



TFF Voriconazole Powder for Inhalation

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Disclosure: Paid Consultant of TFF Pharma



*Advanced Technology
for Better Drug
Delivery Options*

Safe Harbor Statement

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This document contains forward-looking statements concerning TFF Pharmaceuticals, Inc. (“TFF”, the “Company,” “we,” “us,” and “our”). The words “believe,” “may,” “will,” “potentially,” “estimate,” “continue,” “anticipate,” “intend,” “could,” “would,” “project,” “plan,” “expect” and similar expressions that convey uncertainty of future events or outcomes are intended to identify forward-looking statements. These forward-looking statements include, but are not limited to, statements concerning the following:

- our future financial and operating results;
- our intentions, expectations and beliefs regarding anticipated growth, market penetration and trends in our business;
- the timing and success of our plan of commercialization;
- our ability to successfully develop and clinically test our product candidates; and
- our ability to file for FDA approval of our product candidates through the 505(b)(2) regulatory pathway.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially. Among those factors are: (i) no drug product incorporating the TFF platform has received FDA pre-market approval or otherwise been incorporated into a commercial drug product, (ii) the Company has no current agreements or understandings with any large pharmaceutical companies for the development of a drug product incorporating the TFF Platform and (iii) those other risks disclosed in the section “Risk Factors” included in the Company’s 2019 Annual Report on Form 10-K filed March 26, 2020 with the SEC. TFF Pharmaceuticals cautions readers not to place undue reliance on any forward-looking statements. TFF Pharmaceuticals does not undertake, and specifically disclaims, any obligation to update or revise such statements to reflect new circumstances or unanticipated events as they occur, except as required by law.

This document contains only basic information concerning TFF. Because it is a summary it does not contain all of the information you should consider before investing. Please refer to our reports and registration statements on file with the SEC for more comprehensive information concerning TFF Pharmaceuticals.



TFF Brittle Matrix and Powders



DRUG/EXCIPIENT
IN SOLUTION



RAPID-FREEZING ON
A CRYOGENIC DRUM



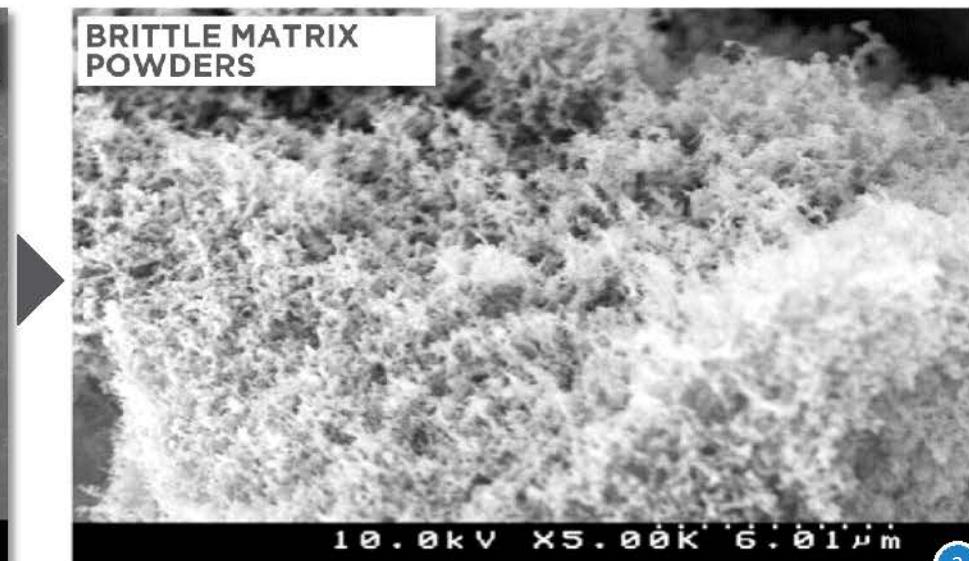
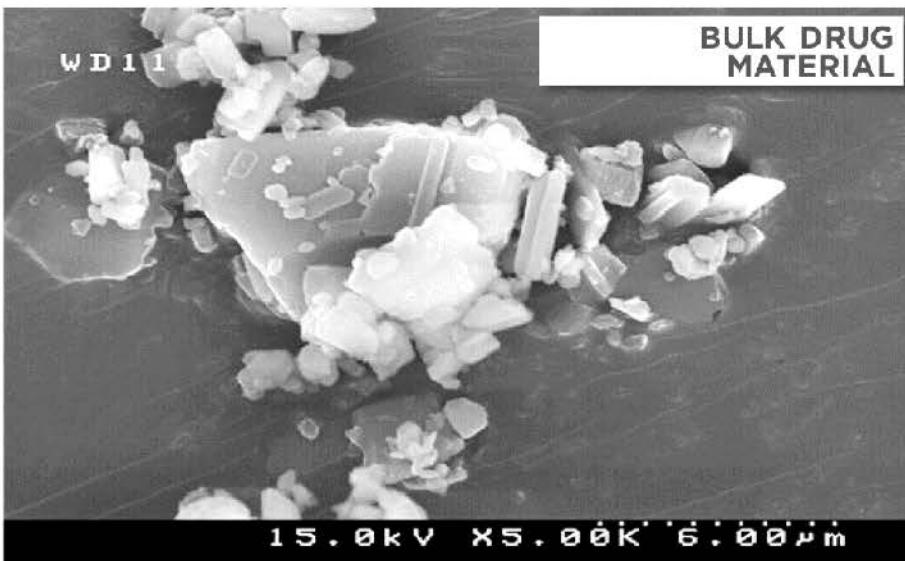
SOLVENT REMOVAL
BY LYOPHILIZATION



POWDER FILLING
IN CAPSULE



COMMERCIALIZED
PRODUCT



Voriconazole Phase 1 Trial Program

Double Blind Placebo Controlled Design

Part A: SAD

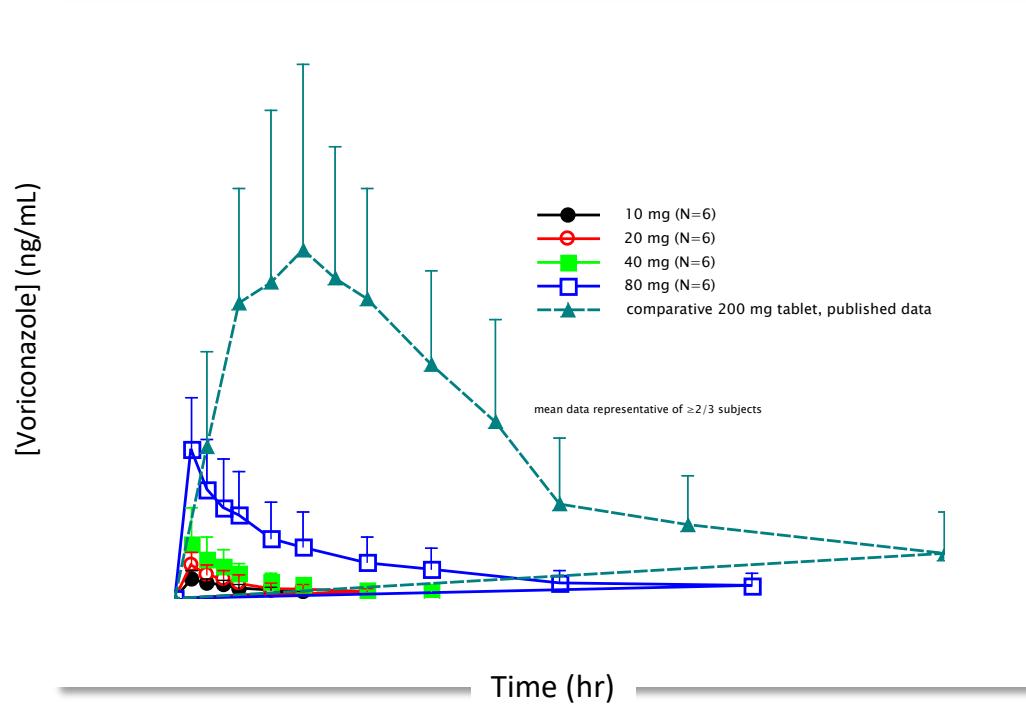
- Normal volunteers
- Single inhaled dose
- 6+2 volunteers per cohort
- Dose levels of 10, 20, 40 and 80 mg
- Endpoints:
 - Blood/Sputum exposure
 - Tolerability
 - Pulmonary Function (FEV1)
 - Vision/renal toxicity

Part B: MAD

- Normal volunteers
- Inhaled dosing 2x/day – 7 Days (13 doses)
- 6+2 volunteers per cohort
- Dose levels of 10, 20, 40 and 80 mg
- Endpoints:
 - Blood/Sputum exposure (Day 1 and 7)
 - Tolerability
 - Pulmonary Function (FEV1)
 - Vision/renal toxicity

Voriconazole Development: SAD Pharmacokinetic Profiles

Comparisons of inhalation plasma concentrations to published 200 mg oral data



Oral Bioavailability
estimated at 80%

Voriconazole Development Program

SAD/MAD DSMB summary

TFF-V1-001

A Randomized, Double-Blind, Placebo Controlled, Single-Dose and Multiple Dose Dose-Ranging Study of Voriconazole Inhalation Powder in Healthy Adult Subjects

In summation, there were no reported clinically significant adverse events, laboratory test results, ECG's or vital signs observed by the DSMB. There were no clinically meaningful relationships or trends observed for differences between vital signs, liver function tests, spirometry, visual examinations, pulse oximetry and ECGs as a function of dose or treatment. From the safety data that was made available to the DSMB, Voriconazole Inhalation Powder at the 80 mg dose level (MAD Cohort 4) was well tolerated and adequately demonstrated safety and tolerability to dosing at that level.

We as the DSMB have no reservations to the continuation of study drug development for Voriconazole Inhalation Powder.

Clinical Trial Design – Monotherapy Approach

- Inclusion – IPA Patients transitioning from IV to Oral
 - Probable (?) and/or Confirmed – Positive Aspergillus culture or PCR
 - Chest CT – Radiographic evidence of disease
 - Biomarker – Gallactomannan positivity
 - Patient Population –
 - Hematological malignancy patients following chemotherapy
 - Bone marrow transplant
 - Lung transplant

Do we include Patients with Possible or Probable disease?

How many patients from a group are needed for broad approval?

- Exclusion – evidence of angio-invasive or systemic disease
- 3 cohorts – Double Dummy Design – All Patients get treatment
 - 40 mg and 80 mg BID Inhaled voriconazole + oral placebo
 - Placebo inhaled + Vfend oral

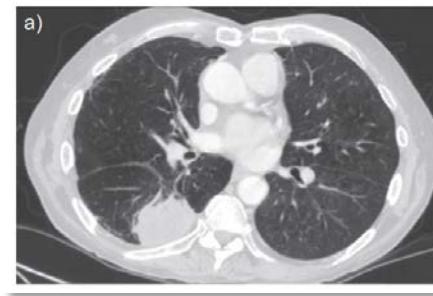
Voriconazole Pivotal Trial Dose Selection

Remarkably efficient inhaled antifungal monotherapy for invasive pulmonary aspergillosis

To the Editors:

Voriconazole is a broad-spectrum antifungal agent that is effective against moulds such as *Aspergillus fumigatus*. It inhibits the cytochrome P450-dependent 14- α -lanosterol demethylase, preventing the conversion of lanosterol to ergosterol. This results in the accumulation of toxic methylsterols in the fungal wall and the inhibition of fungal growth [1]. Voriconazole is available as an intravenous infusion solution containing a cyclo-

protein. By that time, the patient had developed polyneuropathy and progressive increases in liver enzyme levels. Consequently, antifungal treatment was halted, which normalised liver enzymes but was also associated with a worsened clinical condition and elevated C-reactive protein and leukocytes. Therefore, in July 2010, the patient started monotherapy with inhaled voriconazole at an initial total dose of 40 mg *t.i.d.* that was reduced to 40 mg *b.i.d.* after 2 weeks and was



Hilberg et al. European Resp. Journal 2012 Jul;40(1):271-3

- 40 mg *t.i.d* for 2 weeks then 40 mg *b.i.d.* to 3 months
- Monotherapy – no systemic antifungal added
- No systemic escape reported

Clinical Trial Design - Outcomes

- Endpoints:
 - Efficacy Endpoint(s)
 - All cause mortality
 - Aspergillus culture/PCR clearance
 - Improved lung function
 - Clearance of radiographic lesions
 - Decreased galactomannan in blood

Is stable disease (i.e. stable FEV1, no CT lesion growth, no detectable gallactomannan) success or is it a treatment failure???

- Safety Endpoints
 - Withdrawal due to adverse events
- How many clinical sites? *Enrollment rate estimate 0.1 pt/site/month*
 - Defining a limited population for LPAD approval

Potential Advantages of TFF Voriconazole

- ✓ Delivers the IDSA recommended agent for Aspergillus directly to site of infection
- ✓ Higher local concentrations
 - greater efficacy
- ✓ Reduced systemic exposure
 - lower toxicity
 - Potential for reduced Drug-Drug interactions
- ✓ Heat stable and easy-to-Use



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