ATTACHMENT # 2

to the

UNOPPOSED MOTION OF THE NATIONAL SPASMODIC TORTICOLLIS ASSOCIATION, THE NATIONAL SPASMODIC DYSPHONIA ASSOCIATION, ALLIED EDUCATIONAL FOUNDATION, AND WASHINGTON LEGAL FOUNDATION FOR LEAVE TO FILE AS *AMICI CURIAE* IN SUPPORT OF PLAINTIFF'S MOTION FOR PRELIMINARY INJUNCTION

in

Civil Action No. 1:09-cv-01879 (JDB)

BRIEF OF THE NATIONAL SPASMODIC TORTICOLLIS ASSOCIATION, THE NATIONAL SPASMODIC DYSPHONIA ASSOCIATION, ALLIED EDUCATIONAL FOUNDATION, AND WASHINGTON LEGAL FOUNDATION AS *AMICI CURIAE* IN SUPPORT OF PLAINTIFF'S MOTION FOR PRELIMINARY INJUNCTION

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

ALLERGAN, INC., Plaintiff, v. UNITED STATES OF AMERICA; UNITED STATES FOOD & DRUG ADMINISTRATION; DR. MARGARET HAMBURG, Commissioner of the United States Food & Drug Administration; and KATHLEEN SEBELIUS, Secretary of the United States Department of Health & Human Services, Defendants.	Civil Action No. 1:09-cv-01879 (JDB)

BRIEF OF THE NATIONAL SPASMODIC TORTICOLLIS ASSOCIATION, THE NATIONAL SPASMODIC DYSPHONIA ASSOCIATION, ALLIED EDUCATIONAL FOUNDATION, AND WASHINGTON LEGAL FOUNDATION AS *AMICI CURIAE* IN SUPPORT OF PLAINTIFF'S MOTION FOR PRELIMINARY INJUNCTION

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page

CASES

STATUTES AND REGULATIONS

LEGISLATIVE HISTORY

SCHOLARLY AUTHORITIES

OTHER AUTHORITIES

STATEMENT OF INTEREST OF *AMICI CURIAE*

The undersigned *amici* are organizations that are troubled by the current federal enforcement regime, which aggressively seeks to limit – through both civil and criminal means – speech by manufacturers about so-called "off-label" uses of FDA-approved drugs.[1] Such speech can be critically important to the prescribing decisions of medical professionals, and when such speech is truthful, accurate, and nonmisleading, it deserves full First Amendment protection.

The National Spasmodic Torticollis Association (NSTA) is a non-profit organization whose mission is to support people affected with spasmodic torticollis (also known as cervical dystonia (CD)), a painful and debilitating movement disorder of the neck that affects 3 in 10,000 people; to promote awareness of and education about CD; and, critically important here, to advance research aimed at treating, and ultimately curing, this disease. Currently, the most effective treatments for CD involve botulinum toxins (including Botox, manufactured by Allergan Neuroscience). Before receiving FDA approval, Botox was used off-label to treat CD, and it currently is prescribed off-label to treat other forms of dystonia – such as spasmodic dysphonia, which affects speech through involuntary muscle movements of the voice box. NSTA supports the dissemination of truthful, accurate, nonmisleading information about off-label uses of prescription drugs as a means to ensure safe and effective medical treatment.

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[1] *See* Compl. ¶¶ 49-50; *e.g.*, *United States v. Caronia*, 576 F. Supp. 2d 385 (E.D.N.Y. 2008) (sustaining indictment against a medical science liaison who disseminated truthful, accurate, non-misleading information about an off-label use); *United States v. Harkonen*, No. 08-00164, 2009 WL 1578712 (N.D. Cal. June 4, 2009) (sustaining indictment against CEO based on manufacturer's issuance of a press release announcing clinical trial data relating to an off-label use of an approved prescription drug), *jury verdict of guilt entered*, 2009 WL 3187564 (Sept. 29, 2009); Press Release, DOJ (Sept. 2, 2009), http://tinyurl.com/nm2pro (announcing that Pfizer would pay a criminal fine of $1.3 billion to settle charges that it "promoted" off-label uses and dosages); Press Release, DOJ (Sept. 29, 2008), http://tinyurl.com/ygvy8la (announcing that Cephalon would pay a criminal fine of $450 million to settle charges of off-label promotion).

The National Spasmodic Dysphonia Association (NSDA) is a non-profit organization dedicated to advancing medical research into the causes of and treatments for spasmodic dysphonia, promoting physician and public awareness of the disorder, and providing support for affected persons and their families. Spasmodic dysphonia is a neurological voice disorder that causes the vocal cord to spasm, and is estimated to affect 30,000 to 50,000 people. Off-label use of Botox is considered the standard of care for treating spasmodic dysphonia. Because spasmodic dysphonia is often diagnosed by a neurologist or even a family practitioner, but is treated by an otolaryngologist, this disorder tends to fall between specialties. It therefore is particularly important for the physicians who encounter it to have as much information as possible about treatment protocols.

The Allied Educational Foundation (AEF) is a non-profit charitable foundation based in Englewood, New Jersey. Founded in 1964, AEF is dedicated to promoting education in diverse areas of study, such as law and public policy, and has appeared as *amicus curiae* on a number of occasions. AEF has filed briefs supporting the First Amendment rights of commercial entities to speak truthfully on matters of public importance.

The Washington Legal Foundation (WLF) is a non-profit public interest law and policy center with supporters in all 50 states. It devotes a substantial portion of its resources to defending and promoting free enterprise, individual rights, business civil rights, and a limited and accountable government. WLF has appeared in numerous federal and state courts in cases raising issues closely related to those presented here. Of particular relevance, WLF, on behalf of a group of concerned health care practitioners, brought the first successful challenge to the constitutionality of Food and Drug Administration (FDA) restrictions on speech regarding lawful, off-label uses of FDA-approved products. *See WLF v. Friedman*, 13 F. Supp. 2d 51 (D.D.C. 1998)

(hereinafter "*WLF I*"), *appeal dismissed sub nom. WLF v. Henney*, 202 F. 3d 331 (D.C. Cir. 2000) (hereinafter "*WLF II*").

INTRODUCTION

The undersigned *amici curiae* submit this brief to assist the Court's consideration of the important public health and First Amendment issues implicated by the threat of enforcement that currently looms over manufacturers' dissemination of information to physicians relating to new – so-called "off-label" – uses of FDA-approved prescription drugs.[2] Allergan's Complaint is important in this regard because it squarely presents the question whether the First Amendment permits the federal government to ban truthful, accurate, and nonmisleading speech to physicians regarding off-label uses of FDA-approved prescription drugs. The importance, prevalence, and value of off-label uses are well-known to health care professionals, but the courts have had little occasion to analyze the constitutionality of federal enforcement efforts – in large measure because manufacturers typically cannot as a practical matter litigate these issues in court, due to the threat of exclusion from participation in Medicare and other federal health-care programs. *Amici* therefore welcome and support Allergan's effort to present these issues for judicial review.

To evaluate the First Amendment issues presented by Allergan's Complaint and motion for preliminary injunction, it is important to understand the lawfulness and medical importance of off-label use, and the corollary importance of appropriate dissemination by manufacturers of truthful, accurate, and nonmisleading information about such use. Allergan already has de-

[2] "The uses that are approved by the agency are sometimes referred to as 'labeled' uses because they appear in the product's approved labeling. Uses that do not appear in the labeling and are not approved by the agency are referred to as 'unapproved,' 'unlabeled,' 'off-label,' or 'extra-label' uses." Citizen Petition Regarding the Food and Drug Administration's Policy on Promotion of Unapproved Uses of Approved Drugs and Devices; Request for Comments, 59 Fed. Reg. 59,820, 59,820 (Nov. 18, 1994).

scribed the chill on manufacturer speech created by the current regime. To avoid burdening the Court with duplicative briefing, this brief therefore is limited to two principal topics. *First*, we explain the vital importance of off-label uses in modern medicine, and why overregulating speech about those uses is contrary to the public health. *Second*, supplementing Allergan's own discussion of First Amendment issues, we highlight three foundational First Amendment principles that are important to the proper resolution of this dispute.

It is important to be clear about the specific and limited type of speech at issue here – namely, speech that (1) is truthful, accurate, and nonmisleading; (2) is directed to physicians or other qualified health care professionals; and (3) relates to off-label uses of FDA-approved prescription drugs. There can be no dispute that it is entirely lawful for medical professionals to prescribe FDA-approved prescription drugs for off-label uses, consistent with the standard of care, as part of their practice of medicine. Manufacturers, moreover, have broad access to information regarding their products, including about off-label uses. It therefore is critical that manufacturers be able to communicate truthful, accurate, and nonmisleading information regarding such uses to the physicians making the prescribing decisions. This information is often vital to proper and effective patient care, and trained heath care professionals are uniquely well-suited to understand and use it properly. The First Amendment simply does not permit the government to impose a *de facto* ban on truthful speech by the speakers having the best access to relevant information, particularly where it is directed to an audience in the best position to critically evaluate and use that information.

ARGUMENT

I. PROVIDING TRUTHFUL, ACCURATE, NONMISLEADING INFORMATION ABOUT OFF-LABEL USES OF APPROVED PRESCRIPTION DRUGS IS IMPORTANT TO ENSURE SAFE AND EFFECTIVE MEDICAL TREATMENT.

A. The Off-Label Use Of FDA-Approved Prescription Drugs Is Lawful.

Any evaluation of prescription drug manufacturers' speech concerning off-label uses of their products must be informed by one foundational fact: "Once a drug product has been approved for marketing, a physician may, in treating patients, prescribe the drug for uses not included in the drug's approved labeling." Proposed New Drug, Antibiotic, and Biologic Drug Regulations, 48 Fed. Reg. 26,720, 26,733 (proposed June 9, 1983).[3] The decision whether to prescribe an approved drug for an off-label use is a quintessentially medical judgment that must be based on current science, and the FDA disclaims authority to interfere with such judgments. *Id.* So long as a physician complies with state medical practice standards, including the use of due care, he or she may depart from the conditions of use set forth in approved labeling for a drug – including, notably, using the drug to treat another condition or disease entirely. This court, among others, has recognized that off-label uses are lawful and often necessary. *See Ass'n of Am. Physicians & Surgeons, Inc. v. FDA*, 226 F. Supp. 2d 204, 206 (D.D.C. 2002) ("[w]hen … FDA approves a drug, it [is] approve[d] for [a] particular use" but "the FDCA does not regulate how the drug may be prescribed"); *see also Sigma-Tau Pharms., Inc. v. Schwetz*, 288 F.3d 141, 147 (4th Cir. 2002) (recognizing "the longstanding practice of Congress, the FDA, and the

[3] *See also* 21 C.F.R. § 312.2(d) (exemption from FDA regulations for "the use in the practice of medicine for an unlabeled indication of a new drug product approved" by the Agency); Legal Status of Approved Labeling for Prescription Drugs; Prescribing for Uses Unapproved by the Food and Drug Administration, 37 Fed. Reg. 16,503, 16,503 (proposed Aug. 15, 1972) ("[T]he physician may, as part of the practice of medicine, lawfully prescribe a different dosage for his patient, or may otherwise vary the conditions of use from those approved in the package insert, without informing or obtaining the approval of the Food and Drug Administration.").

courts not to interfere with physicians' judgments and their prescription of drugs for off-label uses"). When a manufacturer engages in speech regarding off-label uses, it therefore is speaking about *lawful uses of lawful products*.

B. Off-Label Uses Are Common, Often Representing The Standard Of Care.

1. The phrase "off-label use" may carry an implication of questionable medical practice, but the truth is quite the contrary. Off-label uses are "common, can be a source of innovation, and in some settings may represent the standard of care." Donna T. Chen et al., *U.S. Physician Knowledge of the FDA-Approved Indications and Evidence Base for Commonly Prescribed Drugs: Results of a National Survey*, 2009 Pharmacoepidemiology & Drug Safety (footnotes omitted). "For some diseases, such as non-small cell lung cancer and cystic fibrosis, off-label uses either are the only therapies available, or are the therapies of choice." *Comments of the Medical Information Working Group on FDA's "Good Reprint Practices" Draft Guidance*, 4 (Apr. 18, 2008), *available at* http://tinyurl.com/yh6ha6v (citing Susan G. Poole and Michael J. Dooley, *Off-Label Prescribing in Oncology*, 12 Support Care Cancer 302 (2004)). A 2002 study likewise found that off-label prescriptions were common for managing dermatologic conditions, and reflected the standard of care. Joel Sugarman et al., *Off-Label Prescribing in the Treatment of Dermatologic Disease*, 47 J. Am. Acad. Dermatol. 217 (2002).

Government officials themselves have recognized the benefits of off-label uses. In 1992, the FDA's Deputy Commissioner for External Affairs stated that "off-label drug use is often essential to good medical practice, and in some areas – oncology and pediatrics in particular – off label uses are often considered necessary. In fact, it is on this edge that science and medicine move forward to benefit patients with intractable illness." Carol Scheman, Prescription Drug Marketing and Promotion—An FDA Perspective, Address Before the PMA Public Affairs Section, Mid-Year Meeting, Apr. 15, 1992. In 1998, an FDA Information Sheet noted that "[g]ood

medical practice and the best interests of the patient require that physicians use legally available drugs, biologics and devices according to their best knowledge and judgment." FDA, "Off-Label" and Investigational Use of Marketed Drugs, Biologics, and Medical Devices – Information Sheet, *available at* http://tinyurl.com/mj3n37 (last visited Nov. 18, 2009); *see also* Dissemination of Information on Unapproved/New Uses for Marketed Drugs, Biologics, and Devices, 63 Fed. Reg. 31,143, 31,153 (proposed June 8, 1998) ("FDA has long recognized that in certain circumstances, new (off-label) uses of approved products are appropriate, rational, and accepted medical practice."). The FDA's Good Reprint Practices Guidance recently reaffirmed that position, noting that "off-label uses or treatment regimens may be important and may even constitute a medically recognized standard of care." FDA, Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs or Cleared Medical Devices (Jan. 2009), http://tinyurl.com/ykvjr4z.[4]

Indeed, where an off-label use represents the standard of care, it is not merely lawful but effectively may be *required*: Under such circumstances a physician reasonably could fear that the *failure* to prescribe drugs off-label could amount to malpractice. *See Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 349-51 & n.5 (2001); *WLF II*, 202 F.3d at 333. In 1994, the Vice President of the American Medical Association (AMA) warned that, "'[i]n some cases, if you didn't use the drug in the off-label way you'd be guilty of malpractice.'" Fran Kritz, *FDA*

[4] This sentiment was echoed by GAO's Director of Health Services Quality and Public Health Issues, who has testified that "a drug given off-label may have been proven to be safer and more beneficial than any drug labeled for that disease." *Off-Label Drug Use and FDA Review of Supplemental Drug Applications: Hearing Before the Subcomm. on Human Resources and Intergovernmental Relations of the H. Comm. on Government Reform and Oversight*, 104th Cong. 12 (1996) (statement of Sarah F. Jaggar, Director of Health Services Quality and Public Health Issues, Health, Education, and Human Services Division, GAO), *available at* http://tinyurl.com/yhxojqy.

Seeks to Add Drugs' New Uses to Labels, Wash. Post, Mar. 29, 1994, at Z11. Thus, at its 1997 Annual Meeting, the AMA explained that

> [t]he prevalence and clinical importance of prescribing drugs for unlabeled uses are substantial. Unlabeled indications are especially common in oncology, rare diseases, and pediatrics. Thus, the prescribing of drugs for unlabeled uses is often necessary for optimal patient care.

1997 Annual Meeting of the American Medical Association, 4, Reports of the Council on Scientific Affairs, http://tinyurl.com/ykowbgx. And, a 2005 AMA resolution noted that "[u]p to date, clinically appropriate medical practice at times *requires* the use of pharmaceuticals for 'off-label' indications." Memorandum of the AMA House of Delegates, Resolution 820, Off-Label Use of Pharmaceuticals (Sep. 21, 2005), http://tinyurl.com/yfpwmyo (emphasis added).

Not surprisingly, then, off-label use is common in medical practice across the United States. For example, a 2003 study found that fully 57% of physicians prescribe drugs off-label at least 10% of the time, and indeed 21% of physicians do so more than 30% of the time. Daniel B. Klein & Alexander Tabarrok, *Do Off-Label Drug Practices Argue Against FDA Efficacy Requirements?*, Indep. Ins. Working Paper No. 47, 10 (Apr. 16, 2003), *available at* http://tinyurl.com/ylgvcpq.

2. The fact that off-label use can be essential is demonstrated by certain medical specialties in which such uses are particularly prevalent. In some such areas, the FDA's drug approval process lags years behind medical research and its embrace by the medical community. *See Richardson v. Miller*, 44 S.W.3d 1, 13 n.11 (Tenn. Ct. App. 2000) ("Because the pace of medical discovery runs ahead of the FDA's regulatory machinery, the off-label use of some drugs is frequently considered to be 'state-of-the-art' treatment. In some circumstances, an off-label use of a particular drug or device may even define the standard of care.") (citation omitted). One study reported that off-label uses that later came to be recognized by the FDA appeared in official

compendia on average 2.5 years before FDA recognition. J.H. Beales III, *New Uses for Old Drugs*, *in Competitive Strategies in the Pharmaceutical Industry* (Robert B. Helms ed., 1996). Off-label use in "[c]linical practice often precedes, rather than follows, clinical trials." Daniel B. Klein & Alexander Tabarrok, *Who Certifies Off-Label?*, 27 Reg. 60, 61 (2004).

This is true, for example, in oncology, where research is intensive and lives are at stake. As early as 1991, the General Accounting Office (GAO) issued a report documenting that "[a] third of all drug administrations to cancer patients were off-label, and more than half of the patients received at least one off-label drug." GAO, *Off-Label Drugs: Reimbursement Policies Constrain Physicians in Their Choice of Cancer Therapies* 3 (Sept. 1991), *available at* http://tinyurl.com/yfg53rl. In 2005, the National Comprehensive Cancer Network estimated that "50% to 75% of all uses of drugs and biologics in cancer care in the United States are off-label." Michael Soares, *Off-Label Indications for Oncology Drug Use and Drug Compendia: History and Current Status*, 1 J. Oncol. Pract. 102, 104 (2005), *available at* http://tinyurl.com/yzoqo2p.

This happens in large part because oncologists "are regularly faced with few approved treatment options, especially if the first treatment didn't work." Am. Cancer Soc., Off-Label Drug Use (Mar. 13, 2007), http://tinyurl.com/ygxobso. A doctor faced with a lack of FDA-approved therapy will naturally do precisely what one would expect: follow the science. *See* FDA, *Guidance for Industry: IND Exemptions for Studies of Lawfully Marketed Drug or Biological Products for the Treatment of Cancer*, 4 (Jan. 2004), *available at* http://tinyurl.com/m29jrs ("Off-label therapy with cancer drugs is common in practice. When there is no established therapy for a cancer, or stage of cancer, it is common for oncologists to try different regimens or combinations of established drugs."). "Some cancer drugs are found to be effective against a variety of tumor types," even though they may not have been approved for use

with all of those types. Nat'l Cancer Inst., *Understanding the Approval Process for New Cancer Treatments – Q&A: Off-Label Drugs* (Jan. 6, 2004), *available at* http://tinyurl.com/3zfty (emphasis omitted). Moreover, "[c]ancer chemotherapy often involves the use of multiple drugs … [and] [c]ancer treatment is always evolving" – again, leading to a standard of care that is ahead of FDA approval. Accordingly, "[f]requently the standard of care for a particular type or stage of cancer involves the off-label use of one or more drugs." *Id.* (emphasis omitted).

A similar situation exists in psychiatry. Like oncology, psychiatry is a field in which multiple treatment attempts and methods may be necessary before a remedy is found that works for a particular patient's unique biochemistry. It also is a field, like oncology, in which a drug that treats one disease or disorder may prove useful in treating a related or similar one. Patients often are treated based on symptoms rather than a specific diagnosis, and there are even psychiatric disorders for which no approved drug has an indication, such that off-label use is the *only* option for drug therapy. Kavi K. Devulapalli & Henry A. Nasrallah, *An Analysis of the High Psychotropic Off-Label Use in Psychiatric Disorders*, 2 Asian J. Psych. 29 (2009). Even if FDA has approved a drug for a particular condition, the patient may fall outside the labeled patient population, or might need a higher or lower dosage. As a result, uses of approved drugs in ways that depart from approved labeling are predominant in psychiatry. For example, in 2003, antipsychotics had a 60% rate of off-label use, *see* Randall S. Stafford, *Regulating Off-Label Drug Use – Rethinking the Role of the FDA*, 358 New Engl. J. Med. 1427, 1427 (2008), *available at* http://tinyurl.com/yzywxx4.

Off-label uses are routine in neurology, the field principally at issue in this case:

> Neurologists … routinely use medications off label, such as tricyclic antidepressants, anticonvulsants, corticosteroids, azathioprine, mycophenolate mofetil, cyclophosphamide, and IV immunoglobulin, to treat disorders

> ranging from neuropathic pain and migraines to inflammatory disorders of the central and peripheral nervous systems.

Joseph Kass, *Ethical Perspectives in Neurology*, 14 Continuum Lifelong Learning Neurol. 205, 206 (2008), *available at* http://www.aan.com/globals/axon/assets/5583.pdf. In fact, "[o]ff-label prescription is … an integral and standard part of neurological practice.… [W]ithout off-label prescription, the clinical observation of new benefits would not occur, and treatment of rare neurological or sleep disorders would practically stop." *Guidance For Off-Label Use of Drugs*, 7 The Lancet Neurology 285, 285 (Apr. 2008), *available at* http://tinyurl.com/yhfb255.

Of particular relevance here, some 50,000 Americans in their 40s and 50s lose their ability to speak normally and to be understood, when a neurological disorder known as spasmodic dysphonia (likely influenced by an inherited gene in the basal ganglia and triggered later in life) causes the larynx muscles to spasm uncontrollably when the person attempts to speak. This disorder can mean job loss, social isolation, and extreme distress. Once triggered, the disorder cannot be cured and remains a lifelong disability. No oral medications have been found to ease the condition. To date, the scientific and medical communities have found only two ways to enable such patients to resume a normal life: (i) experimental surgeries that cut key neural connections from the brain (with mixed results for future vocalization) and (ii) injections of botulinum toxin, such as Botox, through the throat and into the muscle groups controlling opening and closing of the larynx. Although the injections are difficult and painful and often result in a whispered voice for several weeks after the shot, when the voice returns the patients have 4–6 months of normal speaking voice before another injection is required. Botox has been approved by the FDA for use in certain of the other focal dystonias (localized involuntary spasms), and otolaryngologists, neurologists, and scientific researchers throughout the country are in agreement that this is the

only relief available to these patients. The affected patient community is so limited, however, that it would not be economically rational to seek FDA approval of Botox for this use.

C. Manufacturers Are In A Unique Position To Provide Truthful, Accurate, And Nonmisleading Information About Off-Label Uses To Medical Professionals.

Because of the importance of off-label use in clinical practice, the public interest is best served when physicians have as much truthful, accurate, and nonmisleading information as possible regarding such uses. *See* Dissemination of Information on Unapproved/New Uses for Marketed Drugs, Biologics, and Devices, 63 Fed. Reg. 64,556, 64,579 (Nov. 20, 1998) (recognizing the "public health gains associated with the earlier dissemination of objective, balanced, and accurate information on important unapproved uses of approved products"); *see also* Paul E. Kalb & Paul E. Greenberg, *Legal and Economic Perspectives Concerning US Government Investigations of Alleged Off-Label Promotion by Drug Manufacturers*, 27 Pharmacoeconomics 623, 623 (2009), *available at* http://tinyurl.com/yzcjfrs ("Physicians' decisions to prescribe off label are informed by the available scientific literature, and it stands to reason that the more truthful, nonmisleading data available, the more informed their decisions will be."). The practitioners who comprise the audience for such information are trained professionals who are able to evaluate it intelligently. And there is no question that these doctors can and often must prescribe drugs off-label as science advances – a fact acknowledged by the FDA's recognition of the importance of off-label use. The question is whether they will do so with the best possible information.

Manufacturers are particularly well-positioned to provide this information because of their access to it. As the FDA long has recognized, "[s]cientific departments within regulated companies generally maintain a large body of information on their products," 59 Fed. Reg. at 59,823, including data on off-label uses, and particularly information regarding the risks of such

uses and measures available to physicians to make those uses safer for patients.[5] In short, manufacturers tend to know their own products best. *See generally Wyeth v. Levine*, 129 S. Ct. 1187, 1202 (2009) (manufacturers "have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge"); *e.g.*, Compl. ¶ 54 ("Allergan monitors and reports every available adverse event report received following treatment with Botox® anywhere in the world."). And, they have the resources to share this information, because they are in direct touch with prescribers. Simply put, no one is better positioned to ensure that prescribers have important new information about the drugs they prescribe and administer to their patients. Accordingly, the "[d]issemination of independently derived scientific information about unlabeled uses by manufacturers to physicians can help physicians have access to the latest, scientifically credible information." 1997 Annual Meeting of the American Medical Association, *supra*, at 4; *see also More Information for Better Patient Care: Hearing of the Senate Comm. on Labor and Human Resources*, 104th Cong. 81 (1996) (statement of Dr. Gregory H. Reaman, Director, Medical Specialty Services, Children's National Medical Center) ("Pharmaceutical and biotechnology companies obviously have an interest in supporting new uses of their products, but they also happen to be in the best position to share information with the physician community at the earliest possible time, when it may really make a difference in treatment options.").

Notably, the FDA itself recognizes the value of manufacturer-to-physician speech regarding off-label uses. FDA policy purports to allow a manufacturer to respond to a question posed

[5] FDA does not itself test new drugs before approval but rather reviews data and information submitted to the Agency by the manufacturers of those products. *See* 21 U.S.C. § 355(b). Moreover, prescription drug manufacturers are required to monitor a wide range of sources of information on the risks and benefits of their products in clinical practice, and to report such information to FDA in accordance with specific regulatory requirements. *See, e.g., id.* § 355(k); 21 C.F.R. § 314.80.

by a health care provider regarding an off-label use. *See* Citizen Petition Regarding the Food and Drug Administration Policy on Promotion of Unapproved Uses of Approved Drug and Devises; Request for Comments, 59 Fed. Reg. 59,820, 59,823 (Nov. 18, 1994). However, if the manufacturer provides the same information on its own initiative, then it runs the risk of enforcement action for forbidden off-label "promotion," which the government argues is criminal through its interpretation of the FDCA's misbranding and new drug provisions. In short, for speaking without first having been invited to do so, a manufacturer risks criminal prosecution.[6]

The harm caused by the restraint on manufacturers' speech about emerging scientific research (and about other information concerning new uses) is manifest. And, critically, this harm cannot be cured by changing a drug's labeling through the supplemental approval process. Under the FDA's regulations, the *only* way to add a new indication to labeling – to convert an "off-label" use to an "on-label" use – is to conduct clinical trials and submit the resulting data, together with other information, to the FDA for review. 21 C.F.R. § 314.70(c)(6)(iii)(A-D). But there is no clear regulatory pathway for a manufacturer to provide treating physicians with information relating to an off-label use while that use is under FDA review. *See id.* § 312.55(b) (allowing a manufacturer to provide physicians with risk information pertaining to a use under investigation *only if* the physicians are "investigators" as defined in 21 C.F.R. § 312.3). The

[6] From a public health and First Amendment perspective, it is no answer to say that manufacturers can communicate adequately to prescribers about off-label uses by simply waiting for and responding to unsolicited requests for information. Prescribers must know something about the off-label use before they can make a request, and many physicians will not, or cannot, take the time or initiative to reach out to a corporate medical affairs department. More importantly, given the limited nature of the relevant policy, even once an inquiry has been received, a manufacturer still risks enforcement action on the theory that it has provided information that was not specifically requested. *See* 59 Fed. Reg. at 59,823 (to be covered by the policy, and therefore exempt from the ban on off-label promotion, information provided to prescribers must be "responsive" to an unsolicited inquiry); *see also supra* n.1 (describing federal enforcement efforts, including cases involving manufacturer response to requests where the requests were allegedly solicited).

time required for FDA approval often is measured in years, and would deprive physicians of vital treatment information in the interim. Nor is it always possible to convert off- to on-label uses. For instance, it may be unethical to conduct the necessary study, as in a circumstance where the off-label use represents the standard of care and patients cannot ethically be randomized to a placebo arm; and many doctors understandably will not encourage their patients to enter into a study where they might end up with a placebo rather than standard-of-care therapy.[7]

In addition, labeling itself does not always provide enough information for physicians to decide whether a drug will be safe or effective for every use, and is not intended to be comprehensive. The labeling contains "a *summary* of the essential scientific information needed for the safe and effective use of the drug," 21 C.F.R. § 201.56(a)(1) (emphasis added), and the highlights of prescribing information "'do not include all of the information needed to use'" a drug "'safely and effectively,'" *id.* § 201.57(a)(1). Simply put, "[m]uch critical information that the [FDA] has at the time of approval may fail to make its way into the drug label and relevant journal articles." Lisa M. Schwartz & Steven Woloshin, *Lost in Transmission: FDA Drug Information That Never Reaches Clinicians*, 361 New Engl. J. Med. 1717, 1717 (2009), *available at* http://tinyurl.com/yhfgo7k. Unless manufacturers can speak with greater freedom about emerging science relating to their medicines, the medical community will continue to use drugs off-

[7] *See* 21 C.F.R. § 314.126(a) (citing the necessity of "adequate and well-controlled investigations"); FDA, Basic Questions and Answers About Clinical Trials, *available at* http://tinyurl.com/ybetlog ("Comparison with a placebo can be the fastest and surest way to demonstrate therapeutic effectiveness of new products."); (last visited Nov. 18, 2009) Joseph T. Flynn, *Ethics of Placebo Use in Pediatric Clinical Trials: The Case of Antihypertensive Drug Studies*, 42 Hypertension 865, 866 (2003) ("Use of placebo is especially suspect if an accepted treatment exists for a given condition and the potential subject is to be withdrawn from or denied active treatment in order to be enrolled in the study.").

label without receiving all relevant safety and efficacy information. Due regard for public health demands that doctors be fully informed and, as we discuss next, so does the First Amendment.

II. THE FIRST AMENDMENT PROTECTS TRUTHFUL, ACCURATE, AND NONMISLEADING SPEECH REGARDING LAWFUL OFF-LABEL USES OF APPROVED PRESCRIPTION DRUGS.

This case fundamentally concerns truthful, accurate, nonmisleading speech about a lawful use of a lawful product. The speech, moreover, is of uncommonly high value, concerning the proper and safe use of a prescription drug. It is of great concern to the audience to which it is directed: physicians treating patients. And that audience is an audience not of lay consumers but of experts, individuals who have professional training that enables them to evaluate speech of this kind. Nothing could be clearer as a matter of First Amendment first principles than that the government may not indiscriminately prevent such speech, whether through direct prohibition, indirect regulation, or overbroad investigative and enforcement activity that chills its exercise. No First Amendment case begins to allow anything of the kind. On the contrary, for more than 30 years, the Supreme Court has rejected governmental attempts to paternalistically limit, confine, or dictate public discussion of lawful products. *See generally United States v. Caputo*, 517 F.3d 935, 938-39 (7th Cir.) (discussing *Virginia State Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748 (1976)), *cert. denied*, 129 S. Ct. 94 (2008).

Because Allergan has presented a full doctrinal analysis under the First Amendment, this submission is confined to three essential points that flow from the important facts about off-label use set forth above. *First*, the First Amendment is directly implicated when the government seeks to limit prescription drug manufacturers' truthful, accurate and non-misleading speech regarding off-label uses of approved products. *Second*, the speech at issue here is not commercial. Although uttered by an actor that presumably could gain financially, the content of the speech is scientific – or at a minimum, mixed – and lies at the heart of what the First Amendment is meant

to protect. Restrictions on such speech should be subjected to strict scrutiny. *Third,* even if this scientific speech were treated as commercial, and restrictions on it therefore were subject only to intermediate scrutiny, the result would be no different. This is because the government's consumer-protection rationale for restricting this speech amounts to an impermissibly paternalistic effort to control the flow of information, with the effect of excluding particular well-informed speakers from the discussion of scientific subjects. Such paternalism is particularly misplaced in light of the expert audience to which these communications are directed.

A. The First Amendment Protects Manufacturers' Speech Regarding Off-Label Uses Of Their Lawful Products.

Current federal enforcement efforts aimed at off-label promotion restrict prescription drug manufacturers' speech, and therefore implicate the First Amendment. Under this regime, a manufacturer is entitled to speak *relatively* freely about any labeled use, but faces criminal sanctions if it "promotes" a use that is not set forth in approved labeling, even if that use is lawful and represents optimal medical practice, and even if the information provided is truthful, accurate, and nonmisleading. Moreover, because the line between what is lawful and what is forbidden does not follow the line between truth and falsity, some entirely truthful speech is potentially criminalized by this regime. That is the very picture of a forbidden content-based restriction: "'Regulations which permit the Government to discriminate on the basis of the content of the message cannot be tolerated under the First Amendment.'" *Simon & Schuster, Inc. v. Members of the N.Y. State Crime Victims Bd.*, 502 U.S. 105, 116 (1991). The First Amendment concerns are all the more serious given the severity of the criminal and other penalties at issue. *See, e.g.*, *supra* n.1.

It is no answer to argue, as the Government sometimes has done, that these federal enforcement efforts are aimed at conduct rather than speech, of which the speech concerning off-

label uses is mere evidence. *Cf. Wisconsin v. Mitchell*, 508 U.S. 476, 489 (1993) ("The First Amendment … does not prohibit the evidentiary use of speech to establish the elements of a crime or to prove motive or intent."). To be sure, there is a "'distinction between making speech the crime … and using speech to prove the crime.'" *State v. Halstien*, 857 P.2d 270, 279-80 (Wash. 1993) (emphasis omitted). In this context, however, it manifestly is the speech itself that is at issue – the enforcement regime targets, and is premised upon, manufacturer speech concerning off-label uses. As Judge Lamberth pointedly noted in *WLF I*:

> This court is hard pressed to believe that the agency is seriously contending that "promotion" of an activity is conduct and not speech, or that "promotion" is entitled to no First Amendment protection. There may certainly be a "line" between education and promotion as regards a drug manufacturer's marketing activities, but that is the line between pure speech and commercial speech, not between speech and conduct.

13 F. Supp. 2d at 59; *accord Caronia*, 576 F. Supp. 2d at 394-95. Put otherwise, "[t]he Supreme Court has never accepted the notion that truthful speech can be regulated in order to prevent harm where the sole embodiment of that harm is the speech itself." Richard A. Samp, *Courts Are Arriving at a Consensus on Food and Drug Administration Speech Regulation*, 58 Food & Drug L.J. 313, 324 (2003); Richard M. Cooper, *The WLF Case Thus Far: Not With a Bang but With a Whimper*, 55 Food & Drug L.J. 477, 484 (2000) ("[I]f evidence of protected speech is somehow relevant and otherwise admissible at a trial for engaging in unprotected speech, then such evidence may be admitted. The *target* of the enforcement action, however, may not be protected speech." (emphasis added)). Here, the government's goal is to prevent manufacturer speech about off-label uses, and the government's decision to target that speech for punishment is not purified from a constitutional perspective by filtering it through criminal statutes that purport to criminalize something of which the speech is the *sine qua non*.

That the First Amendment applies here is made clear by the Supreme Court's resolution of a similar issue in *Thompson v. Western States Medical Center,* 535 U.S. 357 (2002). The statute at issue in *Western States* did not directly prohibit speech – there, advertising – but did sanction it, providing that a pharmacist who advertised would not be exempted from the new drug approval provisions of the FDCA. *Id.* at 360. Notwithstanding the lack of a direct prohibition on speech, the Supreme Court nevertheless invalidated the statute on First Amendment grounds. *Id.* at 377. Accordingly,

> After *Western States*, FDA can no longer assert that its use of speech as a proxy for conduct is exempt from First Amendment scrutiny. Its use of speech to determine when a regulated drug or device will be treated as 'new' for purposes of approval requirements … or as 'misbranded' … must survive exacting First Amendment standards.

A. Elizabeth Blackwell & James M. Beck, *Drug Manufacturers' First Amendment Right to Advertise and Promote Their Products for Off-Label Use: Avoiding a Pyrrhic Victory*, 58 Food & Drug L.J. 439, 445-46 (2003). Nor did the fact that FDA had exerted extensive authority over both the pharmaceutical industry in general, and pharmacists in particular, prevent the Court from invalidating the unconstitutional restraint on pharmacist speech. Indeed, the notion that the government may restrict speech because it restricts relevant conduct has matters precisely backwards: "[T]he First Amendment directs that government may not suppress speech as easily as it may suppress conduct, and that speech restrictions cannot be treated as simply another means that the government may use to achieve its ends." *44 Liquormart, Inc. v. Rhode Island.* 517 U.S. 484, 510-13 (1996) (plurality).[8]

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[8] *See also United States v. Wenger*, 427 F.3d 840, 846 n.1 (10th Cir. 2005) ("[T]he Supreme Court has rejected the idea that the power to extensively regulate in a certain area includes the authority to regulate speech without raising First Amendment concerns."); *WLF I*, 13 F. Supp. 2d at 60-62 (rejecting the FDA's argument that it may restrict off-label promotion without implicating the First Amendment because of the pervasiveness of the FDCA's statutory scheme); *Com-*
(Footnote Continued)

B. Truthful, Accurate, Nonmisleading Speech About Off-Label Uses of Approved Prescription Drugs Is Entitled To Full First Amendment Protection.

Truthful, accurate, nonmisleading speech that implicates issues of both scientific inquiry and public health is high-value speech, and restrictions on it should be subject to strict scrutiny. According to the Complaint, the use of Botox to treat spasticity represents an established medical practice, and has for years. Compl. ¶¶ 54-56, 59-63. Allergan has submitted spasticity-related indications for FDA approval, *id.* ¶¶ 57-58, and the FDA itself has recognized that Botox's off-label use to treat juvenile cerebral palsy is a "'very effective means to relieve a very important problem'" and that it should not be discouraged. *Id.* ¶ 75. Allergan wishes to disseminate scientific information regarding spasticity, *id.* ¶¶ 76, 81-82, and, like any manufacturer, is well positioned – if not uniquely so – to comment on its own products, *id.* ¶ 80. It proposes to limit its audience to licensed physicians, and to reiterate that neither the uses nor the information it will be providing have been approved by the FDA. *Id.* ¶¶ 77-79.

Nonetheless, notwithstanding that Plaintiff's proposed speech could be limited to the dissemination of truthful, accurate, and nonmisleading scientific information regarding a matter of

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modity Trend Serv. v. CFTC, No. 97 Civ 2362, 1999 U.S. Dist. LEXIS 15877, at *32-33 (N.D. Ill. Sept. 28, 1999) (rejecting the suggestion that restrictions on investment advice should be exempt from First Amendment scrutiny because the industry was subject to a comprehensive regulatory scheme).

Nor is there any basis to suppress the speech as "misleading," *cf. Central Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n*, 447 U.S. 557, 566 (1980) ("For commercial speech to come within [the First Amendment], it at least must concern lawful activity and not be misleading."), simply because it pertains to a use the FDA has not approved. "FDA exaggerates its overall place in the universe" in suggesting that "all scientific claims about … prescription drugs are presumptively untruthful or misleading until the FDA has had the opportunity to evaluate them." *WLF I*, 13 F. Supp. 2d at 67; *see also Pearson v. Shalala*, 164 F.3d 650, 655 (D.C. Cir. 1999) (the argument that unverified health claims lacking significant scientific agreement are "inherently misleading" due to their potential impact on lay consumers "is almost frivolous"). Notably, moreover, the government's suppression of off-label speech is in no way confined to false or misleading speech.

clear public concern to a limited audience of learned professionals, we anticipate that the government will argue, as it has in the past, that this is mere "commercial speech" entitled to only intermediate protection. *See generally Central Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n*, 447 U.S. 557, 564 (1980) (setting forth the test for evaluating restrictions on commercial speech). For the reasons set out in Plaintiff's moving papers, the restrictions on Plaintiff's speech cannot survive *Central Hudson* scrutiny. *See* Mem. of Law in Support of Mot. For Prelim. Inj., Dkt. No. 3, at 21-24. *Amici* submit, however, that the speech at issue here is not properly categorized as commercial speech in the first place, and even if it were, strict scrutiny still should apply.

1. Commercial speech "usually [is] defined as speech that does no more than propose a commercial transaction." *United States v. United Foods, Inc.*, 533 U.S. 405, 409 (2001); *Dun & Bradstreet, Inc. v. Greenmoss Builders, Inc.*, 472 U.S. 749, 790 (1985) (plurality) ("Commercial speech [is] defined as advertisements that do no more than propose a commercial transaction.") (quotation marks and brackets omitted).[9] Elsewhere, the Court has spoken of commercial speech as "expression related *solely* to the economic interests of the speaker and its audience." *Discovery Network*, 507 U.S. at 422 (emphasis added); *see also United States v. Philip Morris USA, Inc.*, 566 F.3d 1095, 1143 (D.C. Cir. 2009) (per curiam) ("Commercial speech is defined as 'expression related solely to the economic interests of the speaker and its audience' or 'speech proposing a commercial transaction.'") (quoting *Central Hudson*, 447 U.S. at 561-62).

The speech at issue here – which Allergan explains is truthful, accurate, nonmisleading speech from prescription drug manufacturers to medical professionals about the safety and effi-

[9] *See also City of Cincinnati v. Discovery Network, Inc.*, 507 U.S. 410, 422 (1993); *Bd. of Trs. v. Fox*, 492 U.S. 469, 473-74 & 482 (1989) (whether speech proposes a commercial transaction "is the test for identifying commercial speech" and "is what defines commercial speech").

cacy of unlabeled uses of prescription drugs – does not remotely fit either description. Whatever analysis might apply to consumer-oriented advertising, this proposed speech to medical professionals does much "more than propose a commercial transaction," *United Foods*, 533 U.S. at 409, and does not relate "solely to the economic interests" of the manufacturers or the physicians, *Philip Morris*, 556 F.3d at 1143. Rather, this speech has scientific and medical/clinical value. According to the Complaint, this speech would provide "guidance to physicians as [to] what steps they can take, if they use Botox® for spasticity, to achieve the desired effect while reducing the risk of adverse events and improving the overall risk-benefit profile." Compl. ¶ 76; *see generally id.* ¶¶ 77-87 (detailing its proposed speech). Truthful and nonmisleading speech concerning the safe administration of a prescription drug will assist medical professionals, who then can make independent scientific judgments about whether, when, and how to use this information.

A rule by which this speech would receive lessened protection merely because it could financially benefit the manufacturer would be utterly unworkable, and would provide insufficient protection for all sorts of high-value speech. *Cf. First Nat'l Bank v. Bellotti*, 435 U.S. 765, 776-77 (1978) (corporate speech on a matter of public concern remains "indispensable to decision-making in a democracy" regardless whether the speech or topic would materially affect its business). Charitable solicitation, for instance, is driven by a financial motive, as indeed is much speech about charitable causes that, it is hoped, will spawn donations. Financial motivations also stand, at least in significant part, behind many forms of artistic expression, but there is no doctrinal support for the notion that the sale of artwork obviates its First Amendment protection. Much academic research is tied up with financial considerations, whether in the form of grant proposals or tenure considerations. It would make little sense to deprive these valued forms of

speech of their First Amendment protection because of some partial economic motivation or benefit. *See Bd. of Trs. v. Fox*, 492 U.S. 469, 482 (1989) (distinguishing "speech for a profit" from "speech that *proposes* a commercial transaction, which is what defines commercial speech"; "Some of our most valued forms of fully protected speech are uttered for a profit." (emphasis in original)); *Rubin v. Coors Brewing Co.*, 514 U.S. 476, 494 (1995) (Stevens, J., concurring in the judgment) ("[E]conomic motivation or impact alone cannot make speech less deserving of constitutional protection[.]"). The same is true here. As noted above, and set forth more fully in the Complaint, the speech here goes directly to scientific and medical concerns. Accordingly, even assuming that it also has some financial motivation, the result is simply to render the speech "mixed," and it should retain full First Amendment protection: "It is not clear that a professional's speech is necessarily commercial whenever it relates to that person's financial motivation for speaking. But even assuming, without deciding, that such speech in the abstract is indeed merely 'commercial,' we do not believe that the speech retains its commercial character when it is inextricably intertwined with otherwise fully protected speech." *Riley v. Nat'l Fed'n of Blind*, 487 U.S. 781, 795-96 (1988) (citation omitted).[10]

[10] In *WLF I*, Judge Lamberth concluded that the speech at issue there was commercial speech that deserved only intermediate protection. *See* 13 F. Supp. 2d at 64-65. This conclusion was based on *Bolger v. Youngs Drug Products Corporation.* In *Bolger*, unlike here, the pamphlets at issue were "conceded to be advertisements." 463 U.S. 60, 66 (1993). Moreover, although *WLF I* properly recognized that manufacturer speech about off-label uses "present[s] one of those complex mixtures of commercial and non-commercial elements," 13 F. Supp. 2d at 62 (internal quotation marks omitted), it failed to acknowledge the legal conclusion that flows from this premise: that, under *Riley*, the speech therefore deserves full First Amendment protection. *See* 487 U.S. at 795-96. This is another reason that *Bolger* does not control here. In *Bolger*, the Court noted that nothing would prevent the defendant companies from speaking on the issues outside of the commercial context. *See* 463 U.S. at 68 ("A company has the full panoply of protections available to its direct comments on public issues[.]"). Where, by contrast, off-label promotion is concerned, a company faces the threat of civil and criminal liability for engaging in

(Footnote Continued)

2. For closely related reasons, even if this speech were properly termed "commercial," its restriction still should be subjected to strict scrutiny. "The mere fact that messages propose commercial transactions does not in and of itself dictate the constitutional analysis that should apply to decisions to suppress them." *44 Liquormart,* 517 U.S. at 501 (opinion of Stevens, Kennedy, and Ginsburg, JJ.); *id.* at 518 (Thomas, J., concurring in part and concurring in the judgment); *Nike, Inc. v. Kasky*, 539 U.S. 654, 676-79 (2003) (Breyer and O'Connor, JJ., dissenting from dismissal) (communications that "are not purely commercial in nature" warrant strict First Amendment scrutiny); *Riley*, 487 U.S. at 795; *see Western States*, 535 U.S. at 367-68 (listing cases questioning the applicability of *Central Hudson* intermediate scrutiny in particular circumstances); *cf. Bates v. State Bar of Ariz.*, 433 U.S. 350, 363 (1977) (commercial speech "'must be distinguished by its content'").

A principal rationale for singling out some forms of speech for lesser First Amendment protection – that is, applying intermediate scrutiny under *Central Hudson* rather than traditional strict scrutiny – is "the importance of avoiding deception and protecting the consumer from inaccurate or incomplete information." *Rubin*, 514 U.S. at 493 (Stevens, J., concurring in the judgment). This rationale collapses in circumstances where the regulation "neither prevents misleading speech nor protects consumers from the dangers of incomplete information." *Id.* at 492. In the absence of such a concern, there is no basis "for upholding a prohibition against the dissemination of truthful, nonmisleading information … merely because the message is propounded in a commercial context." *Id.* at 493; *44 Liquormart*, 517 U.S. at 501 (opinion of Stevens, Kennedy, and Ginsburg, JJ.) ("[W]hen [the Government] entirely prohibits the dissemination of truthful,

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such speech in any arena, and so the commercial and non-commercial aspects of speech truly are intertwined.

nonmisleading commercial messages for reasons unrelated to the preservation of a fair bargaining process, there is far less reason to depart from the rigorous review that the First Amendment generally demands.").

This is all the more so in light of the manifest benefits of the sort of speech at issue here. A proper First Amendment analysis should consider "the amount of beneficial speech prohibited by" the regulation. *Western States*, 535 U.S. at 376. In *Western States*, the Court stated that even if the government had been able to justify a ban on advertisements regarding compounded drugs, the ban would still have been unconstitutional because it prohibited valuable communications: That the ban "prohibit[s] … seemingly useful speech" should "confirm[] … that the prohibition is unconstitutional." *Id.* at 377. That concern applies with even greater force when, as here, the speech is directed to an audience of experts with years of professional training. Accordingly, these restrictions "should be subjected to the same stringent review as any other content-based abridgment of protected speech." *Rubin*, 514 U.S. at 497 (Stevens, J., concurring in the judgment). And if, as alleged, the federal enforcement regime as applied here works to suppress information about state-of-the-art medical treatments that is truthful, accurate, and nonmisleading, it is manifestly unconstitutional.

C. Under Any First Amendment Standard, Speech Restrictions Cannot Be Sustained When They Amount To Paternalistic Efforts By The Government To Control The Content Of Scientific Discussions Concerning The Safety And Efficacy Of Lawful Uses Of Lawful Products.

Under either constitutional test – that is, whether the scrutiny this Court applies is strict or intermediate – the First Amendment forbids the government from paternalistically limiting the flow of information to the marketplace concerning lawful transactions in lawful products. The Supreme Court has roundly and repeatedly rejected the notion that such speech (so long as it is truthful and nonmisleading) can be abrogated in an effort to protect the recipients of that infor-

mation from themselves. "There is, of course, an alternative to this highly paternalistic approach. That alternative is to assume that … information is not in itself harmful, that people will perceive their own best interests if only they are well enough informed, and the best means to that end is to open the channels of communication rather than to close them." *Virginia State Bd.*, 425 U.S. at 770; *Linmark Assocs. v. Twp. of Willingboro*, 431 U.S. 85, 96-97 (1977) (the government may not act "to prevent its residents from obtaining … information" on the ground that they "will make decisions inimical to what the [government] views as [their] self-interest").[11]

This rule applies with force to truthful, nonmisleading speech related to off-label uses of approved products when, as we have emphasized above, such speech addresses a matter of public health and is directed to a sophisticated audience of learned professionals. Government suppression of such speech cannot be reconciled to the First Amendment:

> [I]f a given use is lawful, and thus can be written about freely in newspapers or blogs, and discussed among hospitals … doesn't it make a good deal of sense to allow speech by the [drug's] manufacturer, which after all will have the best information? Why privilege speech by the uninformed? The manufacturer has an incentive to slant the speech in its favor and may withhold bad news, but many listeners (especially professionals such as physicians) understand this and can discount appropriately. That, at any rate, is the anti-paternalist view of [*Virginia State Board*] and the cases that followed in its wake.

Caputo, 517 F.3d at 939. What instead results from the current enforcement regime is a distorted presentation of information to medical professionals. The government exercises its ability to

[11] *Accord Bates*, 433 U.S. at 375 ("[W]e view as dubious any justification that is based on the benefits of public ignorance."); *Peel v. Atty. Registration & Disciplinary Comm'n,* 496 U.S. 91, 105 (1990) (plurality) (rejecting "the paternalistic assumption" that the recipients of attorney advertisements will be misled by claims of specialized expertise); *Rubin*, 514 U.S. at 497 (Stevens, J., concurring in the judgment) ("Any 'interest' in restricting the flow of accurate information because of the perceived danger of that knowledge is anathema to the First Amendment …."); *44 Liquormart*, 517 U.S. at 510 (plurality) ("[W]e conclude that [the government] does not have the broad discretion to suppress truthful, nonmisleading information for paternalistic purposes ….").

speak, as in the form of press releases concerning proposed uses. Compl. ¶ 65. It forces the manufacturer to speak consistent with the government's own views. *Id.* ¶¶ 59-63, 72-74. And then it *forbids* the manufacturer from supplementing the discussion with relevant information about these uses, simply because the FDA has not approved them. *Id.* ¶¶ 69-70. This stage-managed conversation is bad for public health, and flatly inconsistent with basic First Amendment values: Forcing a manufacturer "to toe the government's line, or shut up, is unconstitutional." *Caputo*, 517 F.3d at 939 (citing *Western States*, 535 U.S. 357).

The restriction on manufacturer-to-physician communications distorts the information flow concerning off-label uses of prescription medications. It is legal for a physician to prescribe off-label; it is legal for an academic to study off-label uses; and it is legal for the government, outside advocacy groups, and any other non-manufacturer speakers to comment on off-label uses. Yet the manufacturer may not communicate to a treating physician additional truthful, accurate, and nonmisleading scientific information without risking criminal prosecution, civil lawsuits, and exclusion from federal health care programs. *See* Compl. ¶¶ 48-50. The First Amendment forbids regulation that seeks to exclude a speaker or suppress one side of a discussion about the lawful use of a lawful product. *See Bellotti*, 435 U.S. at 784-85 ("[T]he legislature is constitutionally disqualified from dictating … the speakers who may address a public issue."); *Central Hudson*, 447 U.S. at 573 (Blackmun and Brennan, JJ., concurring in the judgment). If the Government has concerns about, or disagrees with, the information a manufacturer provides with regard to its approved drug products, it may respond with "'more speech, not enforced silence.'" *Lorillard Tobacco Co. v. Reilly*, 533 U.S. 525, 586 (2001) (Thomas, J., concurring in the judgment) (quoting *Whitney v. California*, 274 U.S. 357, 377 (1927) (Brandeis, J., concurring)); *Bates*, 433 U.S. at 375 ("[T]he preferred remedy is more disclosure, rather than less.");

see also Caputo, 517 F.3d at 939 (the solution is to "allow the FDA to supply warnings via its own speech").[12]

CONCLUSION

For the reasons set forth above, the undersigned *amici curiae* urge the Court to grant the relief requested in Allergan's Complaint and Motion for Preliminary Injunction.

[12] Any concern that communications from a prescription drug manufacturer to a physician regarding the safety and efficacy of an off-label use would convey the impression that the use was FDA-approved (a dubious proposition to say the least) is more than met by Allergan's proposal to reiterate that neither the use in question nor the information pertaining to it has been approved by the FDA. *See* Compl. ¶¶ 77-79; *see also Western States*, 535 U.S. at 376 ("Even if the Government … had an interest in preventing misleading [promotion], this interest could be satisfied by the far less restrictive alternative of requiring each compounded drug to be labeled with a warning that the drug had not undergone FDA testing and that its risks were unknown."); *Pearson*, 164 F.3d at 657 (concluding that the FDA was constitutionally required to pursue a disclaimer regime rather than ban potentially misleading health claims).

Dated: November 19, 2009

Respectfully submitted,

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