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UNITED STATES DISTRICT COURT FOR THE
CENTRAL DISTRICT OF CALIFORNIA

MICHAEL KRANTZ, INDIVIDUALLY, AND ON BEHALF OF THE ESTATE OF JANIS KRANTZ, DECEASED, LAUREN GREGORY, AND JOSHUA KRANTZ,

Plaintiffs,

vs.

REGENERON PHARMACEUTICALS, INC. and SANOFI AVENTIS US, LLC

Defendants.

Case No.: ____________________

COMPLAINT FOR DAMAGES AND

DEMAND FOR JURY TRIAL

1. Strict Products Liability/Failure to Warn
2. Negligence
3. Negligent Misrepresentation
4. Gross Negligence

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TABLE OF CONTENTS

I. PARTIES 1

II. JURISDICTION AND VENUE 1

III. FACTS 2

A. Overview 2

B. The Plaintiff 6

C. The Importance of SJS and TEN 7

D. Laws Governing the Approval and Labeling of Prescription Drugs 9

E. Summary of Regulatory History of Libtayo 12

F. Newly Acquired Safety Information 16

i. *Undisclosed Cases of Serious Skin Reactions from Scientific Literature and in Libtayo Clinical Trials* 16

ii. *Increased Risk of SJS and TEN to Subpopulations (Females)* 24

iii. *Foreign Libtayo Labeling Discloses More SJS/TEN Safety Data*.26

iv. *Increase in Severe Skin Reaction Adverse Events and Undisclosed Safety Signal Analysis* 29

G. Mrs. Krantz' Prescribing Physician Relied on Defendants' False and Misleading Safety Information 31

IV. CAUSES OF ACTION 35

STRICT PRODUCTS LIABILITY/FAILURE TO WARN 35

NEGLIGENCE 38

NEGLIGENT MISREPRESENTATION 41

GROSS NEGLIGENCE... 46

V. REQUEST FOR RELIEF 47

1
2
3
4
5
6
7
8
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10
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Plaintiffs Michael Krantz, individually and on behalf of the estate of Janis Krantz, Lauren Gregory, and Joshua Krantz (collectively, "Plaintiffs") file this Original Complaint against Defendants Regeneron Pharmaceuticals, Inc. ("Regeneron") and Sanofi-Aventis US, LLC ("Sanofi" and collectively with Regeneron, "Defendants").

I. PARTIES

1. Plaintiff Michael Krantz is the spouse and administer of the estate of the decedent, Janis Krantz, and is a resident of Long Beach, California.

2. Plaintiff Joshua Krantz is the adult son of decedent, Janis Krantz, and is a resident of Long Beach, California.

3. Plaintiff Lauren Gregory is the adult daughter of decedent, Janis Krantz, and is a resident of San Marcos, California.

4. Defendant Regeneron Pharmaceuticals, Inc. is a New York corporation with its principal place of business at 777 Old Saw Mill River Road, Tarrytown, NY 10591.

5. Defendant Sanofi-Aventis U.S. LLC is a New Jersey corporation with its principal place of business at 55 Corporate Drive, Bridgewater, NJ 08807.

II. JURISDICTION AND VENUE

6. This Court has subject matter jurisdiction over this lawsuit pursuant to 28 U.S.C. §1332 because there is diversity of citizenship between the parties and

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the amount in controversy exceeds $75,000. The Court has jurisdiction over Defendants because they engaged in business in this Judicial District and the State of California in connection with the transactions and occurrences giving rise to this action, and because the wrongful conduct challenged herein was directed at, took place in, and/or had foreseeable injurious effects in this Judicial District and the State of California. The Court also has jurisdiction over Defendants because they have continuously and systematically engaged in business in this Judicial District and the State of California such that they have subjected themselves to personal jurisdiction in this Court for all purposes.

7. Venue is proper pursuant to 28 U.S.C. §1391(b)(2) and (c)(1) because Plaintiffs' claims arose from events taking place within this Judicial District, and Plaintiffs reside in and Mrs. Krantz was injured in this Judicial District.

III. FACTS

A. Overview

8. Janis Krantz was a 73-year-old woman when she suffered a fatal Stevens-Johnson syndrome ("SJS") and toxic epidermal necrolysis ("TEN") adverse drug reaction to Libtayo. SJS and TEN are life-threatening and permanently disabling skin reactions with mortality rates ranging from 30% to as high as 80%.

9. This case involves warnings that Defendants have never included in the U.S. Libtayo product label, as well as existing warning language in the U.S.

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Libtayo label that is severely understated. Specifically, there is no warning in Defendants' U.S. label advising prescribing physicians i) that Libtayo causes SJS and TEN and that cases of SJS and TEN occurred in patients taking the drug; ii) that there is an increased risk of SJS/TEN from Libtayo beyond what is disclosed in the U.S. label; iii) about frequency or incidence data that would allow U.S. prescribing physicians to place the increased risk of SJS/TEN in context when assessing the risk-benefit profile of Libtayo against safer and more efficacious drugs; iv) that cases of SJS/TEN (including fatal cases) occurred in Libtayo clinical trials; v) that certain subpopulations including those occupied by Mrs. Krantz (females) are at an increased risk of SJS and TEN; or vi) that patients receiving Libtayo should be subject to strict medical monitoring for the early signs of SJS/TEN and warned to seek specialized medical treatment at the first sign of these reactions. These categories of missing warnings are collectively referred to in this Complaint as the "Krantz Warnings."

10. Instead, the 2021 version of Defendants' U.S. Libtayo label (in place at the time of Mrs. Krantz' prescription and death) vaguely stated that cases of SJS and TEN had occurred with PD-1/PDL-1 blocking antibodies[1] (as a class effect) without disclosing the known fact that Libtayo itself had caused cases of SJS and

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[1] PD-1 inhibitors and PD-L1 inhibitors are a group of immune checkpoint inhibitor anticancer drugs. Libtayo is one of many different types of PD-1/PD-L1 inhibitors.

TEN. Incredibly, Defendants revised their 2018 U.S. Libtayo launch label to remove the warning language in the 2018 label acknowledging that cases of SJS and TEN have occurred in connection with Libtayo. Defendants also weakened their U.S. Libtayo SJS and TEN warnings even though i) additional cases of SJS and TEN were reported to Defendants in their own clinical studies and scientific literature between 2018-2022, and ii) Defendants strengthened their SJS and TEN warnings on the Libtayo label in foreign countries during this four-year period between the U.S. launch of Libtayo and Mrs. Krantz' death.

11. Notably, Mrs. Krantz' sophisticated prescribing physician agrees that the SJS/TEN warnings on the U.S. Libtayo are deficient. Dr. Nilesh Vora – a highly credentialed oncologist and Medical Director of the Todd Cancer Institute in Long Beach, California – has executed a sworn declaration in which he testifies that i) Defendants failed to adequately warn him of the increased risks of SJS and TEN from Libtayo, and ii) he would not have prescribed Libtayo to Mrs. Krantz if Defendants had informed him of those risks.

12. In stark contrast to their conduct in the United States, Defendants do warn prescribing physicians and patients in foreign countries of the risk of SJS and TEN from Libtayo and disclose to prescribers overseas that fatal cases of TEN (*e.g.*, the adverse reaction that killed Mrs. Krantz) have occurred in connection with Libtayo in Defendants' clinical trials. In foreign countries, Defendants also

recommend that doctors closely monitor their patients for serious skin reactions after starting the drug and instruct doctors to immediately send potential Libtayo SJS/TEN victims for emergency medical treatment with physicians experienced in handling these life-threatening reactions.

13. "There is an inherent tension between the desire for profit and scientific decisions that suggest warnings may well shrink the customer base because of the cautionary tone struck by the warnings."[2] That profit motive drove Defendants' wrongful conduct that caused Mrs. Krantz' death.

14. Libtayo is one of the most heavily marketed and profitable drugs in Defendants' history. Defendants' net sales of Libtayo amounted to nearly $448 million in 2022 alone – the vast majority of which (approximately $375 million) took place in the United States. Defendants' blockbuster sales and profits also resulted in an increased number of adverse reactions to their drug, including additional cases of SJS/TEN.

15. Defendants know about the risk of Libtayo-caused SJS and TEN, and they know how to warn about those risks. They have vast financial resources and internal processes in place to warn U.S. patients and physicians about the increased risk of SJS and TEN Libtayo presents to its users. Defendants chose to inadequately

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[2] *Hodges v. Pfizer, Inc.,* 14-cv-4855, 2015 WL 13804602, at *10 (D. Minn. Dec. 17, 2015) (SJS/TEN case handled by Plaintiff's counsel).

warn U.S. prescribing physicians of the risk of SJS and TEN from their drug and Mrs. Krantz died as a result.

B. The Plaintiff

16. On April 18, 2022, Mrs. Krantz presented to Long Beach Memorial Care hospital with complaints of malaise, diffuse rash, and swelling of the left face after receiving a new immunotherapy, cemiplimab, on April 11. She was evaluated by the on-call oncologist who diagnosed her with a mucocutaneous toxicity to an immune checkpoint inhibitor, cemiplimab, presenting with a diffuse, coalescing maculopapular rash after receiving her first Libtayo infusion. The treatment plan was to discontinue Libtayo and continue steroids. She was discharged home on April 20 and instructed to take Prednisone and follow up with her physicians.

17. On April 23, an ambulance was called to Mrs. Krantz' residence after her rash progressed despite taking steroids as instructed, and she was transported to Long Beach Memorial. Her physicians noted she had blisters and sloughing of skin. Her skin had peeled off her entire back, abdomen, and extremities. She complained that she was experiencing excruciating pain. The doctors diagnosed her with diffuse body rash, suspected SJS and TEN secondary from cemiplimab, secondary sepsis, and respiratory failure.

18. On April 24, Mrs. Krantz was transferred to UCI Burn hospital where she was diagnosed with SJS and TEN caused by Libtayo. The initial dermatology

consultation noted that she developed a diffuse desquamative eruption involving multiple mucosal surfaces, consistent with SJS/TEN with a total body surface area (TBSA) involvement of approximately 90% and a SCORETEN of 4. All of the physicians at UCI concluded that Mrs. Krantz' SJS/TEN reaction was caused by Libtayo.

19. Mrs. Krantz was evaluated by the Burn Team, Ophthalmology, ENT, Pulmonary and OB-GYN consults during the burn unit stay at UCI. They also performed a skin biopsy that was consistent with SJS/TEN. Infectious diseases were ruled out as the primary cause of her SJS/TEN.

20. The treating doctors strongly recommended that the family agree to a do-not-resuscitate order and, following an incredibly difficult family decision, Mrs. Krantz was transitioned to a palliative care patient. Mrs. Krantz died on April 30 after suffering the excruciating effects of her SJS/TEN reaction for three weeks. The death certificate notes that her primary cause of death was SJS/TEN caused by CPI therapy (Libtayo).

C. The Importance of SJS and TEN

21. Due to the magnitude of injury and high mortality rates, SJS and TEN are two of the most serious and scrutinized adverse drug reactions. Stern, R.S., *et al.* 21 AM. J. ACAD. DERMATOL. 317-322 (1989) (commenting that because of high mortality/morbidity SJS/TEN is the most important drug-related cutaneous eruption

with respect to assessing risk vs. benefits of drugs); Mockenhaupt *et al.*, 128 J. INVEST. DERMATOL. 35-44 (2007) ("…SJS and TEN have a significant impact on public health because of high mortality, frequently lasting disability"); Roujeau *et al.*, 333 N.E.J.M. 1600-1607 (1995) ("Although infrequent, these conditions [SJS and TEN] may kill or severely disable previously healthy people. A few cases have prompted the withdrawal of newly released drugs.").

22. SJS/TEN's impact on public health is unquestionably important. It has been reported that the costs associated with the treatment of SJS/TEN patients in the United States alone exceeds $125 million per year – five times higher than the cost associated with any other hospital admission. Hsu, *et al.*, "Morbidity and Mortality of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in United States Adults," J. INVESTIGATIVE DERM. (2016).

23. It is therefore not surprising that the FDA requires drug companies such as Defendants to pay special attention to these potentially fatal serious adverse drug reactions (a clinically significant risk under FDA regulations) in order to reduce the number of cases of SJS/TEN occurring in consumers such as Mrs. Krantz.[3]

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[3] FDA Guidance for Industry: Safety Reporting Requirements for INDs and BA/BE Studies (Dec. 2012), https://www.fda.gov/downloads/Drugs/Guidances/UCM227351.pdf ("Certain serious adverse events are informative as single cases because they are uncommon and are known to be strongly associated with drug

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D. Laws Governing the Approval and Labeling of Prescription Drugs

24. The facts and allegations set forth in the complaint must be viewed through the regulatory framework and heightened duties of care imposed on drug makers. The Federal Food, Drug, and Cosmetic Act ("FDCA" or the "Act") requires manufacturers that develop a new drug product to file a New Drug Application ("NDA") in order to obtain approval from the Food and Drug Administration ("FDA") before selling the drug in interstate commerce. 21 U.S.C. §355.

25. An NDA is the formal step a drug sponsor takes to request that the FDA consider approving a new drug for marketing in the United States. 21 C.F.R. §314.50. An NDA should include all animal and human data and analyses of the data, as well as information about how the drug behaves (pharmacokinetics and pharmacodynamics) in the body and how it is manufactured. 21 C.F.R. §314.50. A key component of the new drug approval process is the evaluation of the information regarding the safety and efficacy of the proposed drug. *Id.* Thus, the NDA must contain a section reporting on foreign or domestic clinical data regarding the proposed new drug. 21 C.F.R. §314.50(d)(5).

26. The application must also contain a description and analysis of all clinical studies (controlled or uncontrolled) relied upon in evaluating the safety and

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exposure. Some examples, including…Stevens-Johnson syndrome.").

efficacy of the drug. 21 C.F.R. §314.50(d)(5)(ii). The NDA should also include "a description of any other data or information relevant to an evaluation of the safety and effectiveness of the drug obtained or otherwise received by the applicant from any source, foreign or domestic, including commercial marketing experience, reports in the scientific literature, and unpublished scientific papers." 21 C.F.R. §314.50(d)(5)(iv).

27. These FDA regulations in the premarketing phase require the drug sponsor to submit all safety information either to the IND or NDA – foreign or domestic – regardless of the source.[4] Changes in foreign labeling should also be disclosed in the IND or NDA filings. *Id.*

28. Manufacturers with an approved NDA must review all adverse drug experience information obtained by or otherwise received by them from any source, including but not limited to post-marketing experience, reports in the scientific literature, and unpublished scientific papers. 21 C.F.R. §314.80(b).

29. Under what is known as the Changes Being Effected ("CBE") regulation, a manufacturer with an approved NDA can make certain changes to its

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[4] Good Review Practice: Clinical Review of Investigational New Drug Applications, FDA, CDER, December 2013, p. 15, also citing FDA regulations, 21 C.F.R. §312.32; and FDA Reviewer Guidance, "Conducting a Clinical Safety Review of a New Product Application and Preparing a Report on the Review," FDA CDER, February 2005.

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label without prior FDA approval by simply sending the FDA a "supplemental submission." 21 C.F.R. §314.70(c)(6)(iii).

30. Changes to the labeling a manufacturer can make pursuant to CBE without prior FDA approval include those to "add or strengthen a contraindication, warning, precaution, or adverse reactions for which the evidence of causal association satisfies the standard for inclusion in the labeling under § 201.57(c) of this chapter" and "to add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product." 21 C.F.R. §314.70(c)(6)(iii)(A) and (C).

31. A manufacturer must revise its label "to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug; a causal relationship need not have been definitively established." 21 C.F.R. §201.57(c)(6). Adverse reactions must be added to the label where there "is some basis to believe there is a causal relationship between the drug and the occurrence of the adverse event." *Id*. at §201.57(c)(7).

32. An August 22, 2008 amendment to these regulations provides that a CBE supplement to amend the labeling for an approved product must reflect "newly acquired information." 73 Fed. Reg. 49609. "Newly acquired information" is not limited to new data but also includes "new analysis of previously submitted data." "[I]f a sponsor submits adverse event information to FDA, and then later conducts

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a new analysis of data showing risks of a different type or of greater severity or frequency than did reports previously submitted to FDA, the sponsor meets the requirement for 'newly acquired information.'" *Id*. at 49607.

33. The critical purpose of post marketing safety requirements is to ensure that the benefit of the drug outweighs the risk at all times during the life cycle of the product. 21 C.F.R. §§314.50, 314.80, and 314.81. If new safety information, including information from clinical trials, foreign countries or other information not previously disclosed to and considered by the FDA, comes to light that calls that balance into question, the FDA requires sponsors (like Defendants) to initiate risk management strategies to address the safety risk, including updating the professional label.[5]

E. Summary of the Regulatory History of Libtayo

34. Libtayo (cemiplimab) is a recombinant human IgG4 monoclonal antibody that targets the programmed death-1 receptor (PD-1) and is part of the pharmacologic class of programmed death receptor-1 (PD-1) blocking antibodies.

35. On December 22, 2014, Defendants submitted their Investigational Drug Application (IND) #123950 to the FDA for their new biological drug

[5] The requirement to actively assess safety data and to update the product label is also set forth in 21 C.F.R. §201.56 and 21 C.F.R. §1.21, which require the prescription labeling to be neither false nor misleading in any particular.

identified as cemiplimab or REGN2810. The IND for cemiplimab included the clinical protocol for Study R2810-ONC-1423 entitled, "A First-in-Human (FIH) Study of Repeat Dosing with REGN2810, a Monoclonal, Fully Human Antibody to Programmed Death -1 (PD-1), as Single Therapy and in Combination with Other Anti-Cancer Therapies in Patients with Advanced Malignancies."

36. After this initial protocol was submitted to study cemiplimab for the treatment of cutaneous squamous cell carcinoma ("CSCC"), Regeneron and Sanofi submitted Amendments to the cemiplimab IND to seek approval use cemiplimab in Study #1423 to treat various kinds of advanced cancers, including NSCLC, head and neck cancer, breast cancer, advanced solid tumors in patients previously treated with another anti-PD-1/PDL1 antibody, and other advanced solid tumors.

37. On September 10, 2015, a pre-IND meeting was held with FDA officials from the Division of Oncology (DOP2) to discuss the development program for REGN2810 in treating CSCC based on preliminary efficacy data from the CSCC expansion cohorts of Study 1423.

38. On December 7, 2015, IND 127100 was submitted and contained the protocol for Study R2810-ONC-1540 (Study# 1540), entitled "A Phase 2 Study of REGN2810, a Fully Human Monoclonal Antibody to Programmed Death – 1 (PD-1), in Patients with Advanced Cutaneous Squamous Cell Carcinoma."

39. On January 11, 2016, Defendants started their Phase 1 study to evaluate the effectiveness of cemiplimab REGN2810 to treat lymphoma.

40. On November 30, 2017, Defendants submitted a Biologics License Application (BLA) for cemiplimab (Libtayo, REGN2810), a new molecular entity, pursuant to the regulations under 21 CFR 601. The proposed initial indication for cemiplimab that was submitted to the FDA in 2017 was the following indication:

> For the treatment of patients with metastatic cutaneous squamous cell carcinoma (CSCC) or patients with locally advanced CSCC, who are not candidates for curative surgery or radiation.

41. Only one set of clinical study data from the two trials was submitted by Defendants to support the safety and effectiveness of cemiplimab for that same proposed indication, Study #1540.

42. Serious adverse reactions caused by cemiplimab were experienced by at least 28% of clinical trial patients. Serious adverse reactions that occurred in at least 2% of patients included serious skin reactions called bullous skin reactions. One of the most common toxicities associated with cemiplimab was maculopapular rashes, which were categorized by Defendants as "immune-related adverse events" or "imARs."

43. Immune-mediated dermatologic reactions, including erythema multiforme and pemphigoid, occurred in at least 1.7% (9/534) patients receiving cemiplimab, including six Grade 3 (1.1%) events. Temporary interruption of

cemiplimab was required in five patients (0.9%) for adverse skin reactions. Systemic corticosteroids were required in all patients with dermatologic reactions, including 89% who received high dose corticosteroids. Dermatologic reactions resolved in 33% of patients.

44. During Study #1504, two patients experienced a fatal skin adverse reaction after receiving a single dose of cemiplimab, and a third patient developed life-threatening myositis and myasthenia gravis following two doses of cemiplimab.

45. These fatal cases of SCAR events, including EM, SJS and TEN were not disclosed in the Libtayo launch labeling in 2018. Even today, the U.S. Libtayo label has not disclosed these clinical trial cases of Libtayo-caused SJS and TEN to U.S. prescribers.

46. On September 28, 2018, the U.S. FDA approved Defendants' Libtayo NDA for the treatment of cutaneous squamous cell carcinoma.

47. Regeneron and Sanofi entered into an Immuno-oncology License and Collaboration Agreement in 2015. Pursuant to this agreement, the companies split Libtayo's worldwide operating profits equally and co-commercialized Libtayo in the U.S., with Sanofi solely responsible for commercialization outside the U.S.

48. In 2022, Regeneron announced that it had completed the acquisition of Sanofi's stake in Libtayo, providing Regeneron with exclusive worldwide

development, commercialization, and manufacturing rights to the drug. Today, Regeneron owns and captures 100% of global net sales for Libtayo.

F. Newly Acquired Safety Information

49. Both before and after Libtayo's FDA approval in 2018, new safety information emerged that should have prompted Defendants to immediately and unilaterally change the Libtayo label without FDA approval pursuant to the CBE-0 process in 21 C.F.R. §314.70 to warn for the increased risks of SJS/TEN. Defendants failed to disclose this important safety information to the FDA and have never attempted to add the Krantz Warnings to the Libtayo label through the CBE-0 process or otherwise.

i. Undisclosed Cases of Serious Skin Reactions from Scientific Literature and Libtayo Clinical Trials

50. Defendants know that it is critically important to disclose all serious adverse events occurring in their clinical trials. The FDA also requires Defendants to regularly review and update the Libtayo label to identify new safety information arising from clinical trials:

> Applicants are urged to review at least annually the content of the adverse reactions section [of the label] to ensure that the information remains current. We expect the labeling to be consistent with newly acquired information from controlled clinical trials or spontaneous reports and with the evolution of labeling in the pertinent drug class. . . The applicant must update the labeling when new information becomes

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> available that causes the labeling to become inaccurate, false, or misleading.[6]

51. Even a single case of a SJS or TEN occurring in a clinical trial is a significant safety event that requires safety surveillance by the drug manufacturer. Defendants are well-aware of the FDA's concern regarding just 1-2 cases of SJS/TEN occurring in clinical trials:

> IND sponsors [*i.e.*, Defendants] must still promptly report to the FDA and investigators serious, unexpected suspected adverse reactions occurring during clinical trials. Unlike a myocardial infarction in an elderly subject, a *single occurrence* of Stevens–Johnson syndrome (SJS) would reach this threshold. Not only is SJS unexpected and serious, it is known to be strongly associated with drug exposure. A report of SJS would clearly be informative about the safety of the investigational drug and could have important effects on patient monitoring and care.[7]

52. Defendants also know that cases of SJS and TEN occurred in the Libtayo trials. Published literature details numerous cases of serious skin reactions and deaths that have never been disclosed in the U.S. Libtayo labeling. Defendants funded, designed, and monitored these studies and were fully aware prior to Mrs. Krantz' Libtayo prescription and resulting death of the significant increased incidence of serious skin reactions, including cases of SJS/TEN that led to

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[6] FDA Guidance for Industry (CDER): Adverse Reactions Section of the Labeling for Human Prescription Drug and Biological Products (January 2006).
[7] Sherman and Woodcock *et al.*, U.S. FDA, "New FDA Regulation to Improve Safety Reporting in Clinical Trials," N Engl J Med., 365:1 nejm.org, July 7, 2011.

withdrawal of Libtayo patients from clinical studies along with SCAR-related hospitalizations and deaths.

53. Defendants initially and unsuccessfully tested Libtayo as a potential treatment for lymphoma. In 2017, Topp, *et al.* published an abstract of their international (including U.S. sites) clinical study of Libtayo therapy in 60 patients with lymphoma. In that trial, Defendants had an unexpected and serious case of TEN that resulted in a drug-attributed fatality and an exceedingly high incidence of TEN of 1 per 60 patients. The early fatal case of TEN was a serious safety signal, one that occurred well before Defendants initiated their Phase II and Phase III skin cancer studies. In contrast to their overseas labels and disclosures to foreign prescribers, Defendants' U.S. Libtayo label has never disclosed this clinical trial fatal case of TEN or any other SJS or TEN fatality to U.S. prescribing physicians. Among other labeling deficiencies, Mrs. Krantz' prescribing physician has sworn under oath that had he known about the occurrences of SJS/TEN in Libtayo clinical trials or the fatal cases of TEN, he would not have prescribed Libtayo to Mrs. Krantz.

54. The following table identifies serious skin reactions, including SJS and TEN, that occurred in Defendants' clinical studies since 2017:

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Author/Trial	**Skin Reaction / Grade**	**Incidence**
Topp, *et al.* 12/2017 NCT02651662[8]	(1) TEN in Arm 1 Grade: 5 (fatal)	1 per 60 (1.7%)
Migden, *et al.* 7/2018 NCT02383212[9]	Phase 1: (1) Maculopapular Rash[10] Grade: =/>3 Phase 2: (1) Dermatitis Bullous[11] Rash: 9 Maculopapular rash: 6 (Total=15) (5) Other types of rashes[12] and blisters were reported	Phase 1: 1 per 26 or 3.8% Phase 2: 1 per 59 or 1.7% (15%) (10%)
Migden, *et al.* 2020 NCT02760498	(1) Atopic Dermatitis Grade: =/>3	1 per 78 (1.28%)

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[8] Topp, MS, *et al.* Safety and Preliminary Antitumor Activity of the Anti-PD-1 Monoclonal Antibody REGN2810 Alone or in Combination with REGN1979, an Anti-CD20 x Anti-CD3 Bispecific Antibody, in Patients with B-Lymphoid Malignancies. *Blood*, 2017;130 (Suppl. 1):1495; https://clinicaltrials.gov/ct2/show/NCT02651662.

[9] Migden, MR, *et al.* PD-1 Blockade with Cemiplimab in Advanced Cutaneous Squamous-Cell Carcinoma. *NEJM* July 2018, 379;4:341-35; https://clinicaltrials.gov/ct2/show/NCT02383212

[10] Migden, *et al.* 2018, Appendix, Table S3, S4.

[11] Migden, *et al.* 2018, reported in Supplementary Appendix at Table S7.

[12] Migden, *et al.*2018; 1-generalized rash, 1 drug eruption, 1 dermatitis, 1 mouth ulceration, 1 stomatitis at Table S7.

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		Total incidence of rash was between 20-23%[13]
Papadopolous *et al.* 3/2020 NCT02383212	(1) Pruritic Rash Grade: =/>3	1 per 60 (1.7%)[14]
Rischkin, *et al.* 6/2020 NCT02760498[15]	Maculopapular Rash Grade: =/>3	1 per 56 (1.79%) Group 3 Total Rash in Group 3 was 28.6%
Kitano, *et al.* 11/2020 NCT03233139[16]	(1) Bullous dermatitis Grade: UNK	1 per 13 (7.7%)
Sezer, *et al.* 2/2021 NCT03088540[17]	(3) Rash Grade: 3 (1) Maculopapular Rash	3 per 355 (1%) 1 per 355 (0.3%)

[13] Migden, MR, *et al.* Cemiplimab in locally advanced cutaneous squamous cell carcinoma: results from an open-label, phase 2, single-arm trial. *Lancet Oncol* Feb. 2020;21(2):294-305; Migden, *et al.* 2020, Table 3.
[14] Papadopoulos, KP, *et al.* First-In-Human Study of Cemiplimab Alone or In Combination with Radiotherapy and/or Low-dose Cyclophosphamide in Patients with Advanced Malignancies. *Clin Cancer Res* March 2020; *Clin Cancer Res* 2020; 26:1025–33; Out of 32 patients with irAEs.
[15] Rischin, D, *et al.* Phase 2 study of cemiplimab in patients with metastatic cutaneous squamous cell carcinoma: Primary analysis of fixed-dosing, long-term outcome of weight-based dosing. *Journal for Immunotherapy of Cancer* June 2020*,* 8, 1-8. e000775
[16] Kiton, S, *et al.* Dose exploration results from Phase 1 study of cemiplimab, a human monoclonal programmed death (PD)-1 antibody, in Japanese patients with advanced malignancies. *Cancer Chemotherapy and Pharmacology* (2021) 87:53–64. Published online Nov. 4 2020; https://clinicaltrials.gov/ct2/show/NCT03233139.
[17] Sezer, A, *et al.* Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial. *Lancet* Feb. 2021; 397: 592–604; https://clinicaltrials.gov/ct2/show/NCT03088540.

	Grade: 3 Total Serious Rashes	4 per 355 (1.13%) Total Rashes: 6.2%
Valentin, *et al.* 3/2021[18] GP-2020-27 CE	Severe Skin Reaction Grade: =>3	1 per 30 (3.3%) All SAEs occurred in elderly patients.
Stratigos, *et al.* 5/2021 NCT03132636[19] Group 2 only	Rash[20] Grade: =>3	1 per 84 (1%)
Hober, *et al.* 7/2021 NCT05302297[21]	(1) TEN[22] Grade: 5 (1) DRESS[23] Grade: 4	1 per 245(0.4%) 1 per 245 (0.4%)
Rischkin, *et al.* 8/2021[24]	(1) Rash	5 per 193 (2.6%) - pooled

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[18] Valentin, J, *et al.* Real world safety outcomes using cemiplimab for cutaneous squamous cell carcinoma.
Journal of Geriatric Oncology 2021, 12: 1110–1113.
[19] Stratigos, AJ, *et al.* Cemiplimab in locally advanced basal cell carcinoma after hedgehog inhibitor therapy: an open-label, multi-centre, single-arm, phase 2 trial. *Lancet Oncol* 2021 May-Jun;22(6):848-857; https://clinicaltrials.gov/ct2/show/NCT03132636.
[20] Stratigos, *et al.*, rash cited in Table 3.
[21] Hober, C, *et al.* Cemiplimab for Locally Advanced and Metastatic Cutaneous Squamous-Cell Carcinomas: Real-Life Experience from the French CAREPI Study Group. *Cancers* July 2021, 13, 3547:1-14; https://clinicaltrials.gov/ct2/show/NCT05302297.
[22] Hober, et al, Investigator attributed TEN reaction to cemiplimab and cause of death in elderly patient. Authors discussed risk of SJS and TEN with PD-1 inhibitors; stated warnings should be provided to prescribing physicians.
[23] Hober, *et al.*, Investigator attributed the DRESS reaction to cemiplimab.
[24] Rischkin, *et al.* Integrated analysis of a phase 2 study of cemiplimab in advanced cutaneous squamous cell carcinoma: extended follow-up of outcomes

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NCT02760498	Grade: =>3 (2) Maculo papular rash Grade: =>3 (1) Atopic Dermatitis[25] Grade: =>3 (1) Autoimmune Dermatitis Grade: =>3	
Baggi, *et al.* 9/15/2021[26] REAL CEMI Study #: N4181	(1) Rash[27] Grade: 3-4	1 per 131 (0.8%)
Strippoli, *et al.* 11/2021[28] National Cancer Institute of Bari, Italy	(1) Bullous erythema Grade: 3	1 per 30 (3.3%) Most common AE in elderly was skin toxicity was 33.3%
Rios-Vinuela, *et al.*, 2022[29]	(1) Bullous pemphigoid	Total Rashes

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and quality of life analysis. *Journal for ImmunoTherapy of Cancer* Aug. 2021;1-9:e002757.

[25] Rischkin, *et al.*, this case of atopic dermatitis was previously reported in *Migden*, *et al.* 2020.

[26] Baggi, A, *et al.* Real world data of cemiplimab in locally advanced and metastatic cutaneous squamous cell carcinoma. *European Journal of Cancer*, Sept. 2021;157:250-258.

[27] Baggi, *et al.* - Serious Rash occurred in elderly patient. Nine other rashes (Grades 1-2) were reported in the analysis.

[28] Strippoli, S, *et al.* Cemiplimab in an Elderly Frail Population of Patients with Locally Advanced or Metastatic Cutaneous Squamous Cell Carcinoma: A Single-Center Real-Life Experience From Italy. *Front. Oncol.* Nov. 2021; 11:1-12. 686308.

[29] Rios-Vinuela, E, *et al.* Cemiplimab in Advanced Cutaneous Squamous Cell Carcinoma: Real-World Experience in a Monographic Oncology Center. *ACTAS Dermo-Sifiliograficas* 2022, 113:610-615.

Fundacion Instituto Valenciano de Oncologia	(1) Rash	2 per 13 (15.3%)
Gross, *et al.* 2022[30]	(1) Bullous dermatitis Grade: =>3	1 per 79 (1.3%) Rash was one of the most common AEs at 14%

55. The incidence of serious cutaneous reactions (including SJS and TEN) in several of Defendants' clinical studies (Topp, *et al.*, Migden, *et al.*, Hober *et al.*, Rischin, *et al.*, Strippoli, *et al.*, Stratigos, *et al.*, among others) was exceedingly high and included unexpected fatalities associated with Libtayo-induced SJS and TEN. This safety information has never been included in Defendants' U.S. Libtayo label (pre- or post-approval) or otherwise disclosed to U.S. prescribing physicians in other safety communications.

56. In 2021, Chen, *et al.*[31] conducted a post-marketing disproportionality analysis of adverse events reported to the U.S. FDA FAERs pharmacovigilance database associated with immune checkpoint inhibitors ("ICIs"). Using a dataset of

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[30] Gross, ND, *et al.* Neoadjuvant Cemiplimab For Stage II to IV Cutaneous Squamous-Cell Carcinoma. *NEJM* 2022; 387:1557-1568.
[31] Chen, C, *et al.* Immune-related adverse events associated with immune checkpoint inhibitors: An updated comprehensive disproportionality analysis of the FDA adverse event reporting system. *International Immunopharmacology* June 2021; 95, 107498: 1-10.

January 2004 – December 2019, the aim of the study was to comprehensively evaluate and characterize ICI-associated immune-related adverse events ("irAEs") to further prevention and management of the safety profiles for each ICI.

57. A total of 32,441 reports of ICI-associated irAEs were gathered for all ICIs. Among the Anti PD-1 ICIs, Libtayo had the highest ROR for all irAEs with a ROR of 2.42 (95% CI, 1.94-3.01). Among the various toxicities assessed between the ICIs, this study showed that cemiplimab had the highest fatality proportion of renal and skin toxicities of the class of study drugs. In fact, Libtayo had a two times higher proportion of fatal skin events than compared to either pembrolizumab or nivolumab. Supp. Table 6. Libtayo had 16% proportionality for fatal skin reactions, which was twice as high as the other drugs in the PD-1 class for fatal irAEs.

58. This high incidence and the clinical trial cases of SJS/TEN identified above were not fully and adequately disclosed to the FDA, to U.S. prescribing physicians, or to Mrs. Krantz' prescribing physician through the Libtayo label labeling either pre- or post- NDA approval of the drug.

ii. *Increased Risk of SJS and TEN to Subpopulations (Females)*

59. Since 1998, the FDA has required drug companies such as Defendants to follow the "Demographic Rule,"[32] which requires drug companies to assess and

[32] 21 C.F.R. § 314.50(d)(5).

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warn for subpopulation risks by age, gender, and racial subgroups.[33] Under the Demographic Rule, Defendants are required to assess subpopulation risk information from published and unpublished studies, the global scientific literature, data from the FDA's adverse event database, their Libtayo safety database and provide subpopulation risk information in the warnings, precautions, and adverse reactions sections of the Libtayo labeling. 21 C.F.R. § 314.50.

60. The FDA has informed drug manufacturers that research has shown that biological differences between men and women (differences due to sex chromosome or sex hormones) may contribute to variations seen in the safety and efficacy of drugs, biologics, and medical devices. The FDA's regulations and guidance acknowledge that understanding mechanisms of sex differences in medical product development is crucial for regulatory decisions and optimal treatment outcomes.[34]

61. Although numerous studies have reported that females are at a higher risk of SJS/TEN than males,[35] Defendants' Libtayo label does not warn for the

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[33] FDA Guidance for Industry: Adverse Reactions Section of the Labeling For Human Prescription and Biological Products-Content and Format, March of 2006.
[34] https://www.fda.gov/science-research/womens-health-research/understanding-sex-differences-fda.
[35] Bigby, M, "Drug-Induced Cutaneous Reactions: A report from the Boston Collaborative Drug Surveillance Program on 15,438 consecutive inpatients, from 1972-1982," *JAMA*, 1986; 256:3358-3363; Rademaker, M., "Do Women Have More Adverse Drug Reactions?" *Am J Clin. Dermatol*. 2001: 2(6): pp.349-351;

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increased risk of SJS and TEN to the female subpopulation occupied by Mrs. Krantz.

iii. *Foreign Libtayo Labeling Discloses More SJS/TEN Safety Data*

62. The Libtayo prescription labels in Canada, Australia, and European Union countries (among others), contain stronger warnings for serious skin reactions, including SJS/TEN. As one example, the Libtayo label in Canada discloses more SJS/TEN safety data to prescribing physicians than the U.S. label:

U.S. Libtayo Label
LIBTAYO can cause immune-mediated rash or dermatitis. The definition of immune-mediated dermatologic adverse reaction included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. Exfoliative dermatitis, including Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and DRESS (Drug Rash with Eosinophilia and Systemic Symptoms), has occurred with PD-1/PD-L1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold or permanently discontinue LIBTAYO depending on severity. Immune-mediated dermatologic adverse reactions occurred in 1.6% (13/810) of patients receiving LIBTAYO, including Grade 3 (0.9%) and Grade 2 (0.6%)

Pouyanne, P, et. al., "Admissions to Hospital caused by adverse drug reactions: cross sectional incidence study, BMJ, Vol. 320, pg. 1036, 2000; Fattinger, K, et. al., *Br J Clin. Pharrnacol*., Epidemiology of drug exposure and adverse drug reactions in two Swiss departments of internal medicine, Vol. 49, pp. 158-67, 2000; Martin, RM, *Br J Clin. Pharrnacol.*, Age and Sex distribution of suspected adverse drug reactions to newly marketed drugs in general practice in England: analysis of 48 cohort studies, Vol. 46, pp. 505-511,1998; Naldi, L, *et al.*, "Cutaneous reactions to drugs. An analysis of spontaneous reports in four Italian regions," *BCJP*, 48, 839–846, 1999.

adverse reactions. Dermatologic adverse reactions led to permanent discontinuation of LIBTAYO in 0.1% of patients and withholding of LIBTAYO in 1.4% of patients.
Canadian Libtayo Label
Immune-mediated skin adverse reactions, defined as requiring use of corticosteroids with no clear alternate etiology, including rash, erythema multiforme, pemphigoid, and Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN) *(some cases with fatal outcome)* have been observed (see ADVERSE REACTIONS). *Monitor patients for signs and symptoms of suspected severe skin reactions and exclude other causes.* Manage patients with treatment modifications and corticosteroids at an initial dose of 1 to 2 mg/kg/day prednisone or equivalent, followed by a corticosteroid taper for Grade 2 lasting longer than 1 week, severe (Grade 3) or life-threatening (Grade 4) skin adverse reaction. Withhold LIBTAYO for Grade 2 lasting longer than 1 week or severe (Grade 3) skin adverse reaction. Resume if skin adverse reaction improves and remains at Grade 0 to 1 after corticosteroid taper to less than 10 mg/day prednisone or equivalent. *For symptoms or signs of SJS or TEN, withhold LIBTAYO and refer the patient for specialized care for assessment and treatment. Permanently discontinue LIBTAYO for life-threatening (Grade 4) skin adverse reaction or if SJS or TEN is confirmed (see DOSAGE AND ADMINISTRATION).* *Cases of SJS/TEN/stomatitis including fatal TEN occurred following 1 dose of LIBTAYO in patients with prior exposure to idelalisib, who were participating in a clinical trial evaluating LIBTAYO* in Non-Hodgkins Lymphoma (NHL), and who had recent exposure to sulfa containing antibiotics. *Two patients experienced fatal mucocutaneous toxicity after a single dose of cemiplimab monotherapy*, and a third patient developed myositis and myasthenia gravis following 2 doses of cemiplimab. Manage patients immediately with treatment modifications and corticosteroids as described above. (emphasis supplied)

63. In contrast to their foreign labels, Defendants have never included warnings in the U.S. Libtayo label for the close monitoring of patients receiving Libtayo for the initial signs of SJS and TEN, or warnings to send patients with those

early warning signs for "specialized care for assessment and treatment." And the Libtayo label does not disclose to U.S. prescribing physicians that Libtayo has caused fatal cases of TEN or contain warnings regarding SJS and TEN in the WARNINGS section that disclosing the risk of these serious life-threatening skin reactions directly from Libtayo (rather than a vague and generalized reference to the PD class of drugs).

64. In fact, Defendants' 2018 Libtayo launch labeling discloses more SJS/TEN safety information than the 2021 label in effect at the time of Mrs. Krantz' death. Given that Defendants received notice of additional cases of Libtayo-induced SJS and TEN in clinical trials and additional articles were published identifying the drug's risk of SJS and TEN in the interim, there was no conceivable safety basis for Defendants to weaken their 2018 U.S. launch labeling *while at the same time strengthening their SJS/TEN warnings overseas*. To this day, Defendants' U.S. Libtayo label does not disclose to U.S. prescribing physicians the degree of relative risk, the severity (disabling and fatal outcome), the confirmed causal relationship, the source of the adverse event reports (clinical studies versus post-marketing experience), the disparate impact on at-risk populations, the need for medical monitoring and specialized treatment at the first sign of SJS/TEN, or the frequency of serious skin reactions (including SJS/TEN) from Libtayo.

65. Nor have Defendants ever disclosed to the FDA all of the cases of serious skin reactions occurring in Libtayo clinical trials; that Defendants' Libtayo labels overseas disclose more safety information regarding the risk of SJS and TEN to prescribing physicians and patients than Defendants' U.S. drug label; or the scientific and medical basis for disclosing more safety information to physicians and consumers overseas in comparison to the safety information provided to physicians and consumers in the U.S.

iv. *Increase in Severe Skin Reaction Adverse Events and Undisclosed Safety Signal Analysis*

66. Under FDA regulations, Defendants are required to fully disclose to the FDA all adverse event data they received about the use of Libtayo. Adverse drug events are important because drug companies are required to use them to assess causality and to identify safety signals.

67. Defendants' Libtayo adverse events are stored in their global safety database and are directly accessible to Defendants. Defendants failed to review and report to the FDA all serious cases of Libtayo-related serious skin reaction adverse events maintained in Defendants' adverse event databases and did not fully disclose their internal safety signal analysis of those serious skin reaction adverse events to the FDA. The FDA maintains a publicly available adverse event reporting system (the FAERS database) that is known to Plaintiff's prescribing physician and discussed in the medical community. If Defendants had disclosed all Libtayo-

related serious skin reaction adverse events to the FDA before Mrs. Krantz was prescribed Libtayo, Plaintiff's prescribing physician would have had access to that safety data and also been informed of those serious skin reaction adverse events through continuing medical education conferences and scientific literature that would have reported on those adverse events and the increase in adverse events. Had Defendants made this safety information available to Mrs. Krantz's prescribing physician, Dr. Vora would not have prescribed Libtayo to Mrs. Krantz and she would not have been injured and died.

68. In addition to failing to report all cases of serious skin reactions to the FDA, Defendants "soft coded"[36] relevant Libtayo serious skin reaction adverse events (including cases of SJS and TEN) and failed to adequately track, analyze, and report safety signals that emerged from these adverse events to the FDA.

69. In addition to the safety information discussed above, Defendants knew or should have known about an increase in the number of Libtayo serious skin reactions and SJS/TEN adverse events before Libtayo was prescribed to Mrs. Krantz. Defendants' failure to report serious skin reaction adverse events (including cases occurring in clinical trials), soft coding of serious skin reaction adverse events

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[36] "Soft coding" occurs when a drug company, during the adverse event data entry process, selects a medical term to code the adverse event that is less severe than the correct adverse event term.

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as less severe medical events and the increase in SJS and TEN adverse events constitute newly acquired information that Defendants never disclosed to the FDA or Plaintiff's prescribing physician.

70. While the FDA was aware of SJS/TEN reports in connection with Libtayo, Defendants did not disclose to the FDA the true and increased frequency and severity of these serious skin reaction adverse events (including SJS and TEN) or the results of their internal safety signal analysis of these adverse events. Defendants should have but did not study and disclose the increase in serious skin reaction adverse events to the FDA.[37]

G. Mrs. Krantz' Prescribing Physician Relied on Defendants' False and Misleading Safety Information

71. Due in part to the availability of numerous skin cancer treatments, Mrs. Krantz' physician Dr. Nilesh Vora assessed the risks and benefits of the use of various skin cancer treatments, including Libtayo, for Mrs. Krantz. In evaluating the appropriate drug for Mrs. Krantz, Dr. Vora intended to select the drug or treatment option that would be the most tolerable for Mrs. Krantz, have the lowest

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[37] SJS and TEN should be included on "designated medical events" lists (DMEs) in order to closely monitor and assess the drug's safety because SJS and TEN triggers a safety signal on the basis of only a few cases as they are rare, medically serious, and associated with a high drug-attributable risk. Schotland, *et al.*, "Target Adverse Event Profiles for Predictive Safety in the Post-market Setting," Clinical Pharmacology & Therapeutics, 109(5):1232-1243 (2021); Hauben, *et al.*, "Early Postmarketing Drug Safety Surveillance: Data Mining Points to Consider," Annals of Pharmacotherapy 38(10): 1625-1630 (2004).

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potential for harm for serious skin reactions, and be most effective in treating her skin cancer.

72. For the purpose of assessing the risks and benefits of prescribing Libtayo to Mrs. Krantz in April 2022, among other professional background and Libtayo-related information, Dr. Vora relied on his education, training and experience; the branded U.S. Libtayo label; Defendants' sponsored medical and pharmaceutical websites; continuing medical education conferences where Libtayo was discussed; Defendants' medical literature on Libtayo; discussions with Defendants' sales representatives and at the times they visited his office to sell and promote Libtayo; Dear Healthcare Professional (DHCP) letters; and promotional materials provided by Defendants regarding Libtayo, among other documents and communications.

73. Defendants did not advise Dr. Vora of any comparative risk analyses for serious skin reactions such as SJS/TEN among the different cancer medications. He was not made aware of the higher frequencies of SJS/TEN and serious skin reactions from Libtayo in comparison to other drugs in its class or the increased risk of SJS/TEN to females. Defendants did not disclose to Dr. Vora the increase in serious skin reaction adverse events, unreported cases of serious skin reactions (including those occurring in clinical trials), or Defendants' soft coding of Libtayo-related serious skin reaction adverse events. Nor did Defendants advise him of the

safety information Defendants disclose to prescribing physicians in foreign countries, including but not limited to fatal cases of SJS and TEN; clinical trial cases of SJS and TEN; the high comparative risk of SJS and TEN from Libtayo; the causal relationship between Libtayo and SJS/TEN; or the instructions included in foreign labeling for the close monitoring for the early warning signs of SJS/TEN and the need to immediately send potential SJS/TEN patients for specialized medical care.

74. In prescribing Libtayo to Mrs. Krantz, Dr. Vora relied on Defendants to fairly and accurately disclose the serious skin reaction safety data associated with Libtayo to him. He was not aware of the inaccurate, false and misleading safety information described above, or Defendants' omission from and affirmative misrepresentations contained in the Libtayo label and prescribing information with regard to serious skin reactions and SJS/TEN. Dr. Vora would not have prescribed Libtayo to Mrs. Krantz if he known of the material safety data and information described in this Complaint.

75. As an oncologist, Dr. Vora has the option to prescribe many different cancer medications to his patients. It is impractical to place the burden on or expect every physician to manage a medical practice, effectively treat their patients, and review all of the available safety literature regarding every drug that may be applicable to their practice. These obvious impracticalities are, in part, why federal regulations place the burden on drug companies such as Defendants to disclose all

material safety information regarding the safe use of their drugs. Defendants at all times knew it was their duty and legal responsibility to do so. It is Dr. Vora's practice to rely on safety information provided by drug companies like Defendants (including but not limited to prescribing information disseminated in labeling and Medication Guides, DHCP letters, sales literature and communications, symposiums and medical conferences), and he was exposed to, reviewed and relied upon the safety information referenced above when he was analyzing the safest and most effective cancer medication to use with Mrs. Krantz in April 2022.

76. Had the prescribing information for Libtayo accurately disclosed the risk of serious skin reactions (including SJS and TEN), Dr. Vora would not have prescribed Libtayo to Mrs. Krantz, would have prescribed a safer alternative drug or course of medical treatment to or no additional treatment for Mrs. Krantz, and Mrs. Krantz would not have died from a Libtayo-induced SJS/TEN reaction.

77. Defendants knew physicians such as Dr. Vora would rely upon the completeness and accuracy of the safety information contained in the Libtayo label, and Dr. Vora did in fact rely on that information in prescribing Libtayo to Mrs. Krantz.

78. At the time Defendants made the above-described misrepresentations and nondisclosures, Mrs. Krantz and Dr. Vora were ignorant of the falsity of the representations and reasonably believed them to be true. In fact, Defendants knew

that prescribing physicians like Dr. Vora were unaware of the increased risks of SJS and TEN, because Defendants concealed such risks from them.

79. Plaintiffs' serious injuries, as described above, are the foreseeable and proximate result of Defendants' failure to correct false and misleading information they disseminated to physicians, which contained inaccurate, misleading, deceptive, materially incomplete, and/or otherwise inadequate information concerning the efficacy, safety, and serious skin reaction side effects of Libtayo.

80. But for the above misrepresentations, actions, and omissions of Defendants, Mrs. Krantz would not have suffered the catastrophic and fatal injuries giving rise to this case.

IV. CAUSES OF ACTION[38]

STRICT PRODUCTS LIABILITY/FAILURE TO WARN

81. Plaintiffs incorporate by reference each and every paragraph of this complaint as set forth in full below.

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[38] Plaintiffs' claims are distinct from a global challenge to Defendants' general (and inadequate) skin reaction warnings. Specifically, Plaintiffs' claims in this case are limited to i) pre- and post-approval claims relating to warnings that have never been in the Libtayo label (*e.g.*, the Krantz Warnings), and ii) post-approval claims relating to Defendants' vastly understated warnings and references that were in the label following approval and at the time of Plaintiffs' injuries on the basis that new safety information (addressed in the Complaint) has emerged since NDA approval. Plaintiffs further allege that Defendants could and should have unilaterally changed the U.S. Libtayo label to include the Krantz Warnings following NDA approval through the CBE-0 process. In fact, Defendants have

82. Defendants designed, manufactured, marketed, distributed, and supplied Libtayo. As such, Defendants had a duty to adequately analyze the product in conformance with the standards of care to ensure that the risks and benefits of the drug were sufficient for the safe and effective use of the drug for its approved indications, and to warn healthcare providers, including Plaintiff's prescribing physician, of the health risks and dangers associated with using the medication, both in the premarketing and post-approval lifecycle phases of Libtayo.

83. Libtayo was in the exclusive control of Defendants and was sold without adequate directions of use and without adequate warnings. More specifically, Defendants should have included the Krantz Warnings in the Libtayo label.

84. As a direct and proximate result of the defective condition of Libtayo, manufactured, marketed and/or supplied by Defendants, and as a direct and proximate result of negligence, gross negligence, willful, oppressive, cruel and wanton misconduct, or other wrongdoing and actions of Defendants described herein, Plaintiffs suffered personal injuries, damages and economic loss as alleged herein.

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changed their still-deficient skin reaction warnings following NDA approval.

85. Upon information and belief, Defendants knew of the defective nature of Libtayo, but continued to manufacture, market, and sell the medication to maximize sales and profits at the expense of public health and safety, in knowing, conscious, and deliberate disregard of the foreseeable harm caused by the medication, and in violation of its duty to provide an accurate, adequate, and complete directions for use and warnings concerning the use of Libtayo.

86. Defendants failed to adequately warn Plaintiff's prescribing physician of the dangerous propensities of Libtayo, which were known or should have been known to Defendants, as they were scientifically readily available.

87. Defendants knew and intended for Libtayo to be prescribed by physicians and be used by persons with a prescription, without any inspection for defects. Defendants also knew that hospitals, clinics, and physicians and users, such as Plaintiff, would rely upon the representations made by Defendants in their product labels and in other promotion and sales materials upon which Plaintiff and her prescribing physician did so rely.

88. As a direct and proximate result of Defendants' sale of Libtayo without adequate directions of use and adequate warnings regarding the risk of serious skin reactions set forth herein and in the Krantz Warnings, Plaintiffs suffered harm and permanent injuries.

89. Defendants' conduct in the packaging, warning, marketing, advertising, promotion, distribution, and sale of Libtayo was despicable, cruel and committed with a willful, conscious or reckless disregard of the rights and safety of consumers such as Mrs. Krantz, thereby entitling Plaintiffs to punitive damages in an amount to be determined at trial that is appropriate to punish Defendants and deter them from similar conduct in the future.

NEGLIGENCE

90. Plaintiffs incorporate by reference each and every paragraph of the complaint as though set forth in full herein.

91. Defendants owed a duty to Plaintiff's prescribing physicians and Plaintiff to use reasonable care in labeling, manufacturing, marketing, supplying, distributing and selling Libtayo, including a duty to ensure that Libtayo did not cause users to suffer from unreasonable, unknown, and dangerous side effects from SJS and TEN.

92. Defendants failed to exercise reasonable care and failed to warn of the known risks associated with the risks of Libtayo with respect to serious skin reactions. The product lacked sufficient warnings regarding the hazards and dangers to users of Libtayo and serious skin reactions and failed to provide safeguards to prevent the injuries and damages sustained by the Plaintiff. Defendants failed to properly analyze and report on the safety profile of Libtayo prior to its sale and, as

a result, subjected users to an unreasonable risk of injury when the product was used as directed.

93. In addition to those reasons set forth above, Defendants breached their duty and were negligent in their actions, misrepresentations, and omissions in the following ways:

- Failed to exercise due care in marketing, labeling and manufacturing Libtayo in order to avoid the aforementioned risks to individuals, including Plaintiff, during Libtayo's lifecycle;
- Failed to include adequate directions for use and warnings with Libtayo to alert prescribers and Plaintiff of its potential risks and side effects;
- Failed to adequately and properly analyze the safety profile of Libtayo after placing it on the market by not disclosing all risks in its studies, applications, labeling, marketing and advertising materials and documents;
- Failed to conduct sufficient clinical analysis on Libtayo, which if properly performed would have shown that Libtayo had serious side effects, including but not limited to the increased risks of serious skin reactions, including SJS and TEN from clinical trials, scientific literature and spontaneous reporting of SJS and TEN, and the increased risks of serious skin reactions in the female subpopulation;
- Failed to adequately warn Plaintiff's prescribing physician regarding the increased risks of serious skin reactions, including SJS and TEN from clinical trials, scientific literature and spontaneous reporting of SJS and TEN, and the increased risks of serious skin reactions in certain subpopulations, including the female subpopulation;
- Failed to conduct adequate pharmacovigilance and prepare a pharmacovigilance assessment and plan to mitigate the risks of serious skin reactions in certain subpopulations, including the female subpopulation; and

- Failed to warn Plaintiff's prescribing physician as outlined above through various communication vehicles, including the Libtayo labeling, patient medication guides, Dear Healthcare Provider letters, press releases, and other risk communication options.

94. Defendants knew or should have known that Libtayo caused unreasonably dangerous risks and serious side effects of which Plaintiff and Plaintiff's prescribing physician would not be aware. Defendants nevertheless advertised, marketed, sold, and/or distributed Libtayo, despite knowing of its unreasonable risks of injury associated with serious skin reactions, like SJS and TEN.

95. Defendants knew or should have known that consumers such as Plaintiff would suffer injury as a result of Defendants' failure to exercise reasonable care as described above.

96. Defendants knew or should have known of the defective nature of Libtayo, as set forth herein, but continued to manufacture, market, and sell Libtayo so as to maximize sales and profits at the expense of the health and safety of the public, Plaintiff and Plaintiff's prescribing physician, in conscious and/or negligent disregard of the foreseeable harm caused by the medication.

97. Defendants failed to disclose to Plaintiff and Plaintiff's prescribing physician facts known or available to Defendants in order to ensure continued and increased sales of Libtayo. This failure to disclose deprived Plaintiff and Plaintiff's

prescribing physician of the information required to weigh the true risks of taking Libtayo against its benefits.

98. As a direct and proximate result of Defendants' negligence as outlined above, Plaintiffs suffered harm as alleged herein, including severe pain and suffering, loss of enjoyment of life, economic loss, out-of-pocket costs of medical tests and treatment, future medical care and/or services, and other costs.

99. Defendants' conduct was despicable, cruel and committed with a willful, conscious or reckless disregard of the rights and safety of consumers such as Plaintiff, thereby entitling Plaintiffs to punitive damages in an amount to be determined at trial that is appropriate to punish Defendants and deter them from similar conduct in the future.

NEGLIGENT MISREPRESENTATION

100. Plaintiffs incorporate by reference each and every paragraph of this complaint as though set forth in full herein.

101. Defendants owed a duty to disseminate accurate and adequate information concerning Libtayo, and to exercise reasonable care to ensure that it did not, in those undertakings, create unreasonable risks of personal injury to others.

102. Defendants disseminated to physicians (including Plaintiff's prescribing physician), through the U.S. Libtayo label, the publication of a PDR monograph, DHCP letters and other mediums, information concerning the efficacy,

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safety profile and understated side effects of Libtayo, with the intention that physicians (including Plaintiff's prescribing physician) would rely upon that information when making a decision concerning whether to prescribe Libtayo for their patients.

103. Defendants had a duty to ensure that the information contained in the package inserts, patient information leaflets, and medication guides accompanying its prescription drug products is accurate, adequate, complete, and is not misleading. Defendants had a duty to monitor the medical literature and post marketing adverse events and to report the data affecting the safety of the drug to the FDA and Plaintiff's prescribing physician.

104. Defendants knew that Plaintiff's prescribing physician would rely upon Libtayo labeling and safety information disseminated from Defendants, and that many patients would be likely to use Libtayo as a result of Defendants' labeling and safety communications and advertising efforts.

105. From 2014-present, Defendants breached their duty to Plaintiff's prescribing physician and Plaintiff because Defendants mispresented material significant safety and efficacy data regarding Libtayo through the omission of the Krantz Warnings. These omission of fact and misrepresentations include Defendants' knowing failures to include the Krantz Warnings in the Libtayo

labeling and knowing failures to place Plaintiff's prescribing physician on notice of the following material safety risks, among others:

- Libtayo has an elevated risk and higher frequency of serious skin reactions, including DRESS, SJS and TEN than disclosed in the labeling;
- Libtayo has an elevated risk and higher frequency of serious skin reactions, including SJS and TEN, that are materially greater than what is disclosed in the U.S. label;
- Libtayo clinical trials detected cases of SJS and TEN (including fatal cases), which are not disclosed in the U.S. Libtayo label;
- Libtayo has a substantially increased risk for serious skin reactions compared to other checkpoint inhibitors;
- The U.S. Libtayo label does not warn prescribing physicians that SJS/TEN from Libtayo has resulted in fatalities;
- The Libtayo label has not been updated with the post-approval peer-reviewed literature, clinical trial cases, and spontaneous reports that reflect high reporting rates of SJS and TEN;
- Foreign country labeling for Libtayo provides stronger SJS/TEN warnings and directions to prescribing and treating physicians than the U.S. label;
- The post-approval peer-reviewed Libtayo literature and spontaneous reporting reflects higher reporting rates of SJS and TEN than disclosed in the labeling; and
- The Libtayo label did not adequately disclose the existence of early warning signs of SJS and TEN, caution that stopping Libtayo at the first sign of these symptoms and instruct prescribing and treating physicians to warn patients to immediately see expert medical care for SJS and TEN in order to reduce mortality and morbidity even though Defendants knew that the only effective treatment for mitigating the development of SJS and TEN is early discontinuation of the drug.

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106. From 2014-present, Defendants knew or should have known through the exercise of reasonable care, that the labeling for Libtayo grossly understated and misrepresented, the risks and/or degree of risks of severe skin reactions associated with Libtayo as described above.[39]

107. Defendants made the misrepresentations in the Libtayo label and marketing materials referenced herein without any reasonable ground for believing them to be true. From 2014-present, these misrepresentations were made directly by Defendants in the Libtayo labeling and in Defendant-sponsored publications and other written materials directed to physicians (including Plaintiff's prescribing physician) and Plaintiff with the intention of inducing reliance by Plaintiff's prescribing physician and by Plaintiff.

108. The representations by Defendants were in fact false and misleading and were intended to induce reliance on those misrepresentations and the purchase and use of Libtayo and Defendants knew or should have known that those

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[39] *Rayes v. Novartis Pharmaceuticals Corp.*, No. 21-55723, 2022 WL 822195, at *2 (9th Cir. March 18, 2022) (reversing district court's order dismissing case on pleading fraud with specificity basis; noting omissions from drug label satisfies Rule 9(b), stating "Rayes's allegation that Novartis intentionally understated the risk of Beovu on the product label satisfies Rule 9(b)'s particularity requirement."); *White v. Novartis,* No. 16-4300, 2018 WL6133637 (C.D. Cal. Mar. 7, 2018) (order denying Rule 12(b)(6) motion to dismiss fraud and negligent misrepresentation claims in SJS case handled by Plaintiffs' counsel that involved a black box SJS/TEN warning).

misrepresentations would result in the ingestion of Libtayo by consumers such as Plaintiff. Had Plaintiff or her prescribing physician known of the true facts and those facts concealed by Defendants, Plaintiff's prescribing physician would not have prescribed Libtayo to Plaintiff and Plaintiff would not have used Libtayo and died. The reliance by Plaintiff's prescribing physician on Defendants' misrepresentations at the time of Dr. Vora's prescription to Mrs. Krantz and each time he reviewed the Libtayo label between 2018 - April 2022 was justified because such misrepresentations were made by Defendants, who were in a position to know and did know the true facts.

109. As a direct and proximate result of Defendants' negligent misrepresentations, Plaintiffs suffered harm as alleged herein, including severe pain and suffering, loss of enjoyment of life, economic loss, out-of-pocket costs of medical tests and treatment, future medical care and services, among other costs.

110. Defendants' conduct was despicable, cruel and committed with a willful, conscious or reckless disregard of the rights and safety of consumers such as Plaintiff, thereby entitling Plaintiffs to punitive damages in an amount to be determined at trial that is appropriate to punish Defendants and deter them from similar conduct in the future.

GROSS NEGLIGENCE

111. Plaintiffs incorporate by reference each and every paragraph of this complaint as though set forth in full herein.

112. Defendants had the duty to exercise reasonable care in manufacturing, marketing, labeling, selling, and/or distributing Libtayo including a duty to ensure that Libtayo did not cause users to suffer from unreasonable and dangerous side effects, like SJS and TEN.

113. Defendants failed to exercise reasonable care in manufacturing, marketing, labeling, selling, and/or distributing Libtayo for the reasons set forth above.

114. As a direct result of Defendants' gross negligence, willful and wanton misconduct, and other wrongdoing which constitute a deliberate act or omission with knowledge of a high degree of probability of harm and reckless indifference to the consequences, Mrs. Krantz was prescribed Libtayo, was injured and died.

115. Defendants continued to promote the efficacy and safety of Libtayo, while providing little or no warnings, and downplayed the risks of SJS/TEN, even after Defendants knew of the risks and injuries associated with its use.

116. Defendants' conduct was despicable, cruel and committed with a willful, conscious or reckless disregard of the rights and safety of consumers such as Plaintiffs, thereby entitling Plaintiffs to punitive damages in an amount to be

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determined at trial that is appropriate to punish Defendants and deter them from similar conduct in the future.

DEMAND FOR JURY TRIAL

Plaintiffs demand a jury trial on all counts in this Complaint.

V. REQUEST FOR RELIEF

WHEREFORE, Plaintiffs pray for judgment and relief as follows:

1. Actual, compensatory and punitive damages;
2. Loss of consortium, survival, and wrongful death damages;
3. Past and future pain, suffering and mental anguish damages;
4. Restitutionary relief; and
5. Plaintiffs request all other and further relief to which they are entitled at law and equity.

DATED: September 21, 2023 Respectfully submitted,

By: */s/ Robert A. Mosier*

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