IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

AMARIN PHARMA, INC., DR. JONATHAN HERBST, DR. ERIC RISHE, DR. PETER GOTTESFELD, and DR. RALPH YUNG, Plaintiffs, v. UNITED STATES FOOD & DRUG ADMINISTRATION 10903 New Hampshire Avenue Silver Spring, Maryland 20993, UNITED STATES OF AMERICA Serve to: U.S. Attorney General 950 Pennsylvania Avenue NW Washington, DC 20530, STEPHEN OSTROFF, M.D., in his official capacity as Acting Commissioner of Food and Drugs 10903 New Hampshire Avenue Silver Spring, Maryland 20933, and SYLVIA MATHEWS BURWELL, in her official capacity as Secretary of the Department of Health & Human Services 200 Independence Avenue SW Washington, DC 20201, Defendants.	)	Civil Action No. 1:15-cv-03588-PAE Oral Argument Requested

REPLY MEMORANDUM OF LAW IN SUPPORT OF MOTION FOR PRELIMINARY INJUNCTION

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PRELIMINARY STATEMENT

The approach taken by FDA in this case will be familiar to students of its prior behavior. It has long been standard operating procedure for FDA to seek to escape from First Amendment-centered judicial review of its regulations. As Professor Rodney Smolla put it in his recent assessment of the very body of law that is at issue in this case, "the government appears to employ a deliberate strategy to avoid making law in this area, using its coercive power to force settlements or its interpretive power to deftly alter regulatory positions so as to avoid a frontal First Amendment assault on its position." Rodney A. Smolla, *Off-Label Drug Advertising and the First Amendment*, 50 Wake Forest L. Rev. 81, 84-85 (Spring 2015).[1]

In this case, however, FDA's efforts have been anything but deft. FDA is simply wrong that almost nothing remains at issue in the case except Amarin's desire to state, without risk of criminal prosecution, that "supportive but not conclusive research shows that EPA and DHA may reduce the risk of coronary heart disease"—the very language that FDA acknowledges would *not* be false or misleading if Amarin were to "repackage and relabel [its] product as a dietary supplement." June 5th Ltr. ("Ltr.") 10, 12; *see also* Opp'n 9, 15. That certainly is at issue (*see* § II.c, *infra*) but so is far more.

The Complaint seeks a declaration that "Amarin has a First Amendment right to engage in truthful and non-misleading speech about Vascepa®,[2] even if that speech is off-label

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[1] For example, in a case before the United States Court of Appeals for the D.C. Circuit, the "stage . . . appeared set for [the court] to consider a difficult constitutional question of considerable practical importance"—whether FDA could limit off-label speech by drug companies—until the government at oral argument made that question "disappear before [the court's] eyes" by conceding that the challenged provisions did not vest FDA with such authority. *Washington Legal Found.* v. *Henney*, 202 F.3d 331, 335 (D.C. Cir. 2000). Other examples of FDA's strategic efforts in this vein are referenced at pages 18-19 of the amicus curiae brief filed on behalf of Pharmaceutical Research and Manufacturers of America (Dkt. 48).

[2] Vascepa® has a safety profile comparable to that of a placebo and is acknowledged by FDA to

promotion" and a preliminary injunction enjoining the defendants from taking any legal action against Amarin for its "proposed off-label promotion of Vascepa®." Compl. ¶ 17; Prayer for Relief § C. The Complaint states that Amarin "now finds itself unable to engage in a full and truthful dialogue with healthcare professionals about the success of the ANCHOR trial and the effectiveness of Vascepa® . . ." *Id.* ¶ 93. It asserts that "FDA's effective all-out ban on any discussion initiated by Amarin of off-label use of Vascepa® prevents doctors from receiving essential information." *Id.* ¶ 98. Doctor Plaintiffs assert that they wish to engage in a "full and frank" and "full and free" dialogue with Amarin about off-label use of Vascepa®. Gottesfeld Decl. ¶ 8; Rishe Decl. ¶ 10; Herbst Decl. ¶ 8; Yung Decl. ¶ 9.[3] And the Complaint states—in the most straightforward manner—that Amarin not only wishes to communicate with healthcare professionals "through written materials and digital media about its product" but also to "proactively engag[e] in a dialogue with doctors and other healthcare professionals about Vascepa®" in a truthful and non-misleading manner. Compl. ¶ 126; Ketchum Decl. ¶ 166; Ketchum Reply Decl. ¶¶ 37-38, 42.

Nothing in FDA's June 5 letter to Amarin or in its brief to this Court recognizes the company's First Amendment right to do or say any of these things. The letter contemplates no such dialogues or discussions at all, but only academic presentations in what FDA refers to as

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significantly reduce triglycerides in patients with persistently high triglycerides, among other favorable effects. Ketchum Decl. Exs. 3, 4, 9. The emphasis by Dr. Woodcock in her Declaration (*see* ¶¶ 10, 14, 15, 34, 46) and by Public Citizen in its amicus brief (*see* pp. 3, 11, 16, 17) on safety issues is of no moment in this as-applied challenge since FDA itself has emphasized in its June 5 letter that the favorable "safety profile" of Vascepa® was one of the factors that had led it not to object to certain of Amarin's proposed communications. Ltr. 6. Another factor cited was "Amarin's commitment to complete the REDUCE-IT trial" (*id.*) a commitment it has explicitly reaffirmed in the Ketchum Reply Declaration, ¶ 7, filed simultaneously with this submission.

[3] The government incorrectly asserts that "Amarin raises only an as-applied challenge regarding communications with health care providers, not payors." *Id.* But payors are referred to in the Complaint as "managed care professionals," Compl. ¶ 122, and Amarin's claims apply to these potential recipients of Amarin's proposed speech as well.

"educational or scientific settings." Ltr. 7. Neither FDA's letter nor its brief acknowledges the right of Amarin's representatives to seek to *promote* Vascepa®, truthfully and in a non-misleading manner, to doctors in their offices. In fact, it is now clear (if there were any previous doubt about it) that such activities could subject Amarin to significant risk of criminal prosecution. FDA's brief to this Court is unambiguous that any dissemination of "the reprints and summaries about unapproved uses in a manner not described in the June 5 letter" may be considered by FDA "as evidence of intended use," and thus potentially criminal. Opp'n 9. And FDA asserts that only if the "journal reprints and summaries of the ANCHOR trial results" are disseminated in the particular manner set forth in its June 5 letter—which says not a word about *dialogue* or *discussions*, let alone meetings in which Amarin sales representatives proactively discuss Vascepa®—would Amarin be free of significant risk. *Id*.; Ltr. 6-8; Ketchum Reply Decl. ¶¶ 37-38, 42.

On the merits, the government's refusal to accept the lessons of *Caronia* and cases relied on in that ruling leads it to refight old, lost battles. The government again asserts, as it did in *Caronia*, that Plaintiffs' as-applied challenge would "establish precedent that would return the country to the pre-1962 era." Opp'n 1.[4] And the government again claims, as it did in *Caronia*, that "promotional materials" are unprotected by the First Amendment, as if *Caronia* had never held that "the government cannot prosecute pharmaceutical manufacturers and their representatives under the FDCA for speech promoting the lawful, off-label use of an FDA-approved drug," 703 F.3d at 169. There is much in this case about which the parties disagree.

[4] *See* Brief of United States at 71, *United States* v. *Caronia*, 703 F.3d 149 (2d Cir. 2012) ("Allowing drug manufacturers to promote drugs for off-label uses . . . would turn the regulatory clock back more than seventy years, to the regime of *caveat emptor*."). FDA nowhere contends the world has become less safe since *Caronia*.

ARGUMENT

I. THIS CASE PRESENTS A LIVE CONTROVERSY

Only two months ago, FDA told Amarin in its "Complete Response Letter" that "if [Vascepa®] is marketed" for off-label use Amarin could face prosecution under the FDCA's "misbranding" provisions. Ketchum Decl. Ex. 9. Still more recently, FDA reasserted on the first page of its June 5 letter to Amarin its authority to pursue "misbrand[ing]" prosecutions for off-label promotion. It closed the letter with another warning that Amarin risked prosecution if it uttered its proposed health claim set forth above on page one. Ltr. 10.[5] The government now claims that Amarin "cannot show a credible threat of prosecution" in light of its June 5 letter. Opp'n 16. As we have shown above, that statement is inaccurate. Substantial issues of the highest import remain for judicial resolution.[6]

The government argues that the June 5 letter "makes clear that Amarin is free to

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[5] Contrary to the government's suggestion, Amarin was not required to "ask for FDA's views regarding [its] proposed communications before filing the Complaint." Opp'n 8. Although FDA states that it "regularly provides its views on pharmaceutical companies' proposed marketing statements," *id.*, the only provision it cites to (21 C.F.R. § 202.1(j)(4)) is used primarily to provide pre-publication review of direct-to-consumer advertisements. *See* FDA, Draft Guidance, *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs Guidance for Industry*, 8 (April 2015). In light of the many warning letters sent by FDA to companies for allegedly promoting their products off-label, FDA's public statements about off-label promotion and Amarin's already-years-long dialogue with FDA (*see* Ketchum Decl. ¶¶ 105, 112), which culminated in a threat from FDA that promotion of Vascepa® for off-label use would be considered "misbrand[ing]," it was necessary for Amarin to turn to this Court to vindicate its rights. *See* Ketchum Reply Decl. ¶¶ 39, 42, 44.

[6] Even if FDA's letter had fully addressed Amarin's concerns, it would not moot Amarin's claims. The government may not "escape the pitfalls of litigation by simply giving in to a plaintiff's individual claim without renouncing the challenged policy." *See Legal Assistance for Vietnamese Asylum Seekers* v. *Dep't of State, Bureau of Consular Affairs*, 74 F.3d 1308, 1311 (D.C. Cir. 1996). Far from renouncing its off-label promotion ban, the June 5 letter and the government's brief reassert its intent to prosecute off-label promotion by drug manufacturers. *See* Ltr. 1, n.1; Opp'n 9. Further, FDA's letter is non-binding and represents only FDA's "current thinking" on the matter. Ltr. 1. Nothing prevents FDA from simply changing its mind. *See Hispanic Leadership Fund, Inc.* v. *Walsh*, 42 F. Supp. 3d 365, 375 (N.D.N.Y. 2014).

engage in virtually all of its proposed speech without fear of civil and criminal liability." Opp'n 49. But the June 5 letter actually "makes clear," by what it says and what it does not, that Amarin may only do so safely on terms set by FDA that are inconsistent with the First Amendment. By limiting any off-label speech by Amarin to "distribution of summaries and reprints of the ANCHOR trial and journal article reprints" in scientific settings, it seeks to prevent Amarin from promoting its product—precisely what this lawsuit seeks to establish it may do.

Finally, FDA's letter does not even purport to bind the Department of Justice and therefore has no bearing at all on the relief Plaintiffs seek against that entity with regard to its prosecution of off-label promotion under the False Claims Act. Multiple live controversies remain for judicial adjudication.[7]

II. AMARIN IS ENTITLED TO PRELIMINARY INJUNCTIVE RELIEF

a. FDA Regulations Threaten Amarin's Speech

The centerpiece of the government's defense is that FDA's regulations banning off-label promotion do not actually prohibit manufacturer speech. Such promotion, FDA asserts, plays only an "evidentiary" role in determining whether a manufacturer intends its drug to be used off-label and therefore violates the FDCA. Opp'n 18, 20-21. This speech-as-evidence argument is, on its face, a charade. By definition, a drug company's promotion of its product for

[7] The only cases the government cites in support of its case-or-controversy argument are readily distinguishable. In *American Library Association* v. *Barr*, 956 F.2d 1178, 1196 (D.C. Cir. 1992), the court held that plaintiffs did not face a credible threat of prosecution where the government had a "longstanding policy" against invoking the statute except in limited circumstances and because plaintiffs' speech activities would not violate the statute. In *Rafferty* v. *Judicial Council for the District of Columbia Circuit*, No. CIV. A. 95–CV–1499, 1996 WL 451052, at *4 (D.D.C. Aug. 5, 1996), plaintiff failed to establish a credible threat of prosecution because officials had never prosecuted a witness in a federal judicial complaint proceeding for disclosing truthful information and the policy at issue did not apply to plaintiff.

off-label use is, *in and of itself*, a reflection of its intent that its drug be used off-label. The promotion—the speech—*is* the illegal act.

The government's speech-as-evidence tautology with respect to off-label promotion has not been lost on commentators or courts. Professor Smolla explains:

> The FDA and its prosecutors invoke a . . . circularity. There is nothing illegal about promoting off-label drug uses. But there's a catch (there's always a catch). No drug may be promoted if it is misbranded. Any drug promoted for use other than a use approved by the FDA (i.e., any drug promoted for an off-label use) is, by definition, "misbranded." And much like the military in *Catch-22*, which claims it is not penalizing the pilot merely for *asking* to be grounded, but rather is simply using "the ask" as evidence of the pilot's sanity, the FDA claims it is not penalizing the promoter of off-label uses for the promotion *itself*, but rather as evidence of misbranding. While seductively clever, the government's argument is too clever by half. Here is its flaw: the . . . evidentiary-use principle is valid *only* when the elements of the underlying crime or tort do not themselves require expressive activity. In such cases it is possible to coherently separate the use of speech as evidence of a nonspeech element from the imposition of liability for the speech itself. When expressive activity is a necessary element of the crime or tort, however, no such separation is possible. . . . Unlike the racially motivated beating in [*Wisconsin* v.] *Mitchell*, [508 U.S. 476 (1993),] conduct that was not intrinsically linked to expression at all, it is *impossible* to conceive of a prosecution for the introduction of a misbranded drug into interstate commerce predicated on the promotion of the drug's off-label uses *without* making the expressive promotion of the off-label use an element of the crime.

Smolla, at 114-115 (emphasis in original).

FDA acknowledges that the conduct to which off-label promotion is directed—off-label drug use—is lawful. Indeed, FDA acknowledges off-label use can be "truly medically necessary." Opp'n 41. As a result, the "illegal" conduct for which speech is used as "evidence" must be something other than off-label drug use. It is nothing but speech itself. As Judge Royce Lamberth observed in striking down certain FDA off-label anti-promotion policies as failing First Amendment scrutiny:

> In claiming that the speech at issue involves "illegal activities," the FDA does not seriously press any argument that off-label prescriptions are illegal. Rather, the agency . . . asserts that the speech cannot survive the first prong of the *Central*

> *Hudson* test because a drug or device is considered to be misbranded as a matter of law if it is promoted by the manufacturer for an off-label use. *See* 21 U.S.C. § 352. Therefore, when a manufacturer disseminates information about a drug product that diverges from the treatments included on the label, that manufacturer may be engaged in misbranding, which is illegal. *See, e.g.*, 62 Fed.Reg. at 64079. However, the tautological nature of this argument exposes its shortcomings. The proper inquiry is not whether the speech violates a law or a regulation, but rather whether the conduct that the speech promotes violates the law. The Supreme Court formulates the restriction this way: "[T]he First Amendment does not protect commercial speech *about unlawful activities.*" *44 Liquormart*, 517 U.S. at 497 n. 7 (emphasis added). Were the FDA's characterization of what constitutes "lawful activity" accurate, First Amendment protections for commercial speech could be all but eviscerated by the government: First Amendment challenges to speech restrictions would be defeated by noting that Congress had made the speech illegal, and therefore unlawful activity is at issue.

Washington Legal Found. v. *Friedman*, 13 F. Supp. 2d 51, 66 (D.D.C. 1998) *appeal dismissed, judgment vacated in part sub nom. Washington Legal Found.* v. *Henney*, 202 F.3d 331 (D.C. Cir. 2000); *see also* Coleen Klasmeier & Martin H. Redish, *Off-Label Prescription Advertising, the FDA and the First Amendment: A Study in the Values of Commercial Speech Protection*, 37 Am. J.L. & Med. 315, 343 (2011).

b. The Government's Speech Restrictions Cannot Survive First Amendment Scrutiny

In *Caronia*, heightened scrutiny was held required because the ban on off-label promotion is both content-based and speaker-based. The same is true here. Prohibiting off-label promotion is—as in *Caronia*—content-based because it "distinguishes between 'favored' and 'disfavored' speech on the basis of the ideas or views expressed.'" 703 F.3d at 165. And, like *Caronia*, it is speaker-based "because it targets one kind of speaker—pharmaceutical manufacturers—while allowing others to speak without restriction." *Id.*

In the very recent ruling of the Supreme Court in *Reed* v. *Town of Gilbert*, the Court went still further, concluding that "[g]overnment regulation of speech is content based if a law applies to particular speech because of the topic discussed or the idea or message expressed."

— S.Ct. —, 2015 WL 2473374, at *7 (June 18, 2015). For that proposition, the Court cited *Sorrell* v. *IMS Health, Inc.*, 134 S. Ct. 2655 (2011), which is at center-stage in this case. In *Reed*, the Court made plain that "[a] law that is content based on its face is subject to strict scrutiny regardless of the government's benign motive, content-neutral justification, or lack of 'animus towards the ideas' contained in the regulated speech." *Id.* at *7 (citation omitted). All such regulations, the Court held, are "presumptively unconstitutional and may be justified only if the government proves that they are narrowly tailored to serve compelling state interests." *Id*. at *6.

Whether couched as "heightened scrutiny" or the more familiar "strict scrutiny" referred to in *Reed*, the government cannot come close to meeting its burden since it cannot even meet the *Central Hudson*-imposed burden of showing that the challenged regulation goes no further than necessary to accomplish the sought end, let alone the narrow tailoring standard of *Reed.*

Caronia held as a matter of law that FDA's prohibition of off-label promotion provided "only ineffective or remote support" for the government's asserted interests in "preserving the efficacy . . . of the . . . approval process and reducing patient exposure to unsafe and ineffective drugs." 703 F.3d at 166-67. The third prong test of *Central Hudson* thus could not be met.[8]

With respect to *Central Hudson*'s fourth prong, the Supreme Court has stated, that "[i]f the First Amendment means anything, it means that regulating speech must be a last—not first—resort." *Thompson* v. *Western States Med. Center*, 535 U.S. 357, 373 (2002). In that

[8] Although the government purports to have identified a series of additional "substantial interests" (Opp'n 27) such as "motivating robust scientific research" (*id.* 27) and "ensuring that drugs bear labeling that contains both accurate information and adequate directions for use" (*id.* 29), these interests are merely rephrasings of the interests recognized in *Caronia*. The government's remaining asserted interests relate to the effects on health of fraudulent activities, for instance preventing "unscrupulous players from making deceptive or unsubstantiated claims." *Id.* 28. These interests are irrelevant to Plaintiffs' as-applied challenge: Amarin seeks to engage in speech that is truthful and non-misleading, a proposition FDA does not dispute. *Id.* 18, n.11.

respect, *Caronia* concluded that "numerous" alternatives are available to the government[9] and on that basis held that the government's off-label promotion ban failed *Central Hudson*'s fourth prong. The government now revisits these alternatives and—unsurprisingly—has "found them all inadequate." Opp'n 38.

In support of that conclusion, the government has submitted a declaration from Dr. Janet Woodcock, with respect to the "numerous" *Caronia* alternatives.[10] Dr. Woodcock devotes a single paragraph (in one instance, two paragraphs) to each. She makes no representations that FDA has explored these alternatives beyond the context of this litigation (which has been pending for less than two months), or who at FDA had input in any such considerations or authority over the conclusions reached. She does not cite in her Declaration, or attach to it, any documentary evidence to support her conclusions. Once, she references—but does not provide or cite to—"studies" (*id.* ¶ 49) in support of a conclusion as to one alternative. *See Edenfield* v. *Fane*, 507 U.S. 761, 771 (1993) (*Central Hudson* not satisfied in part because officials "present[ed] no studies" relevant to analysis). Indeed, she cites no concrete *factual* information at all in addressing the *Caronia* alternatives other than two brief anecdotes about specific drugs. Woodcock Decl. ¶ 47. She speculates as to certain outcomes, stating that they "would likely" (*id.* ¶¶ 43, 52); "may" (*id.* ¶ 44); or "could" (*id.* ¶ 49) occur. *See Rubin* v. *Coors Brewing Co.*, 514 U.S. 476, 490 (1995) (finding government's submission of "anecdotal evidence" and "educated guesses" insufficient: "[t]hese various tidbits . . . cannot overcome the irrationality of the

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[9] The government could, the Court held, (1) directly regulate off-label drug use, (2) provide guidance that differentiates between misleading and false promotion, exaggerations and embellishments, and truthful or non-misleading information; (3) develop a warning or disclaimer system; (4) develop different "safety tiers" for off-label drugs; (5) create ceilings or caps on off-label prescriptions; and (6) prohibit certain dangerous off-label uses altogether. 703 F.3d 167-68.

[10] More detailed responses to Dr. Woodcock's Declaration are set forth in the Declarations of Dr. Scott Gottlieb and Dr. Paul H. Rubin.

regulatory scheme"). She provides no representation that she, or anyone at FDA, actually implemented any of the alternatives before concluding them inadequate. *See In re R.M.J.*, 455 U.S. 191, 206 (1982) (striking down portions of a rule regulating lawyer advertising in part because "[t]here is no indication in the record of a failed effort to proceed along such a less restrictive path"). This is far from the "showing" *Central Hudson* contemplates. 447 U.S. 557, 570 (1980)

The most obvious way to address FDA's concerns about off-label drug use would be, as *Caronia* states, to do so "directly" by simply banning such use. 703 F.3d at 168. Dr. Woodcock acknowledges that such an approach "would be effective" in advancing the government's asserted interests in "motivating scientifically robust research" and in "ensuring that new uses of an approved drug are proven to be safe and effective before they are used to treat patients." Woodcock Decl. ¶ 43. She then states, however, that it would also "fail to take into account the interests behind allowing healthcare providers to determine the best treatment options for individual patients." *Id*. That may well be accurate—Amarin itself hardly favors a ban on off-label use—but it is no response to the First Amendment requirement that speech may not be suppressed or punished if alternatives exist. Dr. Woodcock uses the same reasoning to dismiss other alternatives as well, *id.* ¶¶ 45, 51, and they are insufficient for the same reason. There is inherent tension between FDA's interests in protecting patients from the risks attendant to off-label drug use on the one hand, and ensuring that drugs meet FDA's "gold standard" by way of pre-market approval (*id.* ¶ 31) on the other. But the fact of that tension is not a basis for limiting First Amendment-protected speech.

c. Amarin's Qualified Health Claim Is Protected Speech

The foregoing analysis applies with equal force to Amarin's proposed qualified health claim that "supportive but not conclusive research shows that consumption of EPA and

DHA omega-3 fatty acids may reduce the risk of coronary heart disease."[11] Examples of such research are set forth in Exhibit A to the Complaint and at Exhibits 10, 50, 52, 96-103, and 142 of the Ketchum Declaration. In its June 5 letter, FDA does not argue that this claim is untrue or inherently misleading; it simply asserts that it may be "potentially misleading." Ltr. 10. But speech that is only potentially misleading is, in any event, "commercial speech protected by the First Amendment" if it is "presented in a way that is not deceptive." *Alexander* v. *Cahill*, 598 F.3d 79, 95 (2d Cir. 2010) (internal quotation marks and citations omitted).

In *Pearson* v. *Shalala*, the D.C. Circuit evaluated under *Central Hudson* plaintiffs' challenge to FDA regulations requiring sellers of dietary supplements to obtain FDA authorization before labeling such supplements with health claims. 164 F.3d 650 (D.C. Cir. 1999). Striking down the regulations, the *Pearson* court held that banning health claims about dietary supplements was "a rather indirect route" to protecting public health, since the government did not assert that dietary supplements themselves threatened public health. *Id.* at 656. The court also rejected the notion that "'the public is better kept in ignorance than trusted with correct but incomplete information.'" *Id.* at 657 (quoting *Bates* v. *State Bar of Arizona*, 433 U.S. 350, 374-375 (1977)). *Pearson* held "that the government ha[d] violated the First Amendment by declining to employ a less draconian method—the use of disclaimers—to serve the government's interest." *Id.* at 654. The same is true here.

FDA asserts that the statement Amarin seeks to make about Vascepa® would be transformed into being truthful and non-misleading if Amarin marketed it as a dietary supplement rather than as a drug. Ltr. 10. But a truthful statement made to lay consumers by supple-

[11] FDA has stated that it "believe[s]" that certain additional disclaimers, over and above those proposed by Amarin, "would be appropriate." Ltr. 7. As explained in the Ketchum Reply Declaration ¶¶ 13-24, while some of the proposed additions are acceptable, the content of others could make Amarin's speech about Vascepa® misleading.

ment manufacturers is surely no less truthful when made to sophisticated doctors, and in the latter instance it is far less likely to mislead. That is particularly evident where, as here, such a statement would be made only in conjunction with disclosures that "FDA has not approved Vascepa® to reduce the risk of coronary heart disease" and that "the effect of Vascepa® on the risk of cardiovascular disease mortality and morbidity has not yet been determined." Compl. ¶ 124.

d. FDA's Off-Label Promotion Ban is Unconstitutionally Vague

Since *Caronia* held in 2012 that the government may not prosecute pharmaceutical manufacturers for off-label promotion, FDA has stated that *Caronia* would not "significantly affect" FDA's regulation of off-label promotion (*see* Kurtzberg Decl. Ex. 7). But FDA has not made at all clear what, if any, promotional activities drug manufacturers may engage in with respect to off-label use of their products that would *not* subject them to potential criminal sanctions. Or just what speech by such companies about off-label uses FDA would deem—or not deem—to constitute a "new intended use" of its drugs. In light of the enormous risks, criminal and civil, for drug companies that wish to engage in off-label promotion, that lack of clarity is alone sufficient to create a situation that is so "standardless that it authorizes or encourages seriously discriminatory enforcement" in violation of the Fifth Amendment. *FCC* v. *Fox Television Stations, Inc.*, 132 Sup. Ct. 2307, 2317 (2012).

The government's opposition papers on this motion seek to introduce a new standard, apparently drafted to respond to those questions. In doing so, it has "open[ed] a new front of uncertainty," one that is "so shapeless" that it cannot be used "to condemn someone to prison." *Johnson* v. *United States*, — S.Ct. —, 2015 WL 2473450, at *7 (June 26, 2015). The government, in this case, now states that "the dissemination of information about an unapproved

use would not, by itself, cause a violation of the FDCA when such information is neither false or misleading and is not relevant or sufficient to infer a new intended use." Opp'n 35; *see also* Woodcock Decl. ¶ 23. But this creates more ambiguity than even existed before. The government does not explain why or how the truth or falsity of information about the use of a drug even bears on whether a "new intended use" is contemplated. The language does not clarify what is meant by importing the concept of "relevance" in making that determination. Is all speech by drug companies about off-label use to be deemed relevant because all such companies seek to sell their products? What speech of drug companies could be deemed irrelevant?

Such uncertainty, coupled with credible threats of very real threats of criminal prosecution or massive civil liability, is constitutionally unacceptable. "[T]he due process protection against vague regulations does not leave regulated parties at the mercy of noblesse oblige." *Fox*, 132 Sup. Ct. at 2317.

e. The Government's Interpretation of the False Claims Act Fails First Amendment Scrutiny

The parties agree that at least in most circumstances the use of Vascepa® in treatment of patients with persistently high triglycerides should bar any FCA claim since it is supported by citation in statutorily approved compendia. But there may be certain circumstances in which Vascepa® does not meet additional State-specific reimbursement requirements.[12]

[12] A state has discretion to ensure that it is reimbursing only for those goods and services that are safe and effective. For example, a state may create a "'formulary,' which has the effect of excluding coverage of, or payment for, certain Medicaid-eligible drugs." *Pharmaceutical Research & Mfrs. of America* v. *Meadows*, 304 F.3d 1197, 1201-02 (11th Cir. 2002); 42 U.S.C. § 1396r-8(d)(1)(B)(iv). And as one state health agency has asserted, "it is unreasonable and defies logic to assert . . . that [a state health agency] lacks discretion to assess whether to cover off-label uses simply because they appear in Compendia . . . ." Reply Br. of Defendant-Appellant, *Edmonds* v. *Florida*, No. 06-11745-JJ, 2006 WL 2364857, at *3 (11th Cir. July 31, 2006).

The government has secured billions of dollars from drug companies by bringing claims under the False Claims Act for allege off-label promotion. See Pls.' Br. 14-15 n.5. The consequences of prosecution, let alone an adverse judicial ruling, would be devastating for a small company like Amarin. The government states that "it is difficult to see how, assuming the truth of the facts alleged in the complaint . . . a false claim would arise," Opp'n 46, but fails to provide any assurance that it will not prosecute Amarin for its proposed speech.[13] "[W]here threatened action by *government* is concerned, we do not require a plaintiff to expose himself to liability before bringing suit to challenge the basis for the threat—for example, the constitutionality of a law threatened to be enforced." *MedImmune, Inc.* v. *Genentech, Inc.*, 549 U.S. 118, 128-29 (2007) (emphasis in original). Indeed, "it was the very purpose of the Declaratory Judgment Act to ameliorate" such "dilemma[s]." *Abbott Labs.* v. *Gardner*, 387 U.S. 136, 152 (1967) (pre-enforcement review by pharmaceutical manufacturers).

On the merits, the government argues that Amarin may be liable under the FCA if its off-label promotion "caus[es] the submission of a false claim for payment." Opp'n 47. It does not matter, the government asserts, "whether a party causes the submission of a false claim by words, conduct, or by a combination of both." *Id.* Of course, it matters. Protected speech cannot be used as a basis for civil liability, *see N. A. A. C. P.* v. *Claiborne Hardware Co.*, 458 U.S. 886, 926 (1982), and if, as *Caronia* concludes, "[a] pharmaceutical representative's promotion of an FDA-approved drug's off-label use is speech" protected by the First Amendment, 703 F.3d at 161, civilly prosecuting Amarin under the FCA for its promotional speech would necessarily violate Amarin's First Amendment rights.

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[13] Indeed, by only "assuming" that Vascepa® is supported by citation in statutorily approved compendia, the government is apparently unwilling even to concede even that fact.

CONCLUSION

The motion for a preliminary injunction should be granted.

Dated: New York, New York
June 30, 2015

Respectfully submitted,

CAHILL GORDON & REINDEL LLP

By: _____

Floyd Abrams
Joel Kurtzberg
Michael B. Weiss
80 Pine Street
New York, New York 10005
Telephone: (212) 701-3000
Facsimile: (212) 269-5420

Attorneys for Plaintiffs

Of counsel:

Joseph T. Kennedy
Senior Vice President, General Counsel
c/o Amarin Pharma, Inc.
1430 Route 206
Bedminster, NJ 07921
Telephone: (908) 719-1315
Facsimile: (908) 719-3012

Attorney for Plaintiff Amarin Pharma, Inc.