

Kevin M. McDonough (#41892005)
LATHAM & WATKINS LLP
885 Third Avenue
New York, New York 10022
(212) 906-1200

Allen M. Gardner (*PHV* forthcoming)
Sarah M. Gragert (*PHV* forthcoming)
LATHAM & WATKINS LLP
555 Eleventh Street, N.W., Suite 1000
Washington, D.C. 20004
(202) 637-2200

*Attorneys For Plaintiff Pacira
BioSciences, Inc.*

**UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY**

PACIRA BIOSCIENCES, INC.,

Plaintiff,

v.

AMERICAN SOCIETY OF
ANESTHESIOLOGISTS, INC.,
EVAN D. KHARASCH, NASIR
HUSSAIN, RICHARD BRULL,
BRENDAN SHEEHY, MICHAEL K.
ESSANDOH, DAVID L. STAHL,
TRISTAN E. WEAVER, FARAJ W.
ABDALLAH, BRIAN M. ILFELD,
JAMES C. EISENACH, RODNEY A.
GABRIEL, AND MARY ELLEN
McCANN,

Defendants.

Civil Action No. 2:21 Civ. 9264

**COMPLAINT and DEMAND
FOR JURY TRIAL**

Plaintiff Pacira BioSciences, Inc. (“Pacira”), by and through its attorneys, hereby brings this Complaint against Defendants American Society of Anesthesiologists (“ASA” or “the Society”), Evan D. Kharasch, Nasir Hussain, Richard Brull, Brendan Sheehy, Michael K. Essandoh, David L. Stahl, Tristan E. Weaver, Faraj W. Abdallah, Brian M. Ilfeld, James C. Eisenach, Rodney A. Gabriel, and Mary Ellen McCann, and states as follows:

NATURE OF THE ACTION

1. This is a trade libel action regarding false and misleading statements made about EXPAREL, a pain medication drug, in the February 2021 issue of *Anesthesiology*, the ASA’s “official” medical journal.¹ Pacira is the manufacturer of the only liposomal bupivacaine product approved by the U.S. Food and Drug Administration (“FDA”), brand name EXPAREL. EXPAREL (bupivacaine liposome injectable suspension)² is a non-opioid pain medication proven to prolong post-surgery pain relief.

2. In the February 2021 issue of *Anesthesiology*, the ASA, reflecting a bias against EXPAREL amongst the editorial staff at *Anesthesiology*, published three

¹ ASA Publ’ns, *About the Journal*, <https://pubs.asahq.org/anesthesiology/pages/about-the-journal> (last visited Apr. 13, 2021).

² The Complaint uses both “EXPAREL” and “liposomal bupivacaine” to refer to the bupivacaine liposome injectable suspension product manufactured and sold by Pacira.

articles, and other related content, that seriously disparage Pacira’s product EXPAREL. The challenged journal articles, as well as the related podcast and Continuing Medical Education (“CME”) content on the ASA’s website, contain false and misleading conclusions, based on faulty scientific research that does not satisfy applicable standards within the scientific community. These conclusions create the false impression that EXPAREL—a drug approved by the FDA and used by over eight million patients over the past nine years—is not an effective pain medication. As a result, Pacira has suffered and will continue to suffer significant pecuniary harm as both existing and potential customers who have seen the disparaging articles, have either canceled contracts for EXPAREL, declined to purchase EXPAREL, or are considering removing EXPAREL from hospital formularies.

PARTIES

3. Pacira is a pharmaceutical company, and a leading provider of non-opioid pain management. Pacira is the manufacturer of the drug EXPAREL, a non-opioid pain medication.

4. Pacira’s headquarters are located at 5 Sylvan Way, Parsippany, New Jersey, and the company is incorporated in Delaware, making Pacira a citizen of both New Jersey and Delaware.

5. The ASA is a professional medical association centered on the practice of anesthesiology. The ASA is headquartered at 1061 American Lane, Schaumburg, Illinois, 60173, and incorporated in New York, making it a citizen of Illinois and New York.

6. The ASA's membership is open to physicians practicing in anesthesiology as well as anesthesiologist assistants and scientists interested in anesthesiology; other non-physicians who nevertheless provide anesthesia care may join as educational members.³ Active members of the ASA must also be members of a component society; component societies are located in each of the 50 states, including New Jersey, as well as the District of Columbia and Puerto Rico.⁴ The ASA has over 54,000 members,⁵ including members located in New Jersey.

7. The ASA publishes a peer-reviewed medical journal, *Anesthesiology*.⁶

8. Dr. Evan Kharasch is the editor-in-chief of *Anesthesiology* and a Professor of Anesthesiology at the Duke University School of Medicine in Durham, North Carolina, located at Department of Anesthesiology, Box 3094, 905 S. Lasalle,

³ ASA, *Membership Eligibility*, <https://www.asahq.org/member-center/membership-eligibility> (last visited Apr. 13, 2021).

⁴ ASA, *Component Societies*, <https://www.asahq.org/about-asa/component-societies> (last visited Apr. 13, 2021).

⁵ See *supra* note 3.

⁶ The Complaint uses both “*Anesthesiology*” and the “Journal” to refer to the peer-reviewed medical journal published by the ASA.

GSRB1 Room 20031, Durham, NC 27710. He holds a Ph.D. and an M.D. from Northwestern University. Dr. Kharasch oversaw the publication of the challenged articles, and is a longstanding proponent of opioid-based treatments. On information and belief, Dr. Kharasch knew or recklessly disregarded the fact that statements contained in the February articles were false or misleading when he either approved them for publication or permitted them to be published.

9. Dr. Nasir Hussain holds an M.D. and an M.Sc., and is an anesthesiology resident at the Ohio State University College of Medicine in Columbus, Ohio, located at The Ohio State University Wexner Medical Center Doan Hall, Department of Anesthesiology, 410 W. 10th Ave., Columbus, OH, 43201. Dr. Hussain was the lead author of the meta-analysis entitled, “Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia: A Systematic Review and Meta-analysis.” On information and belief, Dr. Hussain knew or recklessly disregarded the fact that his statements about EXPAREL were false or misleading.

10. Dr. Richard Brull holds an M.D. and is a Professor of Anesthesia at the University of Toronto, and Chair in Ambulatory Anesthesia and Women’s Health at Women’s College Hospital in Toronto, Ontario, located at University of Toronto, Women’s College Hospital, 76 Grenville Street, Toronto ON, M5S182. Dr. Brull co-authored “Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal

Bupivacaine for Peripheral Nerve Block Analgesia: A Systematic Review and Meta-analysis.” On information and belief, Dr. Brull knew or recklessly disregarded the fact that his statements about EXPAREL were false or misleading.

11. Dr. Brendan Sheehy is a resident in anesthesiology at The Ohio State University College of Medicine in Columbus, Ohio, located at Ohio State University Wexner Medical Center, Doan Hall, Department of Anesthesiology, 410 W. 10th Ave., Columbus, OH, 43201. He holds an M.D., and is a co-author of “Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia: A Systematic Review and Meta-analysis.” On information and belief, Dr. Sheehy knew or recklessly disregarded the fact that his statements about EXPAREL were false or misleading.

12. Dr. Michael K. Essandoh is an anesthesiologist at The Ohio State University’s Wexner Medical Center in Columbus, Ohio, located at Ohio State University Wexner Medical Center, Doan Hall, Department of Anesthesiology, 410 W. 10th Ave., Columbus, OH, 43201. He holds an M.D., and is a co-author of “Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia: A Systematic Review and Meta-analysis.” On information and belief, Dr. Essandoh knew or recklessly disregarded the fact that his statements about EXPAREL were false or misleading.

13. Dr. David L. Stahl also co-authored “Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia: A Systematic Review and Meta-analysis.” Dr. Stahl is an intensivist and anesthesiologist at The Ohio State University Wexner Medical Center in Columbus, Ohio, located at Ohio State University Wexner Medical Center, Doan Hall, Department of Anesthesiology, 410 W. 10th Ave., Columbus, OH, 43201. He holds an M.D. On information and belief, Dr. Stahl knew or recklessly disregarded the fact that his statements about EXPAREL were false or misleading.

14. Dr. Tristan E. Weaver is an anesthesiologist at The Ohio State University in Columbus, Ohio, located at Ohio State University Wexner Medical Center, Doan Hall, Department of Anesthesiology, 410 W. 10th Ave., Columbus, OH, 43201. He, too, holds an M.D., and co-authored the meta-analysis “Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia: A Systematic Review and Meta-analysis.” On information and belief, Dr. Weaver knew or recklessly disregarded the fact that his statements about EXPAREL were false or misleading.

15. Dr. Faraj W. Abdallah is the final co-author of “Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia: A Systematic Review and Meta-analysis.” Dr. Abdallah is an Associate Professor of Anesthesiology and Pain Medicine at The Ottawa Hospital

in Ottawa, Ontario, located at University of Ottawa, Department of Anesthesiology & Pain Medicine, the Ottawa Hospital, General Campus, 501 Smyth Road, Ottawa, ON, K1H8L6. He holds an M.D. and M.Sc. On information and belief, Dr. Abdallah knew or recklessly disregarded the fact that his statements about EXPAREL were false or misleading.

16. Dr. Brian Ilfeld is the lead author of the second article in question, “Clinical Effectiveness of Liposomal Bupivacaine Administered by Infiltration or Peripheral Nerve Block to Treat Postoperative Pain: A Narrative Review.” Dr. Ilfeld holds an M.D. and an M.Sc., and is Professor of Anesthesiology In Residence at the University of California, San Diego (UCSD) in La Jolla, California, located at University of California, San Diego, Jacobs Medical Center at UC San Diego Health, Department of Anesthesiology, 9300 Campus Point Drive, La Jolla, CA 92037. On information and belief, Dr. Ilfeld knew or recklessly disregarded the fact that his statements about EXPAREL were false or misleading.

17. Dr. James C. Eisenach co-authored “Clinical Effectiveness of Liposomal Bupivacaine Administered by Infiltration or Peripheral Nerve Block to Treat Postoperative Pain: A Narrative Review.” Dr. Eisenach holds an M.S. and an M.D. He is a Professor of Anesthesiology at Wake Forest University School of Medicine in Winston-Salem, North Carolina, located at Wake Forest University School of Medicine, Bowman Gray Center for Medical Education, 475 Vine Street,

Winston-Salem, NC 27101. On information and belief, Dr. Eisenach knew or recklessly disregarded the fact that his statements about EXPAREL were false or misleading.

18. Dr. Rodney A. Gabriel also co-authored “Clinical Effectiveness of Liposomal Bupivacaine Administered by Infiltration or Peripheral Nerve Block to Treat Postoperative Pain: A Narrative Review.” Dr. Gabriel is an Assistant Clinical Professor of Medicine at the University of California, San Diego in San Diego, California, located at University of California, San Diego, Jacobs Medical Center at UC San Diego Health, Department of Anesthesiology, 9300 Campus Point Drive MC7770, La Jolla, CA 92037. He holds an M.D. from the University of California, San Francisco. On information and belief, Dr. Gabriel knew or recklessly disregarded the fact that his statements about EXPAREL were false or misleading.

19. Finally, Dr. Mary Ellen McCann holds an M.D. and is a Senior Associate in Perioperative Anesthesia in the Boston Children’s Hospital’s Departments of Anesthesia and Critical Care and Pain Medicine, and an Associate Professor of Anesthesia at Harvard Medical School. Her place of business is located at Boston Children’s Hospital, Department of Anesthesiology, Critical Care & Pain Medicine, 300 Longwood Avenue, Bader, 3rd Floor, Boston, MA, 02115. Dr. McCann authored the third piece, “Liposomal Bupivacaine: Effective, Cost-effective, or (Just) Costly?” and appeared as a guest on *Anesthesiology*’s podcast to

discuss her editorial. On information and belief, Dr. McCann knew or recklessly disregarded the fact that her statements about EXPAREL were false or misleading.

JURISDICTION AND VENUE

20. This Court has subject matter jurisdiction pursuant to 28 U.S.C. § 1332(a)(1). Pacira is incorporated in Delaware and its principal place of business is located in New Jersey, making Pacira a citizen of Delaware and New Jersey. The ASA is incorporated in New York, and its principal place of business is in Illinois, making the ASA a citizen of New York and Illinois. On information and belief, none of the individual defendants reside in New Jersey. Complete diversity therefore exists between the parties, and the amount that Pacira seeks in damages exceeds \$75,000.

21. This Court has personal jurisdiction over the ASA by virtue of the activities it conducts in New Jersey. On information and belief, the ASA has members located in New Jersey, as well as subscribers to its official journal *Anesthesiology* located in New Jersey. On information and belief, the ASA has purposefully availed itself of the benefits and protections of New Jersey state law by conducting activities here.

22. This Court has personal jurisdiction over the individual defendants Kharasch, Hussain, Brull, Sheehy, Essandoh, Stahl, Weaver, Abdallah, Ilfeld, Eisenach, Gabriel, and McCann because, on information and belief, the individual

defendants have sufficient minimum contacts with New Jersey and because the effects of their conduct have been felt in New Jersey. Trade libel is an intentional tort, and the individual defendants' disparaging statements regarding liposomal bupivacaine were directed at Pacira, the only FDA-approved manufacturer of liposomal bupivacaine, brand-name EXPAREL. Pacira is headquartered in New Jersey, and has felt the effects of the individual defendants' conduct—lost revenue, lost customers, and damage to EXPAREL's reputation as an effective product—in New Jersey. The individual defendants likewise targeted the forum by publishing their false and misleading statements about EXPAREL in *Anesthesiology*, a national publication available in New Jersey, and on information and belief, with subscribers in New Jersey.

23. Venue is proper in this Court pursuant to 28 U.S.C. § 1391. Pacira resides in this district due to the location of its headquarters in Parsippany, New Jersey, and Pacira's cause of action arose in this action due to the pecuniary harm Pacira's business suffered as a result of the ASA's libelous and disparaging remarks about Pacira's product, which caused several of Pacira's customers to cancel their supply contracts for EXPAREL, or remove EXPAREL from their formularies. A substantial part of the events giving rise to the claim therefore occurred in New Jersey.

STATEMENT OF FACTS

EXPAREL (Liposomal Bupivacaine) and the Opioid Crisis

24. The opioid crisis facing the United States is unparalleled. Americans consume and produce more opioids than any other country in the world. According to the U.S. Centers for Disease Control and Prevention, the number of opioid overdoses has quadrupled since 1999.⁷ This is unsurprising, given that opioid prescriptions quadrupled during this period as well, triggering the present crisis. *Id.* In 2015, the amount of opioids prescribed in the United States was enough for every American to be medicated around the clock for three weeks. *Id.* In that same year, nearly two-thirds of drug overdoses were linked to opioids, especially Percocet, OxyContin, heroin, and fentanyl. *Id.* The opioid epidemic is not one that began on a street corner: in many cases, it began in doctor's offices and hospitals. *Id.*

25. Addressing the opioid epidemic will require a multi-faceted strategy, but any such strategy must include changes to the way the medical community treats and manages patient pain. "The era of opioids as the gold standard for pain

⁷ *The President's Commission on Combating Drug Addiction and the Opioid Crisis*, Appendix 3, at 115, available at <https://www.hsdl.org/?search&exact=United+States.+President%27s+Commission+on+Combating+Drug+Addiction+and+the+Opioid+Crisis&searchfield=publisher&collection=limited&submitted=Search&advanced=1&release=0>.

management is over.”⁸ Pacira’s corporate mission is to provide a non-opioid pain management option to every patient. As noted above, Pacira is the manufacturer of EXPAREL, the brand name for the sole liposomal bupivacaine product approved for sale in the United States. Liposomal bupivacaine is a long-lasting, non-opioid, non-narcotic pain medication used to treat post-surgical pain.

26. EXPAREL is used as a local anesthetic administered at the time of surgery to control pain and reduce or eliminate the use of opioids for post-surgical pain.⁹ EXPAREL contains specially formulated bupivacaine—it encapsulates bupivacaine in liposomal chambers and is designed to release into the body over a prolonged period of time as the chamber walls break down.¹⁰ In this respect, it is able to deliver prolonged pain relief over non-liposomal bupivacaine. Because EXPAREL works for longer periods of time, patients may need fewer doses of other pain medications, including opioids, after surgery.¹¹

27. EXPAREL is approved by the FDA for two indications. In 2011, EXPAREL was approved for single-dose infiltration into the surgical site for local

⁸ Pacira, *Commitment*, <https://www.pacira.com/commitments> (last visited Apr. 13, 2021).

⁹ Pacira, *EXPAREL*, <https://www.pacira.com/products/exparel> (last visited Apr. 13, 2021).

¹⁰ EXPAREL, *Frequently Asked Questions*, <https://www.exparel.com/patient/faq> (last visited Apr. 13, 2021).

¹¹ *Id.*

postoperative analgesia. In 2018, EXPAREL was approved as an interscalene brachial plexus nerve blocking agent (blocking the nerves in the neck, near the shoulder) to produce postsurgical regional analgesia.¹² And just last month, the FDA approved EXPAREL for use in children ages 6 to 17, making it the first long-acting anesthetic ever approved for pediatric use.¹³ To date, over 8 million patients have been treated with EXPAREL.¹⁴

28. Pacira sells EXPAREL to hospitals, ambulatory surgical centers, and healthcare providers all over the country. The primary customers of EXPAREL are the Department of Defense, hospitals, and ambulatory surgical centers. EXPAREL is purchased for use by surgeons and anesthesiologists to provide long-lasting non-opioid post-surgical pain relief. In 2019 and 2020, sales of EXPAREL represented approximately 96% of Pacira's total revenues.¹⁵ EXPAREL thus represents a crucial part of Pacira's business.

¹² See *supra* note 9.

¹³ EXPAREL, *Pediatric*, <https://www.exparel.com/hcp/specialty/pediatrics> (last visited Apr. 13, 2021).

¹⁴ EXPAREL, *Non-Opioid EXPAREL*, <https://www.exparel.com/patient/non-opioid-pain-medication> (last visited Apr. 13, 2021).

¹⁵ Press Release, Pacira, Pacira BioSciences Reports Full-Year 2019 Preliminary Revenue of \$421.0 Million (Jan. 9, 2020), <https://investor.pacira.com/news-releases/news-release-details/pacira-biosciences-reports-full-year-2019-preliminary-revenue#:~:text=Full%20year%20EXPAREL%20net%20product,to%20%241.3%20million%20in%202018>; Press Release, Pacira, Pacira Reports Record Revenue

Anesthesiology

29. *Anesthesiology* (the “Journal” or “*Anesthesiology*”) is the “official journal of the American Society of Anesthesiologists.”¹⁶ As such, it claims to “lead[] the world in publishing and disseminating the highest quality work to inform daily clinical practice and transform the practice of medicine in the specialty.”¹⁷ The Journal publishes 12 issues a year, and has a top impact factor ranking of 1 out of 32 in the field of anesthesiology.¹⁸ An impact factor ranking is one metric used to measure the importance of an academic journal within its field, measuring the frequency with which the journal is cited.¹⁹

30. The Journal is available in both print and online forms; indeed, the ASA provides free online access to certain highlighted articles, and free access to many

for 2020 of \$429.6 Million (Jan. 7, 2021), <https://investor.pacira.com/news-releases/news-release-details/pacira-reports-record-revenue-2020-4296-million#:~:text=Full%20year%20EXPAREL%20net%20product,to%20%24407.9%20million%20in%202019.&text=Full%20year%20iovera%C2%B0%20net,to%20%247.9%20million%20in%202019>.

¹⁶ *See supra* note 1.

¹⁷ *Id.*

¹⁸ Wolters Kluwer, *Anesthesiology*, <https://www.wolterskluwer.com/en/solutions/lippincott-audience-solutions/media-kits/anesthesiology> (last visited Apr. 13, 2021).

¹⁹ Clarivate, *Journal Citation Reports: Learn the Basics*, <https://clarivate.libguides.com/jcr> (last visited Apr. 13, 2021).

previously published articles.²⁰ A subscription is included as a free benefit for ASA members, but subscriptions are also available to any individual for a fee, as well as to institutions.²¹ The Journal has approximately 51,502 subscribers in total, including 43,332 print subscribers, and 8,170 online subscribers. The website receives, on average, 422,964 visits per month.²²

Bias of the Editor-in-Chief of *Anesthesiology*

31. Dr. Evan Kharasch, the Editor-in-Chief of *Anesthesiology* appears to have a significant bias against EXPAREL, in favor of opioids for treatment of pain. As Editor-in-Chief, he has final say over the content published in each issue, and on information and belief, is using his position to advance a pro-opioid agenda and disparage competitive alternatives like EXPAREL. In fact, Kharasch has previously made public statements disparaging products like EXPAREL. For example, Dr. Kharasch authored an editorial in an April 2020 issue of *Anesthesiology* in which he described using non-opioid drugs like EXPAREL, which seek to reduce opioid use post-surgery, as an “arbitrary and commercially influenced” approach to

²⁰ ASA Publ’ns, *Issues: Volume 134, Issue 5*, <https://pubs.asahq.org/anesthesiology/issue> (last visited Apr. 12, 2021); *see also* ASA Publ’ns, *Issues: Volume 132, Issue 1*, <https://pubs.asahq.org/anesthesiology/issue/132/1> (prior publications).

²¹ ASA Publ’ns, *Anesthesiology Access Options*, <https://pubs.asahq.org/anesthesiology/pages/access-options> (last visited Apr. 13, 2021).

²² *See supra* note 18, at Audience tab.

management of postoperative pain, that “presently lack[s] compelling evidence.”²³ Asking whether “the elimination of intraoperative opioid use [is] a reasonable goal,” Kharasch wrote that “[w]e appear poised to fundamentally change anesthesia practice without having a rational basis for doing so.”²⁴ Kharasch’s own research interests include studies supporting opioid use in post-surgery patients.²⁵

32. The anti-EXPAREL bias of *Anesthesiology* and its Editor-in-Chief is also apparent from a comparison of the covers of the journal’s January 2021 and February 2021 issues. The January 2021 cover highlighted a meta-analysis that reviewed an anesthesiology procedure called a “quadratus lumborum block,” used for cesarean delivery.²⁶ The meta-analysis—conducted by the same lead author, Dr. Hussain—reached an unfavorable conclusion regarding the effectiveness of that

²³ Evan D. Kharasch et al., *Rational Perioperative Opioid Management in the Era of the Opioid Crisis*, 132 *Anesthesiology* 603-05 (Apr. 2020).

²⁴ *Id.*

²⁵ See, e.g., Evan D. Kharasch, *Opioid-Free Anesthesia: Time to Regain Our Balance*, 134 *Anesthesiology* 509-14 (Apr. 2021) (arguing that “Opioid-free anesthesia may be feasible. Nevertheless, it appears neither logical nor beneficial to patients.”); James P. Rathmell et al., *Frontiers in Opioid Pharmacology*, 128 *Anesthesiology* 865 (May 2018); Evan D. Kharasch, *Intraoperative Methadone: Rediscovery, Reappraisal, and Reinvigoration?*, 112 *Anesthesia & Analgesia* 13 (Jan. 2011).

²⁶ ASA Publ’ns, *Issues: Volume 134, Issue 1*, <https://pubs.asahq.org/anesthesiology/issue/134/1> (last visited Apr. 13, 2021).

procedure.²⁷ The cover of the January publication stated simply, “Quadratus Lumborum Block for Ceasarean Delivery.”²⁸ In clear contrast, the EXPAREL meta-analysis also reached an unfavorable conclusion regarding the treatment, but the February cover contained the pejorative teaser: “Liposomal Bupivacaine Is Not Superior to Standard Local Anesthetics.” *See* Ex. 7, *Anesthesiology* Feb. 2021 cover.

33. On information and belief, Kharasch has also used his position as Editor-in-Chief to suppress information favorable to EXPAREL, in order to further his pro-opioid agenda. Pacira understands that *Anesthesiology* rejected publication of a letter to the editor that reported favorable experience with EXPAREL, and which expressed concern about the over-generalizations contained in the meta-analysis published in the February 2021 issue.

The February 2021 Issue of *Anesthesiology* Disparages EXPAREL

34. Consistent with Dr. Kharasch’s bias against EXPAREL, including the bias conveyed on the cover of the February 2021 issue of *Anesthesiology*, the February 2021 issue focuses on the efficacy of EXPAREL, and contains significant

²⁷ Dr. Nasir Hussain et al., *Postoperative Analgesic Effectiveness of Quadratus Lumborum Block for Cesarean Delivery under Spinal Anesthesia: A Systematic Review and Meta-analysis*, 134 *Anesthesiology* 72-87 (Jan. 2021).

²⁸ *See supra* note 26.

false and misleading representations of fact that seriously disparage Pacira's product EXPAREL.

35. As noted above, the cover of the issue states that "Liposomal Bupivacaine Is Not Superior to Standard Local Anesthetics," with no accompanying qualifying or explanatory information. *See* Ex. 7, *Anesthesiology* Feb. 2021 cover. The issue also contains three articles—a purported meta-analysis, a so-called narrative review, and an editorial based on the meta-analysis and narrative review—that contain false and misleading statements and conclusions that disparage EXPAREL. These representations were also advanced in the ASA's CME program and podcast. The three articles are:

- a. *Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia: A Systematic Review and Meta-analysis*, authored by Defendants Nasir Hussain, Richard Brull, Brendan Sheehy, Michael K. Essandoh, David L. Stahl, Tristan E. Weaver, and Faraj W. Abdallah ("Hussain Article") (attached as Ex. 1). This article was at one point one of the "most viewed" articles on the ASA's website, where the article is offered for anyone to view for free.
- b. *Clinical Effectiveness of Liposomal Bupivacaine Administered by Infiltration or Peripheral Nerve Block to Treat Postoperative Pain: A Narrative Review*, authored by Defendants Brian M. Ilfeld, James C. Eisenach, and Rodney A. Gabriel ("Ilfeld Review") (attached as Ex. 2).
- c. *Liposomal Bupivacaine: Effective, Cost-effective, or (Just) Costly*, authored by Defendant Mary Ellen McCann ("McCann Editorial") (attached as Ex. 3).

36. All three articles and the Journal cover create the illusion of rigorous and reliable scientific analysis using carefully curated data and technical jargon. The truth is anything but. Each article is riddled with errors, some of which are such egregious deviations from standard practice as to make clear that the authors designed their analyses to arrive at a predetermined outcome.

37. Three significant problems in particular are common to all three articles. First, the articles rely heavily on pain studies that make no attempt to account for the fact that patients receive other medication beyond the test drugs. Basic ethics dictate that patients cannot be left in pain; they are provided opioids and other pain medication as needed. Thus, it is no surprise that patients in groups receiving EXPAREL and those receiving alternative medications may report similar pain scores, because additional analgesics control the pain. This is a common problem with many pain studies. Rather, it is important to look to studies that gather the data needed to make calculations to account for the additional pain medicine. The authors of all three studies rely heavily on trials that did not do that.

38. Second, all three articles (and the issue cover) reach blanket, unqualified conclusions that EXPAREL is not effective—in any type of use or any type of surgery. Without limiting their conclusions to specific infiltration methods for specific surgical procedures, the statements are false. The amount of benefit that EXPAREL provides a patient varies significantly by the type of surgery the patient

underwent and how EXPAREL was used (i.e., direct infiltration near the wound site or a peripheral nerve block to the major nerves that provide sensation to the surgical area). However, even if there are some procedures for which EXPAREL may not provide much additional benefit over alternative anesthetics (e.g., procedures that do not cause pain much beyond 24 hours), there are certain procedures for which EXPAREL is undoubtedly effective—rendering the blanket conclusion false.

39. Third, in order to reach their conclusions, the authors of all three articles choose to discredit industry-sponsored trials as supposedly biased simply because of their funding source, even though industry-funded trials often produce the best data because they have sufficient funding for more robust trials (as was the case with the EXPAREL trials), and even though the authority on proper meta-analysis and review procedure (the Cochrane Collaboration) does *not* identify industry-funding as an indicator of bias.

40. In addition to these flaws, the articles suffer from other individual problems that result in their false conclusions.

The Hussain Article

41. Among myriad other problems, the authors of the Hussain Article appear to have cherry-picked selective studies that are likely to provide an unfavorable view of EXPAREL, excluded those that would result in the opposite conclusion, focused on surgical procedures for which EXPAREL is not approved or

not commonly used, and used contorted methods and calculations that are contrary to accepted practices for conducting a meta-analysis. At least one anesthesiologist member of the ASA, familiar with EXPAREL and its uses, expressed surprise and concern at the “unbalanced selection” of the studies used in the meta-analysis. There are hundreds of studies on the use of EXPAREL, yet the authors of the meta-analysis relied on only nine highly curated studies in reaching their conclusions.

42. The authors also employ a flawed method known as “crude pooling” rather than the methodologically correct approach known as “stratified pooling.” Crude pooling can lead to inaccurate and misleading results that do not reflect trial outcomes. For this reason, this methodology is widely recognized as an incorrect method.

43. Additionally, the authors fail to account for statistical heterogeneity of the studies on which the meta-analysis relies, even though scientific standards require such heterogeneity to be accounted for. Studies vary in their populations (e.g., types of patients, surgeries, peripheral nerve blocks), the types of medication involved and how that medication is administered (e.g., whether patients were given EXPAREL only or mixed with normal bupivacaine; what doses were used), outcome definitions (e.g., how the study measures patient pain experiences), and designs (e.g., what methods were used to guard against common biases in the data, or missing data). In order to draw meaningful conclusions from comparing these studies, these

differences must be accounted for through heterogeneity analyses. The Hussain Article's failure to do so contravenes the standards of medical research and precludes clinically meaningful conclusions.

44. These are only some of the many shortcomings of the Hussain Article. Yet the authors create the false impression that their conclusions were reached only after a rigorous and thorough analysis of all relevant and available data, when that could not be further from the truth.

45. It is also worth noting that two of the authors, Brull and Abdallah, practice in Canada, where EXPAREL is not available. Thus, these authors are likely commenting on a product they have never actually used. Again, it is difficult to believe that these errors and omissions, combined, were all unintentional.

46. On information and belief, the authors knew or recklessly disregarded the fact that such practices were likely to bias the results of the meta-analysis. The errors in this article were not inadvertent. Among other evidence of intent, the use of crude pooling is universally condemned as an improper approach to meta-analysis. The authors' selection of trials for review shows an intent to cherry-pick studies unfavorable to EXPAREL, while excluding multiple favorable studies for manufactured reasons, or no reason at all. The authors' failure to account for clinical diversity likewise demonstrates intent. Some of these errors could be due to

ignorance, but on balance, they demonstrate an intent to choose methodologies that would bias the results.

The Ilfeld Review

47. In addition to the three substantial problems above, the conclusions of the Ilfeld Review are false for additional reasons. Among other things, they never discuss the most relevant anesthesia procedure: direct infiltration of EXPAREL versus continuous infiltration of bupivacaine via catheter. Continuous infiltration of bupivacaine most closely approximates what EXPAREL offers patients. Together, those studies present results favorable to EXPAREL. The authors also raise spurious reasons to dismiss, discredit, or flatly ignore other studies that are favorable to EXPAREL, and then do not tell the truth about the biases and problems with studies that are not favorable to EXPAREL.

48. These errors are likely not inadvertent and are, instead, the result of actual malice. Like the authors of the Hussain Article, Ilfeld et al. disregarded the large body of research favorable to EXPAREL, and made other design choices in the study that appear intended to bias the results, ignoring industry-accepted guidelines. Even the simple fact that the authors chose a narrative review, a form of study which gives authors a great deal of flexibility to inject their subjective views into the research, creates concern that the study was molded to reach a particular outcome. And the authors' execution of the Cochrane Bias Risk Assessment evinces

an intent to conceal shortcomings of numerous studies unfavorable to EXPAREL, as the authors conclude that they had low risk of bias or only “some concerns,” a proper assessment reveals that they have considerable risks of bias.

49. As further evidence of intent, two of the authors of this article, Defendants Ilfeld and Gabriel, failed to disclose certain financial conflicts of interest—but had disclosed those conflicts in other recent articles. The incomplete disclosures give the misleading impression that the conclusions in the article are based on objective assessments from unbiased observers. In fact, the two authors had an interest in reaching particular conclusions.

50. It is standard ethics in medical publications for authors to disclose relevant financial interests. Indeed, the “Instructions for Authors” provided by *Anesthesiology*, as well as the recommendations for the “Disclosure of Financial and Non-Financial Relationships and Activities, and Conflicts of Interest” maintained by the International Committee of Medical Journal Editors (“ICMJE”), hold that accurate disclosures are necessary to ensure public confidence in science.²⁹ As the ICMJE disclosure guidelines state, it is ultimately the readers that must be able to

²⁹ See ASA Publ’ns, *Instructions for Authors*, <https://pubs.asahq.org/anesthesiology/pages/instructions-for-authors-general#coi> (last visited Apr. 13, 2021); ICMJE, *Disclosure of financial and Non-Financial Relationships and Activities, and Conflicts of Interest*, www.icmje.org/recommendations/browse/roles-and-responsibilities/author-responsibilities--conflicts-of-interest.html (last visited Apr. 13, 2021).

make their own judgments regarding whether an author's relationships and activities are pertinent to a paper's content. These judgments require transparent disclosures.³⁰ To be complete, such disclosures must include any financial relationships, such as employment and consultancies. *Anesthesiology* and other academic standards therefore require complete disclosure of all funding sources supporting a given work or its authors, even if such support is indirect, so as to avoid both actual and perceived conflicts.

51. The financial disclosures provided in connection with this article state that coauthor Gabriel had not “performed consulting work for any private company in the last 6 [years].” Ex. 2, Ilfeld Review at 334. Yet the Open Payments database maintained by the Centers for Medicare & Medicaid Services shows that Gabriel received a \$2,500 consulting payment from Heron Therapeutics, Inc. (“Heron”) as recently as October 2019.³¹ Heron is a primary competitor of Pacira, and a manufacturer of a long-acting bupivacaine formulation.³²

52. Similarly, Ilfeld, the lead author of the article, failed to disclose conflicting interests. Ilfeld's profile on UCSD's website states that he received over

³⁰ See ICMJE, *supra* note 29.

³¹ Open Payments Data, *Rodney Allanigue Gabriel*, <https://openpaymentsdata.cms.gov/physician/2789991> (last visited Apr. 13, 2021).

³² Heron Therapeutics, *HTX-011 (ZYNRELEF)*, <https://www.herontx.com/HTX-011> (last visited Apr. 13, 2021).

\$14 million in U.S. Department of Defense funding for research involving treatment modalities that compete with EXPAREL.³³ Similarly, Ilfeld has authored multiple journal articles, including two articles published in 2020,³⁴ and an article published in March 2021,³⁵ in which he disclosed that UCSD received funding from Heron. Notably, Ilfeld did not simply forget his disclosure obligations in connection with the February 2021 article; to the contrary, he disclosed Pacira consulting payments that he received between 2011 and 2014. *See* Ex. 2, Ilfeld Review at 334. Ilfeld’s simultaneous failure to disclose the Department of Defense funding he received, as well as the relationship between Heron Therapeutics and his employer, is thus all the more striking.

³³ UC San Diego, *UCSD Profiles: Brian Ilfeld*, <https://profiles.ucsd.edu/brian.ilfeld> (last visited Apr. 13, 2021)

³⁴ *See* John J. Finneran et al., *Suture-method versus Through-the-needle Catheters for Continuous Popliteal-sciatic Nerve Blocks: A Randomized Clinical Trial*, 132 *Anesthesiology* 854-66 (Apr. 2020) (disclosing, in relevant part, that “Dr. Ilfeld’s institution has received funding for a different research project from a manufacturer of a long-acting bupivacaine formulation, Heron Therapeutics”); Brian M. Ilfeld et al., *Letter Regarding “Repeated Intercostal Nerve Blocks With Liposomal Bupivacaine for Chronic Chest Pain: A Case Report”*, 14 *A&A Practice* 67 (Jan. 2020) (disclosing, in relevant part, that Ilfeld’s “institution has received funding and/or product for his research from ... Heron Therapeutics” and that Ilfeld “performed consulting work for Pacira more than 3 years ago (last: November 2014)”).

³⁵ *See* Brian M. Ilfeld et al., *Ambulatory continuous peripheral nerve blocks to treat postamputation phantom limb pain: a multicenter, randomized, quadruple-masked, placebo-controlled clinical trial*, 162 *Pain* 938-55 (Mar. 2021) (disclosing, on behalf of Ilfeld and one other author, that the “University of California has received funding and product for other research projects from ... Heron Therapeutics”).

53. By failing to provide the relevant disclosures discussed above, Gabriel and Iffeld have violated the ethics of medical journals and the standards of the broader scientific community regarding conflicts of interest.³⁶ Their article therefore creates the false and misleading impression that it presents a disinterested analysis of the effectiveness of EXPAREL, when in fact the authors, sponsored by Pacira's competitors, had a vested interest in disparaging the effectiveness of Pacira's product. Again, the errors and omissions in this article, particularly the erroneous disclosures, are too numerous to have been accidental.

The McCann Editorial

54. The McCann Editorial rehashes the conclusions of the Hussain and Iffeld articles, and then proceeds to criticize Pacira and EXPAREL for EXPAREL's cost, suggesting that Pacira is lining its pockets with revenue from an ineffective drug. These statements and insinuations are false.

55. Dr. McCann strongly insinuates that the FDA approved EXPAREL with insufficient evidence. However, she is overly dismissive of placebo studies, which demonstrate that EXPAREL is an effective pain medication, and which members of her own committee believed constituted sufficient evidence. She also implies that customers purchase EXPAREL due only to Pacira's marketing efforts,

³⁶ See *supra* note 29.

but the fact that licensed physicians have chosen to use EXPAREL in novel ways, far beyond the methods for which Pacira markets it, demonstrates that statement is false. They use EXPAREL because it works.

56. The false conclusions of the McCann Editorial also appear to be the product of actual malice. The editorial relied heavily on, and adopted, the conclusions of the Hussain and Ilfeld Review to show that there is no clinical difference between EXPAREL and other available products. In adopting the conclusions, McCann—the former Chair of the FDA Anesthetic and Analgesic Drug Products Advisory Committee—blessed the articles with her authoritative imprimatur, magnifying their disparaging effects. Yet, Dr. McCann appears to make no effort to check the accuracy or methodology of their analyses and simply places her stamp of approval on them. Many of the errors in the Hussain and Ilfeld articles are too obvious to ignore, yet McCann apparently did just that. Given the weight that her credentials would lend to the conclusions of those articles, it was incumbent upon her to make sure the conclusions were right. Nevertheless, on information and belief, McCann turned a blind eye to these problems and fully endorsed both articles in their entirety and adopted their conclusions without recognizing any shortcomings. McCann likewise systematically disregards studies favorable to EXPAREL, on the basis that the studies are “tainted,” by industry funding or bias—even where no such bias is identified in the underlying study.

57. On information and belief, Pacira understands that Dr. McCann wrote this editorial at the request of the editors of *Anesthesiology*, and that the editors of *Anesthesiology* did not solicit commentary regarding EXPAREL from anyone else in advance of publishing the February 2021 issue. Indeed, the editorial indicates that it was accepted for publication in December 2020, months before the other articles were published—meaning that the article has to have been solicited by the ASA and the editors of *Anesthesiology*. Ex. 3, McCann Editorial at 139. Why the editors sought out Dr. McCann, what the editors asked Dr. McCann to write, what background information Dr. McCann was provided, and the degree of influence that the editors exerted over Dr. McCann’s writing have not been publicly disclosed. While invited editorials may reflect the biases of their authors, the readers of *Anesthesiology* should be made aware if such a guest editorial reflects biases of the journal itself. Again, the letter creates the misleading impression that the conclusions regarding the effectiveness of EXPAREL are based on objective analysis, and the lack of disclosure calls that objectivity into question.

Podcasts and CME Based on the February 2021 Issue of *Anesthesiology* Disparaged Pacira’s Product

58. The ASA also published on its website content adjacent to and based on the February 2021 issue of *Anesthesiology*, including content based on the misrepresentations or misleading statements found in the three articles above. This

content likewise disparaged EXPAREL, and, together with the articles, has caused pecuniary harm to Pacira.

CME Activity

59. For a fee, the ASA offers a CME program linked to its *Anesthesiology* articles. Each month, the ASA chooses articles from that month's issue, and writes six questions associated with the articles.³⁷ Those who have subscribed to the CME program can access the questions online, and receive credit that can be used to satisfy medical licensure requirements.³⁸ The Hussain and Ilfeld articles from the February 2021 issue of *Anesthesiology* were among the articles chosen for this program. *See* Ex. 6, CME Instructions. The questions in the CME activity restate as fact the various flawed and misleading conclusions reached by these articles about the effectiveness of EXPAREL, and then use them as *accredited teaching material* for healthcare providers. *See* Exhibit 4, ASA Journal CME Posttest.

60. For example, Question 2 asks, "Which of the following is true regarding studies comparing liposomal bupivacaine to aqueous local anesthetics?" Ex. 4, ASA Journal CME Posttest at 2-3. Choice B, which says that a high percentage of randomized control trials showed that infiltration of the surgical site with liposomal

³⁷ ASA, *Journal CME – 2021 Full Subscription*, <https://www.asahq.org/shop-asa/e021j00w00> (last visited Apr. 13, 2021).

³⁸ *Id.*

bupivacaine provides inferior analgesia to a peripheral nerve block with local anesthetics, is indicated as true, yet is in fact false. *Id.* Studies that have compared EXPAREL infiltration to peripheral nerve blockade have shown statistically significant findings in favor of EXPAREL, and certainly did not demonstrate that EXPAREL was *inferior* to alternatives. Indeed, even the conclusion of the Husain Article was only that EXPAREL was “not superior.” Ex. 1, Hussain Article at 1.

61. Similarly, Question 1 asks whether a majority of studies reporting positive results for liposomal bupivacaine compared to aqueous local anesthetics or placebo were deemed to be high risk for bias. Ex. 4, ASA Journal CME Posttest at 2. This question assumes that funding source is considered a primary component when determining the risk of bias in clinical trials. The question misleads the reader to assume that the authors’ opinion of bias is the same as the standard accepted definition of bias, which refers to the validity of findings based on various parameters. The question creates the impression that industry-sponsored studies finding positive results from EXPAREL are necessarily biased and cannot be trusted—a particularly troubling and misleading impression given the failure of the authors of the Ilfeld Review to adequately disclose their financial connections to the manufacturers of EXPAREL competitors. Nor does it address the fact that a very large portion of studies that do not report favorable results for liposomal bupivacaine rated as having high risks of bias.

62. Moreover, in promoting the bias against EXPAREL, the CME activities violate standards promulgated by the Accreditation Council for Continuing Medical Education (“ACCME”), the body that regulates CME programs. Because physicians are likely to apply knowledge obtained through CME activities to their practices, it is critical that these CME activities provide balanced and accurate information. For this reason, ACCME states that “independence” of medical education from industry influence is the cornerstone of accredited continuing education. Industry corporations, such as pharmaceutical companies, insurance companies, and medical device companies are ineligible to provide accredited CME activities (known as “ineligible companies”). The burden is on CME providers, like the ASA, to implement safeguards to protect the independence of CME activities and ensure that CME activities offered are balanced, evidence-based, and based on best practices.

63. In order to ensure that CME activities and CME providers meet these crucial goals, accredited providers must comply with ACCME’s Standards for Integrity and Independence in Accredited Continuing Education (ACCME Integrity Standards).³⁹ Among other things, Standard 1 requires that CME material be “valid,” meaning, among other things, that the material gives a “fair and balanced

³⁹ ACCME, *Standards for Integrity and Independence in Accredited Continuing Education* (Dec. 2020), https://accme.org/sites/default/files/2020-12/884_20201210_New%20Standards%20Standalone%20Package.pdf (last visited Apr. 13, 2021).

view of diagnostic and therapeutic options,” and that “[a]ll scientific research referred to, reported, or used in accredited education ... conform[s] to the generally accepted standards of experimental design, data collection, analysis, and interpretation.”⁴⁰ Standard 2 “prevent[s] commercial bias and marketing,” and prohibits influence on CME activities from ineligible companies like pharmaceutical or insurance companies.⁴¹ Finally, Standard 3 requires providers to “identify, mitigate, and disclose relevant financial relationships ... between individuals in control of educational content and ineligible companies.”⁴² This standard also imposes affirmative obligations on providers to collect and disclose information about financial relationships, mitigate conflicts of interest, and exclude owners and employees of industry corporations from CME activities.⁴³ By promoting the biases and scientific flaws present in the challenged articles, and failing to mitigate the conflicts of interest in the Iffeld Review, the CME activity accompanying the February 2021 issue of *Anesthesiology* violated these ACCME standards.

64. Overall, this CME activity compounds the issues identified in the three articles discussed above, violates the ACCME’s standards for CME activities, and

⁴⁰ *Id.* at 5.

⁴¹ *Id.* at 5.

⁴² *Id.* at 6.

⁴³ *Id.*

seems designed to disparage EXPAREL rather than accurately educate medical professionals.

Anesthesiology Podcast

65. *Anesthesiology* produces a podcast that is available on the ASA's website,⁴⁴ and a recent episode discusses the conclusions of both the Hussain Article and the Ilfeld Review regarding EXPAREL, further spreading false and misleading information from the two February 2021 articles to an audience beyond the journal's readers. The podcast has repeated the conclusions of both articles without acknowledging their many flaws. A transcript of the podcast is attached as Exhibit 5.

66. For example, Dr. James Rathmell, the podcast's host, and Defendant Abdallah, one of the authors of the Hussain Article, discussed that article's meta-analysis of "nine randomized trials," but did not address any of the deficiencies mentioned above. *See* Ex. 5, *Anesthesiology Podcast Tr.* at 2. During this discussion, Dr. Rathmell did not pose any questions regarding the underlying issues with the studies' methodology and results. *Id.* Although Defendant Abdallah did briefly acknowledge that the lack of clinical heterogeneity analysis among the analyzed studies may limit the conclusions that can be drawn from the meta-analysis,

⁴⁴ ASA Publ'ns, *Podcasts*, https://pubs.asahq.org/anesthesiology/multimedia/podcasts?mediaType=Podcasts&_ga=2.155153912.1336838194.1617918080-808123890.1613598007 (last visited Apr. 13, 2021).

he asserted that there is sufficient statistical heterogeneity to support the conclusions reached in the article, despite the fact that the studies were marked by substantial differences in numerous respects. *Id.* at 2-3. Once again, this perpetuated the false impression that the studies were based on rigorous science that satisfied scientific standards for meta-analysis, when that is not the case.

67. Dr. Rathmell also interviewed Defendant McCann as part of this podcast. Consistent with her editorial, McCann positively reviewed the Hussain Article and the Ilfeld Review, and failed to acknowledge their scientific and ethical flaws. *See* Ex. 5, Anesthesiology Podcast Tr. at 3-4. Overall, the journal's podcast does not present an open, honest discussion about the *Anesthesiology* EXPAREL articles or the effectiveness of EXPAREL products, and this communication with *Anesthesiology's* readers only perpetuates the articles' inaccuracies and further spreads the falsehoods contained therein.

The ASA and Kharasch Caused the Disparaging Material in the February 2021 Issue to be Published

68. The ASA and Kharasch were responsible for the publication of the challenged articles, CME activity, and podcast that made disparaging remarks about EXPAREL. On information and belief, the fact that the three challenged articles, with their obvious methodological flaws, were published together, is no accident. Further, to amplify the weight a reader would give their false conclusions, Kharasch and the editorial board appear to have solicited McCann's editorial, evidenced by

the fact that the editorial was accepted for publication on December 1, 2020—well before the Hussain and Ilfeld articles were even published. *See* Ex. 3, McCann Editorial at 139. The ASA and Kharasch appear to have made no effort to present a balanced view by including a second editorial favorable to EXPAREL. Indeed, ASA was provided the opportunity to do so and refused, rejecting for publication a letter to the editor critical of the Hussain analysis.

69. Kharasch and the ASA then published these three articles in the February 2021 issue, complete with a cover proclaiming the inaccurate conclusion that “Liposomal Bupivacaine is Not Superior to Standard Local Anesthetics,” *see* Ex. 7, *Anesthesiology* Feb. 2021 Cover, despite knowing this statement was false. Kharasch and the ASA further promoted this false conclusion in both the podcast published on *Anesthesiology*’s website, and the CME activity, which repeat many of the inaccuracies and misstatements of the three articles. When viewed together, this evidence, combined with Kharasch’s well known pro-opioid bias, can only indicate intent by the ASA, the Journal, and its editorial board (led by Kharasch) to disparage EXPAREL.

Pacira’s Business Is Harmed As a Result of the ASA’s Disparagement of EXPAREL

70. The disparaging remarks about EXPAREL contained in the February 2021 of *Anesthesiology* have caused Pacira significant pecuniary harm. In the wake of the issue’s release, Pacira has heard from multiple existing customers who have

seen the issue and read at least one of the disparaging articles noted above. Multiple customers have informed Pacira that they will either discontinue their use of Pacira's product EXPAREL, or are considering discontinuing use of it, based on the flawed and misleading conclusions propagated by the ASA in the challenged articles and materials. Other customers have reached out to Pacira with questions and concerns about the challenged articles, and requesting additional information about EXPAREL.

71. Moreover, Pacira's competitors are capitalizing on the false and misleading statements in the challenged articles in order to promote their own products. For example, recently, Pacira's competitor AVANOS published on its website a "clinical article" on the February 2021 *Anesthesiology* issue, summarizing the Hussain, Ilfeld, and McCann articles and the "shortcomings of liposomal bupivacaine."⁴⁵ AVANOS manufactures the "On-Q Pain Relief System," which it describes as an "opioid-sparing solution that has the data to back it up."⁴⁶ The On-Q system competes directly with EXPAREL in the market for non-opioid pain relief.

⁴⁵ David Schaffner, *Clinical Evidence Does Not Support the Use of Liposomal Bupivacaine, Leaving Patients Without Adequate Post-Surgical Pain Control*, <https://avanospainmanagement.com/wp-content/uploads/2021/03/AVANOS-WhitePaper-Exparel-FINAL.pdf> (last visited Apr. 13, 2021).

⁴⁶ Avanos, *On-Q Pain Management System: The Opioid-Sparing Solution That Has the Data to Back It Up*, <https://avanospainmanagement.com/posts/practice/EXPAREL-in-anesthesiology/> (last visited Apr. 13, 2021).

In addition to the clinical article, AVANOS has an entire webpage devoted to “EXPAREL in Anesthesiology” which highlights certain points from the challenged articles disparaging EXPAREL.⁴⁷

72. Finally, these articles are now being referenced in other medical journal articles, indicating that the misstatements in the articles are being disseminated to an ever-wider audience. *See* Kishan Patel & Mark Zakowski, *Enhanced Recovery After Cesarean: Current and Emerging Trends*, *Current Anesthesiology Reports* (Mar. 2021), at 4. This indicates that the articles will continue to cause harm to Pacira, unless the ASA is required to retract the false and misleading statements.

73. In short, as a result of the ASA’s anti-EXPAREL bias, the false and misleading statements written by the Defendant authors and published by the ASA in the three articles discussed above, as well as the podcast and CME content published by the ASA that has continued to propagate that misinformation, Pacira has lost, and will continue to lose, revenue from discontinued or lost sales of its product.

FIRST CAUSE OF ACTION – TRADE LIBEL

74. The allegations set forth in paragraphs 1 through 73 are incorporated by reference as if set forth here in full.

⁴⁷ *Id.*

75. The ASA has falsely claimed that “Liposomal Bupivacaine Is Not Superior to Standard Local Anesthetics.” *See* Ex. 7, *Anesthesiology* Feb. 2021 Cover. In support of this statement, it has published inaccurate and misleading materials about Pacira’s product EXPAREL, including the three articles discussed above written by the Defendant authors. These articles were published in the February 2021 issue of the ASA’s “official” journal, *Anesthesiology*. *See* Exs. 1-3. The Defendant authors caused these false and misleading statements about EXPAREL to be published by submitting the articles for publication to *Anesthesiology*.

76. The ASA also published accompanying CME and podcast materials on its website, which repeat many of the false and misleading statements contained in the articles. *See* Exs. 4-5.

77. Together, the challenged articles and accompanying materials create the false and misleading impression that EXPAREL is not an effective analgesic, and that this conclusion is supported by credible scientific evidence, when in fact these materials are seriously flawed, do not comply with rigorous scientific and ethical standards, and do not support the conclusions reached.

78. The false statements in the February 2021 issue of *Anesthesiology* were published to print and online subscribers of the journal and eventually will be available to the public for free. *See supra* ¶ 30 & n.20. The Hussain Article, which

is the flawed meta-analysis, is currently available to the public for free on the ASA's website and was one of the "Most Viewed" articles on the website when first published. The false and misleading statements contained in the podcast are also currently available to the public for free on the ASA's website.⁴⁸ And the misleading CME materials are likewise published on the ASA's website and available for anyone to purchase.⁴⁹

79. Defendants' false and misleading statements about EXPAREL could only have been made with malice. On information and belief, the Defendant authors knew or recklessly disregarded the fact that the analyses contained in the challenged articles were seriously flawed, and failed to conform to accepted scientific standards. On information and belief, the Defendant authors knew or recklessly disregarded the fact that their failure to conform to these scientific standards was likely to result in inaccurate conclusions that would create the false and misleading impression that EXPAREL is not an effective product.

80. Moreover, on information and belief, Defendants Ilfeld and Gabriel intentionally failed to disclose their financial relationships with Pacira's competitors. In doing so, they knew or recklessly disregarded the fact that failing to

⁴⁸ *See supra* note 44.

⁴⁹ ASA, *Education Center*, <https://education.asahq.org/totara/> (last visited Apr. 13, 2021).

make appropriate financial disclosures about their financial arrangement with Pacira's competitors would create the false and misleading impression that the conclusions reached in their article were based on objective evidence rather than their own financial interests.

81. On information and belief, the ASA and Defendant Kharasch intended to further their anti-EXPAREL bias in publishing these false, misleading, and disparaging statements about EXPAREL. The ASA's—and Defendant Kharasch's—review of the challenged articles prior to publication was deficient. On information and belief, the ASA and Defendant Kharasch knew or recklessly disregarded the fact that the conclusions reached in the challenged *Anesthesiology* articles, and further disseminated in the companion podcast and CME materials, were misleading about the efficacy of EXPAREL and based on flawed studies that do not satisfy the relevant scientific standards. Moreover, on information and belief, the ASA and Kharasch deliberately suppressed material favorable to EXPAREL in order to further their biased campaign.

82. As the official, peer-reviewed publication of the ASA, and the most cited medical journal on anesthesiology, *see supra* ¶¶ 29-30, statements made by the ASA in *Anesthesiology* carry significant weight in the medical and pharmaceutical industry. On information and belief, Defendants knew or recklessly disregarded the fact that their false or misleading statements about EXPAREL could significantly

affect the market for Pacira's product EXPAREL, and interfere with Pacira's ability to sell its product.

83. Defendants' false and misleading statements regarding EXPAREL have caused Pacira pecuniary loss. Based on the statements made in the February 2021 issue of *Anesthesiology*, several of Pacira's existing customers have discontinued, or are threatening to discontinue, their use of EXPAREL. Pacira has also lost potential customers who expressed interest in purchasing a supply of EXPAREL, but then backed out after seeing Defendants' disparaging statements about EXPAREL.

PRAYER FOR RELIEF AND DEMAND FOR JURY TRIAL

WHEREFORE, Pacira hereby demands trial by jury on all issues in the above matter, and respectfully requests:

(1) An order requiring the removal of the following materials from the ASA's website:

- a. *Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia: A Systematic Review and Meta-analysis*, authored by Defendants Nasir Hussain, Richard Brull, Brendan Sheehy, Michael K. Essandoh, David L. Stahl, Tristan E. Weaver, and Faraj W. Abdallah;
- b. *Clinical Effectiveness of EXPAREL Administered by Infiltration or Peripheral Nerve Block to Treat Postoperative Pain: A Narrative Review*, authored by Brian M. Ilfeld, James C. Eisenach, and Rodney A. Gabriel;
- c. *Liposomal Bupivacaine: Effective, Cost-effective, or (Just) Costly*, authored by Mary Ellen McCann;

- d. The February 2021 *Anesthesiology* podcast and accompanying podcast transcript; and
 - e. The February 2021 Continuing Medical Education (“CME”) quiz questions related to the February 2021 issue of *Anesthesiology*;
- (2) An order requiring Defendant ASA to retract items (a)-(e) above in the next issue of *Anesthesiology*;
- (3) An order barring defendants Evan D. Kharasch, Nasir Hussain, Richard Brull, Brendan Sheehy, Michael K. Essandoh, David L. Stahl, Tristan E. Weaver, Faraj W. Abdallah, Brian M. Ilfeld, James C. Eisenach, Rodney A. Gabriel, and Mary Ellen McCann from publishing or further disseminating items 1(a)-(e);
- (4) Compensatory damages for Pacira’s economic and financial losses resulting from the ASA’s false or misleading statements;
- (5) Punitive damages;
- (6) Attorneys’ fees, costs, and interest; and
- (7) Any other relief the Court deems just and proper.

Dated: April 14, 2021

Respectfully submitted,

LATHAM & WATKINS LLP

/s/Kevin M. McDonough

Kevin M. McDonough (#41892005)
LATHAM & WATKINS LLP
885 Third Avenue
New York, New York 10022
(212) 906-1200

Allen M. Gardner (*PHV* forthcoming)
Sarah M. Gragert (*PHV* forthcoming)
555 Eleventh Street, N.W., Suite 1000
Washington, D.C. 20004
(202) 637-2200

*Attorneys for Plaintiff Pacira
BioSciences, Inc.*