

**UNITED STATES OF AMERICA**  
**Before the**  
**SECURITIES AND EXCHANGE COMMISSION**

**SECURITIES EXCHANGE ACT OF 1934**  
**Release No. 58690 / September 30, 2008**

**ADMINISTRATIVE PROCEEDING**  
**File No. 3-13264**

**In the Matter of**

**INSPIRE PHARMACEUTICALS, INC.,  
CHRISTY L. SHAFFER, and  
MARY B. BENNETT,**

**Respondents.**

**ORDER INSTITUTING CEASE-AND-  
DESIST PROCEEDINGS, MAKING  
FINDINGS, AND IMPOSING A  
CEASE-AND-DESIST ORDER  
PURSUANT TO SECTION 21C OF  
THE SECURITIES EXCHANGE ACT  
OF 1934**

**I.**

The Securities and Exchange Commission (“Commission”) deems it appropriate that cease-and-desist proceedings be, and hereby are, instituted pursuant to Section 21C of the Securities Exchange Act of 1934 (“Exchange Act”) against Inspire Pharmaceuticals, Inc. (“Inspire”), Christy L. Shaffer (“Shaffer”), and Mary B. Bennett (“Bennett”) (collectively, “Respondents”).

**II.**

In anticipation of the institution of these proceedings, Respondents have submitted Offers of Settlement (the “Offers”) which the Commission has determined to accept. Solely for the purpose of these proceedings and any other proceedings brought by or on behalf of the Commission, or to which the Commission is a party, and without admitting or denying the findings herein, except as to the Commission’s jurisdiction over each of them and the subject matter of these proceedings, which are admitted, Respondents consent to the entry of this Order Instituting Cease-and-Desist Proceedings, Making Findings, and Imposing a Cease-and-Desist Order Pursuant to Section 21C of the Securities Exchange Act of 1934 (“Order”), as set forth below.

### III.

On the basis of this Order and Respondents' Offers, the Commission finds<sup>1</sup> that:

#### Respondents

1. Inspire is a biopharmaceutical company incorporated in Delaware and headquartered in Durham, North Carolina. At all relevant times, Inspire's common stock was registered with the Commission pursuant to Section 12(g) of the Exchange Act and was quoted on the Nasdaq National Market under the symbol "ISPH."

2. Shaffer, 50, is a legal resident of North Carolina, and was, at all times relevant, Inspire's Chief Executive Officer and a member of the company's board of directors.

3. Bennett, 51, is a legal resident of North Carolina, and was, at all times relevant, Inspire's Senior Vice President, Communications.

#### Summary

4. Inspire's Forms 10-Q for the first three quarters of its fiscal year 2004 described a clinical trial for Inspire's drug, diquafosol tetrasodium ("diquafosol"), as "confirmatory" and stated that diquafosol had to "replicate" the efficacy demonstrated in an earlier clinical trial. In the context of other public statements made by Inspire and Shaffer concerning diquafosol, these statements created the impression that the particular standard by which diquafosol had to demonstrate efficacy in the new clinical trial (the "primary endpoint") was the same as a primary endpoint that diquafosol had successfully achieved in a previous clinical trial. In fact, the primary endpoint was different from the primary endpoints of previous clinical trials for diquafosol. On February 9, 2005, Inspire announced that diquafosol had failed to achieve the trial's primary endpoint, which the company specifically identified for the first time. Inspire's stock closed at \$8.88 per share, representing a drop of more than 44 percent from the previous day's close of \$16 per share.

#### FDA Approval Process

5. Before a drug may be marketed in the United States, it must be approved by the United States Food and Drug Administration ("FDA"). Among other requirements, a drug candidate must demonstrate efficacy in "Phase III" trials, which are generally conducted to determine its efficacy in a patient population by comparing the results of patients taking the drug with the results of patients taking a placebo. A Phase III clinical trial is conducted pursuant to a written protocol, which the trial sponsor typically submits to the FDA for review and approval and then provides to clinicians administering the trial. The protocol typically sets forth, among other things, procedures for the trial and the manner of data analysis. One key component of a Phase III protocol is the "primary endpoint," which is a predefined criterion by which the drug's

---

<sup>1</sup> The findings herein are made pursuant to Respondents' Offers of Settlement and are not binding on any other person or entity in this or any other proceeding.

efficacy is generally measured. A Phase III trial's success is usually determined by whether the data establish the primary endpoint with "statistical significance" with a "p-value less than 0.05." This means that there must be a greater-than-95 percent chance that the effect seen is due to the drug rather than due to mere chance.

6. After successfully completing Phase III clinical trials, a company files a New Drug Application ("NDA") with the FDA. The FDA can approve or reject a drug based upon an NDA submission, or can send an "approvable letter" when a drug can be approved based on specific additional information to be submitted by the sponsor.

### **Relevant Endpoints to Measure Efficacy of Dry Eye Drugs: "Corneal Staining" vs. "Corneal Clearing"**

7. A common test for measuring the impact of a drug on dry eye disease is to use corneal staining. Clinicians (also called "investigators"), who are typically ophthalmologists with experience in treating dry eye disease, periodically administer a fluorescein dye to the corneas of study patients. The dye stains the damaged areas of the cornea caused by dry eye disease. The investigators wait for a period of time after administering the dye and then assess the amount of stain in the patient's corneas. Investigators assign patients a numerical "staining score" corresponding to the residual level of staining (as perceived by the investigators) in the cornea, with a greater score theoretically indicating a greater level of corneal irritation.

8. A primary endpoint based on the corneal staining test that Inspire has used in certain clinical trials has been to measure "a reduction in mean corneal staining." Inspire has, at times, referred to primary endpoints seeking a reduction in mean corneal staining as "corneal staining" as shorthand. For diquafosol to achieve the endpoint of reduction in mean corneal staining, patients receiving diquafosol have to show a higher reduction in the level of corneal staining as compared to patients receiving placebo at specific points in time.

9. Another endpoint based on the corneal staining test is the statistically significant achievement of "corneal clearing." A clinical trial with a "corneal clearing" endpoint is conducted in substantially the same fashion as a trial measuring reduction in mean corneal staining. However, in the former, the investigators determine whether, over a period of time, there is a complete elimination, *i.e.*, "clearing" of residual staining or, in other words, reduction of the staining score to zero. For diquafosol to achieve a corneal clearing endpoint, there must be a statistically significant higher rate of patients receiving diquafosol that achieve corneal clearing versus patients receiving placebo at specific points in time.

10. At the time Inspire filed its May, August, and November 2004 Forms 10-Q, certain clinicians, analysts, and Inspire investors understood that the terms "corneal staining" and "corneal clearing" referred to different endpoints, and believed that "corneal staining" was generally easier to achieve than "corneal clearing."

## Inspire Seeks FDA Approval of Diquafosol

11. In 2002, Inspire reported the results from a Phase III clinical trial of diquafosol designated Study 3-105. Study 3-105 had co-primary endpoints: 1) statistically significant improvement in mean corneal staining scores, and 2) clearing of the symptom of foreign body sensation, both at six weeks. In Study 3-105, diquafosol achieved improvement in mean corneal staining, but failed to meet the subjective endpoint of clearing of foreign body sensation at the same six-week time period.

12. In Study 3-105, diquafosol also achieved statistically significant results in corneal clearing. Corneal clearing was not, however, designated as a predefined endpoint or efficacy measurement in that Study.

13. Although Inspire never specifically mentioned the clearing results from the 3-105 trial in any press release or Commission filing, Inspire did present the clearing results, along with the other results from the Study 3-105, in a presentation at an eye conference in May 2003. That presentation did not describe corneal clearing as an endpoint (either primary or secondary), an “efficacy variable” or an “efficacy measurement” for the 3-105 Study. Inspire also issued a press release in May, noting, among other things, that this paper could be downloaded from Inspire’s website.

14. The corneal clearing results from the 3-105 Study were mentioned in certain reports published in May 2003 by one of the analysts that covered Inspire. However, none of these reports contained any substantive discussion of the clearing results or described corneal clearing as a measure by which Inspire or the FDA evaluated efficacy for diquafosol. Moreover, analysts that covered Inspire between May 2003 and February 2005 published reports in which they surmised that the primary endpoint for the new Phase III clinical trial was the same as in Study 3-105, *i.e.*, a reduction in mean corneal staining.

15. In June 2003, Inspire submitted an NDA to the FDA for diquafosol. The NDA was based in part on the Study 3-105 results, and although Study 3-105 had not achieved both its co-primary endpoints, the FDA accepted the NDA and granted it priority review status.

16. On December 19, 2003, the FDA issued an approvable letter to Inspire which provided two options to gain approval of diquafosol: “[A]n additional adequate and well controlled study demonstrating efficacy in the clearance of corneal staining is needed to support the efficacy of the drug product. Alternatively, additional adequate and well controlled studies demonstrating both subjective and objective improvements in ocular surface health could be submitted.”

17. Inspire elected to conduct an additional clinical trial based on the clearance of corneal staining, and it designed a new Phase III clinical trial, designated as Study 3-109, in which the primary endpoint was the clearance of corneal staining. Inspire designed Study 3-109 to replicate the corneal clearing results achieved in Study 3-105. The initial protocol for Study 3-109 described the primary endpoint as “based on corneal staining” but stated that the specific primary endpoint would not be disclosed for proprietary reasons. In May 2004, the FDA

informed Inspire that the protocol (which is a non-public document) had to specify the primary endpoint as corneal clearing.

### **Related Disclosures**

18. Before Study 3-109, Inspire on occasion had publicly used the term “corneal staining” to refer to the endpoint of a reduction in mean corneal staining. In a press release issued on June 18, 2002, Inspire disclosed that, in Study 3-105, diquafosol had “demonstrated a highly statistically significant improvement . . . over placebo for the primary objective endpoint, corneal staining.”

19. During a January 30, 2004 conference call with analysts and investors, Shaffer stated that Inspire would not be disclosing the details of the 3-109 Study, including its primary endpoint. However, beginning in February 2004, in oral communications with analysts and investors, Shaffer generally described the endpoint of the 3-109 Study as a “measure of corneal staining.”

20. In a May 10, 2004 conference call with analysts, moderated by Bennett, Shaffer was asked by an analyst to “elaborate on the protocol” of Study 3-109. Shaffer replied: “The protocol is very similar in fact to a study that was already run which is our flagship Phase III study, study 105. It’s going to enroll a similar number of patients and generally I would say the eye, the inclusion-exclusion criteria are similar, not quite identical but very close to what we’ve seen before.” The analyst then replied: “Oh, great. Now what’s the, as a reminder, what’s the primary endpoint in 105?” Shaffer then replied: “It’s corneal staining.”

21. Inspire’s Forms 10-Q for the first three quarters of 2004 (filed on May 10, August 9, and November 9, 2004) each described the 3-109 trial as “confirmatory,” and stated that in Study 3-109 diquafosol had to “replicate” the efficacy of an earlier trial.

22. During a conference call on November 4, 2004, in which Study 3-109 was discussed, an analyst asked Shaffer: “Okay, a question on diquafosol . . . just confirm is the primary endpoint corneal staining and will the data be six weeks as opposed to a previous study which was twelve weeks?” Shaffer replied: “The primary endpoint is six weeks and it is a corneal staining endpoint.”

23. In a February 9, 2005 press release, Inspire announced that diquafosol had failed to demonstrate efficacy in Study 3-109, and identified the trial’s endpoint as “corneal clearing.” Some analysts expressed surprise at the revelation of the endpoint, and Inspire’s stock closed at \$8.88 per share, representing a drop of more than 44 percent from the previous day’s close of \$16 per share.

### **Violations of the Federal Securities Laws**

24. Section 13(a) of the Exchange Act and Rule 13a-13 thereunder require issuers of registered securities to file with the Commission quarterly reports prepared in conformity with the requirements of the Commission’s rules and regulations. Courts have held that an implicit

requirement of these provisions is that the information provided in the reports filed with the Commission be accurate and contain no material misrepresentations or omissions. See, e.g., SEC v. IMC International, Inc., 384 F.Supp. 889, 893 aff'd mem., 505 F.2d 733 (5<sup>th</sup> Cir. 1974), cert. denied sub nom. In addition, Exchange Act Rule 12b-20 requires that these periodic reports contain such further material information necessary to ensure that the required statements made in them are not misleading. In determining whether particular statements violate these provisions of the federal securities laws, the focus is not on the technical accuracy of such statements, but instead on whether the statements, taken together and in context, would have misled a reasonable investor. See, e.g., McMahan & Company v. Wherehouse Entertainment, Inc., 900 F.2d 576, 579 (2d Cir. 1990); SEC v. First American Bank and Trust Co., 481 F.2d 673, 678 (8<sup>th</sup> Cir. 1973). No showing of scienter is necessary to establish a violation of Section 13(a) or Rules 12b-20 and 13a-13, Tenex Corp., et al., Exchange Act Rel. No. 41312 (April 20, 1999), 69 SEC Docket 1814, 1834 n. 11, and no finding of scienter has been made.

25. Inspire violated Section 13(a) of the Exchange Act and Rules 12b-20 and 13a-13 thereunder by filing Forms 10-Q on May 10, August 9, and November 9, 2004. Those filings described Study 3-109 as “confirmatory” and “replicating” the efficacy of an earlier trial. Given the context in which those statements were made, and the public understanding of the terms “corneal staining” and “corneal clearing,” this created the impression that the primary endpoint for Study 3-109 was the same as the primary objective endpoint for Study 3-105, *i.e.* a reduction in mean corneal staining. Moreover, although diquafosol had achieved corneal clearing in Study 3-105, corneal clearing was not designated as a predefined endpoint or efficacy standard in that Study.

26. Under Section 21C of the Exchange Act, a person is “a cause” of a company’s violation if the person “knew or should have known” that his or her act or omission would contribute to the company’s violation. Negligence is sufficient to establish liability for “causing” a primary violation that does not require scienter. KPMG Peat Marwick LLP, 54 S.E.C. 1135, 1175 (2001), recon. denied, 55 S.E.C. 1, 4 & n.8 (2001), pet. denied, 289 F.3d 109 (D.C. Cir. 2002).

27. Shaffer and Bennett caused Inspire’s violation of Section 13(a) of the Exchange Act and Rules 12b-20 and 13a-13 thereunder. Shaffer and Bennett were members of Inspire’s “Disclosure Committee,” which was charged with drafting and approving the company’s public disclosures, including Commission filings. As such, Shaffer and Bennett were responsible for the disclosure decisions concerning the details of the diquafosol program. Moreover, Shaffer signed Inspire’s Forms 10-Q that contained the statements at issue.

#### IV.

In view of the foregoing, the Commission deems it appropriate to impose the sanctions agreed to in Respondents’ Offers.

Accordingly, it is hereby ORDERED that, pursuant to Section 21C of the Exchange Act:

- A. Respondent Inspire cease and desist from committing or causing any violations and any future violations of Section 13(a) of the Exchange Act and Rules 12b-20 and 13a-13 thereunder.
- B. Respondent Shaffer cease and desist from causing any violations and any future violations of Section 13(a) of the Exchange Act and Rules 12b-20 and 13a-13 thereunder.
- C. Respondent Bennett cease and desist from causing any violations and any future violations of Section 13(a) of the Exchange Act and Rules 12b-20 and 13a-13 thereunder.

By the Commission.

Florence E. Harmon  
Acting Secretary