Lassman Law+Policy
FDA Regulatory Expertise

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May 23, 2019

VIA ELECTRONIC SUBMISSION

Division of Dockets Management
Department of Health and Human Services
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2019-P-1679; Supplementary Letter Supporting Braeburn's Citizen Petition

Dear Sir or Madam:

At the suggestion of Janet Maynard, M.D., M.H.S., Director of the Food and Drug Administration's Office of Orphan Product Development, and in accordance with 21 C.F.R. § 10.30(g), I am hereby submitting the attached May 20, 2019 letter from Braeburn, Inc. ("Braeburn") to Dr. Maynard in further support of Braeburn's April 5, 2019 Citizen Petition requesting that FDA revoke the orphan drug designation for Sublocade (buprenorphine extended-release) injection.

Thank you for your attention to this matter. Please do not hesitate to let me know if you have any questions.

Sincerely,

Scott M. Lassman
Counsel to Braeburn, Inc.

Attachment

ATTACHMENT

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May 20, 2019

DELIVERED VIA EMAIL

Janet Maynard, MD, MHS
Director
Office of Orphan Products Development
Food and Drug Administration
10903 New Hampshire Avenue
Bldg. 32, Rm. 5292
Silver Spring, MD 20993-0002

Re: NORD Corporate Council Presentation

Dear Dr. Maynard:

I am writing on behalf of Braeburn, Inc. to provide our perspective on the views you expressed about Orphan Drug Designation ("ODD") in your May 16, 2019 presentation at the National Organization for Rare Disorder's Corporate Council meeting. As you know, Braeburn has a keen interest in the FDA's interpretation and application of the Orphan Drug Act, particularly the ODD revocation provisions, because it recently submitted a Citizen Petition requesting that FDA revoke the ODD for Sublocade (buprenorphine extended-release) injection.

- FDA has legal authority to revoke an ODD where new or subsequent information would "invalidate" the original grant of ODD;

- FDA has previously confirmed its ability to revoke ODD where new information shows:

    - The size of the target population was larger than originally estimated (*e.g.*, papaverine, methylnaltrexone and lisinopril oral solution); or

    - The cost recovery justification for ODD was flawed or not supportable (*e.g.*, raloxifene).

We believe that Braeburn's request for ODD revocation for Sublocade is closely aligned to both FDA's statutory powers and the intent of the ODA, especially given the obvious facts that the cost recovery justification made 25 years ago was flawed, and that opioid addiction is clearly not a "bone fide" orphan disease. Thus, we hope that FDA will exercise its ***broad discretion*** under both the ODA and the regulations to revoke ODD for Sublocade.

In your presentation, you said that FDA generally does not revoke ODD when the circumstances of designation change after the fact. You also noted that FDA regulations say this explicitly when ODD is based on prevalence and the prevalence subsequently exceeds 200,000. We are concerned that FDA believes this limits the Agency's ability to consider *any* new information to support revocation. We also are concerned that FDA may view these limitations as

applying even where they are not "explicitly" stated in the regulations, such as when ODD is based on the cost recovery prong rather than the prevalence prong. We hope you will agree that FDA's discretion to revoke ODD is much broader than this.

Neither the statute nor FDA's regulations prohibit the Agency from considering new information to support a revocation decision. On the contrary, FDA's regulations (21 C.F.R. § 316.29(c)) explicitly state that if the Agency "subsequently finds" that a drug was not eligible for ODD at the time of the request, FDA has ample authority to revoke ODD. In most cases, this "subsequent finding" will, of necessity, be based upon *new information*.

Thus, while FDA may not be able to revoke ODD based solely upon changing circumstances (*i.e.*, growth in the relevant patient population beyond 200,000), the Agency retains broad discretion to revoke ODD if those changing circumstances indicate that the original decision itself was flawed. Indeed, it appears FDA did just this when it revoked ODD for a number of drugs, including papaverine, methylnaltrexone and lisinopril oral solution, based upon new information indicating that the potential target population could be significantly larger than originally assumed.

This is particularly the case when ODD is granted under the cost-recovery prong. In such situations, ODD is based almost entirely on *assumptions* about the future marketing and marketplace for the orphan drug. In the past, FDA has sought to ensure that these assumptions are not speculative and that they instead meet the threshold for presenting a "reasonably likely scenario." *See* ODD Review for Raloxifene (Evista), p. 13 (May 20, 2005). If new information demonstrates that the drug is highly profitable, this could indicate that the original assumptions were unreasonable at the time they were made, which would support revocation.

Indeed, in the Evista situation, FDA imposed ongoing reporting requirements on the sponsor – extending even after approval – to substantiate the reasonableness of the Agency's original assumptions regarding cost-recovery. Although FDA did not revoke Evista's ODD, the Agency indicated that if new information obtained after approval failed to substantiate the reasonableness of its original assumptions, FDA could use the new information to revoke ODD under its regulations.

There is thus clear Agency precedent supporting FDA's broad discretion to revoke ODD, particularly in the cost recovery area, whenever new information indicates that the Agency's original assumptions were unreasonable. This is exactly the situation raised in Braeburn's Citizen Petition.

In short, we think it is important to understand the breadth of the Agency's discretion to revoke ODD, particularly when necessary to respond to a public health crisis like the opioid epidemic. Beyond the legal aspects involved here, of course, there is an overwhelming public health need to increase the options available to treat opioid use disorder.

We appreciate your consideration of this view. If you have any questions, please do not hesitate to contact me.

Sincerely,

Scott M. Lassman
Counsel to Braeburn, Inc.