



FOOD AND DRUG ADMINISTRATION

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**Meeting Date and Time:** 4/7/2011; 3:00PM ET  
**Meeting Type:** Teleconference  
**Application Number:** 125348  
**Product Name:** AzFicel-T  
**Sponsor Name:** Fibrocell, Inc.

**Meeting Attendees:**

**FDA Attendees**

Yao Yao Zhu (OCTGT)  
Agnes Lim (OCTGT)  
John Thomas (OCTGT)  
Craig Zinderman (OBE/DE/TBSB)  
Thomas Buttolph (OBE/DE/TBSB)

**Fibrocell Attendees**

Dana Weinberger  
John Maslowski  
Kevin Hennegan

**1.0 BACKGROUND**

FDA/CBER requested a teleconference with the sponsor to notify the sponsor that if the product is approved, FDA anticipates instituting a post-market requirement for a study to further assess safety signals identified with AzFicel-T (AzF).

**2.0 DISCUSSION**

**2.1 Safety Signals**

Dr. Zinderman introduced the two safety issues that FDA anticipates including in a PMR (post-market requirement): potential for skin cancer to occur in the area of AzF injections and the risk of immune mediated hypersensitivity reactions such as leukocytoclastic vasculitis (LV). Dr. Zinderman noted that risk of cancers in the area of the AzF injection could come from transfer of abnormal cells from the biopsy site or local development of cancer cells at the injection site. The single Basal Cell

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Cancer case in the clinical trials was noted although the relatedness of this case to the product versus part of the background incidence of BCC, a relatively common condition, is unknown. The LV case in the Histopathology study was briefly discussed and noted to possibly be temporally related to product administration but also have possible other causes for LV in this patient.

## **2.2 PMR**

Dr. Zinderman explained that if the product is approved, a post-market study would be expected to further characterize these risks in an AzF-treated population larger than the population studied in the clinical trials. Based on the background incidence of BCC in the U.S., a sample size of 2700 enrolled patients would be needed to detect a 3-fold increase in AzF-treated patients.

The sponsor had no initial discussion on the PMR or the safety signals but noted that an additional teleconference would be needed to include the sponsor's appropriate clinical personnel.

FDA noted that a registry type of study would be a reasonable study plan for AzF because, due to the autologous nature of the product, all patients and physicians are identified and known to the sponsor. Given that the safety signals under study include the risk of tumorigenicity, a follow-up period longer than the 12 month period proposed in the Pharmacovigilance Plan would be needed, at least 2 years.

FDA further indicated that a preliminary proposal be submitted to the BLA with sufficient time for the review team to review and provide comments prior to the end of the BLA timeline. A specific due date for this proposal was not identified since the sponsor indicated that an additional telecon would be needed for further discussion, however, FDA indicated that the submission of a proposal in 4-5 weeks would be optimal. FDA noted that this preliminary proposal should include the size of the study, study design, methods for follow-up contact, and adverse outcomes to be collected.

Additionally, the sponsor should propose a due date for submission of a final protocol for a post-market study. The due date can be after the end of the current BLA timeline. The sponsor should also propose a date for completion of the study.

The sponsor asked if the study requirement would potentially lead to an extension of the timeline of the BLA review. FDA indicated that the Final Protocol could be submitted after the end of the BLA timeline and would not be expected to impact the timeline.

Noting that neither safety issue is clearly linked to product administration, the sponsor asked if the issue of a post-market study would affect decisions about including these two safety issues in the label. FDA indicated that the label is under review; the content will be determined from review of the materials in the BLA and this is a separate issue from the post-market study. Once the review on Prescribing Information (PI) is finalized internally by FDA, a teleconference will be initiated soon for discussion of FDA's recommendations regarding specific items of the PI.

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### **3.0 ISSUES REQUIRING FURTHER DISCUSSION**

The sponsor indicated that they would work through Lori Tull to arrange an additional telecom to further discuss the issues raised in this meeting.