IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSSACHUSETTS

ZOGENIX, INC., 12400 High Bluff Drive, Suite 650 San Diego, CA 92130, Plaintiff, v. DEVAL PATRICK, in his official capacity as GOVERNOR OF THE COMMONWEALTH OF MASSACHUSETTS, Massachusetts State House, Office of the Governor, Room 105, Boston, MA 02133, and CHERYL BARTLETT, RN, in her official capacity as DEPARTMENT OF PUBLIC HEALTH COMMISSIONER, Massachusetts Department of Public Health 250 Washington Street, Boston, MA 02108. Defendants.	Civil Action No. _____ **DEMAND FOR JURY TRIAL**

VERIFIED COMPLAINT

Plaintiff Zogenix, Inc. ("Zogenix"), by its undersigned counsel, hereby brings this Verified Complaint against Defendants Deval Patrick, solely in his official capacity as Governor of the Commonwealth of Massachusetts ("Governor Patrick"), and Cheryl Bartlett, RN, solely in her official capacity as Commissioner of the Department of Public Health ("Commissioner Bartlett"), and states and alleges the following:

1. This is an action seeking temporary, preliminary and permanent injunctive relief, a declaratory judgment, and other appropriate relief to set aside as unconstitutional the recent actions of the Governor and Commissioner to ban the prescribing, ordering, dispensing, and administration of a pain medication deemed safe and effective by the federal Food and Drug Administration ("FDA") and specifically approved by FDA as safe and effective for marketing and sale in the United States.

2. Zogenix's product, Zohydro™ ER (Hydrocodone Bitartrate Extended-Release Capsules), was approved by FDA on October 25, 2013 for the management of severe pain in patients requiring continuous around-the-clock opioid therapy.

3. The active ingredient in Zohydro™ ER, hydrocodone, has been available in FDA-approved products since 1943 and is the same active ingredient found in a number of immediate-release hydrocodone combination analgesic products currently on the market. Products containing hydrocodone in combination with acetaminophen are some of the most commonly prescribed opioid analgesics currently available in Massachusetts and elsewhere for the treatment of chronic pain.

4. Zohydro™ ER is the first single-entity hydrocodone product available on the market and is the only hydrocodone product subject to schedule II controls under the Controlled Substances Act and the Massachusetts Controlled Substances Act – the most restrictive schedule available for an FDA-approved product.

5. Notwithstanding that FDA already has determined Zohydro™ ER to be safe and effective – and approved it for marketing and sale in the United States – Governor Patrick recently issued an "emergency declaration" empowering Commissioner Bartlett to issue an order prohibiting the prescribing, ordering, dispensing, or administration of hydrocodone-only

extended release drug products, a category that only includes Zohydro™ ER. Ex. A. The single substance ban will be lifted only when Commissioner Bartlett "has determined that adequate measures are in place to safeguard against the potential for diversion, overdose, and abuse…." *Id.* at 2.

6. When FDA approved Zohydro™ ER, it considered but rejected the idea of requiring the drug to utilize abuse-deterrent technology. Thus, in effectuating the present ban, the Commonwealth is attempting to override the reasoned decision by FDA not to require abuse-deterrent technology for Zohydro™ ER and taking upon itself the responsibility for regulating the safety of drugs already approved by FDA as safe and effective.

PARTIES

7. Plaintiff Zogenix, Inc. is a Delaware corporation with its principal place of business at 12400 High Bluff Drive, Suite 650, San Diego, California, 92130. Zogenix holds an approved New Drug Application, No. 202880, for Zohydro™ ER.

8. Defendant Deval Patrick is the Governor of the Commonwealth of Massachusetts. Governor Patrick maintains an office at the Massachusetts State House, Office of the Governor, Room 105, Boston, Massachusetts, 02133.

9. Defendant Cheryl Bartlett is the Commissioner of the Massachusetts Department of Public Health. Upon information and belief, Commissioner Bartlett maintains an office at the Massachusetts Department of Public Health, 250 Washington Street, Boston, Massachusetts, 02108.

JURISDICTION AND VENUE

10. Jurisdiction in this Court is grounded upon and proper under 28 U.S.C. § 1331 in that this is a civil action arising under the laws of the United States; and 28 U.S.C. §§ 2201-2202

in that there exists between Zogenix and the Defendants an actual, justiciable controversy as to which Zogenix requires a declaration of its rights by this Court as well as temporary, preliminary and permanent injunctive relief to prohibit the Defendants from violating federal laws and regulations and abridging its rights protected under the U.S. Constitution.

11. Venue is proper in this Court under 28 U.S.C. § 1391(b) because this is a civil action in which the Defendants maintain their offices and conduct business in this judicial district. Moreover, a substantial part of the events giving rise to the claims herein occurred within this judicial district.

12. Zogenix has standing to bring the present lawsuit because Defendants' actions have caused Zogenix actual injury, which is redressable through the specific relief requested herein. As a pharmaceutical company manufacturing and selling pain medication through interstate commerce pursuant to its approval by the FDA, Zogenix's operations also fall within the zone of interests to be protected by the Contract and dormant Commerce Clauses of the U.S. Constitution, as well as general federal preemption principles.

13. This case is ripe for adjudication. As further discussed below, the enforcement of the emergency declaration and order will result in an immediate and concrete invasion of Zogenix's legally protected interests under federal law.

NATURE OF THE CASE

1. Statutory Process for FDA Approval of Drugs:

14. Congress has vested FDA with responsibility for reviewing and approving all new prescription drugs sold in the United States. To that end, the Food, Drug, and Cosmetic Act ("FDCA") requires all new prescription drugs to obtain FDA approval under a new drug application ("NDA") before they can enter the marketplace. 21 U.S.C. § 355(a), (b).

15. Prior to receiving FDA approval, brand name or "pioneer" drug manufacturers must demonstrate the safety and effectiveness of their products. See 21 U.S.C. § 355(b). Drug manufacturers can accomplish this in several different ways: (i) they can submit full reports of safety and effectiveness, id. § 355(b)(1); (ii) they can submit full reports of safety and effectiveness where at least some of the information required for approval comes from studies not conducted by or for the applicant, id. § 355(b)(2); or (iii) they can submit information establishing that the proposed product is identical in specified characteristics to a previously approved product, id. § 355(j).

16. An NDA applicant is required to submit extensive clinical evidence that the drug product is safe and effective; a list of the components of the drug; a statement of the drug's composition; a description of the manufacturing, processing, and packaging of the drug; samples of the drug as necessary; patent information on any patent that it claims will protect the drug product or its uses; and proposed labeling for the drug. 21 U.S.C. § 355(b)(1). To establish safety and effectiveness, an NDA must include "full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use." 21 U.S.C. § 355(b)(1)(A).

17. Upon receipt of an NDA, FDA is charged with performing a thorough analysis of the drug's safety and effectiveness—a process that requires the agency to carefully balance the benefits and risks to patients. 21 U.S.C. §§ 355(c), (d). FDA will approve an NDA only when all necessary data are submitted or referenced to establish the product's safety and effectiveness. *Id*. And FDA will refuse to approve an NDA if it finds that the application and the data presented to support the application do not establish the safety and effectiveness of the product. 21 U.S.C. § 355(d); 21 C.F.R. § 314.125.

18. All drugs have some ability to cause adverse effects. Thus, FDA's safety assessment of a drug is determined by:

> whether its benefits outweigh its risks. This benefit-risk assessment is the basis of FDA's regulatory decisions in the pre-market and post-market review process. It takes into account the extensive evidence of safety and effectiveness submitted by a sponsor in [an NDA], as well as many other factors affecting the benefit-risk assessment, including the nature and severity of the condition the drug is intended to treat or prevent, the benefits and risks of other available therapies for the condition, and any risk management tools that might be necessary to ensure that the benefits of the drug outweigh its risks. This assessment involves both quantitative analyses and a subjective qualitative weighing of the evidence. Structured Approach to Benefit-Risk Assessment in Drug Regulatory Decision-Making, PDUFA V Plan (FY 2013-2017), Draft of February 2013 at 1, *available at* http://patientnetwork.fda.gov/sites/default/files/fda_benefit-risk_draft_plan_final_for_posting.pdf.

19. At the time of initial approval of an NDA, FDA also may require a risk evaluation and mitigation strategy ("REMS") for the drug if it is determined to be necessary to ensure that the benefits of a drug outweigh the drug's risks. 21 U.S.C. § 355-1. A REMS for an NDA product must include a timetable for submission of assessments of the REMS. 21 U.S.C. § 355-1(d). In addition, FDA may require that a REMS include any or all of the other REMS elements set out in the FDCA if specific criteria are met. 21 U.S.C. § 355-1(e), (f). Such additional elements may include elements to assure safe use ("ETASU"). FDA may require a REMS with ETASU if the drug has been shown to be effective but is associated with a serious adverse drug experience and can only be approved if such elements are required as part of a strategy to mitigate a specific serious risk listed in the labeling of the drug. 21 U.S.C. § 355-1(f)(1). The FDCA specifically provides that the serious risks that can be considered in requiring a REMS include adverse events occurring from an overdose of the drug, whether accidental or intentional, and adverse events occurring from abuse of the drug. 21 U.S.C. 355-1(b).

20. ETASU can include a requirement that healthcare providers who prescribe the drug have particular training or experience; pharmacies, practitioners, or health care settings that dispense the drug are specially certified; the drug be dispensed to patients only in certain healthcare settings; the drug be dispensed to patients with evidence or other documentation of safe use conditions; each patient using the drug be subject to certain monitoring; and each patient using the drug be enrolled in a registry. 21 U.S.C. § 355-1(f). Before imposing the ETASU, FDA must ensure that the ETASU are commensurate with the specific risks listed in the drug's labeling and not unduly burdensome on patient access to the drug, taking into consideration patients with serious or life-threatening diseases or conditions and patients who have difficulty accessing healthcare. In addition, such ETASU must conform with elements to assure safe use for other drugs with similar, serious risks and be designed to be compatible with established distribution, procurement, and dispensing systems for drugs so as to minimize the burden on the healthcare delivery system. 21 U.S.C. § 355-1(f)(2).

2. Zohydro™ ER

21. Zogenix submitted an NDA for its drug Zohydro™ ER on May 1, 2012 under Section 505(b)(2) of the FDCA. 21 U.S.C. § 355(b)(2); Ex. B at 4. After eighteen months of careful scrutiny, FDA approved Zohydro™ ER on October 25, 2013 for the management of pain severe enough to require daily, around-the clock, long-term opioid treatment for which alternative treatment options are inadequate. Ex. C at 1.

22. Unlike all other hydrocodone products on the market used for chronic pain, Zohydro™ ER does not contain acetaminophen, thereby avoiding the potential for acetaminophen toxicity in patients for whom Zohydro™ ER is indicated. The use of products containing acetaminophen in high doses over long periods of time has the potential to cause liver

injury, acute liver failure, or even death. Acetaminophen overdose is a leading cause of acute liver failure in the United States, with 63 percent of unintentional acetaminophen overdoses attributed to the use of opioid-acetaminophen combination products. *See* Ex. D at 1. The availability of an acetaminophen-free formulation of extended release hydrocodone is an important therapeutic option for certain chronic pain patients.

23. Thus, Zohydro™ ER provides an important treatment option for patients on immediate release hydrocodone who need an extended-release product; for patients who are at risk for hepatic injury from acetaminophen; and for patients on other ER opioids in which another option for opioid rotation is of value.

24. During the approval process for Zohydro™ ER, FDA considered requiring abuse-deterrent technologies for the drug but ultimately concluded that the overall risk-benefit balance of Zohydro™ ER was sufficient to support approval of the NDA without an abuse-deterrent formulation. FDA outlined its reasoning in its Summary Approval. Ex. B. Among other factors, FDA emphasized the medical benefits of an acetaminophen-free hydrocodone to treat chronic pain patients, noting that a patient being treated with a combination hydrocodone product would be able to switch to Zohydro™ ER and reduce the number of doses per day and maintain a consistent blood level, "which is widely believed to be provide better long-term pain control and to reduce the 'rush' associated with high blood levels that appear to be sought after by opioid abusers." *Id.* at 33. In addition, for patients who have responded well to hydrocodone products but now need a higher dose due to tolerance or increased pain arising from to their underlying condition, Zohydro™ ER would permit prescribers to titrate those patients to an appropriate dose of hydrocodone without the development of toxicities associated with the hydrocodone combination products. *Id.* FDA also stated that the technology used to produce abuse-deterrent

opioid formulations "is still in the nascent stages." *Id.* Further, FDA has concluded that it is not "in the interest of public health at this time to require all opioid products or all [extended release/long-acting] opioid products" to feature the abuse deterrent formulation. *See* Ex. E at 3. In addition to abuse-deterrent formulations' known ineffectiveness at affecting abuse by swallowing whole pills, FDA noted that "the availability of opioid formulations that are not abuseable, that are not potentially addictive, and that do not have the potential to cause respiratory depression and death in overdose is not likely in the near future." Ex. B. at 33.[1]

25. FDA instead determined that there were effective measures in place to protect patients while still making Zohydro™ ER available for patients in need: The labeling of the product includes prominent warnings about abuse, a boxed warning about the known serious risks of addiction, abuse, and misuse, and statements urging prescribers to assess each patient's risk before prescribing the drug and to monitor patients regularly for the development of addiction, abuse, and misuse. And Zohydro™ ER – unlike all other hydrocodone products – is included in the Extended Release/Long-Acting Opioid Analgesics REMS designed to reduce serious adverse outcomes resulting from inappropriate prescribing, misuse, and abuse. FDA concluded that these measures combined were sufficient to support approval of the product. Ex. B at 31.

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[1] The Drug Enforcement Administration (DEA), in consultation with the Department of Health and Human Services (HHS), recently proposed to reschedule all hydrocodone combination products from Schedule III to Schedule II because they share the same potential for abuse as a single-agent hydrocodone formulation, such as Zohydro™ ER. Schedules of Controlled Substances: Rescheduling of Hydrocodone Combination Products from Schedule III to Schedule II, 79 Fed. Reg. 11037 (Feb. 27, 2014). Federal regulators thus have determined that drug products that combine hydrocodone with other active pharmaceutical ingredients neither mitigate nor diminish their potential for abuse. Accordingly, it appears that Defendants did not rely on any principled or evidence-based justification for distinguishing Zogenix's single-agent hydrocodone formulation from hydrocodone combination products, in terms of the potential for abuse.

3. Zogenix's Contracts

26. Zogenix maintains contracts with wholesalers who supply, and retailers who operate, Massachusetts pharmacies. In fact, pursuant to these contracts, several pharmacies already have stocked Zohydro™ ER.

27. Zogenix also contracts with Inflexxion, a Massachusetts company that developed cutting-edge abuse tracking methods in conjunction with the federal National Institutes of Health ("NIH").

4. Governor Patrick's Declaration of a Public Health Emergency

28. Without warning to or discussion with Zogenix regarding the safety and effectiveness of Zohydro™ ER, on March 27, 2014, Governor Patrick issued a press release (the "Press Release") announcing that the Governor had declared a public health emergency in Massachusetts and that the Governor had directed the Department of Public Health ("DPH") to take several action steps aimed at combatting opioid overdoses. *See* Ex. F. The Press Release announced that the declared public health emergency provided "emergency powers" to Commissioner Bartlett to, among other actions: "[i]mmediately prohibit the prescribing and dispensing of any hydrocodone-only formulation (commonly known as Zohydro) until determined that adequate measures are in place to safeguard against the potential for diversion, overdose, and misuse." *Id.* at 1-2.

29. That same day, the Governor issued a one-page Declaration of Emergency under M.G.L. chapter 17, section 2A, citing general concerns about opioid addiction and concluding that "an emergency exists which is detrimental to the public health" in Massachusetts. Ex. G at 2.

30. Also on March 27, 2014, the Commissioner and Public Health Council ("PHC") approved an emergency order (the "Order") providing: "No registered individual practitioner shall prescribe or order, and no one shall dispense or administer any hydrocodone bitartrate product in hydrocodone-only extended-release formulation until the Commissioner has determined that adequate measures are in place to safeguard against the potential for diversion, overdose and abuse." Ex. A. There is exactly one "hydrocodone bitartrate product in hydrocodone-only extended-release formulation": Zohydro™ ER.

31. The Commissioner and DPH explained the Order in a March 27, 2014 memorandum as follows: "This order will protect against overdose and abuse of hydrocodone-only extended-release formulation [sic], and provides the means for the Commissioner to lift the prohibition when there are adequate safety measures, such as an abuse-deterrent formulation, which will then allow for the prescribing of hydrocodone-only products to patients with severe pain without running as great a risk that the medication will be diverted or abuse [sic]." Ex. G.

32. This memorandum came as a surprise to Zogenix; it was never consulted before the memorandum issued. And the memorandum doubtless came as a surprise to FDA. As previously noted, during the course of the approval process for Zohydro™ ER, FDA expressly considered whether abuse-deterrent technology should be required for the drug, and it concluded that the benefits of the formulation outweighed any attendant risks. Ex. B at 30-33. Thus, in banning Zohydro™ ER pending its implementation of abuse-deterrent technology, and in determining that the drug is not safe in its current formulation, the Commonwealth placed itself squarely in opposition to the FDA's expert determination and in conflict with federal law. But it did so without any indication that it developed or considered the same factual record surrounding Zohydro™ ER that was presented to the FDA in connection with the agency's determination.

Prohibiting the sale of Zohydro™ ER in Massachusetts also is inconsistent with the Commonwealth's obligations under the drug rebate Medicaid statute. 42 U.S.C. § 1396r-8.

33. Defendants' ban will have an impact on patients beyond the borders of Massachusetts. On March 31, 2014, the director of the Prescription Monitoring and Drug Control division of the DPH issued a Circular Letter to all providers who were Massachusetts Controlled Substance Registrants that informed the providers of the emergency declaration and order and supplied sample "Q&As" that might arise from the Defendants' actions. Ex. A at 2. One question asked whether a Massachusetts provider could still prescribe hydrocodone-only extended release drugs, i.e., Zohydro, to residents of other states. *Id.* The response stated, "No. The order states that no provider registered in Massachusetts shall prescribe any hydrocodone bitartrate product in hydrocodone-only extended-release formulation in Massachusetts." *Id.*

5. <u>The Need for Prompt Judicial Intervention:</u>

34. Defendants' actions will cause real and irreparable harm for patients in Massachusetts with chronic pain. Zohydro™ ER addresses a specific set of patient needs. It fills a noticeable and important gap for chronic pain patients - an acetaminophen-free, extended-release product suitable for round-the-clock pain treatment. While there are other opioid products on the market, some patients are unable to achieve adequate pain relief from, or unable to tolerate, other active ingredients in FDA-approved combination opioid products. This therapy also provides an additional tool for the common practice of opioid rotation in patients with chronic pain. Zohydro™ ER provides an important option for patients while also being the most comprehensively regulated hydrocodone product on the market.

35. Without access to Zohydro™ ER, hydrocodone patients in Massachusetts will either have to remain on immediate release therapy, with a 4-6 hour dosing interval, or be

converted to a different drug substance if they require around the clock care or face risks from the ubiquitous presence of acetaminophen in the immediate-release combination products.

36. Responsive to Massachusetts' concerns related to opioid misuse, and as discussed above, fully 63 percent of unintentional acetaminophen overdoses can be attributed to the use of opioid combination pain medicines. Ex. D at 1. Each year, about 50,000 to 60,000 patients are admitted to emergency rooms for acetaminophen poisoning, and on average more than 500 die each year of acetaminophen related liver toxicity. *Id.* at 5. Depriving Massachusetts patients of access to Zohydro™ ER will not alleviate the hydrocodone safety problems in the state and will compromise public knowledge of the unique contribution that the product has made to preventing acetaminophen poisoning.

37. In addition, Defendants' conduct, unless enjoined, will cause immediate and irreversible harm to the reputation and goodwill of Zohydro™ ER and Zogenix and will irreparably disrupt the launch of this product. The Commonwealth's actions are likely to cause physicians, pharmacists, and patients – both in Massachusetts and across the country - wrongly to believe that Zohydro™ ER is not safe and effective.

38. The longer that physicians associate Zohydro™ ER with unacceptable risks of opioid abuse, the more the reputation of the drug itself and Zogenix at large will be compromised.

39. Health care providers may also have to turn to competing hydrocone-based products, regardless of health risks to patients who will benefit from the unique formulation of Zohydro™ ER. This conversion would further lower Zogenix's standing in the market and reduce its overall market share.

40. Zogenix also stands to suffer substantial lost sales in Massachusetts as a result of the ban. It has projected millions of dollars in sales for Zohydro™ ER in Massachusetts in the coming years.

41. Zogenix has invested over $75 million on the research and development of Zohydro™ ER since 2007. Zohydro™ ER is one of Zogenix's only two FDA-approved and marketed products. Wall Street analyst and company projections had expected Zohydro™ ER to become Zogenix's leading product in terms of revenue by 2015 and the overwhelming majority of Zogenix' product revenue in 2016 and beyond. But after Governor Patrick's announcement, the average stock price for Zogenix dropped 31 percent, from $3.72 (Mar. 3 – 26, 2014) to $2.58 (Apr. 4, 2014), resulting in lost market capitalization in the hundreds of millions of dollars.

CLAIMS FOR RELIEF

Count I
(United States Constitution: Preemption)

42. Zogenix realleges, reasserts, and incorporates by reference herein each of the allegations contained in paragraphs 1 through 41 of the Complaint as though set forth fully herein.

43. The Supremacy Clause of the United States Constitution provides that federal laws made under the authority of the United States shall be the "supreme law of the land," the laws of any state to the contrary notwithstanding. U.S. CONST. art. VI, § 2.

44. The Supremacy Clause mandates that federal law preempts any state regulation that poses an obstacle to the accomplishment and execution of the full purposes and objectives of Congress.

45. Under the Food, Drug, and Cosmetic Act ("FDCA"), Congress has delegated to the U.S. Food and Drug Administration ("FDA") the authority to protect and promote the public

health by approving for public use "safe and effective" drugs. The FDA has approved Zohydro™ ER as a safe and effective drug.

46. The ban broadly prohibits the prescription, ordering, dispensation, or administration of any hydrocodone bitartrate product in hydrocodone-only, extended-release formulation, until the Department of Public Health Commissioner has determined that "adequate measures" are in place to safeguard against overdose or abuse.

47. Zohydro™ ER is the only drug on the market in Massachusetts meeting the definition of a hydrocodone bitartrate product in hydrocodone-only, extended-release formulation.

48. Taken as a whole, the ban represents an impermissible effort by Massachusetts to establish its own drug approval policy and directly regulate the availability of drugs within the state. It conflicts with the FDA's mandate under the FDCA, disregards federal policies, undermines the FDA's comprehensive regulatory scheme for nationally-effective drug approvals, and otherwise impedes the accomplishment and execution of the full purposes and objectives of federal law.

49. The ban also specifically undermines the FDA's assessment that Zohydro™ ER is a safe and effective product that may be distributed in all fifty states. In so doing, it impedes the FDA's Congressional mandate to approve a range of safe treatments to promote the public health.

50. Plaintiff has no adequate remedy at law for the violation of the Supremacy Clause.

51. The ban will cause substantial, imminent, and irreparable injury to Plaintiff unless the ban is vacated and Defendants are enjoined from enforcing the ban.

Count II
(United States Constitution: Contract Clause)

52. Zogenix realleges, reasserts, and incorporates by reference herein each of the allegations contained in paragraphs 1 through 51 of the Complaint, as though set forth fully herein.

53. The Contract Clause of the United States Constitution provides that no state shall pass any law "impairing the obligation of contracts." U.S. CONST. art. I, § 10, cl. 1.

54. The ban broadly bans any prescription, ordering, dispensation, or administration of Zohydro™ ER in Massachusetts.

55. Zogenix has valid contracts with wholesalers who supply Zohydro™ ER to Massachusetts pharmacies. These wholesalers already have stocked products at retail locations within the state. Because their subject matter has become illegal under the Massachusetts ban, these contracts between Zogenix and its wholesalers are now substantially impaired. The ban also will impair Zogenix's ability to receive payment under its contract terms.

56. Zogenix also has valid contracts with Inflexxion, a company retained to track abuse patterns for Zohydro™ ER within Massachusetts. The ban irretrievably frustrates the purpose of the agreement and impairs Zogenix's ability to receive the services for which it bargained.

57. For the reasons set forth herein, the ban does not reflect a significant and legitimate public purpose. The state has not appropriately explained the contours of a public emergency necessitating the drastic step it has taken. Furthermore, it applies only to ban Zohydro™ ER while ignoring both the unique advantages of Zohydro™ ER to specific patients and the dangers of other hydrocodone products and opioid products.

58. For the reasons set forth herein, the ban is not based upon reasonable conditions and is not of a character appropriate to the state's stated public purpose. The ban is *ultra vires* and could never be adequately tailored, to the extent that Massachusetts lacked authority to ban Zohydro™ ER in the first place. Moreover, it is too grossly under- and over-inclusive to reflect any level of tailoring, on its own terms.

59. Plaintiff has no adequate remedy at law for the violation of the Contracts Clause.

60. The ban will cause substantial, imminent, and irreparable injury to Plaintiff unless the ban is vacated and Defendants are enjoined from enforcing the ban.

Count III
(United States Constitution: Commerce Clause)

61. Zogenix realleges, reasserts, and incorporates by reference herein each of the allegations contained in paragraphs 1 through 60 of the Complaint, as though set forth fully herein.

62. The Commerce Clause of the U.S. Constitution prevents a state from taking any action which may fairly be deemed to have the effect of impeding the free flow of trade between the states.

63. Prescription drug regulation is an arena that is inherently national in nature in that the FDA has long set uniform standards for drug regulation across all states.

64. The ban imposes significant burdens on interstate commerce because it interferes with the FDA's national and uniform system of regulation. If Massachusetts (and other states) are allowed to make determinations as to what drug formulations are appropriately safe, the result will be a patchwork of state-specific regulation governing how prescription drugs are designed and formulated that would effectively eviscerate the mission of the FDA and create 50

different (and potentially conflicting) sets of rules for deciding what constitutes safe and effective pharmaceuticals.

65. The ban also imposes significant burdens on interstate commerce because it harms patients living in Massachusetts, as well as patients residing outside of Massachusetts who see health care providers in the state. Because health care providers are prohibited from prescribing or dispending Zohydro™ ER to any patients (regardless of their state of residence), patients across several states will not be able to access Zohydro™ ER, thus impacting commerce beyond the borders of the state.

66. The burden imposed on interstate commerce by the ban is clearly excessive in relation to the putative local benefits touted by Defendants. The total prohibition on prescribing and dispensing Zohydro™ ER is the most excessive form of action that can be taken. By contrast, the putative local benefits of limiting opioid abuse are both hypothetical and minimal, given the FDA's consideration of the issue and decision to approve the drug.

67. Zogenix has no adequate remedy at law for the violation of the Commerce Clause.

68. The ban will cause substantial, imminent, and irreparable injury to Zogenix unless the ban is vacated and Defendants are enjoined from enforcing the ban.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff respectfully prays for the following relief:

A. A declaration pursuant to 28 U.S.C. § 2201 that the Governor's and Commissioner's conduct in effectuating a ban on the prescription, ordering, dispensing, and administration of Zohydro™ ER violates the United States Constitution;

B. Temporary, preliminary and permanent injunctive relief and/or a final order enjoining the Defendants from implementing or enforcing the Declaration of Emergency, the

Commissioner's Order or any other action banning the prescription, ordering, dispensing, and administration of Zohydro™ ER. In the alternative, temporary, preliminary and permanent injunctive relief and/or a final order vacating the Governor's Declaration of Emergency, the Commissioner's Order, and any other conduct undertaken by or at the direction of Defendants relating to the Commonwealth's effort ban Zohydro™ ER;

C. An order awarding plaintiff's costs, expenses and attorneys fees; and/or

D. Such other and further relief as the Court deems just and proper.

DEMAND FOR JURY TRIAL

Plaintiff respectfully demands a trial by jury of any and all issues triable of right before a jury.

Dated: April 7, 2014

Respectfully Submitted,

ZOGENIX, INC.,

By Its Attorneys

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VERIFICATION OF COMPLAINT

I, the undersigned, having read the allegations of the foregoing Verified Complaint, hereby certify based upon my personal knowledge and under penalty of perjury that the factual allegations asserted in the Verified Complaint are true and correct, and that matters asserted upon information and belief are believed to be true and correct.

Executed this 7th day of April, 2014.

Stephen J. Farr. Ph.D.
President, Zogenix, Inc.