IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

FERRING PHARMACEUTICALS INC., Plaintiff, v. SYLVIA MATHEWS BURWELL, in her official capacity as SECRETARY, UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES, and STEPHEN OSTROFF, M.D., in his official capacity as ACTING COMMISSIONER OF FOOD AND DRUGS, FOOD AND DRUG ADMINISTRATION, Defendants.	Civil Action No. 1:15-cv-802 (RC) **ORAL HEARING REQUESTED**

MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT OF PLAINTIFF'S MOTION FOR RECONSIDERATION

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Dated: April 5, 2016

Pursuant to Rule 54(b), Ferring respectfully submits this motion for reconsideration for the limited purpose of addressing one aspect of this Court's March 15, 2016 Memorandum Opinion. Specifically, in finding that FDA's interpretation of the NCE exclusivity statute was not arbitrary and capricious, this Court stated: "*If there were, in fact, situations in which a drug was eligible for five-year exclusivity under the FDA's prevailing interpretation but failed to receive it because of the order in which it was approved, those circumstances might render the FDA's policy arbitrary and capricious*." Mem. Op. at 28.

Ferring respectfully points out that there were indeed drug products that were denied NCE exclusivity precisely because of the order in which they were approved. In fact, one such drug product was at issue in the very Citizen Petition Response challenged in this APA case. As noted in Ferring's original brief, FDA's February 2014 Citizen Petition Response denied NCE exclusivity to three drug products - Ferring's PREPOPIK, Gilead's STRIBILD, and Bayer's NATAZIA. A.R. 201-202. One of those drugs – STRIBILD – exemplifies the arbitrariness of FDA's NCE exclusivity policy.

STRIBILD contains four active ingredients: elvitegravir (EVG), cobicistat (COBI), emtricitabine (FTC), and tenofovir disoproxil fumarate (TDF). A.R. 201. The application for STRIBILD was submitted on October 26, 2011. A.R. 850. FDA approved STRIBILD on August 27, 2012. A.R. 201. At the time it approved STRIBILD, FDA had previously approved FTC and TDF in other drug products, but had never approved EVG, COBI or any salt, ester, or other form of these moieties in any other drug product. A.R. 201 FDA denied NCE exclusivity to STRIBILD based on its prior NCE exclusivity policy. A.R. 216. FDA subsequently approved

EVG and COBI on September 24, 2014.[1] Because those drug substances were approved *after* the fixed dose combination STRIBILD, they were also denied NCE exclusivity.[2] Had EVG and COBI been approved before STRIBILD, all three drugs would have been granted NCE exclusivity under FDA's own policies.[3]

Similarly, FDA approved GlaxoSmithKline's ANORO ELLIPTA (umeclidinium bromide; vilanterol trifenatate) on December 18, 2013.[4] At that time, FDA had not previously approved a drug product containing umeclidinium bromide (or any other form of the moiety umeclidinium). As with STRIBILD, FDA denied NCE exclusivity to ANORO ELLIPTA. *2016 Orange Book* at ADA 219-220 of 225 (showing three-year exclusivity for ANORO ELLIPTA). GlaxoSmithKline subsequently submitted an application for INCRUSE ELLIPTA, a single-entity version of umeclidinium bromide, on April 29, 2013.[5] Upon approval of INCRUSE

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[1] www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails; www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails. The application for EVG was submitted on June 27, 2012. A.R. 109. The application for COBI was submitted on June 28, 2012. *Id*.

[2] Approved Drug Products with Therapeutic Equivalence Evaluations, 36th ed. (2016) ("2016 Orange Book") at ADA 41 of 225 (showing three-year exclusivity award for TYBOST (cobicistat)), www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/UCM071436.pdf; *id*. at ADA 65 of 225 (showing three-year exclusivity award for VITEKTA (elvitegravir)).

[3] As a reminder, FDA's "umbrella policy" provided that if a single-entity drug product containing a new active ingredient is approved before a fixed-dose combination drug product containing the same active ingredient, both products—the single-entity and the combination—receive the benefit of the single-entity product's five-year NCE exclusivity. 54 Fed. Reg. 28872-01, 28897 (July 10, 1989). This is true even when the gap between approvals is measured not in years or months, but in hours. *Id.*

[4] Approval Letter for ANORO ELLIPTA, *available at* http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2013/203975Orig1s000ltr.pdf. The application for ANORO ELLIPTA was submitted on December 18, 2012. *Id*.

[5] Approval Letter for INCRUSE ELLIPTA, *available at* http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2014/205382Orig1s000ltr.pdf.

ELLIPTA in April 2014, FDA also denied this product NCE exclusivity. *Id*. at ADA 219 of 225 (showing no exclusivity for INCRUSE ELLIPTA). Had the order of approvals been reversed, INCRUSE ELLIPTA would have been awarded NCE exclusivity that would also have protected ANORO ELLIPTA.

A third example is Organon USA's NUVARING (ethinyl estradiol; etonogestrel). FDA approved NuvaRing in 2001.[6] Five years later, in July 2006, FDA approved one of NUVARING's active ingredients, etonogestrel, in the single-drug product NEXPLANON.[7] Because the single-entity product was approved after the fixed-dose combination, neither product benefited from NCE exclusivity.[8]

In contrast, Ferring's original motion for summary judgment gave several examples of drug products that were approved in the reverse order, including EDARBYCLOR, COMPLERA, and NESINA. *See* Ferring Mem. in Supp. of Mot. for Summ. J. 25-27. All three of those fixed-dose combination drug products contained both previously-approved active ingredients and at least one active ingredient that had recently been approved through an application by the same sponsor. *Id*. And for each of these drug products, FDA granted both the single-entity drug

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[6] Approval Letter for NUVARING, *available at* http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2001/21187ltr.pdf. The application for NUVARING was submitted on December 28, 1999. *Id.*

[7] Approval Letter for NEXPLANON, *available at* http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2006/021529s000_ltr.pdf. The application for NEXPLANON was submitted on September 30, 2003. *Id.*

[8] *See* Exclusivity Summary for NDA 21187 at 3 (denying NCE exclusivity to NUVARING because of prior ethinyl estradiol approvals), *available at* http://www.accessdata.fda.gov/drugsatfda_docs/nda/2001/21-187_NuvaRing_admindocs_P1.pdf (page 5 of 36 in linked document); Exclusivity Summary for NDA 21529 at 2-3 (denying NCE exclusivity to NEXPLANON because of prior NUVARING (etonogestrel) approval), *available at* http://www.accessdata.fda.gov/drugsatfda_docs/nda/2006/021529s000_AdminCorres.pdf (pages 14-15 of 140 in linked document).

product and the fixed-dose combination drug product NCE exclusivity. *Id.* If the order of the approvals had been reversed and the fixed-dose combination drug product had been approved just hours before the single-ingredient product, *none* of the products would have been awarded NCE exclusivity, because each would have contained a previously approved active ingredient.

This discrepancy is a direct result of FDA's original, flawed statutory interpretation of the NCE exclusivity provision, pursuant to which "a drug" meant "a drug product" rather than "a drug substance." FDA has provided no rational explanation for treating new chemical entities differently depending on whether they are first approved as part of a fixed-dose combination drug product or a single-entity drug product. Its NCE exclusivity policy therefore is arbitrary and capricious. *Bracco Diagnostics, Inc. v. Shalala,* 963 F. Supp. 20, 27-28 (D.D.C. 1997) ("Government is at its most arbitrary when it treats similarly situated people differently."). FDA's NCE exclusivity policy also is unreasonable under Chevron Step 2. *Amarin Pharms. Ireland Ltd. v. F.D.A.*, No. 14-cv-00324 (RDM), --- F. Supp. 3d ---, 2015 WL 3407061, at *17 (D.D.C. May 28, 2015) ("This analysis overlaps substantially with the APA's 'arbitrary and capricious' inquiry," because "[w]hether a statute is unreasonably interpreted is close analytically to the issue whether an agency's actions under a statute are unreasonable.").

Ferring respectfully requests the Court to review its initial decision on the basis of the foregoing issues.

Respectfully submitted,

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