| _  | FOR                             | RM 4 |                | UN  | ITED STATES                          | SEC  | -  | IES ANI<br>ington, D.C  |       | -  | N   | GE COM                               | MISSION  |              | OMB A   | PP                  | ROVAL  |                             |  |
|--|---------------------------------|------|----------------|---|--------------------------------------|------|--|---|-------|--|---|--------------------------------------|--|--------------|---|---------------------|--|-----------------------------|--|
| o Check this box if no longer subject<br>to Section 16. Form 4 or Form 5<br>obligations may continue. <i>See</i><br>Instruction 1(b).<br>(Print or Type Responses) |                                 |      |                | STATEMENT OF<br>CHANGES IN BENEFICIAL OWNERSHIP<br>Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934,<br>Section 17(a) of the Public Utility Holding Company Act of 1935 or<br>Section 30(h) of the Investment Company Act of 1940 |                                      |      |  |   |       |  |   | Expires: Ja<br>Estimated             | OMB Number: 3235-0287<br>Expires: January 31, 2005<br>Estimated average burden hours<br>per response 0.5 |              |   |                     |  |                             |  |
| 1.   | Name and Addr<br>BVF Partne     |      | orting Person* |   |                                      | 2.   |  | Name and T<br>st Pharmace   |       |  |   |                                      |  | 6.           | . Relationship<br>(Check all ap<br>Director   | plic                | Reporting Person(s)<br>able)<br><u>X</u> 10                          |                             |  |
|  | (Last<br>227 West Monry         | ,    |                | (First) (Midd   |                                      | 3.   | Numbe<br>Person  | S. Identification<br>mber of Reporting<br>rson, if an entity<br>oluntary) |       | 4.   | . Statement f<br>Month/Day<br>January 27, |                                      | y/Year   |              | Officer<br>(give title<br>below)  |                     | (si  | Other<br>(specify<br>below) |  |
|  |                                 |      | (Street)       |   |                                      |      |  |   |       | 5.   |   | If Amendme<br>Original<br>(Month/Day | ,  | - 7.         | (Check Appli<br>Form<br>Person  | icab<br>ı file<br>n | nt/Group Filing<br>le Line)<br>ed by one Reporting<br>d by More than | ţ                           |  |
| Chicago, Illinois 60606  |                                 |      |                |   |                                      |      |  |   |       |  |   |                                      |  | rting Person |   |                     |  |                             |  |
|  | (City)                          |      | (State)        |   | (Zip)                                | Tabl | e I — N  | on-Derivat  | ive S | Securitie                                  | s A                                       | cquired, Dis                         | oosed of, or B   | enef         | ficially Owned  |                     |  |                             |  |
|  | Title of Security<br>(Instr. 3) |      | nsaction Date  | 2A.   | 2A. Deemed Execution<br>Date, if any | 3.   | <ol> <li>Transaction Code 4.<br/>(Instr. 8)</li> </ol> |   | 4.    | . Securities A<br>of (D)<br>(Instr. 3, 4 a |   |                                      |  |              | Amount of 6<br>Securities<br>Beneficially<br>Owned at End<br>of Month (Instr.<br>3 and 4) |                     | Ownership<br>Form: Direct<br>(D) or Indirect<br>(I)<br>(Instr. 4)    | I<br>H<br>O                 | Nature of<br>Indirect<br>Beneficial<br>Ownership<br>(Instr. 4) |
|  |                                 | (Mo  | onth/Day/Year) |   | (Month/Day/Year)                     |      | Code   | V   |       | Amount                                     | t   | (A) or<br>(D)                        | Price  |              |   |                     |  |                             |  |
|  | Common Stock                    | 1/2  | 7/03           |   |                                      |      | Р  |   |       | 1,900                                      |   | А                                    | \$0.9156   |              |   |                     | (1)  |                             | (1)(2)   |
|  | Common Stock                    | 1/2  | 7/03           |   |                                      |      | Р  |   |       | 1,000                                      |   | А                                    | \$0.9156   |              |   |                     | (1)  |                             | (1)(3)   |
|  | Common Stock                    | 1/2  | 7/03           |   |                                      |      | Р  |   |       | 4,000                                      |   | А                                    | \$0.9156   |              |   |                     | (1)  |                             | (1)(4)   |
|  |                                 |      |                |   |                                      |      |  |   |       |  |   |                                      |  |              | 2,106,100   |                     |  |                             |  |
|  |                                 |      |                |   |                                      |      |  |   |       |  |   |                                      |  |              |   |                     |  |                             |  |
|  |                                 |      |                |   |                                      |      |  |   |       |  |   |                                      |  |              |   |                     |  |                             |  |

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly. \*If the form is filed by more than one reporting person, *see* Instruction 4(b)(v).

PERSONS WHO ARE TO RESPOND TO THE COLLECTION OF INFORMATION CONTAINED IN THIS FORM ARE NOT REQUIRED TO RESPOND UNLESS THE FORM DISPLAYS A CURRENTLY VALID OMB CONTROL NUMBER.

| FO | FORM 4 (Continued) Table II — Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities) |      |   |                       |    |  |   |    |                  |                      |                |    |     |  |       |                                 |  |
|----|---|------|---|-----------------------|----|--|---|----|------------------|----------------------|----------------|----|-----|--|-------|---------------------------------|--|
| 1. | Title of Derivative<br>Security<br>(Instr. 3)   | 2.   | Conversion or 3.<br>Exercise Price<br>of Derivative<br>Security | Transacti<br>(Month/I |    | 3A.<br>)                               | Deemed Execu<br>Date, if any<br>(Month/Day/Ye |    | 4.               | Transac<br>(Instr. 8 | tion Code<br>) | 5. |     |  | 6.    | Date Exercisat<br>Date (Month/E | le and Expiration<br>Day/Year)                                 |
| _  |   |      |   |                       |    |  |   |    |                  | Code                 | V              |    | (A) | (D)  |       | Date<br>Exercisable             | Expiration<br>Date   |
| _  |   |      |   |                       |    |  |   |    |                  |                      |                |    |     |  |       |                                 |  |
|    |   |      |   |                       |    |  |   |    |                  |                      |                |    |     |  |       |                                 |  |
| _  |   |      |   |                       |    |  |   |    |                  |                      |                |    |     |  |       |                                 |  |
| 7. | Title and Amount of (Instr. 3 and 4)  | Unde | erlying Securities  |                       | 8. | Price of Der<br>Security<br>(Instr. 5) | ivative                                       | 9. | Sec<br>Ow<br>Rep | ned Follo            | neficially     | )  | 10. | Ownership Form<br>Derivative Securi<br>Direct (D) or Ind<br>(Instr. 4) | ities | :                               | Nature of<br>Indirect<br>Beneficial<br>Ownership<br>(Instr. 4) |
|    | Title   |      | Amount or Nur<br>Shares   | nber of               |    |  |   |    |                  |                      |                |    |     |  |       |                                 |  |
|    |   |      |   |                       |    |  |   |    |                  |                      |                |    |     |  |       |                                 |  |

## Explanation of Responses:

- (1) The shares reported in this response are beneficially owned by BVF Partners L.P., a Delaware limited partnership ("Partners"), the designated filer of this joint filing on Form 4, and by its general partner, BVF Inc., a Delaware corporation ("BVF Inc."), which is also an investment advisor to Partners. Partners is the general partner of Biotechnology Value Fund, L.P., a Delaware limited partnership ("BVF, L.P.") and Biotechnology Value Fund II, L.P., a Delaware limited partnership ("BVF2, L.P."), both investment limited partnerships. Partners also is the manager of BVF Investments, L.L.C., a Delaware limited liability company ("Investments"). Pursuant to the operating agreement of Investments, Partners is authorized, among other things, to invest the funds of Ziff Asset Management, L.P., the majority member of Investments, in the shares of Common Stock reported in Table I as being beneficially owned by Investments. Mark N. Lampert is the sole shareholder and sole director of BVF Inc., and is an officer of BVF Inc. This joint filing on Form 4 shall not be demed an admission that Mark N. Lampert is, for purposes of Section 16 of the Securities Exchange Act of 1934, as amended, or otherwise, the beneficial owner of any equity securities covered by this joint filing.
- (2) Shares beneficially owned by BVF, L.P.
- (3) Shares beneficially owned by BVF2, L.P.
- (4) Shares beneficially owned by Investments.

|    |   | BVF Partne                       | BVF Partners L.P.   |                    |  |  |  |  |  |  |
|----|---|----------------------------------|---|--------------------|--|--|--|--|--|--|
|    |   | By:                              | BVF Inc., its general partner                                       |                    |  |  |  |  |  |  |
|    |   | By:                              | /s/ MARK N. LAMPERT   | January 29, 2003   |  |  |  |  |  |  |
|    |   |                                  | **Signature of Reporting Person                                     |                    |  |  |  |  |  |  |
|    | ** Intentional misstatements or omissions of facts of   | constitute Federal Criminal Viol | ations.   |                    |  |  |  |  |  |  |
|    | See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).   |                                  |   |                    |  |  |  |  |  |  |
|    | Note: File three copies of this Form, one of which mus<br>If space is insufficient, <i>see</i> Instruction 6 for proc |                                  |   |                    |  |  |  |  |  |  |
| ot | ential persons who are to respond to the collection of informat   | ion contained in this form are n | ot required to respond unless the form displays a currently valid O | MB Control Number. |  |  |  |  |  |  |
| )  | RM 4 (Continued)  |                                  |   |                    |  |  |  |  |  |  |
| اؤ | ing of the names and addresses of other reporting persons   | :                                |   |                    |  |  |  |  |  |  |
|    | Biotechnology Value Fund, L.P.<br>227 West Monroe Street, Suite 4800  | BIOTECI                          | BIOTECHNOLOGY VALUE FUND, L.P.                                      |                    |  |  |  |  |  |  |
|    | Chicago, Illinois 60606   | By: BV                           | By: BVF Partners L.P., its general partner                          |                    |  |  |  |  |  |  |
|    |   | By:                              | BVF Inc., its general partner                                       |                    |  |  |  |  |  |  |
|    |   |                                  | By: /s/ MARK N. LAMPERT   | January 29, 200    |  |  |  |  |  |  |
|    |   |                                  | **Signature of Reporting Person<br>Authorized Signatory             | Date               |  |  |  |  |  |  |
|    | Biotechnology Value Fund II, L.P.   | BIOTECI                          | BIOTECHNOLOGY VALUE FUND II, L.P.                                   |                    |  |  |  |  |  |  |
|    | 227 West Monroe Street, Suite 4800<br>Chicago, Illinois 60606   | By: BV                           | By: BVF Partners L.P., its general partner                          |                    |  |  |  |  |  |  |
|    |   | By:                              | BVF Inc., its general partner                                       |                    |  |  |  |  |  |  |
|    |   |                                  | By: /s/ MARK N. LAMPERT   | January 29, 200    |  |  |  |  |  |  |
|    |   |                                  | **Signature of Reporting Person<br>Authorized Signatory             | Date               |  |  |  |  |  |  |
| 3. | BVF Investments, L.L.C.<br>227 West Monroe Street, Suite 4800   | BVF INV                          | ESTMENTS, L.L.C.  |                    |  |  |  |  |  |  |
|    | Chicago, Illinois 60606   | By: BV                           | F Partners L.P., its manager  |                    |  |  |  |  |  |  |
|    |   | By:                              | BVF Inc., its general partner                                       |                    |  |  |  |  |  |  |
|    |   |                                  | By: /s/ MARK N. LAMPERT   | January 29, 200    |  |  |  |  |  |  |
|    |   |                                  | **Signature of Reporting Person<br>Authorized Signatory             | Date               |  |  |  |  |  |  |
|    | BVF Inc.<br>One Sansome Street, 31st Floor  | BVF INC                          | BVF INC.  |                    |  |  |  |  |  |  |
|    | San Francisco, California 94104   | By: /s/                          | MARK N. LAMPERT   | January 29, 200    |  |  |  |  |  |  |
|    |   |                                  | ignature of Reporting Person<br>uthorized Signatory                 | Date               |  |  |  |  |  |  |
|    | Mark N. Lampert<br>One Sansome Street, 31st Floor   | By: /s/                          | MARK N. LAMPERT   | January 29, 200    |  |  |  |  |  |  |
|    | San Francisco, California 94104   |                                  | ignature of Reporting Person<br>uthorized Signatory                 | Date               |  |  |  |  |  |  |

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, *see* Instruction 6 for procedure.

Potential persons who are to respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Control Number.