PETER SHUMLIN
Governor

State of Vermont
OFFICE OF THE GOVERNOR

May 19, 2014

Steven P. Hollman
Hogan Lovells US LLP
Columbia Square
555 Thirteenth Street, NW
Washington, DC 20004

Re: Your public records act request

Dear Mr. Hollman,

Attached please find records in response to your public record act request dated May 1, 2014.

I understand you have also received records in response to a request to the Department of Health. I have withheld certain records – emails between and among the Governor's senior staff, the Governor, and the Commissioner of Health and his General Counsel – that may be responsive to your request as executive privileged communications and/or attorney client communications pursuant to 1 V.S.A. § 317(c)(1) and (c)(4).

If you feel any records have been withheld in error, you may appeal to the Governor's Chief of Staff, Elizabeth Miller.

Sincerely,

Sarah London
Counsel to the Governor

London, Sarah

From: Hoag, Jamie (GOV) <jamie.hoag@state.ma.us>
Sent: Tuesday, April 29, 2014 8:30 AM
To: London, Sarah
Subject: FW: Zogenix v. Patrick
Attachments: Verified Amended Complaint.pdf

Importance: High

Sarah – Here is the amended complaint.

Jamie Hoag
Deputy Chief Legal Counsel
Office of the Governor
617-725-4038 (direct)
617-851-3650 (cell)

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSSACHUSETTS

ZOGENIX, INC., Plaintiff, v. DEVAL PATRICK, in his official capacity as GOVERNOR OF THE COMMONWEALTH OF MASSACHUSETTS, and CHERYL BARTLETT, RN, in her official capacity as DEPARTMENT OF PUBLIC HEALTH COMMISSIONER, and CANDACE LAPIDUS SLOANE, M.D., KATHLEEN SULLIVAN MEYER, ESQ., MARIANNE E. FELICE, M.D., ROBIN RICHMAN, M.D., PAUL R. DeRENSIS, ESQ., MICHAEL E. HENRY, M.D., in their official capacities as members of the MASSACHUSETTS BOARD OF REGISTRATION IN MEDICINE, 200 Harvard Mill Square, Suite 330, Wakefield, Massachusetts, 01880, Defendants.	Civil Action No. 1:14-cv-11689 **DEMAND FOR JURY TRIAL**

VERIFIED AMENDED COMPLAINT

Plaintiff Zogenix, Inc. ("Zogenix"), by its undersigned counsel, hereby brings this Verified Amended Complaint against Defendants Deval Patrick, solely in his official capacity as Governor of the Commonwealth of Massachusetts ("Governor Patrick"), Cheryl Bartlett, RN, solely in her official capacity as Commissioner of the Department of Public Health ("Commissioner Bartlett"), and the members of the Massachusetts Board of Registration in Medicine (the "BORIM"), solely in their official capacities, 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, Commissioner, and BORIM relating to Plaintiff's drug Zohydro™ ER, including: (1) explicitly banning the prescribing, ordering, dispensing, and administration of a pain medication specifically approved as safe and effective by the federal Food and Drug Administration ("FDA") for marketing and sale in the United States; (2) after this Court enjoined Defendants from enforcing their explicit ban, abandoning the explicit ban in favor of draconian requirements imposed upon any effort to prescribe the drug, which effectively create another ban of the drug; (3) singling out a particular extended release opioid product and treating it differently from all other opioids having similar qualities by imposing excessive restrictions on prescriptions of the drug – even in instances where, in the medical judgment of the prescribing physician, it is appropriate for the treatment of severe chronic pain patients; and (4) imposing the foregoing requirements with the objective of forcing Zogenix to offer Zohydro™ ER in an abuse-deterrent formulation despite the fact that the current formulation was approved as safe and effective by FDA and that FDA explicitly considered and rejected the abuse-deterrent formulation that Defendants seek to force Zogenix to make available.

2. Zogenix's product, Zohydro™ ER (Hydrocodone Bitartrate Extended-Release Capsules), was approved by FDA on October 25, 2013 for the management of pain severe enough to require daily around-the-clock, long term opioid treatment and for which alternative treatment options are inadquate.

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 already 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. Hydrocodone is a type of opioid; there are many others, including morphine, codeine, methadone, and oxycodone, hydromorphone, tapentadol, dentanyl, and oxycodone. All of these opioids are available in extended release/long acting formulations.

5. Zohydro™ ER is the first single-entity hydrocodone product available on the market, the first extended release hydrocodone product, and 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. Many other opioid products that contain active ingredients other than hydrocodone – such as morphine, methadone, hydromorphone, oxycodone, oxymorphone, tapentadol, and fentanyl –are subject to state and federal schedule II controls as well.

6. 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 a series of "emergency declarations" empowering Commissioner Bartlett to take

unconstitutional actions that applied to Zohydro™ ER only and not to any of the other opioid products.

7. The first emergency order, dated March 27, 2014, empowered 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 would be lifted only when Commissioner Bartlett "ha[d] determined that adequate measures are in place to safeguard against the potential for diversion, overdose, and abuse...." *Id.* at 2.

8. In response to the original ban, Zogenix filed this action on April 7, 2014, alleging that the ban violated the United States Constitution. (D.E. 1). On that same date, Zogenix also filed a motion for a temporary restraining order and/or preliminary injunction. (D.E. 3-5.) After briefing by both sides and two hearings before the Court, on April 15, 2014, this Court issued an order concluding that Defendants' actions likely were preempted by federal law and declaring that Zogenix was entitled to a preliminary injunction. (D.E. 26.) The Court stayed the order for one week, until April 22, 2014. During that time, Plaintiff's counsel reached out to legal representatives in the Governor's Office and Defendants' litigation counsel to inquire whether Defendants intended to appeal the April 15, 2014 Order. Although Defendants' counsel indicated that the Governor was unlikely to appeal, no mention was made during those discussions of the alternative measures the Governor was about to implement in what appears to be an effort to sidestep this Court's April 15, 2014 Order.

9. The very day that the stay expired, Governor Patrick issued a press release (without any advance notice to or consultation with Zogenix or its counsel), stating that he had directed Commissioner Bartlett to issue a new emergency order requiring doctors to "utilize the

Prescription Monitoring Program (PMP) prior to prescribing a hydrocodone-only extended release medication that is not in an abuse deterrent formulation," which Defendants acknowledged only applied to Zohydro™ ER. Ex. B at 1-2.

10. In addition, on the same day, the BORIM promulgated emergency regulations requiring medical licensees, prior to prescribing Zohydro™ ER to: "1) conduct a risk assessment for a patient, including an evaluation of the patient's risk factors, substance abuse history, presenting conditions, current medications, and PMP data; 2) discuss the risks and benefits of the medication with the patient; 3) enter into a pain management treatment agreement with the patient; supply a letter of medical necessity for the pharmacy that will fill the prescription; and 4) document this information in the patient's medical records." Ex. C at 2. The required letter of medical necessity must "verif[y] that other pain management treatments have failed." Ex. D, 243 CMR 2.07(25)(d).

11. Taken together, these requirements impose such draconian restrictions on physicians' ability to prescribe Zohydro™ ER that they amount to an effective ban of the drug in Massachusetts.

12. The announced actions apply only to any hydrocodone-only extended release medication (i.e., to Zohydro ™ ER) "that is not in an abuse deterrent formulation." Ex. B at 1. Yet FDA specifically considered and rejected the requirement of an abuse deterrent formulation when it granted approval for Zohydro™ ER. Ex. E at 27-29. Dr. Margaret A. Hamburg, Commissioner of Food and Drugs, specifically noted in regard to this determination that "the science of abuse-deterrence is still in its infancy and has yet to be fully tested or proven in actual market or use conditions" and that "abuse deterrent formulations do not prevent someone from taking more pills orally – the most common form of opioid analgesic abuse." Ex. G at 3. Dr.

Hamburg also stressed the importance of balancing potential abuse with "the very real medical needs of the estimated 100 million Americans living with severe chronic pain or coping with pain at the end of life, which is also a major public health problem in this country." *Id.* at 1. In addition to acknowledging the importance of balancing these two complex sets of needs and "apply[ing] sound science as we move forward to achieve this balance," Dr. Hamburg noted the importance of devising "comprehensive policy solutions," such as "requirements for the class-wide E[xtended]R[elease]/L[ong]A[cting] opioid analgesics", and she expressed concern regarding "some misinformation circulating about Zohydro's safety and potency" that "has caused diversion of attention from comprehensive policy solutions to focus on a single drug." *Id.* at 1-3.

13. In spite of these considerations, the Commonwealth, in ordering the original ban and creating a de facto ban in the form of oppressive regulations designed to interfere with the medical judgment of physicians and to require multiple failures in the treatment of a patient's severe chronic pain before Zohydro may be prescribed in Massachusetts, is attempting to override the reasoned decision by FDA to approve Zohydro™ ER for the treatment of severe chronic pain and taking upon itself the responsibility for regulating the safety and effectiveness of drugs already approved by FDA as safe and effective, including dictating a formulation for such drugs that is acceptable to the Commonwealth regardless of whether that formulation requirement conflicts with FDA's specific formulation determination.

14. In addition, by effectuating the new restrictions on prescribing of Zohydro™ ER, the Commonwealth is eschewing any comprehensive approach to the health emergency it identifies. It has taken no such action against any similar opioid drugs currently being misused and abused within the state, and even though more than 30 other extended release/long-acting

opioid-based drug products approved for the same use as Zohydro™ ER contain larger quantities of the active opioid drug than the highest strength of Zohydro™ ER. Instead, the Commonwealth is intentionally singling out one drug to be treated differently from other extended-release/long-acting opioid medications, without any rational basis. These actions violate the United States Constitution.

PARTIES

15. 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.

16. 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.

17. 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.

18. Defendants Candace Lapidus Sloane, Kathleen Sullivan Meyer, Marianne E. Felice, Robin Richman, Paul R. DeRensis, and Michael E. Henry are members of the Massachusetts Board of Registration in Medicine. The BORIM is a department of the Massachusetts Department of Health and Human Services and maintains an office at 200 Harvard Mill Square, Suite 330, Wakefield, Massachusetts, 01880.

JURISDICTION AND VENUE

19. 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.

20. 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.

21. 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, Equal Protection, and dormant Commerce Clauses of the U.S. Constitution, as well as general federal preemption principles.

22. This case is ripe for adjudication. As further discussed below, the enforcement of the emergency declarations and orders 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:

23. 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).

24. 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).

25. 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).

26. 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.

27. 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.

28. 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).

29. 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

30. 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. E at 3. Zohydro™ ER was

developed for patients with severe chronic pain on immediate-release hydrocodone products who would benefit from an extended release product and in whom prescribers determined it appropriate to continue with the same opioid active ingredient while removing the potential for liver toxicity associated with acetaminophen. The pivotal clinical trial in the NDA was an adequate and well controlled clinical study in patients currently taking and tolerating an opioid medication before entering the study. There was no requirement that patients enrolled in the study be shown to have been failing on their opioid therapy. Ex. F at 27-29. 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; the same indication required of other FDA approved extended release opioids. Ex. H at 1. FDA did not find Zohydro™ ER to be safe and effective specifically and only for patients who have failed other pain management treatments. FDA would have required a different set of data than that submitted in the Zohydro™ ER NDA to approve the product with such a condition of use.

31. 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. I at 1. The availability of an acetaminophen-free formulation of extended release hydrocodone is an important therapeutic option for certain chronic pain patients.

32. Zohydro™ ER, however, is not the only extended-release/long-acting opioid product on the market. Currently, there are more than 30 extended-release/long-acting opioid products marketed in the US, including MS Contin, Opana ER, Duragesic, Exalgo, and OxyContin. These medications, which contain active ingredients that can include morphine, oxymorphone, fentanyl, hydromorphone and oxycodone, are subject to Schedule II controls that carefully dictate how physicians prescribe the drugs and how they are tracked. Physicians may choose to prescribe different extended-release/long-acting opioids to patients based on how well the particular patient responds to the underlying active chemical, i.e., hydrocodone, fentanyl, and oxycodone. [1]

33. 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 extended-release opioids in which another option for opioid rotation is of value.

34. The announced actions apply only to hydrocodone-only extended release medication "that is not in an abuse deterrent formulation." Ex. B. 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

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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.

support approval of the NDA without an abuse-deterrent formulation. FDA outlined its reasoning in its Summary Approval. Ex. E. 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 acetaminophen 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. J at 3. In addition to abuse-deterrent formulations' known ineffectiveness at affecting the most common form of 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. E at 33.

35. 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. E at 31.

3. Zogenix's Contracts

36. 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.

37. 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. The Governor's First Declaration of a Public Health Emergency and the Original Ban

38. 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 "Ban 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. K. The Ban 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.

39. 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. L at 2.

40. Also on March 27, 2014, the Commissioner and Public Health Council ("PHC") approved an emergency order (the "Ban 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. M. There is exactly one "hydrocodone bitartrate product in hydrocodone-only extended-release formulation": Zohydro™ ER.

41. The Commissioner and DPH explained the Ban 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. M.

42. 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. E 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.

43. 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. Zogenix's Complaint and the Court's Preliminary Injunction Order

44. In response to the Governor's and the Commissioner's actions to ban the prescribing and dispensing of Zohydro™ ER, on April 7, 2014, Zogenix filed a complaint in this case alleging that the ban was preempted by federal law and violated the Contracts and dormant Commerce Clauses of the U.S. Constitution. After briefing by both sides and two hearings before the Court, on April 15, 2014, this Court issued an order concluding that the Defendants' actions were preempted by federal law and that Zogenix was entitled to a preliminary injunction.

(D.E. 26.) The final sentence of the order stated that the injunction was "stayed until April 22, 2014." (*Id.* at 5.)

45. Within days of the Court's issuance of the preliminary injunction order, counsel for Zogenix reached out to legal counsel on the Governor's staff, in order to provide them with facts about Zohydro™ ER that would better help Defendants understand why the medication provides an important treatment option not currently available to severe chronic pain patients while presenting risks no greater than those of other opioids already on the market. In addition, counsel for Zogenix asked to discuss ways to conclude the case, given the Governor's public statements indicating that he did not anticipate Defendants would appeal the Court's preliminary injunction order. At no time did employees of Defendants or their counsel indicate that they planned to undertake additional actions targeted specifically at Zohydro™ ER in its current formulation. Nor did Defendants rescind the original Ban Order or the first Declaration of Emergency. Thus, despite the court's injunction, these actions appear to remain on the books today.

6. <u>Defendants' Most Recent Conduct: Additional Restrictions on Prescribing Zohydro</u>

46. On the same day that the stay of the Court's preliminary injunction order was lifted, and without prior discussion with or warning to Zogenix or its counsel, the Governor directed Commissioner Bartlett to issue a new emergency order (the "PMP Order") requiring prescribers to "utilize the Prescription Monitoring Program (PMP) prior to prescribing a hydrocodone-only extended release medication that is not in an abuse deterrent formulation," which Defendants acknowledged only applied to Zohydro™ ER. Ex. B at 1-2. Under the PMP Order, prescribers must use the PMP to evaluate a patient's prescription history prior to each instance of issuing a prescription of Zohydro™ ER. Ex. C at 1. According to a Circular Letter

sent to all Massachusetts Controlled Substance Registration Participants on April 24, 2014, because prescriptions for Schedule II medication (such as Zohydro™ ER) can be written for no more than a 30-day supply, the PMP Order "will require the prescriber to check the patient's PMP record, at a minimum, every 30 days while he or she is being prescribed the medication." *Id.* The April 24 Circular Letter also notes that Commissioner Bartlett issued the PMP Order pursuant to the March 27, 2014 PHC vote that resulted in the original ban. *Id.*

47. On the same day, the BORIM, through its members, promulgated emergency regulations requiring licensees, prior to prescribing Zohydro™ ER, to undertake four distinct measures. Ex. C at 2. The emergency regulation, found at 243 CMR 2.07(25), states that prior to prescribing "a hydrocodone-only extended release medication that is not in an abuse deterrent form" (a description that precisely matches Zohydro™ ER in its current, FDA-approved formulation and applies to no other drug), the licensee must:

> (a) Thoroughly assess the patient, including an evaluation of the patient's risk factors, substance abuse history, presenting condition(s), current medication(s) and a check of the online Prescription Monitoring Program;
>
> (b) Discuss the risks and benefits of the medication with the patient;
>
> (c) Enter into a Pain Management Treatment Agreement with the patient that shall appropriately address drug screening, pill counts, safe storage and disposal and other requirements based on the patient's diagnoses, treatment plan, and risk assessment;
>
> (d) Supply a Letter of Medical Necessity as required by the Board of Registration in Pharmacy that includes the patient's diagnoses and treatment plan, verifies that other pain management treatments have failed, indicates that a risk assessment was performed and that the licensee and the patient have entered into a Pain Management Treatment Agreement; and
>
> (e) Document 243 CMR 2.07(25)(a)-(d) in the patient's medical record.

Ex. D.

48. The BORIM emergency regulation notes that the purpose of the regulation "is to enhance the public health and welfare by promoting optimum therapeutic outcomes, avoiding patient injury and eliminating medication errors." *Id.*

49. The PMP Order and the BORIM emergency regulation apply only to Zohydro™ ER, despite the fact that there is no rational basis for claiming that Zohydro™ ER has any more risk of misuse or abuse than any other extended-release/long-acting opioid medication on the market. First, Zohydro™ ER is not the only opioid available without an abuse deterrent formulation; in fact, there is only one opioid medication currently on the market that contains an abuse deterrent formulation, OxyContin. As FDA Commissioner Margaret Hamburg has stated, requiring opioids to contain an abuse deterrent formulation "puts too much faith in the current state of technology. I wish we were there but we are not. It remains a hope more than a reality but there is promise . . . ." Ex. G at 3. Indeed, "the science of abuse-deterrence is still in its infancy and has yet to be fully tested or proven in actual market or use conditions. There are even limits to the abuse-deterrence of OxyContin, the only opioid with a claim on its label that the drug has abuse-deterrent properties." *Id.*

50. FDA Commissioner Hamburg also noted that Zohydro™ ER "is in the same class of [extended-release] and [long-acting] opioids as OxyContin and Opana ER – sharing similar risks of abuse with others in its class." *Id.* This is why Zohydro™ ER "has the same strict labeling and requirements for post market studies, training programs for prescribers, and a Medication Guide for patients," as other Schedule II extended-release/ long-acting opioids in the class. *Id.* Thus, Zohydro™ ER is properly viewed in the context of these Schedule II extended-release/long-acting opioids, and not – as Defendants have compared it – to hydrocodone combination products, which are Schedule III drugs.

51. Because Zohydro™ ER poses no additional risks beyond the risks found to exist with all Schedule II extended-release/long-acting opioids in its class and because the new restrictions limit physician's ability to prescribe only Zohydro™ ER, there is no rational basis for imposing the new restrictions.

52. In practice, the BORIM emergency regulations codified at 243 CMR 2.07(25) constitute a de facto ban on Zohydro™ ER in its current formulation, apparently with the intent to accomplish the same result as the original ban on the prescription and dispensation of the drug in Massachusetts.

53. The BORIM emergency regulations require physicians to jump through numerous and onerous new regulatory hoops in order to prescribe Zohydro™ ER in its current, FDA-approved formulation. None of the requirements applies if a physician chooses to prescribe an opioid other than Zohydro™ ER in its current formulation.

54. Most significantly, the BORIM emergency regulation codified at 243 CMR 2.07(25)(d) mandates that a prescriber of Zohydtro™ ER, *inter alia*, "Supply a Letter of Medical Necessity as required by the Board of Registration in Pharmacy that includes the patient's diagnoses and treatment plan, *verifies that other pain management treatments have failed*, indicates that a risk assessment was performed and that the licensee and the patient have entered into a Pain Management Treatment Agreement" Ex. D (emphasis added). In contrast, FDA's approved indication statement for Zohydro reads: "Indicated for the management of pain severe enough to require daily, around-the-clock, long-term treatment and for which *alternative treatment options are inadequate*." Ex. E at 29 (emphasis added). Although it has done so for other drugs, FDA did *not* require that other treatment alternatives must fail before a physician may prescribe Zohydro™ ER to a patient in need.

55. As a result of its alternative treatment failure requirement, the BORIM emergency regulation codified at 243 CMR 2.07(25)(d) does not practically permit physicians to prescribe Zohydro™ ER while both complying with the new requirements and ensuring appropriate patient care. Under 243 CMR 2.07(25)(d), a regulated prescriber must cycle a patient through multiple pain treatment alternatives and document the failure to achieve adequate pain management and/or unacceptable adverse events —before prescribing Zohydro™ ER. Especially for patients with the very liver health concerns favoring Zohydro™ ER treatment in the first place, the forced preliminary trials of other pain management treatments presents obvious and striking patient health concerns. It should be evident that physicians will be unwilling to subject patients to such inappropriate treatment in order to prescribe Zohydro™ ER. *See* Chou R., Fanciullo G.J., Fine P.G., Adler J.A., Ballantyne J.C., Davies P., *et al.* Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain, 10(2) J. Pain 113-30 (Feb. 2009).

56. According to the Commonwealth's own records, as included in DPH's April 24, 2014 Circular Letter to prescribers, the BORIM emergency regulations apply to approximately 95% of the prescribers of controlled substances in Massachusetts. Ex. C at 2.

57. Because the BORIM emergency regulations extinguish nearly all Massachusetts prescribers' reasonable abilities to ensure appropriate patient treatment and comply with ethics obligations while also following with new state requirements for prescribing Zohydro™ ER, it is extraordinarily unlikely that any practicing physician will consider prescribing Zohydro™ ER in its current formulation for pain patients, including those with liver health risks that otherwise would benefit from treatment with Zohydro™ ER. In effect, the BORIM emergency regulations

once again categorically deny to doctors the choice to prescribe Zohydro™ ER, a drug approved by the FDA as safe and effective for the treatment of severe chronic pain.

7. The Need for Prompt Judicial Intervention:

58. 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 hydrocodone 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 opioid products or FDA approved hydrocodone combination 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.

59. Without adequate 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. Patients also may be subjected to ineffective and potentially risky pain treatments while physicians undertake to comply with the Commonwealth's new requirement that they prove that alternative pain treatments have "failed" before prescribing Zohydro ™ ER.

60. 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. I 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 adequate 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.

61. 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.

62. 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.

63. 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.

64. 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.

65. 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 $2.56 (Apr. 28, 2014), resulting in lost market capitalization in the hundreds of millions of dollars.

CLAIMS FOR RELIEF

Count I
(United States Constitution: Preemption)

66. Zogenix realleges, reasserts, and incorporates by reference herein each of the allegations contained in paragraphs 1 through 65 of the Complaint as though set forth fully herein.

67. 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.

68. 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.

69. 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.

70. The Commonwealth's original 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.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.

71. The more recent restrictions imposed by the Commonwealth constitute an effective ban on Zohydro™ ER, because they make it so difficult to prescribe Zohydro™ ER that physicians are unlikely to do so.

72. Because these new restrictions, including the BORIM emergency regulations, effectively eliminate a Massachusetts physician's option to prescribe Zohydro™ ER consistent with ethical obligations and patient safety, see, e.g., paragraphs 52-57, *supra*, they effectively constitute a de facto ban on the prescription of Zohydro™ ER in the Commonwealth with almost identical effect to the original ban.

73. BORIM emergency regulations codified at 243 CMR 2.07(25) likewise single out Zohydro™ ER, the only hydrocodone bitartrate product in hydrocodone-only, extended-release formulation, as the sole subject of sweeping new requirements imposed upon doctors wishing to prescribe Zohydro™ ER.

74. Taken as a whole, the original ban and BORIM regulations codified at 243 CMR 2.07(25) represent an impermissible effort by Massachusetts to establish its own drug approval policy and directly regulate the availability of drugs within the state. They conflict with the FDA's mandate under the FDCA, disregard federal policies, undermine the FDA's comprehensive regulatory scheme for nationally-effective drug approvals, and otherwise impede the accomplishment and execution of the full purposes and objectives of federal law.

75. The original ban and BORIM regulations codified at 243 CMR 2.07(25) also specifically undermine the FDA's assessment that Zohydro™ ER is a safe and effective product

that may be distributed in all fifty states. In so doing, they impede the FDA's Congressional mandate to approve a range of safe treatments to promote the public health.

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

77. The original ban and BORIM regulations codified at 243 CMR 2.07(25) will cause substantial, imminent, and irreparable injury to Plaintiff unless they are vacated and Defendants are enjoined from enforcing them.

Count II
(United States Constitution: Contract Clause)

78. Zogenix realleges, reasserts, and incorporates by reference herein each of the allegations contained in paragraphs 1 through 77 of the Complaint, as though set forth fully herein.

79. 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.

80. The original ban broadly bans any prescription, ordering, dispensation, or administration of Zohydro™ ER in Massachusetts. In addition, the new restrictions put in place on prescribing Zohydro™ ER in Massachusetts make it difficult for physicians to prescribe the medication for needy patients and make it highly unlikely that physicians will choose Zohydro™ ER. In effect, the BORIM emergency regulations are a de facto ban on the prescription of the drug.

81. 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 original ban and de facto ban under the BORIM regulations, these contracts between Zogenix and its wholesalers are

now substantially impaired. The ban and BORIM regulations also will impair Zogenix's ability to receive payment under its contract terms.

82. The new restrictions on prescribing Zohydro™ ER substantially impair the same wholesaler contracts because they make it so difficult to prescribe Zohydro™ ER that sales are likely to be so low as to negate the purpose of the contracts: to supply retail locations with the medication.

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

84. For the reasons set forth herein, Defendants' actions do not reflect a significant and legitimate public purpose. The state has not appropriately explained the contours of a public emergency necessitating the drastic steps it has taken. Furthermore, their actions single out Zohydro™ ER while ignoring both the unique advantages of Zohydro™ ER to specific patients and the dangers of other hydrocodone products and opioid products.

85. For the reasons set forth herein, Defendants' actions are not based upon reasonable conditions and are 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. In addition, the new restrictions on prescribing Zohydro™ ER single out one medication without any rational connection to the Commonwealth's stated purpose of addressing opioid abuse in general.

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

87. Defendants' actions will cause substantial, imminent, and irreparable injury to Plaintiff unless the orders are vacated and Defendants are enjoined from enforcing the ban and the new restrictions.

Count III
(United States Constitution: Commerce Clause)

88. Zogenix realleges, reasserts, and incorporates by reference herein each of the allegations contained in paragraphs 1 through 87 of the Complaint, as though set forth fully herein.

89. 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.

90. 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.

91. The original ban and the new restrictions on Zohydro™ ER, including the BORIM restrictions on prescribing Zohydro™ ER, impose significant burdens on interstate commerce because they interfere 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 and effective, 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.

92. The original ban and the new restrictions on Zohydro™ ER, including the BORIM restrictions on prescribing Zohydro™ ER, also impose significant burdens on interstate commerce because they harm patients living in Massachusetts, as well as patients residing

outside of Massachusetts who see health care providers in the state. Because under the original ban 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. Similarly, under the new BORIM restrictions, patients being treated by Massachusetts physicians will have to jump through extremely burdensome hoops in order to obtain FDA-approved medication. These burdens, in combination with untenable ethical conflicts required to comply with the BORIM requirement of documenting failed alternative treatments prior to prescribing Zohydro™ ER, will prevent physicians from prescribing Zohydro™ ER and thus impact commerce beyond the borders of the state.

93. 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.

94. Similarly, the burden imposed on interstate commerce by the new restrictions on prescribing Zohydro™ ER rise to the level of a de facto ban and are clearly excessive in relation to the putative local benefits. Because the new restrictions only target Zohydro™ ER, they will not have any meaningful impact on the purported goal of addressing opioid abuse in general.

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

96. Defendants' actions will cause substantial, imminent, and irreparable injury to Zogenix unless the orders are vacated and Defendants are enjoined from enforcing them.

Count IV
(United States Constitution: Equal Protection Clause)

97. Zogenix realleges, reasserts, and incorporates by reference herein each of the allegations contained in paragraphs 1 through 96 of the Complaint, as though set forth fully herein.

98. The Equal Protection Clause of the 14th Amendment to the U.S. Constitution provides that "No state shall . . . deny to any person within its jurisdiction the equal protection of the laws."

99. Commissioner Bartlett's and the BORIM's new restrictions on prescribing Zohydro™ ER intentionally single out one extended-release long-lasting opioid medication to be treated differently than all other similarly situated extended-release/ long acting opioid medications on the market. Further, by doing so, they upset the comprehensive, class-wide policy solutions devised by FDA to apply to all extended release/long acting opioids.

100. There is no rational basis for the difference in treatment of Zohydro™ ER. Because Zohydro™ ER poses no additional risks beyond the risks found to exist with all Schedule II extended-release long-lasting opioids in its class and because the new restrictions limit physician's ability to prescribe only Zohydro™ ER, there is no rational basis for imposing the new restrictions.

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 Ban 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. A declaration pursuant to 28 U.S.C. § 2201 that the Governor's, Commissioner's, and BORIM members' conduct in imposing new restrictions on the prescribing of Zohydro™ ER violates the United States Constitution;

D. Temporary, preliminary, and permanent injunctive relief and/or a final order enjoining the Defendants from implementing or enforcing its administrative and regulatory restrictions on Zohydro™ ER, including but not limited to the Declaration of Emergency, the Commissioner's PMP Order, and/or the BORIM's emergency regulation. In the alternative, temporary, preliminary, and permanent injunctive relief and/or a final order vacating the Governor's Declaration of Emergency, the Commissioner's PMP Order, and the BORIM's emergency regulation and any other conduct undertaken by or at the direction of Defendants relating to the Commonwealth's effort restrict access to Zohydro™ ER;

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

F. 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 28, 2014

Respectfully Submitted,

ZOGENIX, INC.,

By Its Attorneys

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Attorneys for Plaintiff Zogenix, Inc.

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 28th day of April, 2014.

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

London, Sarah

From: Hoag, Jamie (GOV) <jamie.hoag@state.ma.us>
Sent: Wednesday, April 23, 2014 4:12 PM
To: London, Sarah
Subject: FW: GOVERNOR PATRICK ANNOUNCES IMMEDIATE RESTRICTIONS ON POWERFUL NEW PAINKILLER IN RESPONSE TO PUBLIC HEALTH EMERGENCY
Attachments: 2014-4-22 Hydrocodone-only Next Steps.doc

FYI

GOVERNOR PATRICK ANNOUNCES IMMEDIATE RESTRICTIONS ON POWERFUL NEW PAINKILLER IN RESPONSE TO PUBLIC HEALTH EMERGENCY

BOSTON – Tuesday, April 22, 2014 – Massachusetts Governor Deval Patrick today announced several new actions to restrict the availability of hydrocodone-only extended-release medication that is not in abuse-deterrent form (commonly known as Zohydro), including a requirement that doctors complete a risk assessment and utilize the Prescription Monitoring Program before such medications can be prescribed to a patient.

"We are in the midst of a public health emergency around opioid abuse and we need to do everything in our power to prevent it from getting worse," said Governor Patrick. "The broad actions we are taking to address the opioid epidemic will help save lives and give families struggling with addiction new hope."

Today, the Massachusetts Board of Registration in Medicine voted to require individual prescribers to complete a risk assessment and pain management treatment agreement prior to prescribing any patient hydrocodone-only extended-release medication that is not in abuse-deterrent form. The agreement with each patient must address drug screening, pill counts, safe storage and disposal, and other requirements as appropriate in the prescriber's judgment.

Additional state boards that regulate medical and pharmacist practice will meet soon to consider adopting further restrictions around opioids.

At the Governor's direction, Commissioner of Public Health Cheryl Bartlett, RN, also issued an emergency order today requiring prescribers to utilize the Prescription Monitoring Program (PMP) prior to prescribing a hydrocodone-only extended release medication that is not in an abuse deterrent formulation. The PMP tracks prescriptions of controlled substances in the Commonwealth and is an important clinical decision-making tool for preventing misuse, overprescribing or diversion of prescription medications.

Commissioner Bartlett will also issue a notification to all prescribers in Massachusetts informing them of these restrictions. "The introduction of this new painkiller into the market poses a significant risk to individuals

already addicted to opioids and to the public at large," said Commissioner Bartlett. "These new safeguards are critical to prevent misuse."

On March 27, Governor Patrick declared a public health emergency in Massachusetts in response to the growing opioid addiction epidemic. The Governor took the following actions to address the public health emergency: making Naloxone (Narcan) widely available to first responders and through standing orders in pharmacies; dedicating an additional $20 million to treatment and recovery services; accelerating the mandatory enrollment of prescribers in PMP; and re-tasking the Commonwealth's Interagency Council on Substance Abuse and Prevention to address the opioid epidemic and make recommendations on further actions that can be taken.

Today's actions come on the same day as the state's previous ban on all prescribing and dispensing of Zohydro ends.

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DEVAL L. PATRICK
GOVERNOR

JOHN W. POLANOWICZ
SECRETARY

CHERYL BARTLETT, RN
COMMISSIONER

FOR IMMEDIATE RELEASE:
April 22, 2014

FURTHER INFORMATION:
Anne Roach (617) 624-5006

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###

London, Sarah

From: London, Sarah
Sent: Thursday, April 17, 2014 9:19 AM
To: Englander, David
Cc: Chen, Harry
Subject: Re: Emergency Rule Governing Non-ADFs Hydrocodone

Great news, thanks!!

Sent from my iPad

> On Apr 17, 2014, at 8:59 AM, "Englander, David" <David.Englander@state.vt.us> wrote:
>
> A very supportive LCAR unanimously approved the Emergency Rule.
>
> d.

London, Sarah

From: Englander, David
Sent: Wednesday, April 02, 2014 7:29 PM
To: London, Sarah; Allen, Susan; Erickson, Nancy; Chen, Harry; Skovira, Mary
Cc: Miller, Elizabeth; Englander, David
Subject: Emergency Rule - Non-ADF Hydrocones
Attachments: Rule Governing Non-ADFs FINAL.docx

See attached.

d.

Rule Governing the Prescription of Extended Release Hydrocodones Manufactured Without Abuse-Deterrent Formulations

1.0 Authority

This rule is adopted pursuant to 18 V.S.A. § 102 and Act No. 75 of the Acts of the 2013 Sess. (2013) (An act relating to strengthening Vermont's response to opioid addiction and methamphetamine abuse), Section 14(e).

2.0 Purpose

This rule provides requirements for the prescription of extended release hydrocodones lacking abuse-deterrent formulations in order to address potential prescription drug overdose, abuse and diversion.

3.0 Definitions

3.1 "Prescriber" means a licensed health care professional with authority to prescribe controlled substances.

3.2 "Risk Assessment" means utilizing a tool, such as the Screener and Opioid Assessment for Patients with Pain (SOAPP), designed for predicting the likelihood that a patient will abuse or misuse a prescribed controlled substance based on past behavior, genetic predispositions, social or environmental factors or other risks.

3.3 "Hydrocodone" means a semi-synthetic opioid derived from codeine.

3.4 "Controlled Substance Treatment Agreement" means a document that is agreed upon by both the prescriber and the patient acknowledging the rights, responsibilities, and risks of being on controlled substances and the treatment being received.

3.5 "Misuse" means using a controlled substance in a way that is not prescribed.

3.6 "Abuse-deterrent formulations" or "ADF" means one of the following: Physical/Chemical barriers (i.e. physical barriers that prevent chewing, crushing, cutting, grating, or grinding or chemical barriers that can resist extraction of the opioid using common solvents like water); Aversion (i.e. substances that can be combined to produce an unpleasant effect if the dosage form is manipulated prior to ingestion or a higher dosage than directed is used); a formulation such that the drug is lacking in opioid activity until transformed in the gastrointestinal tract (known as a Prodrug); or a combination of the above methods).

4.0 Prescription of Extended Release Hydrocodones without ADFs

Prior to prescribing an extended release hydrocodone that is manufactured without an ADF, the prescriber shall:

4.1 Conduct and document a thorough medical evaluation and physical examination as part of the patient's medical record;

4.2 Evaluate and document relative risks and benefits for the individual patient of the use of hydrocodones that are manufactured without an ADF prior to writing a prescription for such a hydrocodone. The evaluation shall include but not be limited to a Risk Assessment as defined in Section 3.3;

4.3 Document in the medical record that the prescription of a hydrocodone without an ADF is required for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment for which alternative treatment options, including non-pharmacological treatments, are ineffective, not tolerated, or would otherwise be inadequate to provide sufficient management of pain;

4.4 Receive a signed Informed Consent form from the patient, or if the patient is not competent to provide informed consent, from the patient's legal representative, that shall include information regarding the drug's potential for addiction, abuse, and misuse; and the risks associated with the drug of life-threatening respiratory depression; overdose as a result of accidental exposure potentially fatal especially in children; neonatal opioid withdrawal symptoms; and potentially fatal overdose when interacting with alcohol;

4.5 Receive a signed Controlled Substance Treatment Agreement from the patient that shall include requirements such as urine screening (no less frequent than every 120 days), pill counts, safe storage and disposal, and other appropriate conditions as determined by the prescriber to reasonably and timely inform the prescriber if the patient is misusing the prescribed substance;

4.6 Query the Vermont Prescription Monitoring System (VMPS) and review other controlled substances prescribed to the patient prior to the first prescription. For any patient prescribed 40 mg or greater per day, the prescriber shall query the VPMS no less frequently than once every 120 days for as long as the patient possesses a valid prescription for that amount;

4.7 Determine a maximum daily dose, or a "not to exceed value" for the prescription to be transmitted to the pharmacy;

4.8 Write a prescription that must be filled within seven (7) and that does not to exceed 30 days in duration;

4.8 Schedule and undertake periodic follow-up visits and evaluations.

5.0 Follow-ups and Evaluation

At each the follow-up visit(s) required by Section 4.8, the prescriber shall evaluate, determine and document:

5.1 Whether to continue the treatment of pain with hydrocodones not manufactured with an ADF or whether there is an available alternative;

5.2 Whether to refer the patient for a pain management or substance abuse consultation;

5.3 A plan for the discontinuance of prescribed hydrocodone(s) if a patient has failed to adhere to the Controlled Substance Treatment Agreement.

London, Sarah

From: Hoag, Jamie (GOV) <jamie.hoag@state.ma.us>
Sent: Thursday, March 27, 2014 4:33 PM
To: London, Sarah; Richards, Alyson
Subject: FW: GOVERNOR PATRICK DECLARES PUBLIC HEALTH EMERGENCY, ANNOUNCES ACTIONS TO ADDRESS OPIOID ADDICTION EPIDEMIC
Attachments: Governor's Public Health Emergency Declaration 3.27.14.pdf

Sent: Thursday, March 27, 2014 3:29 PM
Subject: GOVERNOR PATRICK DECLARES PUBLIC HEALTH EMERGENCY, ANNOUNCES ACTIONS TO ADDRESS OPIOID ADDICTION EPIDEMIC

Commonwealth of Massachusetts Executive Department
Office of Governor Deval L. Patrick
Press Release

Contact: Heather Nichols, Bonnie McGilpin, Juli Hanscom – 617-725-4025; Alec Loftus (HHS) – 617-573-1612

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GOVERNOR PATRICK DECLARES PUBLIC HEALTH EMERGENCY, ANNOUNCES ACTIONS TO ADDRESS OPIOID ADDICTION EPIDEMIC

Dedicates $20 million to enhance substance abuse treatment programs; Convenes emergency session of Public Health Council to immediately act on emergency measures

BOSTON – Thursday, March 27, 2014 – Governor Deval Patrick today declared a public health emergency in Massachusetts in response to the growing opioid addiction epidemic. The Governor directed the Department of Public Health (DPH) to take several action steps that will combat overdoses, stop the epidemic from getting worse, help those already addicted to recover and map a long-term solution to ending widespread opiate abuse in the Commonwealth.

The use of oxycodone and other narcotic painkillers, often as a route to heroin addiction, has been on the rise for the last few years in Massachusetts. At least 140 people have died from suspected heroin overdoses in communities across the Commonwealth in the last several months, levels previously unseen. From 2000 to 2012, the number of unintentional opiate overdoses increased by 90 percent.

"We have an epidemic of opiate abuse in Massachusetts, so we will treat it like the public health crisis it is," said Governor Patrick. "I have directed DPH to take certain immediate actions and to give me further actionable recommendations within 60 days, to address this challenge and better protect the health of people suffering from addiction and the families and loved ones who suffer with them."

The Governor's Public Health Emergency declaration provides emergency powers to DPH Commissioner Cheryl Bartlett, RN. At the Governor's direction, Commissioner Bartlett will work with the Public Health Council to take the following actions:

1. Universally permit first responders to carry and administer Naloxone (Narcan), a safe and effective opioid antagonist that, when timely administered, can reverse an overdose and save a life. Naloxone will also be made widely available through standing order prescription in pharmacies in order to provide greater access to family and friends who fear a loved one might overdose.

2. Immediately 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. The introduction of this new painkiller into the market poses a significant risk to individuals already addicted to opiates and to the public at large.
3. DPH is mandating the use of prescription monitoring by physicians and pharmacies to better safeguard against abuse or misuse. This was previously a voluntary program.

4. Re-task the Commonwealth's Interagency Council on Substance Abuse and Prevention with added members from public health, provider organizations, law enforcement, municipalities and families impacted by the opiate epidemic, to make recommendations in 60 days on further actions that can be taken, including, but not limited to: how to better coordinate services, ensure a full range of treatment regardless of insurance, and how to divert non-violent criminal defendants struggling with addiction into treatment programs.

The Administration will also dedicate an additional $20 million to increase treatment and recovery services to the general public, to the Department of Corrections and to Sheriffs' Departments.

In conjunction with this public health emergency declaration, Commissioner Bartlett today issued a public health advisory to help education and raise awareness about the treatment options currently available to combat and prevent the spread of opioid addiction.

"These actions will help slow the rise of this dangerous addiction;" said Commissioner Bartlett. "Together, these steps will raise awareness in our communities, help save loved ones who tragically fall down from their disease and build important bridges to long-term recovery."

The Governor also announced today that he will partner with other governors and federal stakeholders to develop a regional action plan to bring an end to the opioid epidemic. Earlier this week, the Governor sent letters to Senator Manchin, Congressman Lynch and Secretary Sebelius in support of efforts at the federal level to ban Zohydro Extended Release (ER).

Supportive Statements:

"This epidemic reaches far beyond the addict," said Senate President Therese Murray. "The costs of drug addiction are high, both to families and the economy, and it poses an extreme threat to the safety of our communities. Recognizing the rising levels of drug abuse in the Commonwealth, we have been trying to address the need for treatment beds and services for the past ten years to get ahead of this crisis. The Senate's Special Committee on Drug Abuse and Treatment Options has been working to find how we can address this difficult and life-threatening problem and I want to thank the Governor and the Department of Public Health for their dedication to finding a solution. In addition to these steps, it is critical that we put in place an education program in elementary schools, similar to the anti-smoking program, so all students are aware of the dangers and effects of addiction by the time they get to middle school. The age of those who are using and overdosing keeps getting

younger and by the time they reach high school it is already too late. It is our responsibility to get ahead of addiction and provide residents with the resources to lead drug-free, independent lives."

"In my role as Chair of the Special Senate Committee on Drug Abuse and Treatment Options, I have met with and heard from countless people with a heart wrenching story to tell," said Senator Jen Flanagan. "I am thankful that the Governor is putting much needed resources into this epidemic. As the Senate Committee continues to travel throughout the Commonwealth to hear from those on the front line, as well as affected families; we are eager to work with the Governor's office and others to enhance the availability treatment options in Massachusetts."

"The steps taken today reinforce that we must renew our focus on prevention – preventing people from starting down the path to addiction by appropriately limiting the prescribing of opiates, preventing deaths through the use of Narcan, and preventing people from being denied treatment because of a lack of programs and lack of insurance coverage," said Senator John Keenan "We have a number of bills making their way through the legislative process that will further enhance these efforts, and together we'll continue our fight to end this epidemic."

"We truly are in a state of emergency when it comes to opiate addiction, and the Commonwealth has had to do a lot with limited resources," said Representative Liz Malia. "Expanding services will fill some of the existing gaps in the system and allow those in need to access treatment in real time – when they need it and in the most appropriate setting."

"Those of us who have spent our careers working in the addiction treatment field have never experienced anything that approaches the current opiate abuse epidemic," said Chuck Faris, CEO of Spectrum Health Systems. "The pain inflicted on families, the increase in crime and the loss of lives is unprecedented. We applaud the Governor for his leadership on this public health challenge. We look forward to his decisive action that will save lives and protect the public."

"On March 26, I was invited to sit with other parents and family members to share experiences of our loved ones' addictions with Governor Patrick and his Administration. I left there with guarded optimism," said Paul Doherty. "His response today is beyond anything I had anticipated or I could have hoped for. I applaud Governor Patrick's quick response to this crisis. Having Governor Patrick recognize the urgency of this epidemic will bring attention and necessary resources to help those who are directly affected by the disease of addiction as well as those who have dedicated their lives to helping those who suffer from this disease."

"I know I speak for each and every one of the over 5,000 members of Learn To Cope, families who struggle every day in finding resources, treatment and hope for our loved ones and all of the families who have lost loved ones to overdose, when I say today we have hope that Governor Patrick, who has heard our concerns and, manning all of the resources at the state's disposal, we are moving forward with solutions to the horrendous epidemic of opiate addiction that is ravaging our Commonwealth and the nation," said Mary D'Eramo, of Learn to Cope.

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OFFICE OF THE GOVERNOR
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STATE HOUSE • BOSTON, MA 02133
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DEVAL L. PATRICK
GOVERNOR

GOVERNOR'S DECLARATION OF EMERGENCY

WHEREAS, as a result of the availability and use of cheap, highly potent heroin, at least 140 people have died from suspected heroin overdoses in the Commonwealth between November 2013 and February 2014 alone;

WHEREAS, as a result of the widespread abuse of other pharmaceutical opiates, the rate of unintentional opioid related overdose deaths has reached levels previously unseen in Massachusetts;

WHEREAS, powerful opiate medications with potential for abuse and overdose are being diverted for non-medical use;

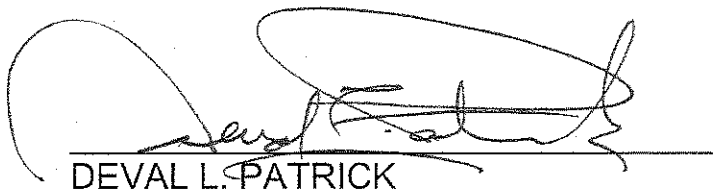
WHEREAS, a majority of individuals receiving services from the Commonwealth's Bureau of Substance Abuse Services in fiscal year 2013 reported opiates as their primary or secondary drug of choice;

WHEREAS, as a result of the struggles of those battling addiction and their loved ones all over the Commonwealth, it is necessary for the Massachusetts Department of Public Health to take action immediately to address this public health emergency;

NOW, THEREFORE, I, Deval L. Patrick, the Governor of the Commonwealth of Massachusetts, pursuant to M.G.L. chapter 17, section 2A, declare that an emergency exists which is detrimental to the public health in the Commonwealth.

This proclamation of a public health emergency is effective immediately and shall remain in effect until notice is given, pursuant to my judgment that the public health emergency has terminated.

Given this 27th day of March in the year of our Lord two thousand and fourteen.



DEVAL L. PATRICK
GOVERNOR
Commonwealth of Massachusetts

London, Sarah

From: London, Sarah
Sent: Tuesday, April 29, 2014 3:23 PM
To: Hoag, Jamie (GOV)
Subject: FW: FYI
Attachments: nejmp1404181.pdf

From: Chen, Harry
Sent: Tuesday, April 29, 2014 2:59 PM
To: London, Sarah
Cc: Cimaglio, Barbara
Subject: FYI

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

Chronic Pain, Addiction, and Zohydro

Yngvild Olsen, M.D., M.P.H., and Joshua M. Sharfstein, M.D.

The recent approval of the long-acting opioid Zohydro ER (hydrocodone bitartrate) by the Food and Drug Administration (FDA) has brought into sharp relief the tension between the twin challenges of chronic pain and addiction.

Chronic pain, which affects tens of millions of people in the United States, is associated with functional loss and disability, reduced quality of life, high health care costs, and premature death. U.S. physicians are now more likely to recognize and treat chronic pain than they have been historically, with the number of prescriptions written for opioids having increased 10-fold since 1990.[1]

Over the same period, however, the rate of overdose deaths in the United States has more than tripled.[2] This is not a coincidence. Many doctors have prescribed opioids for chronic pain without following best practices, understanding the risk for the development of substance-use disorders, or recognizing the red flags that can emerge in clinical practice. There is now evidence from states including our own, Maryland, that some individuals whose path to addiction may have started with a prescription for pain are progressing to heroin.

Enter Zohydro. A single-entity formulation of hydrocodone, Zohydro joins a category of extended-release and long-acting oral opioids that includes Oxycontin (oxycodone hydrochloride), three different versions of extended-release morphine sulfate (MS Contin, Avinza, and Kadian), Exalgo (hydromorphone hydrochloride), Opana ER (oxymorphone hydrochloride), Nucynta ER (tapentadol), and Embeda (morphine sulfate and naltrexone hydrochloride).

Zohydro is a high-potency opioid agonist sold in capsule form, without features to deter crushing and injecting. The FDA explained that it approved Zohydro on the grounds that it is safe and effective for pain when used as directed and may reduce the risk of toxic effects on the liver because, unlike other hydrocodone preparations, it does not contain acetaminophen. But in December 2012, the agency's own advisory committee had voted 11 to 2 against approval, calling for additional safeguards against inappropriate use and diversion. Attorneys general from 29 states have requested that the FDA reconsider its approval of Zohydro. Declaring a public health emergency over the loss of life from overdose and citing the lack of abuse-deterrent features, Massachusetts Governor

Deval Patrick recently took the extraordinary step of banning the prescribing and dispensing of Zohydro in his state. Zogenix, the manufacturer of Zohydro, quickly and successfully challenged the governor's action in federal court. In striking down the ban, Judge Rya W. Zobel acknowledged concerns about the possible misuse of Zohydro but found that the FDA's federal authority preempts state law and that banning the medication would deny appropriate access for patients in pain.

Other states are taking different actions. After his state's health commissioner expressed "dismay" over the FDA approval of Zohydro and called for "getting ahead" of potential problems, Vermont Governor Peter Shumlin announced emergency rules requiring patients to provide informed consent and requiring prescribing physicians to follow a range of specific practices, from drug testing to follow-up care. Failure to do so could lead a physician to lose his or her medical license.

During a recent multiagency call with stakeholders, FDA Commissioner Margaret Hamburg attempted to move the discussion past Zohydro to the agency's broader attempts to address the risks of addiction and overdose.[3] She noted that the agency has supported moving hydrocodone preparations to the more restrictive Schedule II, is relabeling certain prescription opioids with new warnings and narrower indications, is promoting education of prescribers and patients about long-acting opioids, and is seeking to accelerate development of effective nonopioid treatments for pain. The FDA recently approved an autoinjector for the opioid antagonist and reversal agent naloxone.

Hamburg is right that the FDA is doing more than ever before to respond to the overdose epidemic. However, the agency's list of assorted actions is not likely to reduce pressure from elected officials and distraught families who are grappling with an alarming loss of life from overdoses. A more comprehensive and coherent strategy, cutting across the breadth of U.S. health care, is urgently needed.

This strategy need not prioritize chronic pain over addiction or addiction over chronic pain. Rather, it must recognize that both will remain significant and interconnected clinical and public health challenges for the foreseeable future. Millions of people with chronic pain are at risk for addiction or overdose when treated with opioid medications. At the same time, many people with addiction also have chronic pain. Approaches to managing these clinical situations effectively should be a significant focus of research funding, a subject for education in medical and dental schools, and a topic for training in accredited residency programs. A new specialty fellowship in chronic pain and addiction could be developed to foster expertise for consultation to both clinicians and policymakers.

Professional licensing boards can better balance their support of high-quality pain management with effective care for opioid-use disorders. To date, 45 state medical boards have adopted policies on best practices for managing chronic pain with prescription opioids, as recommended by the Federation of State Medical Boards. However, only four of those states have adopted the model policy that encourages ambulatory care physicians to treat opioid-use disorder in their offices with buprenorphine.[4]

The federal government can do more to promote the concurrent treatment of chronic pain and addiction among patients who are at greatest risk for both disorders. For example, we believe that the Substance Abuse and Mental Health Services Administration should provide guidance to physicians practicing in opioid-treatment programs on appropriate ways of using methadone or buprenorphine to treat concomitant opioid-use disorder and chronic pain. Specially designated opioid-treatment programs should be allowed to incorporate comprehensive approaches to chronic pain into their scope of services.

Health care systems can incorporate nonjudgmental screening, brief intervention, and referrals for further assessment and treatment of addiction into all clinical settings where opioids are prescribed. Conversely, addiction-treatment providers can screen patients for pain, recognizing that inadequately treated pain is a risk factor for relapse.

Payers, including Medicare and state Medicaid programs, can use data-analysis tools to spot the red flags of inappropriate prescribing and refer prescribers to medical boards or other state agencies for further review, education, and oversight. Prescription-drug monitoring programs can also identify prescribers in need of assistance. Coherent, evidence-based review of clinical practice can be conducted with the aim of supporting high-quality care for both chronic pain and addiction — and avoiding the unintended consequence of deterring physicians from caring for patients with complex needs.

Public and private insurers can provide as generous coverage for treatment of opioid-use disorder as they do for management of

chronic pain. This standard is infrequently met — for example, it is long past time for Medicare to begin covering the effective care provided in opioid-treatment programs.

It is also time for the FDA to address the intertwining of chronic pain and addiction farther upstream in the drug-development cycle. The agency might consider creating a pathway for development and review of new products and indications for simultaneous treatment of chronic pain and opioid-use disorder. Building on its own work to advance the science of abuse-deterrent formulations, the FDA should also require that prescription opioids meet basic deterrent standards and should facilitate the gradual reformulation of existing products to meet such standards. In declining to apply such a standard to Zohydro, the agency noted that existing deterrent mechanisms have had minimal impact by themselves. However, even modest safeguards have been shown to reduce the potential for inappropriate use.[5] As part of a comprehensive strategy, a set of reasonable requirements for opioid medications is well in line with the FDA's public health mission. Taking such action will deter others with less expertise from filling a perceived void.

In the end, pointing the finger at Zohydro is not going to resolve the tension that exists today between chronic pain and addiction. All concerned about the treatment of chronic pain and all responding to the rise in overdose deaths need to come together to promote high-quality and effective prevention and treatment for both conditions.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

From the Institutes for Behavior Resources (Y.O.) and the Maryland Department of Health and Mental Hygiene (J.M.S.) — both in Baltimore.

This article was published on April 23, 2014, at NEJM.org.

1. Public health grand rounds — prescription drug overdoses: an American epidemic. Atlanta: Centers for Disease Control and Prevention, February 18, 2011 (http://www.cdc.gov/about/grand-rounds/archives/2011/01-February.htm).
2. Policy impact: prescription painkiller overdoses. Atlanta: Centers for Disease Control and Prevention, July 2, 2013 (http://www.cdc.gov/HomeandRecreationalSafety/pdf/PolicyImpact-PrescriptionPainkillerOD.pdf).
3. FDA Commissioner Margaret A. Hamburg statement on prescription opioid abuse. Silver Spring, MD: Food and Drug Administration, April 3, 2014 (http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm391590.htm).
4. Federation of State Medical Boards of the United States. Pain management policies: board by board overview. February 2014 (http://www.fsmb.org/pdf/GRPOL_Pain_Management.pdf).
5. Severtson SG, Bartelson BB, Davis JM, et al. Reduced abuse, therapeutic errors, and diversion following reformulation of extended-release oxycodone in 2010. J Pain 2013; 14:1122-30.

DOI: 10.1056/NEJMp1404181

London, Sarah

From: London, Sarah
Sent: Tuesday, April 29, 2014 9:16 AM
To: Hoag, Jamie (GOV)
Subject: Re: Zogenix v. Patrick

Thanks

Sent from my iPad

> On Apr 29, 2014, at 8:30 AM, "Hoag, Jamie (GOV)" <jamie.hoag@state.ma.us> wrote:
>
> Sarah – Here is the amended complaint.
>
>
> Jamie Hoag
> Deputy Chief Legal Counsel
> Office of the Governor
> 617-725-4038 (direct)
> 617-851-3650 (cell)
>
>
> <Verified Amended Complaint.pdf>

London, Sarah

From: London, Sarah
Sent: Wednesday, April 23, 2014 4:14 PM
To: Hoag, Jamie (GOV)
Subject: Re: GOVERNOR PATRICK ANNOUNCES IMMEDIATE RESTRICTIONS ON POWERFUL NEW PAINKILLER IN RESPONSE TO PUBLIC HEALTH EMERGENCY

Thanks again Jamie.

Sent from my iPad

On Apr 23, 2014, at 4:12 PM, "Hoag, Jamie (GOV)" <jamie.hoag@state.ma.us> wrote:

FYI

GOVERNOR PATRICK ANNOUNCES IMMEDIATE RESTRICTIONS ON POWERFUL NEW PAINKILLER IN RESPONSE TO PUBLIC HEALTH EMERGENCY

BOSTON – Tuesday, April 22, 2014 – Massachusetts Governor Deval Patrick today announced several new actions to restrict the availability of hydrocodone-only extended-release medication that is not in abuse-deterrent form (commonly known as Zohydro), including a requirement that doctors complete a risk assessment and utilize the Prescription Monitoring Program before such medications can be prescribed to a patient.

"We are in the midst of a public health emergency around opioid abuse and we need to do everything in our power to prevent it from getting worse," said Governor Patrick. "The broad actions we are taking to address the opioid epidemic will help save lives and give families struggling with addiction new hope."

Today, the Massachusetts Board of Registration in Medicine voted to require individual prescribers to complete a risk assessment and pain management treatment agreement prior to prescribing any patient hydrocodone-only extended-release medication that is not in abuse-deterrent form. The agreement with each patient must address drug screening, pill counts, safe storage and disposal, and other requirements as appropriate in the prescriber's judgment.

Additional state boards that regulate medical and pharmacist practice will meet soon to consider adopting further restrictions around opioids.

At the Governor's direction, Commissioner of Public Health Cheryl Bartlett, RN, also issued an emergency order today requiring prescribers to utilize the Prescription Monitoring Program

(PMP) prior to prescribing a hydrocodone-only extended release medication that is not in an abuse deterrent formulation. The PMP tracks prescriptions of controlled substances in the Commonwealth and is an important clinical decision-making tool for preventing misuse, overprescribing or diversion of prescription medications.

Commissioner Bartlett will also issue a notification to all prescribers in Massachusetts informing them of these restrictions. "The introduction of this new painkiller into the market poses a significant risk to individuals already addicted to opioids and to the public at large," said Commissioner Bartlett. "These new safeguards are critical to prevent misuse."

On March 27, Governor Patrick declared a public health emergency in Massachusetts in response to the growing opioid addiction epidemic. The Governor took the following actions to address the public health emergency: making Naloxone (Narcan) widely available to first responders and through standing orders in pharmacies; dedicating an additional $20 million to treatment and recovery services; accelerating the mandatory enrollment of prescribers in PMP; and re-tasking the Commonwealth's Interagency Council on Substance Abuse and Prevention to address the opioid epidemic and make recommendations on further actions that can be taken.

Today's actions come on the same day as the state's previous ban on all prescribing and dispensing of Zohydro ends.

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<2014-4-22 Hydrocodone-only Next Steps.doc>