From: James Ciciriello
To: Jamie Warner
Sent: 2/25/2016 3:34:46 PM
Subject: FW: FYI Only: FDA call request letter
Attachments: Meeting Request Ltr 02 24 16 FINAL.pdf

From: Natalie Thoma
Sent: Thursday, February 25, 2016 10:26 AM
To: James Ciciriello
Subject: FW: FYI Only: FDA call request letter

FYI – the latest with regard to Vantrela ER review.

Best regards,
Natalie

Natalie Thoma, RPh
Senior Manager, Regulatory Affairs
Tel: 610-786-7257
Natalie.Thoma@tevapharm.com www.tevapharm.com

From: Susan Larijani
Sent: Wednesday, February 24, 2016 4:15 PM
To: James G King Jr; Shweta Shah; Matthew Wieman; Azhar Choudhry
Subject: FYI Only: FDA call request letter

Dear Medical Affairs colleagues,

Please see below email and attached correspondence to FDA.

Best regards,

Susan

Susan Larijani RN, BSN, Sr Dir Med Info, North America Medical Affairs
Tel: +1-610-786-7187 Cell: +1-484-557-7584 Fax: +1-610-344-0065
Susan.Larijani@tevapharm.com sip:Susan.Larijani@tevapharm.com www.tevapharm.com

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From: Rob Falb
Sent: Wednesday, February 24, 2016 4:01 PM
To: Jeffrey Dierks; Grant Erdel; Douglas Harnish; Susan Larijani; Brian McCormick; Alexander Nikas; Richard Malamut; Jeffrey Martini; Terri Stewart; Patrick Puz
Subject: FDA call request letter

Attached is the letter being sent to the FDA requesting a call to discuss the ad comm.

Robert J. Falb Director, Government and Public Affairs Dept
Tel: 202 639 3800 Fax: 816 508 8160
25 Massachusetts Ave, NW, Suite 440, Washington, DC 20001
Rob.Falb@tevapharm.com

From: Grant Erdel
Sent: Wednesday, February 24, 2016 3:53 PM
To: Rob Falb
Subject: Fwd: vantrela alignment call

Can you forward the letter?

Sent from my iPhone

Begin forwarded message:

From: Jeffrey Dierks <Jeffrey.Dierks@tevapharm.com>
Date: February 24, 2016 at 3:51:34 PM EST
To: Grant Erdel <Grant.Erdel@tevapharm.com>, Douglas Harnish <Douglas.Harnish@tevapharm.com>
Cc: Susan Franks <Susan.Franks@tevapharm.com>, Brian McCormick <Brian.McCormick@tevapharm.com>, Alexander Nikas <Alexander.Nikas@tevapharm.com>, Richard Malamut <Richard.Malamut@tevapharm.com>, Jeffrey Martini <Jeffrey.Martini@tevapharm.com>, Terri Stewart <Terri.Stewart@tevapharm.com>, Patrick Puz <Patrick.Puz@tevapharm.com>, Doris Saltkill <Doris.Saltkill@tevapharm.com>
Subject: RE: vantrela alignment call

Also, would we be able to get a copy of the revised letter?
Thanks in advance-
Jeff

Jeffrey Dierks Director, Pain Care Marketing
Tel: +1-610-786-7899
Jeffrey.Dierks@tevapharm.com www.tevapharm.com

-----Original Message-----
From: Grant Erdel
Sent: Wednesday, February 24, 2016 3:42 PM
To: Douglas Harnish
Cc: Susan Franks; Brian McCormick; Alexander Nikas; Jeffrey Dierks; Richard Malamut; Jeffrey Martini; Terri Stewart; Patrick Puz; Doris Saltkill
Subject: Re: vantrela alignment call

All,

I just got off the phone with Deb. There is a very strong opinion in Israel that we do not want an ad comm and the directive is to work toward that end. There have been many discussions over the course of the week and Deb stressed that the direction is clear. She said that Erez and Michael themselves made edits to the letter and wants it to be sent tomorrow to try and get the call scheduled at the earliest possible date.

There is currently no plan to issue a press release at this time.

As we all know, all the relevant leaders are still together in Israel and available to discuss any concerns raised by this

group.

Thanks,
Grant

Sent from my iPhone

On Feb 24, 2016, at 12:22 PM, Douglas Harnish <Douglas.Harnish@tevapharm.com> wrote:

[X]

[X]

Everyone's calendars are booked so took a chance people could free up
their calendars for a quick call

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Czech Republic (toll free)
800 701 226

Czech Republic, Prague
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Denmark, Copenhagen
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Estonia, Tallinn
+372 622 6550

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UK (national)

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UK (national)
0845 351 3017

UK (toll free)
0800 368 0636

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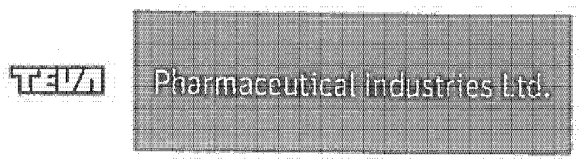

February 24, 2016

Robert M. Califf, M.D.
Acting Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Califf:

On behalf of Teva Pharmaceuticals, we are writing to request a teleconference with you as soon as possible to discuss the review process for our New Drug Application for Vantrela (Hydrocodone) Extended Release (ER). As you know, an estimated one in three American adults experiences chronic pain and we appreciate the agency's commitment to balancing access to much needed, high quality treatment while limiting the potential for misuse and diversion of these products.

Teva believes that abuse deterrent formulations for opioids represent an important tool in the effort to address the epidemic of prescription drug abuse in the United States. Well-controlled clinical studies have demonstrated a significant reduction (up to 60%) in various abuse-related parameters and indicators such as decreased rates of abuse and diversion following the introduction of a reformulated medication into the market. In our shared concern about patients abusing opioids, Teva is committed to investing in the research and development of abuse deterrent technologies and believes that our current application for Vantrela ER, as evidenced by the data package we have submitted including Human Abuse Liability (HAL) studies, represents one of the leading technologies available at this time to reduce the potential for abuse.

Unfortunately, after a robust review process with the agency and an anticipated decision on the application due on October 23, 2015, Teva has recently been notified by Sharon Hertz, M.D. Director, Division of Anesthesia, Analgesia, and Addiction Products, Office of New Drugs that our Vantrela ER application will now be subject to review by an Advisory Committee before final FDA action. This recent decision is a departure from the regulatory pathway Teva has been following with the agency and will delay a product that we believe will provide great public health benefit to patients. Teva is unaware of any outstanding scientific or regulatory deficiencies in the application we have submitted. Any delay in the approval of Vantrela ER will deny patient access to an abuse-deterrent hydrocodone product with unique properties currently not available in the market.

By way of background, Vantrela ER is designed to manage pain through the continuous release of hydrocodone over a 12 hour period. The abuse deterrent characteristics of Vantrela ER are invisible to the patient who needs pain relief but the technology incorporated into the product

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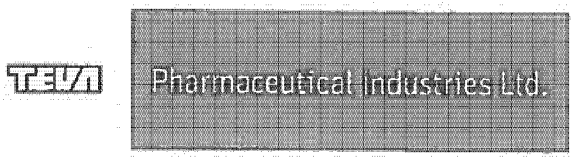

protects against both the intentional and unintentional rapid release of the opioid from the drug product. As evidenced by an extensive in vitro testing regimen and corresponding human PK and liking studies, Vantrela protects against dose dumping through the use of intentionally manipulated drug product via the most common routes of abuse; oral, nasal, and IV. In addition, human PK studies show that Vantrela ER's slow release profile does not change when administered with varying amounts of alcohol, or unintentional dose dumping.

For your review, we have provided a timeline of discussions between Teva and the FDA prior to, and after submission, of our NDA. In these conversations, our understanding is that the agency has been supplied with the necessary information to make a determination on safety, efficacy and the abuse-deterrent label. For your further review, we have provided specific data analysis to evaluate the correlation between our abuse deterrent studies and an abuse deterrent label.

Again, we are requesting a call with you to seek greater clarification from the agency regarding its decision to subject Vantrela ER to an Advisory Committee review. Teva is fully committed to working constructively with the agency to find a resolution and provide timely access to this product for patients who need it.

Thank you very much for your consideration and we look forward to hearing from you as soon as possible.

Sincerely,

Erez Vigodman
President and CEO
Teva Pharmaceutical Industries

Michael Hayden
President Global R&D and Chief Scientific Officer
Teva Pharmaceutical Industries

Enclosures

cc: Janet Woodcock, M.D.
Director, Center for Drug Evaluation and Research

Sharon Hertz, M.D.
Director, Division of Anesthesia, Analgesia, and Addiction Products, Office of New Drugs, Center for Drug Evaluation and Research

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