IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

VELOXIS PHARMACEUTICALS, INC.,	)	
	)	
	)	
Plaintiff,	)	
	)	
-v.-	)	Civil Action No. 14-cv-2126 (RBW)
	)	
	)	
UNITED STATES FOOD AND DRUG ADMINISTRATION, *et al.*,	)	HEARING REQUESTED
	)	
	)	
Defendants.	)	

PLAINTIFF'S REPLY MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT OF ITS MOTION FOR SUMMARY JUDGMENT AND OPPOSITION TO DEFENDANTS' MOTION TO DISMISS, OR IN THE ALTERNATIVE, FOR SUMMARY JUDGMENT

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INTRODUCTION[1]

Plaintiff Veloxis Pharmaceuticals, Inc. ("Veloxis") established in its opening Memorandum in Support of Summary Judgment (the "Memo") that FDA's decision to deny full and final approval to Envarsus XR™, based upon the exclusivity granted to Astagraf XL®, was erroneous as a matter of law. Specifically, Veloxis established that:

- According to the unambiguous statutory language of the FDCA and Congress's clear intent – as confirmed by thirty years of FDA's own precedent – any exclusivity granted to Astagraf XL cannot block approval of Envarsus XR because the Envarsus XR NDA did not rely upon any of the studies or data supporting approval of Astagraf XL or upon FDA's prior findings that Astagraf XL is safe and effective.

- Under the plain language of the FDCA and FDA's own interpretation, the scope of Astagraf XL's exclusivity (if any) is limited to the scope of the "new clinical investigations" essential to its approval. Because Veloxis does not seek approval of Envarsus XR for the specific use studied in Astagraf XL's sole "new clinical investigation," Envarsus XR's full approval is not blocked by Astagraf XL's exclusivity.

- Under the FDCA, a later-in-time drug is blocked only to the extent it shares "conditions of approval" with a drug granted exclusivity. FDA arbitrarily and capriciously concluded that Envarsus XR and Astagraf XL share conditions of approval, ignoring the significant differences between the two drugs.

- Envarsus XR is entitled to immediate final approval because Astagraf XL never was eligible for statutory exclusivity. For drug products like Astagraf XL, exclusivity is available only if an application for approval was submitted to FDA *after* October 2008. Because the initial NDA for Astagraf XL was submitted in 2005, FDA's grant of exclusivity to Astagraf XL exceeded its statutory authority.

Nothing in FDA's Opposition provides a basis to alter these legal conclusions.

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[1] Capitalized terms used in this Reply Memorandum shall have the meaning set forth in Veloxis's opening Memorandum of Points and Authorities in Support of Plaintiff's Motion for Summary Judgment. As in Veloxis's opening Memorandum, Defendants are referred to herein collectively as "FDA."

Unable to rebut these arguments, FDA principally contends that its decision was the result of a reasoned, ordinary-course regulatory decision-making process, to which the Court should afford great deference. This argument misses the mark. First, because FDA's decision contravenes the plain language of the controlling statute and FDA's own regulations, it is not entitled to any judicial deference. Instead, the Court is required to correct FDA's legally erroneous decision by applying the FDCA as intended by Congress.

Second, FDA's assertion that the process it followed in reaching its decision on the Envarsus XR NDA was "ordinary" is remarkable in light of the administrative record in this case. Indeed, the process FDA pursued with respect to the Envarsus XR NDA stands in stark contrast to the principles of transparent and consistent administrative procedure:

- FDA communicated *ex parte* with Astellas, the sponsor of Astagraf XL, regarding the potential blocking impact of Astagraf XL's exclusivity on the Envarsus XR NDA months before reaching out to Veloxis on the same topic and without advising Veloxis of those *ex parte* communications, contrary to Section 505(q) of the FDCA.

- After years of communications with Veloxis regarding the Envarsus XR NDA and Veloxis's plans to pursue approval through a 505(b)(2) application referencing only Prograf – including regular, frequent interactions with the FDA review division during the ten months the Envarsus NDA was pending – FDA first raised the possible application of Astagraf XL's exclusivity with Veloxis on October 27, 2014, three days before Veloxis expected approval of Envarsus XR.

- On October 30, 2014 – despite not having made the threshold determination that Astagraf XL was entitled to any exclusivity – FDA issued its Tentative Approval decision concluding that Envarsus XR's immediate approval was blocked by Astagraf XL's exclusivity.

- FDA's October 30, 2014 decision – which unquestionably constituted "final agency action" based upon which Veloxis could have proceeded to seek judicial relief – also failed to identify the key facts purportedly supporting FDA's decision, including the studies for which Astagraf XL was entitled to exclusivity and the "conditions of approval" purportedly shared by Envarsus XR and Astagraf XL.

- When Veloxis sought clarification on these points and encouraged FDA to reconsider its erroneous decision in an effort to avoid litigation, FDA required Veloxis to frame its inquiry as a "Request for Final Approval" in order to support the legal fiction that FDA's October 30, 2014 decision did not constitute "final agency action."

- In response to Veloxis's inquiry, FDA recognized that the exclusivity granted to Astagraf XL could not block Envarsus XR's immediate approval in conversion kidney transplant patients because Astellas did not study Astagraf XL in that population. When FDA determined that there was no argument that could be advanced to preclude immediate final approval of Envarsus XR for use in the conversion population, it agreed to grant that approval only if Veloxis abandoned its request for full approval.

- Although FDA's Opposition appears to criticize Veloxis for not yet submitting conversion-only labeling, it is FDA that is withholding safe and effective therapy from conversion patients in an effort to avoid a decision from this Court regarding the broader legal implications of FDA's actions. To be clear, FDA appears to be taking the position that Veloxis must abandon this litigation in order to obtain final approval for an indication that FDA concedes is not subject to any claim of exclusivity.

- Even the issuance of FDA's January 12, 2015 "final" letter decision was not ordinary. When drafting that document, FDA already had been served with Veloxis's Complaint and Motion for Preliminary Injunction. In crafting its 53-page response (which is difficult to square with its three-page October 30, 2014 decision), FDA effectively staked out its litigation positions, supported by citations to case law and purported precedent for FDA's October decision. Accordingly, FDA's January 12, 2015 letter decision does not reflect routine agency action to which the Court must defer, but rather an *ex post* attempt to provide rationale for the erroneous legal positions previously adopted but not supported or explained.

In the end, neither FDA's January 12, 2015 letter decision nor its Opposition can obscure that FDA's failure to immediately and fully approve Envarsus XR is erroneous as a matter of law. Accordingly, the Court should find FDA's action to be "in excess of [its] statutory jurisdiction [or] authority," and "arbitrary, capricious, an abuse of discretion, or

otherwise not in accordance with law," 5 U.S.C. §§ 706(2)(A), (2)(C), and grant summary judgment in favor of Veloxis.[2]

ARGUMENT

I. FDA's Decision to Apply Astagraf XL's Exclusivity to Envarsus XR in the Absence of Reliance Is Inconsistent With Congressional Intent and FDA Precedent

A. The Language, Structure, and Purpose of the Hatch-Waxman Amendments All Require Reliance

Under the established two-step framework set out in *Chevron, U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837, 104 S. Ct. 2778 (1984), to determine whether FDA has acted in excess of its statutory authority, the Court must first consider "whether 'Congress has directly spoken to the precise question at issue.'" *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1067 (D.C. Cir. 1998) (quoting *Chevron*, 467 U.S. at 842, 104 S. Ct. at 2781). To do so, "[c]ourts use traditional tools of statutory construction . . . including an examination of the statute's text, structure, purpose, and legislative history." *Watson Labs., Inc. v. Sebelius*, No. 12-1344 (ABJ), 2012 WL 6968224, at *9 (D.D.C. Oct. 22, 2012) (citation omitted) (internal quotation marks omitted). As FDA acknowledges, if Congress's intent is clear from the statute's language, structure, purpose, and history, the agency decision is not entitled to any deference because "'the court, as well as the agency, must give effect to the unambiguously

[2] FDA has filed a Motion to Dismiss or, in the Alternative, for Summary Judgment. FDA's motion requires the Court to review matters outside the pleadings, and thus must be treated as one for summary judgment under Federal Rule of Civil Procedure 56. Fed. R. Civ. P. 12(d); *see also IMS, P.C. v. Alvarez*, 129 F.3d 618, 619 n.1 (D.C. Cir. 1997) (because the district court relied on materials outside the pleadings, including the administrative record, government motion to dismiss under Rule 12(b)(6) "must therefore be converted into a motion for summary judgment"); *Marshall Cty Health Care Auth. v. Shalala*, 988 F.2d 1221, 1226 n.5 (D.C. Cir 1993) (advising that, in agency review cases, "[i]t is probably the better practice for a district court always to convert to summary judgment"). In any event, for the reasons set forth below and in Veloxis's opening Memorandum, Veloxis – not FDA – is entitled to summary judgment.

expressed intent of Congress.'" *Mova Pharm.*, 140 F.3d at 1067 (quoting *Chevron*, 467 U.S. at 842-43, 104 S. Ct. at 2781).

Veloxis's Memo establishes that FDA's application of Astagraf XL's exclusivity to Envarsus XR is erroneous as a matter of law because the Envarsus XR NDA does not reference Astagraf XL as a listed drug, rely upon data supporting Astagraf XL's approval, or rely upon FDA's findings of safety and effectiveness for Astagraf XL. As established in the Memo, (i) the plain language of Section 505(c)(3)(E)(iii) of the FDCA provides that a 505(b)(2) application only will be blocked to the extent that it relies upon data from studies essential to the approval of a drug with exclusivity; and (ii) disregarding this reliance principle upends the statutory scheme established by Congress and essentially eliminates Section 505(b)(2) as a viable regulatory pathway. (*See* Memo at 18-24.)

In response to Veloxis's argument, FDA asserts that the statutory language – including the phrase "relied upon" – only is intended to distinguish 505(b)(1) applications (which are not blocked by exclusivity) from 505(b)(2) applications (which are blocked). (Opp'n at 31-34.) As an initial matter, FDA's interpretation of Section 505(c)(3)(E)(iii) is neither controlling nor sufficient to render the language "ambiguous" for purposes of the *Chevron* analysis. Rather, a court's "review of [an] agency's deviation from the statutory text will occur under the first step of the *Chevron* analysis, in which [the court does] not defer to the agency's interpretation of the statute." *Mova Pharm.*, 140 F.3d at 1068. Indeed, the Supreme Court, D.C. Circuit, and courts in this District have repeatedly rejected FDA interpretations of the FDCA in cases resolved at the first step of the *Chevron* analysis. *See, e.g., Teva Pharm. USA, Inc. v. Sebelius*, 595 F.3d 1303, 1318 (D.C. Cir. 2010) ("the interpretation of the statute that the FDA has adopted . . . fails at *Chevron* step one"); *Mova Pharm.*, 140 F.3d at 1069 ("we think that the

FDA's interpretation cannot survive analysis under the first step of *Chevron*."); *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 121-22, 120 S. Ct. 1291, 1294-95 (2000) (same); *Depomed, Inc. v. HHS*, --- F. Supp. 2d ---, No. 12-cv-1592 (KBJ), 2014 WL 4457225 (D.D.C. Sept. 5, 2014) (same).[3]

Nor is FDA's interpretation of Section 505(c)(3)(E)(iii) logical as a matter of textual interpretation. As Veloxis's Memo establishes, if Congress simply had intended to distinguish 505(b)(2) applications from 505(b)(1) full NDAs, it could have selected far more straightforward language. (Memo at 19-20.) Instead, Congress chose language that expressly ties (i) the clinical studies conducted to support approval of a drug with exclusivity, and (ii) the clinical studies "relied upon" by the applicant that would be blocked by exclusivity. *See* 21 U.S.C. § 355(c)(3)(E)(iii).

Although FDA charges Veloxis with attempting to "load" the phrase "relied upon" in the statute with "a meaning belied by the plain statutory text" (Opp'n at 33), FDA itself repeatedly has confirmed that three-year exclusivity is based upon the listed drug "relied upon" by the 505(b)(2) applicant.[4] Indeed, FDA's regulation implementing Section 505(c)(3)(E)(iii)

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[3] In contrast, the cases FDA cites in the full section it devotes to its plea for deference (Opp'n at 19-22) either do not involve *Chevron* review, were decided at *Chevron* step two, or involve applications of FDA regulations (as to which FDA's interpretation is controlling unless it is "plainly erroneous or inconsistent with the regulation," *Auer v. Robbins*, 519 U.S. 452, 461, 117 S. Ct. 905, 911 (1997) (citation omitted) (internal quotation marks omitted)).

[4] (*See* FDA 01771-1808 (Letter from J. Woodcock, CDER to K. Sanzo, Morgan Lewis & Bockius, LLP et al., at 5 (Oct. 14, 2003) (FDA Docket Nos. 2001-P-0323, 2002-P-0447, 2003-P-0408) ("[w]hile [the] five- and three-year *exclusivity* periods are in effect, FDA may not accept or approve certain applications that rely on the protected product for approval.") (second emphasis added)); FDA 01956-01966 (Letter from J. Woodcock to D. Clissold, Hyman, Phelps & McNamara P.C., at 4 (Sept. 18, 2003) (FDA Docket Nos. 2011-P-0869, 2013-P0995) ("[a] 505(b)(2) applicant is subject to applicable periods of marketing exclusivity granted to the listed drug relied upon . . . .") (emphasis added)).) *See also* *(cont'd)*

includes a reliance requirement. *See* 21 C.F.R. § 314.108(b)(4)(iv) (2014).[5] Earlier this month, FDA reiterated this position in its proposed regulations regarding the approval of 505(b)(2) applications and ANDAs. (*See* Memo at 19 n.8 (quoting Abbreviated New Drug Applications and 505(b)(2) Applications; Proposed Rule, 80 Fed. Reg. 6,802, 6,806 (Feb. 6, 2015) [hereinafter "ANDA & 505(b)(2) Proposed Rule"] ("The timing of approval for a 505(b)(2) application . . . is subject to the patent and marketing exclusivity protections accorded the listed drug(s) *relied upon* . . . .") (emphasis added).) Thus, FDA's own regulation and statements confirm that Veloxis's interpretation is consistent with the FDCA's plain language.

This is not surprising because – as Judge Jackson recently observed in *Takeda Pharmaceuticals U.S.A., Inc. v. Burwell* – "reliance matters" under the Hatch-Waxman statutory scheme. No. 14-cv-1668 (KBJ), 2015 WL 252806, at *24 (D.D.C. Jan. 13, 2015).[6] Indeed, in

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AstraZeneca Pharm. LP v. FDA, 850 F. Supp. 2d 230, 235 (D.D.C. 2012) (upholding FDA interpretation of related FDCA provision as requiring reliance).

[5] In its January 12, 2015 letter decision, FDA argues that the reliance requirement in FDA's regulation only applies to ANDAs submitted pursuant to a suitability petition (*i.e.*, ANDAs for new drugs that have a different active ingredient, route of administration, dosage form, or dosage strength from the listed drug, but for which FDA has determined new studies are not required to demonstrate safety and effectiveness, *see* 21 C.F.R. § 314.93 (2014)). (FDA 00041.) FDA's assertion is unfounded, as there is no statutory or other basis for treating ANDAs submitted pursuant to a suitability petition differently than either other ANDAs or 505(b)(2) applications. To the contrary, FDA has explained that for many drug products an applicant can submit either a 505(b)(2) application or ANDA pursuant to a suitability petition. *See* FDA, Guidance for Industry: Applications Covered by Section 505(b)(2), at 4 (Oct. 1999), *available at* www.fda.gov/downloads/drugs/guidancecomplianceregulatory information/guidances/ucm079345.pdf.

[6] FDA dismisses Judge Jackson's decision in *Takeda Pharmaceuticals* on the grounds that it deals with a different Hatch-Waxman Amendment provision (regarding patent certification), asserting that three-year exclusivity "has nothing to do with patents or patent certifications." (Opp'n at 33-34.) But a statute must be interpreted as a cohesive whole. *See Mova Pharm.*, 140 F.3d at 1067 ("[I]n expounding a statute, we must not be guided by a single sentence or member of a sentence, but look to the provisions of the whole law . . . .") (alteration in original). The patent certification provisions at issue in *Takeda Pharmaceuticals* were

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the absence of a reliance requirement, the *quid pro quo* arrangement designed by Congress – which balances expedited approval pathways with statutory exclusivity protecting innovators against follow-on products that rely upon their data – "is effectively undone." *Id.* at *25. The structure and purpose of the Hatch-Waxman Amendments thus compel reading Section 505(c)(3)(E)(iii), consistent with its plain language, to provide that a 505(b)(2) application is only blocked to the extent it relies upon data supporting approval of a drug with exclusivity.

FDA's Opposition makes no attempt to rebut Veloxis's arguments that FDA's decision is inconsistent with the structure and purpose of the Hatch-Waxman Amendments and will dramatically undercut the viability of the 505(b)(2) pathway. To the contrary, FDA appears to welcome the pathway's elimination, chiding Veloxis for "having submitted Envarsus as a 505(b)(2) application and not a 505(b)(1) NDA" (Opp'n at 32), and choosing "to take advantage of the [505(b)(2)] abbreviated process" (*id.* at 4). Yet Congress created the 505(b)(2) pathway for important public policy reasons: to streamline the approval of competing drug products, and

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enacted along with the exclusivity provision at issue in this case, as part of the Hatch-Waxman Amendments, and both are intended to encourage innovation in light of the abbreviated 505(b)(2) and ANDA pathways. In fact, the legislative history of the Hatch-Waxman Amendments indicates that exclusivity is intended to operate in tandem with the patent certification provision by providing protection to new products that have little or no patent life left when they are approved. *See* 130 Cong. Rec. S10504 (daily ed. Aug. 10, 1984) (statement of Sen. Hatch) (explaining that three-year "new clinical investigation" exclusivity "protects products whose development has taken much time and money in FDA testing and review, but which have little for [sic] no patent life left when they are finally allowed on the market"). For this reason, FDA often discusses "patent and marketing exclusivity protections" in the same breath, as it did in its recent proposed Hatch-Waxman regulations, *see* ANDA & 505(b)(2) Proposed Rule, 80 Fed. Reg. at 6,806 (Feb. 6, 2015 preamble to proposed rule), and January 12, 2015 letter decision (FDA 00023-24). As a result, the significance Judge Jackson places on reliance in the patent certification context is equally applicable in the exclusivity context. Indeed, the *Takeda Pharmaceuticals* decision – as well as FDA's many Citizen Petition decisions emphasizing reliance in the context of patent certification – strongly support Veloxis's position that both the structure and purpose of the Hatch-Waxman Amendments require reliance in the context of three-year exclusivity.

avoid wasteful non-clinical and clinical research that turns patients into guinea pigs and guinea pigs (and other animals) into mortality statistics only to prove what is already known about a drug. (*See* FDA 01771-1808 (Letter from J. Woodcock to K. Sanzo, at 14).) At the same time, Congress provided incentives for innovators to undertake costly and time consuming research, including offering exclusivity to protect against competition from those that would rely upon the innovators' data. FDA may not, through agency action, "change the incentive structure adopted by the Congress." *Ranbaxy Labs. Ltd. v. Leavitt*, 469 F.3d 120, 126 (D.C. Cir. 2006). Yet that is just what will happen in this instance if FDA's decision is allowed to stand.

Here, FDA's decision blocks Envarsus XR – an innovative drug product in which Veloxis invested more than $200 million and ten years of development – based upon exclusivity granted to a drug from which the Envarsus XR development program and NDA derived no benefit. At the same time, it offers Astellas, sponsor of both Prograf and Astagraf XL, an unearned windfall, shielding Astagraf XL from legitimate competition from Envarsus XR, a product that did not rely on its clinical studies or data for expedited approval. This outcome is plainly inconsistent with Congress's intent and is entitled to no deference. *See Mova Pharm.*, 140 F.3d at 1068 (explaining that an agency interpretation that conflicts with Congressional intent – as evidenced by the relevant statute's plain language, structure, and purpose – is entitled to no deference). Rather, the plain language, structure, and purpose of the Hatch-Waxman Amendments all confirm that Congress did not intend a 505(b)(2) application to be blocked by exclusivity granted to another drug product unless it relied upon the clinical data supporting that drug's approval.

FDA, however, maintains that, even if its reading of Section 505(c)(3)(E)(iii) does not comport with the plain language of the statute, the Court nevertheless should defer to FDA's

view as a "reasonable interpretation of the statute." (Opp'n at 38.) FDA's principal authority for its position is the preamble to its 1989 proposed rule. (*Id.*) But that preamble is inconsistent with the statutory language, structure, and purpose, and therefore must be rejected at *Chevron* step one. Moreover, as established in Veloxis's Memo, FDA's 1989 preamble to a proposed rule does not support FDA's plea for deference here. Rather, the position announced in the preamble has been superseded by (i) the preamble to FDA's final rule (Abbreviated New Drug Application Regulations; Patent and Exclusivity Provisions, 59 Fed. Reg. 50,338, 50,360 (Oct. 3, 1994) (explaining that 505(b)(2) applicants "who conduct their own studies to obtain approval" would be treated like 505(b)(1) applicants with respect to those studies, and that commenters who were concerned that a 505(b)(2) applicant would be blocked by exclusivity in such circumstances "misinterpret[ed] the scope of exclusivity")), (ii) numerous Citizen Petition responses and Federal Register notices since 1989 (*see supra* n.3 and ANDA & 505(b)(2) Proposed Rule, 80 Fed. Reg. at 6,806 (Feb. 6, 2015 preamble to proposed rule)), (iii) the precedent identified by Veloxis (*see* Memo at 24-29), and (iv) FDA's acknowledged failure to apply the position advanced in the 1989 preamble even once in the last twenty-five years (FDA 00047). "An agency interpretation of a relevant provision which conflicts with the agency's earlier interpretation is 'entitled to considerably less deference' than a consistently held agency view." *INS v. Cardoza-Fonseca*, 480 U.S. 421, 446 n.30, 107 S. Ct. 1207, 1221 n.30 (1987) (quoting *Watt v. Alaska*, 451 U.S. 259, 273, 101 S. Ct. 1673, 1681 (1981)).

In sum, because Envarsus XR NDA did not (i) reference Astagraf XL as a listed drug; (ii) rely upon any Astagraf XL studies or data; or (iii) rely upon FDA's findings of safety and effectiveness for Astagraf XL, as a matter of law, it cannot be blocked by any exclusivity afforded Astagraf XL.

B. FDA Precedent Similarly Requires Reliance

FDA itself admits that, in the thirty years since the Hatch-Waxman Amendments were enacted, it never has "refused to fully approve a 505(b)(2) application due to the 3-year exclusivity of another NDA on which the subsequent application did not rely." (FDA 00047.) As Veloxis's Memo explains, this agency precedent further serves to confirm that Section 505(c)(3)(E)(iii) is clear in providing that a 505(b)(2) application is only blocked where it relies upon data supporting approval of a drug with exclusivity. (Memo at 24-29.)

In response to Veloxis's examples of FDA precedent confirming this reliance requirement – Concerta®/Metadate CD® and Testim® 1%/Androgel® 1% – FDA criticizes Veloxis for being unable to identify a specific FDA document confirming that lack of reliance was the basis for approving the second-in-time applications. (Opp'n at 34, 36.) But FDA – which, unlike Veloxis, has complete access to the relevant documentation – likewise cannot identify any contemporaneous documentation supporting the position it now asserts (FDA 00049 n.204), instead offering only *post hoc* justifications.

With respect to Concerta and Metadate CD, FDA argues – as it did in its letter decision – that Concerta received exclusivity for its "specific [pharmacokinetic] profile." (Opp'n at 34-35.) But as Veloxis's Memo notes, the administrative record confirms that Concerta and Metadate CD had the same "innovative" pharmacokinetic characteristics: both were "intended to partly mimic immediate release administration by providing an initial bolus in the morning . . . and then providing ongoing coverage over the rest of the day." (FDA 02557.) Given that FDA's own records establish that the two drugs shared the same, new pharmacokinetic characteristics, pursuant to the position FDA asserts in this case, Concerta's exclusivity should have blocked Metadate CD's approval. The only plausible explanation for FDA's approval of Metadate CD during Concerta's exclusivity period is that Metadate CD did not rely upon Concerta for

approval. (*See* FDA 02516 (indicating that Metadate CD relied upon Ritalin® and Ritalin-SR, not Concerta).)

With respect to Testim and Androgel, FDA surmises that Testim was approved during Androgel's exclusivity period because the Testim NDA was considered a 505(b)(1) application. (Opp'n at 36.) But the Testim approval letter demonstrates that FDA's position is untenable. On the date FDA approved Testim, FDA considered the Testim NDA to be a 505(b)(2) application. (FDA 03231.) Even if FDA subsequently reclassified Testim as a 505(b)(1) NDA, it does not explain FDA's decision to approve the drug as a 505(b)(2) during Androgel's exclusivity period. Again, only the fact that the Testim NDA did not rely on Androgel data explains FDA's decision.

FDA also attempts to twist Veloxis's statement in its Memo that the purported "precedent" FDA points to in its letter decision does not "establish a clear FDA position on reliance." (Opp'n at 37.) This statement simply observed that even FDA's examples (which reflect internal agency discussions and not publicly available precedent) do not support FDA's current argument that reliance is not required. For example, publicly available documents regarding the Duoneb decision reveal that FDA indicated that a subsequent 505(b)(2) application would only be blocked if it relied on data supporting approval of a product with exclusivity. (Memo at 27 n.19.)[7] Contrary to FDA's suggestion, Veloxis's Memo establishes that FDA's

[7] FDA incorrectly suggests that Veloxis should not be permitted to rely upon this publicly available document because FDA did not include it in the administrative record it compiled in this case. (Opp'n at 34 n.16.) To the contrary, for the reasons set forth in Veloxis's concurrently filed Motion to Supplement the Administrative Record and statement of points and authorities in support thereof, the Duoneb meeting minutes Veloxis cites are properly included in the administrative record because they were either deliberately or negligently excluded and are adverse to FDA's decision in this matter. *See Styrene Info. and Research Ctr., Inc. v. Sebelius*, 851 F. Supp. 2d 57, 62-64 (D.D.C. 2012) (Walton, J.).

prior actions are consistent with the plain language of the FDCA, its structure and purpose, as well as past FDA statements establishing that reliance is required. Nor does any of the so-called "precedent" cited in FDA's letter decision establish a contrary principle. (Memo at 24-29.)

In the end, FDA admits, and Veloxis's research supports, that until now the agency has never blocked approval of a 505(b)(2) application that does not rely upon data from a drug with exclusivity. (FDA at 00047 ("A search of the Agency's records has not produced another instance where FDA refused to fully approve a 505(b)(2) application due to the 3-year exclusivity of another NDA on which the subsequent application did not rely.").) Equally telling, as FDA certainly would not contest, it consistently has delayed market entry in situations where a drug did rely on the data contained in an NDA with exclusivity. This unswerving course of agency action speaks volumes that cannot be erased by the contrary policy FDA seeks to advance in this case. Rather, FDA's actions confirm Congress's unambiguous intent that 505(b)(2) applications only will be blocked to the extent they "rely upon" data supporting approval of a drug with exclusivity.

II. Astagraf XL is Not Entitled to Exclusivity in *De Novo* Kidney Transplant Patients *With* Induction Because Astellas's Study 158 is Not a "New" Clinical Investigation

FDA's decision to block approval of Envarsus XR also is contrary to law because Veloxis is not seeking approval of Envarsus XR for any exclusivity-protected use. The plain language of the FDCA provides that Section 505(c)(3)(E)(iii) exclusivity may be based only upon "new clinical investigations." 21 U.S.C. § 355(c)(3)(E)(iii). FDA's implementing regulation confirms as much and defines a "[n]ew clinical investigation" as one "the results of which have not been relied on by FDA to demonstrate substantial evidence of effectiveness of a previously approved drug product." 21 C.F.R. § 314.108(a) (2014). Veloxis's Memo established that: (i) Astellas's Study 158 does not qualify as a "new clinical investigation" for

purposes of the Astagraf XL exclusivity determination because Astellas previously submitted the results of Study 158 in seeking an expansion of the Prograf label (Memo at 31-33), and FDA relied on those results in approving the label change; (ii) Astellas's Study 12-03 – the only study that defines Astagraf XL's "new clinical investigation" exclusivity – studied Astagraf XL only in *de novo* kidney transplant patients treated *without* induction (*id.* at 30, 33-34); and (iii) because Veloxis seeks approval of Envarsus XR in populations not studied in Study 12-03 – *de novo* patients treated *with* induction and conversion patients – Astagraf XL's exclusivity cannot block Envarsus XR's full and immediate approval (*id.*).[8]

In response, FDA concedes that it was aware that Study 158 had been submitted and reviewed in connection with the previous Prograf sNDA, but nevertheless deemed it a "new clinical investigation" for purposes of the Astagraf XL NDA. (Opp'n at 26.) FDA provides no viable explanation for its conclusory statement that Study 158 should be considered "new," asserting only that the fact that "FDA reviewed one arm of a study in conjunction with a different application is not dispositive." (Opp'n at 26.) This contention contravenes the plain language of the statute, FDA's implementing regulation, the scientific principles underlying clinical investigations, and the administrative record.

As Veloxis's opening Memo explains, the plain language of Section 505(c)(3)(E)(iii) addresses "new clinical investigations," not "study arms," and an investigation

[8] FDA also criticizes Veloxis for challenging Astagraf XL's exclusivity in this litigation when it did not do so in its November 14, 2014 submission to FDA. (Opp'n at 25.) FDA's criticism is unfounded, as Veloxis only learned the complete basis for FDA's decision, including which studies FDA believed constituted "new clinical investigations," via FDA's January 12, 2015 letter decision.

includes all its arms.[9] As a result, even if FDA had reviewed only one arm of Study 158, that "investigation" nevertheless could not be considered "new" under the statute or FDA's regulation.[10]

Moreover, both the administrative record and basic scientific principles undercut FDA's assertion that it relied on only one arm of Study 158 as part of the Prograf approval. The approved labeling for Prograf explicitly discusses both the Prograf and the Neoral (cyclosporine) arms of Study 158 (described as "Study 2"), the latter of which was used as the "control" arm. (FDA 00221.) Thus, contrary to FDA's claim, the administrative record – as it currently exists – establishes that FDA relied upon at least two arms of Study 158 when it approved the Prograf labeling. (*See also* FDA 02073 (Astagraf XL Exclusivity Request) (stating that Astellas submitted to FDA the "clinical study report for the 158 study (which included data from all three arms of the 158 study)" as part of the Prograf sNDA, and that the current Prograf label "includes 158 study efficacy and safety data" from "the Prograf and Neoral arms" of Study 158).)

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[9] An "arm," also known as a "treatment group," is a "group or subgroup of participants in a clinical trial that receives specific interventions, or no intervention, according to the study protocol." *See* U.S. Nat'l Insts. Of Health, Glossary of Common Site Terms, http://www.clinicaltrials.gov/ct2/about-studies/glossary (last visited Feb. 24, 2015). A clinical investigation typically contains two or more "arms" to compare various dosages of a particular drug and/or test the study drug against a placebo or active control (i.e., another drug intended for the same use). *See* 21 C.F.R. § 314.126 (2014).

[10] FDA's Exclusivity Summary for the Astagraf XL NDA states "[Study 158] . . . has three arms. One of the arms was used to support approval of another NDA." (FDA 01086.) This statement suggests that FDA recognized at the time that its reliance on Study 158 in approving the Prograf sNDA presented an issue for the Astagraf XL exclusivity determination. The Exclusivity Summary asks the reviewer to check "yes" or "no" to the question of whether the study supporting approval has "been relied on by the agency to demonstrate the effectiveness of a previously approved drug." (FDA 01086.) It also instructs the reviewer to check "no" if "the study was relied on only to support the safety of a previously approved drug. (*Id.*) In the case of Astagraf XL, the reviewer did not check either box. (*Id.*)

This makes sense given the basic scientific principles that undergird FDA's entire approval process. An analysis of a single arm of a study – without reference to at least one concurrent control arm – is scientifically flawed (and FDA certainly would not ignore an existing control arm). Indeed, analysis of a single arm of a study does not meet FDA's definition of an "adequate and well-controlled" study required to support a drug approval. *See* 21 C.F.R. § 314.126(b)(2) (2014) ("An adequate and well-controlled study has the following characteristics . . . [t]he study uses a design that permits a valid comparison with a control to provide a quantitative assessment of drug effect.").

As a matter of fact, however, the publicly available Prograf sNDA review package confirms that FDA reviewed the data from all three arms of Study 158 in connection with its approval. (*See, e.g.*, Prograf sNDA Statistical Review, at 14 ("One year efficacy failure (first occurrence of BCAR, graft loss, death or loss to follow-up) was **14%** (30/214), **15.1%** (32/212) and **17.0%** (36/212) in **[Astagraf XL]/MMF**, **Prograf/MMF** and **Neoral/MMF** groups.") (emphasis in original) (Ettinger Decl. Ex. 6).)[11] This is not surprising in that good scientific practice requires consideration of all arms of a single investigation. FDA did just that in reviewing Study 158 in connection with the Prograf sNDA; it may not now attempt to side-step the requirements of the FDCA by contending that it relied on only a portion of Study 158, rendering the study "new" for other purposes.

[11] By separate motion filed concurrently herewith, Veloxis has requested that the Court direct FDA to supplement the administrative record to include the Prograf sNDA Statistical Review. Tellingly, FDA has refused to include in the administrative record this publicly available record, which clearly was before the agency when it determined that Study 158 was "new" for purposes of the Astagraf XL exclusivity determination. As set forth in the accompanying motion, the full record – not a skewed version that "exclude[s] pertinent but unfavorable information" – should be available to the court when considering a challenge under the APA. *Am. Wild Horse Pres. Campaign v. Salazar*, 859 F. Supp. 2d 33, 41 (D.D.C. 2012) (quoting *Fund for Animals v. Williams*, 391 F. Supp. 2d 191, 197 (D.D.C. 2005)).

Contrary to FDA's suggestion, the agency's judgment that Study 158 was "new," is entitled to no deference. Under *Auer v. Robbins*, FDA's interpretation of its own regulation does not control if it is "plainly erroneous or inconsistent with the regulation." 519 U.S. 452, 461, 117 S. Ct. 905, 911 (1997) (citations omitted) (internal quotation marks omitted). That is precisely the case here. Simply put, it is irrelevant whether FDA determined Study 158 qualified as a "new" clinical investigation when it granted exclusivity to Astagraf XL. Under the plain language of the FDCA and FDA's regulation, the study was not "new" because it had been previously relied upon by FDA to demonstrate the efficacy of Prograf. *See* 21 C.F.R. § 314.108(a); (Memo at 31-33). Accordingly, FDA's interpretation is both "plainly erroneous" and "inconsistent with the regulation." *Auer*, 519 U.S. at 461, 117 S. Ct. at 911 (citations omitted) (internal quotation marks omitted).

In addition to failing to establish that Study 158 was "new" for purposes of the Astagraf XL NDA, FDA also fails to respond substantively to Veloxis's argument that the scope of Study 12-03 – the only "new clinical investigation" for which Astagraf XL may receive exclusivity – does not overlap with the uses for which Veloxis seeks approval of Envarsus XR. Instead, FDA attempts to obscure the issue by casting it as a scientific determination made by the agency, which it is not. The clinical trials that, as a matter of law, define the scope of Astagraf XL's exclusivity simply do not cover the patient populations for which Envarsus XR seeks approval. A review of the current Astagraf XL label and proposed Envarsus XR label makes clear – based upon FDA's own scientific analysis – that Envarsus XR's proposed uses are not encompassed in Study 12-03's scope. In the Astagraf XL label, FDA describes Study 12-03 (which it calls "Study 2") with the header "No Induction," and indicates that all of the patients in Study 12-03 were *de novo* kidney transplant patients who received Astagraf XL *without*

induction. (*See* FDA 00346-47 (Clinical Studies discussion).) The approved label also includes separate dosing instructions for using Astagraf XL *without* induction at the doses studied in Study 12-03. (FDA 00321.)[12] In contrast, the proposed Envarsus XL label does not include any instructions for dosing Envarsus XR in *de novo* patients *without* induction. (FDA 01547.) This is because, as evidenced by the Dosage and Administration information in its label, Veloxis only seeks approval in (i) *de novo* patients *with* induction, and (ii) conversion patients. (*Id.*)

As FDA repeatedly asserts in its letter decision and Opposition, FDA "interprets the scope of exclusivity to be related to the scope of the underlying 'new clinical investigations' that were essential to the approval." (Opp'n at 5; FDA 00026.) The FDCA and FDA's implementing regulation clearly define a "new clinical investigation," and it is well within the province of the Court to apply this plain language to the undisputed facts regarding Astellas's clinical trials.[13] In sum, because (i) Study 158 is not a "new" clinical investigation, and (ii) the scope of Study 12-03 does not overlap with the uses for which Veloxis seeks approval of Envarsus XR, Envarsus XR must be approved fully and immediately.

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[12] By contrast, Study 158 is described in the approved Astagraf XL labeling with the header "Study 1 – Induction with Basiliximab" (an antibody drug commonly used for induction) (FDA 00346), and the approved labeling includes separate dosing instructions for *de novo* kidney transplant patients *with* induction that are consistent with the doses used in Study 158 (FDA 00321).

[13] To be clear, Veloxis is not asking this Court to substitute its views of Astellas's scientific studies for those of FDA. Instead, Veloxis only asks the Court to apply FDA's own findings regarding the scope of those studies to define the scope of exclusivity in this case. This is a matter that requires legal – not scientific – judgment, and not one for which FDA is entitled to any deference.

III. FDA's *Post Hoc* Determination of Relevant Conditions of Approval is Arbitrary and Capricious

FDA does not dispute that Envarsus XR and Astagraf XL differ in pharmacokinetic profile, dosage form, dosage strength, and dosing regimen. (*See* Memo at 36-40.) Nevertheless, FDA's letter decision concludes that Envarsus XR is blocked by Astagraf XL's approval because the drugs share a once-daily, extended-release formulation of tacrolimus. (FDA 00019, FDA 00036, Opp'n at 28.) As set forth in Veloxis's opening Memo, this decision is arbitrary and capricious.

Rather than address Veloxis's contentions head-on, FDA instead mischaracterizes Veloxis's argument, incorrectly suggesting that Veloxis asserts "that only drugs that share *all* 'approval characteristics' can be blocked by the three-year exclusivity of a previously-approved drug." (Opp'n at 29.) This is not Veloxis's contention. Rather, Veloxis argues that, in light of the myriad differences between Envarsus XR and Astagraf XL, FDA's decision that the only relevant "conditions of approval" are once-daily extended-release dosing is arbitrary and capricious.

Indeed, FDA's Opposition further confirms the *ad hoc* nature of FDA's selection of relevant conditions of approval. In particular, in discussing the Concerta/Metadate CD precedent, FDA asserts that Concerta was granted narrow exclusivity "limited solely to its unique [pharmacokinetic] profile" and that, as a result, that pharmacokinetic profile was the only relevant "condition of approval" determining whether Metadate CD was blocked by Concerta's exclusivity. (Opp'n at 35.) FDA thus ignores the fact that Concerta and Metadate CD shared general pharmacokinetic characteristics including an immediate-release characteristic combined with a more extended-release pattern. (FDA 02557.) In contrast, when discussing Envarsus XR and Astagraf XL, FDA focuses only on general characteristics, such as their "extended-release"

nature. FDA refuses to extend the logic it now claims applied to Concerta and Metadate CD, asserting that "[e]ven if Envarsus were to have a different 'condition of approval' from Astagraf based on a difference in its [pharmacokinetic] profile" (as it clearly does, *see* Memo at 36-37), Envarsus XR would be blocked by Astagraf XL's exclusivity because that exclusivity is "not as narrow as Concerta's." (Opp'n at 35.)

FDA's Opposition also disingenuously suggests that the relevant "conditions of approval" can be easily discerned by assessing the "innovative change" for which the new clinical investigations supporting exclusivity were required. (Opp'n at 29-30.) Yet as this case demonstrates, it is far from so simple. At the time that FDA grants three-year exclusivity, FDA determines only that a drug is entitled to exclusivity based upon "new clinical investigations." FDA does not determine the scope of exclusivity at that time; rather, it does so only in the context of assessing the potential impact of that exclusivity on another drug's approval.[14] Most importantly, FDA does not make public the precise scope of a drug's exclusivity, and has indicated that its Orange Book exclusivity description cannot be trusted. (FDA 00043.) Accordingly, when Veloxis developed Envarsus XR, discussed and pursued its approval pathway with FDA, Veloxis had no means of knowing whether Astagraf XL would be approved, whether it would be granted exclusivity, or the scope of any such exclusivity. Indeed, the administrative record demonstrates that FDA did not even attempt to determine the scope of Astagraf XL's exclusivity until it was requested to do so by Astellas in connection with its *ex parte* communications with FDA. Astellas obviously understood from public pronouncements that the

[14] (*See* FDA 02034-60 (Letter from J. Woodcock to G. Veron, Sidley Austin, LLP, at 23 (May 25, 2011) (Docket No. FDA-2010-P-0614) ("FDA determines the effect of 3-year exclusivity on a subsequent 505(b)(2) application or ANDA at such time as the application is otherwise ready for approval.").)

Envarsus XR NDA was nearing its approval date. Then, three days before its final decision was due, FDA raised the issue for the first time with Veloxis. Veloxis, which did not rely on Astagraf XL in any way, was stunned to learn that FDA was even considering the issue.[15]

FDA's action in this case has important consequences for drug development generally. As Veloxis's experience demonstrates, if reliance is not required for exclusivity to apply, drug developers will be unable to pursue approval via the 505(b)(2) pathway because they will have no way of knowing, until the eleventh hour, whether their product will be blocked by exclusivity. For example, imagine that a drug developer was planning to submit a 505(b)(2) application for a hypothetical once-a-day, extended-release inhaled tacrolimus product. Even with the benefit of FDA's lengthy letter decision purporting to expound its policy regarding the scope of exclusivity, that developer would have no way of knowing whether the product would be blocked by Astagraf XL's exclusivity. Indeed, a rational developer likely would seek to avoid the situation altogether by submitting a 505(b)(1) NDA, even if doing so meant conducting unnecessary and duplicative testing. Perhaps FDA is content with this level of uncertainty regarding the 505(b)(2) pathway (given its criticism of Veloxis's reliance upon it), but it was not what Congress intended when it designed the Hatch-Waxman Amendments.

IV. Astagraf XL Never Was Entitled to Exclusivity Under Section 505(v)

Veloxis's opening Memo also establishes that Envarsus XR's approval cannot be blocked by Astagraf XL because Astagraf XL was not entitled to exclusivity under Section 505(v) of the FDCA given that tacrolimus is an old antibiotic and the Astagraf XL NDA was

[15] Veloxis promptly replied to FDA's last-minute October 27, 2014 request for Veloxis's view of the impact of Astagraf XL's exclusivity on Envarsus XR. (*See* FDA 00019.) Although FDA claims to have considered Veloxis's submission, there is no evidence in the administrative record reflecting such consideration before FDA issued its October 30, 2014 tentative approval decision.

pending prior to October 8, 2008. (Memo at 40-43.) In response to Veloxis's argument, FDA maintains that Astagraf XL was entitled to exclusivity under the plain language of Section 505(v) because Astellas resubmitted its NDA after October 8, 2008. (Opp'n at 23.) This "plain language" argument, however, ignores the structure, purpose, and history of the relevant statutory language. *See e.g.*, *Ranbaxy Labs.*, 469 F.3d at 124-26 (rejecting FDA "plain language" argument at *Chevron* step one due to inconsistency with statutory purpose and structure); *Teva Pharm.*, 595 F.3d at 1315-17 (same).

The history, purpose, and structure of the QI Act make clear that Astagraf XL is not entitled to exclusivity under Section 505(v). In 1997, Congress amended the FDCA, via FDAMA, to provide that antibiotics would henceforth be approved under Section 505 rather than Section 507. In doing so, Congress explicitly provided that three-year exclusivity would not apply to applications for drug products containing "old antibiotics" (those that were the subject of an approved or pending application prior to FDAMA's enactment). FDAMA §§ 125(d)(1), (d)(2). In 2008, when Congress decided to extend exclusivity to certain NDAs containing old antibiotics, it used the same framework in the QI Act that it used in FDAMA, distinguishing between approved and pending applications, on the one hand, and new applications on the other. 21 U.S.C. §§ 355(v)(1)(B)(i), (v)(3)(B). Indeed, as FDA's Opposition notes, Congress explicitly referred to FDAMA's distinction in Section 505(v)(2), 21 U.S.C. § 355(v)(2). (Opp'n at 23.)

FDA, however, takes the wrong lesson from this reference, arguing that Congress could have used similar language to restrict exclusivity under the QI Act but did not. (Opp'n at 23.) The differences in the language Congress chose to use make perfect sense when one considers Congress's differing purposes in FDAMA and the QI Act. The QI Act granted exclusivity that did not previously exist, whereas FDAMA withdrew exclusivity that otherwise

would apply. As a result, the QI Act specifically identifies those applications that will qualify for the new exclusivity, *i.e.*, new applications, rather than the applications that will not qualify, *i.e.*, pending or approved applications. Congress's grant of exclusivity to new applications submitted after the enactment date thus reflects that applications pending or approved prior to that date – like the Astagraf XL NDA – are not eligible for exclusivity.

This interpretation is supported by the clear legislative history indicating that Congress intended to extend exclusivity only to new and innovative drug products via the QI Act. *See* 154 Cong. Rec. H10171 (daily ed. Sept. 27, 2008) (statement of Rep. Pallone) (indicting that Congress wanted to "encourage and incentivize drug manufacturers to research and develop . . . . new and innovative antibiotic therapies"); 153 Cong. Rec. S5823 (daily ed. May 9, 2007) (statement of Sen. Kennedy) (indicating that Congress wanted to spur development of new antibiotics while "prevent[ing] pharmaceutical manufacturers from abusing the [exclusivity] process to extend the life of old active ingredient drugs"). Because Astagraf XL already was subject to an NDA that was pending at FDA on the date the QI Act was enacted, affording it exclusivity would be inconsistent with Congress's intent.[16] FDA's decision therefore fails at *Chevron* step one.

FDA also argues that the NDA Astellas resubmitted in 2012 is entitled to exclusivity because it included new analyses and perhaps new studies. (Opp'n at 23.) But FDA does not dispute that the two studies upon which Astagraf XL's exclusivity purportedly is based – Studies 158 and 12-03 – were conducted, and were submitted to or requested by FDA, prior to

[16] FDA asserts that Veloxis's position would discourage sponsors from submitting NDAs for antibiotic drug products that were the subject of a previously withdrawn NDA. (Opp'n at 24.) This is a red herring. Veloxis does not argue that Astagraf XL was not entitled to exclusivity because its NDA was withdrawn and resubmitted, but rather because it was pending – and therefore not subject to exclusivity – on the date of the QI Act's enactment.

2008. Moreover, the submission of new data is not a valid indicator of whether an application is new; rather, it is commonplace for applicants to submit new analyses, or even new studies, during various review cycles of the same NDA without withdrawing and resubmitting the NDA.[17] In this case, Astellas was not required to submit a new NDA as a condition to submitting new information to support the approval of Astagraf XL. *See* 21 C.F.R. § 314.110(b) (2014). If Astellas had addressed the deficiencies without withdrawing and submitting a purportedly "new" NDA, there is no question that it would not be entitled to exclusivity under the QI Act. This fact should be dispositive, as FDA has provided no cogent explanation why Congress would make exclusivity hinge on a meaningless administrative maneuver that is wholly within the control of the applicant. *See Teva Pharm.*, 595 F.3d at 1317-18 (rejecting argument that availability of 180-day exclusivity hinged on action within the sole control of a drug company, as this was subject to manipulation and inconsistent with the goals of the Hatch-Waxman Amendments).

V. The Court May Grant The Relief Veloxis Seeks

Finally, Veloxis's Complaint seeks a declaration from the Court that FDA's failure to immediately and fully approve Envarsus XR is in excess of its statutory authority, as well as arbitrary and capricious. Veloxis also seeks injunctive relief in the form of an order

[17] Indeed, documents contained in the administrative record confirm that withdrawal is not required. In particular, the sponsor of Fortesta® was informed by FDA in 2003 that the drug was not approvable based upon the filed NDA. Instead of withdrawing the NDA and submitting a new one, the sponsor followed FDA regulations and resubmitted the same application in 2009 with new information (including a new Phase III clinical trial) seeking to address the identified deficiencies. (*See* FDA 04244-45, FDA 04311, FDA 04317-18, FDA 04955.) Similarly, the sponsor of Androgel® 1.62% was informed that in 2010 it could not be approved based upon the filed NDA. Again, instead of withdrawing the NDA and submitting a new one, the applicant resubmitted the same application in 2010 with new information (including data from two new studies) seeking to address the identified deficiencies. (*See* FDA 05046.)

requiring FDA to immediately and fully approve Envarsus XR. (Compl., Counts I-III and Prayer for Relief.) FDA's Opposition asserts that the Court cannot issue injunctive relief because Veloxis does not address the factors needed to support such relief in its motion for summary judgment. (Opp'n at 38-39.) The Court certainly can do so.

As an initial matter, the record in this case is replete with evidence of the harm that Veloxis and kidney transplant patients have suffered and continue to suffer as a result of FDA's legally erroneous decision. (*See* FDA 01592-1622 (slides presented by Veloxis at Nov. 6, 2014 meeting with FDA); FDA 01626-43 (Veloxis Nov. 14, 2014 submission to FDA), FDA 01644 (Statement of T. Saffer, Nat'l Kidney Found.); FDA 01645-77 (Decl. of Roy M. Bloom, MD); FDA 01751-58 (Veloxis Dec. 8, 2014 submission to FDA and Decl. of Anthony Langone, MD).) And, to the extent FDA argues that Veloxis has not established a likelihood of success on the merits, its opening Memo and this Reply Memo do just that.

Veloxis's motion and Memo more than sufficiently establish that relief is appropriate under the APA, which requires the court to "set aside" agency action that is in excess of statutory jurisdiction or authority, arbitrary, capricious, an abuse of discretion, or not in accordance with law, and also permits the court to "compel agency action unlawfully withheld." 5 U.S.C. § 706(1). This relief can be granted without an analysis of irreparable injury or the balance of equities. Indeed, courts in this District have done just what Veloxis asks this Court to do: grant injunctive relief – in the form of an order requiring FDA to approve a drug – on a motion for summary judgment where a prior motion for preliminary injunction has been denied without prejudice. *See, e.g.*, *Watson Labs.*, 2012 WL 6968224; *see also Pharm. Research & Mfrs. of Am. v. HHS*, No. 13-1501, 2014 WL 2171089 (D.D.C. May 23, 2014) (granting motion

for summary judgment and issuing injunctive relief where motion for summary judgment did not address factors supporting injunctive relief).

In any event, FDA argues a distinction without a difference. As a practical matter, whether the Court grants injunctive relief or grants summary judgment in favor of Veloxis and requires agency action consistent with that judgment, Veloxis cannot legally market Envarsus XR until FDA issues a letter approving the Envarsus XR NDA. *See* 21 U.S.C. § 331(d) (prohibiting introduction or distribution in commerce of a new drug not approved pursuant to Section 505 of the FDCA); (*see also* FDA 00002 (stating that until FDA issues a final approval letter for the Envarsus XR NDA, "this NDA is not approved")). Veloxis's motion for summary judgment and supporting Memo establish that FDA erred as a matter of law when it concluded that (i) Astagraf XL's exclusivity may block Envarsus XR in the absence of reliance, (ii) the scope of Astagraf XL's exclusivity based upon its "new clinical studies" blocks approval of Envarsus XR, (iii) Envarsus XR and Astagraf XL share "conditions of approval" precluding Envarsus XR's approval, and (iv) Astagraf XL was entitled to exclusivity under Section 505(v). In the event the Court grants summary judgment in favor of Veloxis on any of these independent grounds, it certainly may remand the matter to FDA for action consistent with the grant of summary judgment. At that point, FDA will have no choice but to issue the full and final approval of Envarsus XR to which Veloxis is entitled as a matter of law.

CONCLUSION

For the reasons set forth above and in Veloxis's opening Memo, Veloxis respectfully requests that the Court grant summary judgment in favor of Veloxis and grant the relief set forth in Veloxis's Complaint for Declaratory and Injunctive Relief. Veloxis further requests that, in the interest of speeding the resolution of this expedited matter, the Court issue an order resolving this matter as soon as it is prepared to do so, including in advance of issuing a formal memorandum opinion.

Dated: February 24, 2015

Respectfully submitted,
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CERTIFICATE OF SERVICE

I hereby certify that on February 24, 2015, I caused a true and correct copy of the above-entitled Plaintiff's Reply Memorandum of Points and Authorities in Support of Its Motion for Summary Judgment and Opposition to Defendants' Motion to Dismiss, or in the Alternative, for Summary Judgment, to be served via first-class mail and electronic mail to:

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