors, neither of which is relevant here. The court first found that, "because [the plaintiffs] are small companies, the time and person power spent, as well as the millions of dollars in costs, are indeed significant and irreparable losses." *Id.* at 28. Here, Aventis Behring is part of Aventis S.A., one the largest companies in the world. Aventis Behring fails to describe the scope of its expected losses from competition from Alphanate or why those losses are of such significance. The *Bracco* court also found a "second form of imminent harm" resulting from the fact that, without a stay, the plaintiffs' competitor MBI would be the first company to enter the market, which the court found to be "an advantage that can never be fully recouped through money damages or by 'playing catch-up.'" Here, Aventis Behring's product Humate-P® Antihemophilic Factor/von Willebrand Disease (Human) (Humate-P) was the first product in the market for treatment of vWD and, if Alphanate were to be approved for the same vWD indications, it is Alphanate that would be "playing catch-up."

Finally, it is important to note that harm is generally not considered irreparable when the moving party "may be compensated by an award of money damages at judgment." *Hughes Network*, 17 F.3d at 694 (citations omitted). Aventis Behring fails to demonstrate that money damages would be inadequate compensation for the injury it claims will result from the approval of Alphanate for a vWD indication.

## II. Aventis Behring's Petition Is Frivolous And Is Not Being Pursued In Good Faith.

As discussed more fully in Alpha's comments on Aventis Behring's Citizen Petition, filed herewith (Alpha's Petition Comments), Aventis Behring's position here is frivolous and is not being pursued in good faith. Aventis Behring argues in its petition that Alphanate and Humate-P must be deemed the same drug for purposes of orphan exclusivity because the drugs are derived from the same source and are manufactured to produce the same active moiety. Aventis Behring fails to inform the agency that, ten years ago, when Alpha held orphan exclusivity on a related blood derivative product, AlphaNine® Coagulation Factor IX (Human) (AlphaNine), Armour Pharmaceutical (now Aventis Behring) sought to introduce a similar product, Mononine™ Coagulation Factor IX (Human) (Mononine), onto the market. Mononine and AlphaNine were derived from the same raw material (human source plasma collected in U.S.-based plasma collection centers) and contained the same active moiety after manufacturing. Mononine Summary Basis for Approval (1992). The agency nevertheless found the Aventis Behring drug to be different for purposes of orphan exclusivity based on the same types of differences in the risk of viral transmission that are present for Alphanate and Humate-P. *Id.* at 6.

## III. Aventis Behring Has Failed to Demonstrate Sound Public Policy Grounds Supporting the Stay.

Aventis Behring argues that sound public policy supports its position because it claims orphan exclusivity. Aventis Behring asserts the public policy behind the Orphan Drug Amendments. Aventis Behring fails to note, however, the strong public policy evidenced in the Orphan Drug Amendments and in FDA's implementing regulations to ensure that orphan exclusivity should not block the approval of a clinically superior product. As the agency stated in the preamble to its orphan drug regulations, the exception for clinical superiority reflects "the intent of Congress to provide incentives for potential sponsors to develop safer and more effective orphan drugs." 57 Fed. Reg. 62076, 62078 (December 29, 1992). That strong public interest precludes a stay that would block the approval of Alphanate, which, as discussed in Alpha's Petition Comments, is clinically superior to Humate-P.

## IV. The Delay Resulting from the Requested Stay Is Outweighed by Public Health and Other Public Issues.

The needs vWD patients have not been adequately served by the pharmaceutical industry. Currently there is only one drug, Aventis Behring's Humate-P, approved for in vWD patients, and it has a limited safety and effectiveness profile. The product is approved only for "*treatment* of *spontaneous and trauma-induced bleeding episodes* in severe von Willebrand disease, and in mild and moderate von Willebrand disease where use of desmopressin is known or suspected to be inadequate." *See* Humate-P approved package insert.

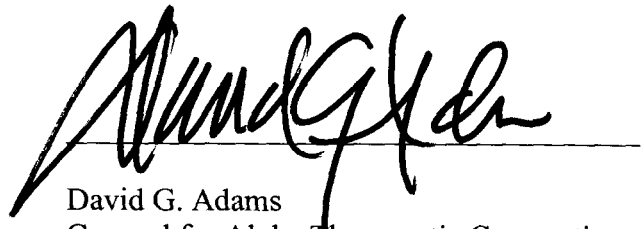
Aventis Behring has failed to complete any studies supporting the use of the product in prevention of surgical bleeding in vWD patients, leaving vWD patients with no approved therapy for this important indication. Alpha, however, has completed a clinical investigation on Alphanate in vWD patients demonstrating that Alphanate is clinically superior to Humate-P and addressing prevention of surgical bleeding.

Although Aventis Behring has failed to provide the vWD community with a product approved for prophylaxis of surgical bleeding, it would deny vWD patients access to Alphanate, which has been studied for this indication. Aventis Behring would further deny vWD patients a second source for treatment of spontaneous and trauma-induced bleeding episodes, even though vWD patients have faced shortages of Humate-P for this use, and even though Alphanate has been demonstrated safer and more effective than Humate-P. The potential harms to health of vWD patients clearly Aventis Behring's selfish interest in monopolization of the market for treatments for vWD.

## CONCLUSION

For all of the foregoing reasons, Aventis Behring's Petition for Stay must be denied.

Respectfully submitted,



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Dear Sir or Madam:

Please accept the attached comments (in four copies) on behalf of Alpha Therapeutic Corporation in response to the Petition for Stay filed by Aventis Behring L.L.C. on October 2, 2002.

Sincerely,

David G. Adams