IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

MERUS N.V., Plaintiff, v. XENCOR, INC., Defendant.	Civil Action No. 24-913-CFC

DEFENDANT XENCOR, INC.'S OPENING BRIEF
IN SUPPORT OF ITS MOTION TO DISMISS
PURSUANT TO FEDERAL RULE OF CIVIL PROCEDURE 12(b)(6)

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XENCOR EXHIBIT 1054
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IPR2025-00604

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Dated: October 10, 2024

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I. NATURE AND STAGE OF THE PROCEEDINGS

On August 5, 2024, Plaintiff Merus N.V. filed a Complaint against Xencor, Inc. alleging infringement of U.S. Patent Nos. 9,358,286 ("the '286 patent"), 9,944,695 ("the '695 patent"), and 11,926,859 ("the '859 patent"). (D.I. 1.) Xencor hereby moves to dismiss this action with prejudice pursuant to Rule 12(b)(6).

II. SUMMARY OF ARGUMENT

Merus's Complaint should be dismissed because Merus has not plausibly alleged (and cannot plausibly allege) that Xencor engaged in any activity outside the scope of 35 U.S.C. § 271(e)(1). This statutory "safe harbor" exempts from alleged infringement activities that are "reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products." *Id.* As the Complaint acknowledges, Xencor is a clinical-stage biopharmaceutical company that operates in the "field of cancer drug ***development***"[1] (D.I. 1 at ¶ 74), and the infringement allegations are directed to Xencor's "antibody ***generation and development work***" on drug candidates (*id.* at ¶¶ 97, 110; *see also id.* at ¶ 74). Such activities fall squarely within the Section 271(e)(1) safe harbor.

[1] Unless otherwise noted, all emphases have been added.

Fully cognizant of the safe harbor issue, and the fact that Xencor does not currently market any products, Merus attempts to plead its way around the statute. But the best Merus can muster are unsupported allegations that Xencor's activities were so "early" that the safe harbor does not apply. Yet, at the same time, Merus broadly requests injunctive relief against all of Xencor's activities (*id.* at 29)—including indisputably safe harbor-protected "clinical pipeline" work (*id*. at ¶ 66). Because Merus's conclusory assertions are both contrary to law and unsupported by any facts, Xencor respectfully requests that the Complaint be dismissed for failure to state a claim under Rule 12(b)(6).

III. STATEMENT OF FACTS

A. Xencor's Groundbreaking Work on Antibody Therapeutics

Antibodies have long been used to treat cancer and other serious diseases. (*Id.* at ¶ 12.) Naturally produced antibodies (as well as traditional forms of manufactured antibodies) are "monospecific," meaning the antibody binds to only one target antigen. (*Id*. at ¶ 15.) Recent antibody development work has focused on antibodies that can target more than one antigen, including antibodies that are "bispecific" (*i.e.*, bind to two different target antigens) or "trispecific" (*i.e.*, bind to three different target antigens). (*Id.*)

Xencor is a leader in the field of bispecific antibodies. It has developed and patented technology for making bispecific antibodies that have highly specific

antigen binding and can be readily purified at manufacturing scale. (D.I. 1, Ex. 14 at 38-49; D.I. 1, Ex. 13 at 16.) Xencor has utilized this technology in creating an extensive pipeline of antibody drug candidates, and is developing "engineered antibody therapeutics to treat patients with cancer and other serious diseases." (D.I. 1, Ex. 13 at 4.)

B. Xencor's Drug Development Programs

Xencor does not currently market any drug products. (*Id.* at 17.) Instead, Xencor has been researching and developing bispecific antibody candidates with the goal of introducing products that, in the future, may be approved by the U.S. Food and Drug Administration ("FDA"). (*Id.*) All of Xencor's drug candidates are designed with a specific target or targets (to which antibody binding would cause a physiological effect) in mind. (*See id.* at 7-10.) For example, Xencor is developing a bispecific antibody drug product designed to bind to human "PD-1" and human "CTLA-4" to treat certain cancers. (D.I. 1 at ¶ 63 (citing https://xencor.com/pipeline/vudalimab/); *see also* D.I. 1, Ex. 13 at 52.) Other Xencor bispecific candidates similarly target known tumor antigens, including "ENPP3," "B7-H3," "CLDN6," "CD20," "STEAP1," "Claudin-18.2," and "PSMA" (D.I. 1, Ex. 13 at 7-10), or are designed to treat various autoimmune diseases (*id.* at 52-53). All of these potential drug products further Xencor's goals of "advancing the development of its XmAb antibody programs for oncology and

other serious diseases" and "building and managing a diversified portfolio of XmAb drug candidates." (*Id*. at 4 (cleaned up).)

Xencor's potential antibody therapeutics are currently in various stages of clinical and preclinical development. (*Id.* at 4 (explaining that Xencor aims to "advance these [bispecific] candidates into clinical-stage development, where [it is] conducting Phase 1 and Phase 2 studies for a broad portfolio of programs, to determine which programs we advance into later stages of development and potentially commercialization").)[2] For example, Xencor's vudalimab antibody is in Phase 2 clinical trials for patients with metastatic castration-resistant prostate cancer, and Phase 1b/2 trials for patients with metastatic non-small cell lung cancer. (D.I. 1 at ¶ 63 (citing https://xencor.com/pipeline/vudalimab/).) XmAb819, another Xencor bispecific antibody, is in Phase 1 clinical trials focused on advanced renal cell carcinoma (*id.* (citing https://xencor.com/pipeline/xmab819/)), and other Xencor candidates are also undergoing Phase 1 or 2 studies (D.1. 1, Ex. 13 at 7-8). The FDA has taken note of the development efforts by Xencor and others, explaining that it "anticipates there will be a spectrum of bispecific antibodies developed for the prevention, treatment,

[2] FDA approval requires extensive preclinical and clinical testing. (D.I. 1 at 22-23.) Preclinical testing includes "laboratory evaluations of product chemistry, stability, and formulation, as well as animal studies to assess the potential toxicity and activity of the product candidate." (*Id.*) Clinical testing includes testing of "safety and efficacy of the product candidate for its intended use." (*Id.*)

or diagnosis of diseases, each with unique considerations for the specific product and targeted indication." (Ex. A, FDA, Bispecific Antibody Development Programs Guidance for Industry (May 2021) at 2.)[3]

C. Merus's Infringement Allegations

Merus alleges that Xencor's activities in developing potential antibody therapeutics have infringed the '286 and '859 patents, which relate to "heterodimeric antibodies" (D.I. 1 at ¶¶ 95, 108), as well as the '695 patent, which relates to methods for "obtaining an antibody that binds to an antigen" (*id.* at ¶¶ 78-79). Even though Xencor does not market any antibody products, Merus filed this lawsuit accusing certain "development" work of infringement. (*Id.* at ¶¶ 97, 110.)

The '286 and '859 patents: Merus's Complaint makes the following allegations of infringement with respect to the '286 and '859 patents:

- "Xencor uses Merus' patented heterodimerization technology to take advantage of certain electrostatic interactions between the constant regions and make stable bispecific antibodies. . . . Xencor refers to its use of Merus' patented heterodimerization technology as its 'XmAb bispecific platform' and ***uses it in many of its antibodies***." (*Id.* at ¶ 63

[3] All Exhibits are attached to the declaration of Simon F. Kung, filed herewith.

(citing Xencor webpages relating to vudalimab and XmAb819 clinical candidates).)

- "Xencor describes the substitutions that are involved in its so-called XmAb technology . . . . Given these amino acid substitutions, all of the early discovery and preclinical ***generation of antibodies*** made, used, offered for sale, sold, and/or imported with Xencor's XmAb bispecific platform infringe Merus' Heterodimerization Patents, as do ***Xencor's clinical pipeline of multispecific antibodies***." (*Id.* at ¶¶ 64-66; *see also* ¶¶ 99, 112-13 (discussing substitutions); ¶¶ 100-02 (discussing alleged manufacturing of antibodies with these substitutions).)
- "Xencor makes extensive use of its infringing XmAb bispecific platform and this platform is ***used throughout Xencor's portfolio of antibodies*** as a fundamental design feature." (*Id.* at ¶ 67.)

Merus also baldly asserts that the alleged infringement "includes both Xencor's own heterodimeric antibody generation and development work and Xencor's 'partnered' heterodimeric antibody generation and development work" (*id.* at ¶¶ 97, 110; *see also id.* at ¶ 58), but these allegations fail to identify any alleged infringing work on any particular antibodies. Merus's infringement allegations are therefore directed to "Xencor's portfolio of antibodies" utilizing Xencor's XmAb® technology, otherwise referred to by Merus as the "XmAb antibodies." (*Id.* at

¶¶ 67, 99, 112-13.) All of Xencor's antibodies utilizing the XmAb® technology are directed to specific antigen targets, and have been (and are being) developed for potential submission to the FDA. (*See* D.I. 1, Ex. 13 at 7-10 (identifying target antigens for all listed XmAb® antibodies).)

In making these infringement allegations, Merus further contends, without any support, that "Xencor's infringing use of Merus' Heterodimerization Patents includes use during the antibody generation and discovery process, which occurs long before any antibody is selected as a possible candidate for regulatory review and/or approval." (D.I. 1 at ¶ 69; *see also id.* at ¶ 65 (referring to unspecified "early discovery" activities).) Merus does not identify any such "early discovery" activities or how these unspecified activities could infringe the '286 and '859 patents, much less fall outside of the safe harbor.

The '695 patent: Merus's only cited evidence of alleged infringement concerning the '695 patent involves what is referred to as "RenLite® mouse" antibody-manufacturing technology that Xencor licensed from a third party, Biocytogen Pharmaceuticals (Beijing) Co., Ltd.:

> Xencor has created common light chain bispecific and/or trispecific antibodies by using the RenLite mouse and biological products of the RenLite mouse, thereby infringing Merus' Common Light Chain Patent. For example, in U.S. Patent Application Publication No. U.S. 2023/0383012 ("the '012 Application"), Xencor describes use of the RenLite mouse and biological products of the RenLite mouse to make multispecific antibodies that bind to, *inter alia*, PD-L1, PD-L2, and/or CD28.

(*Id.* at ¶ 33; *see also* ¶ 53 (discussing the '012 application).) Merus's remaining allegations are either directed at Biocytogen activities (*see id.* at ¶¶ 37-45, 48-52) or amount to no more than conclusory assertions (*see, e.g.*, *id.* at ¶ 46 ("Xencor has immunized RenLite mice with antigens and obtained from the RenLite mice populations of B cells that produce antibodies specific to those antigens"), ¶ 47 ("On information and belief, the antibodies Xencor has generated using RenLite mice share a common light chain – encoded by the fused human V/J gene segments and murine constant region – with a diversity of clonally unrelated heavy chains.")).

Regardless, Xencor's limited work with Biocytogen's antibody-generating technology has long been discontinued.[4] And, once again, Merus's Complaint does not and cannot support any such limited developmental activity falling outside of the safe harbor.

* * *

Despite the fact that Xencor has not yet received permission from the FDA to market any drug product (D.I. 1, Ex. 13 at 7), the Complaint seeks monetary damages as well as broad injunctive relief with respect to Xencor's preclinical and clinical activities (D.I. 1 at 29). Merus's infringement allegations are meritless,

[4] As Xencor explained to Merus during a pre-complaint meeting on July 2, 2024 (*id.* at ¶ 75), Xencor is not pursuing any antibody generated using the discontinued RenLite® mouse.

but regardless, such activities are precisely what the Section 271(e)(1) safe harbor was designed to protect. Merus should not be permitted to interfere with Xencor's efforts to develop potentially lifesaving medications, and its Complaint should be dismissed.

IV. APPLICABLE LEGAL STANDARDS

A. Dismissal Pursuant to Rule 12(b)(6) for Failure to State a Claim

A claim should be dismissed under Rule 12(b)(6) if, accepting all of the facts as true, the plaintiff has failed to state a plausible claim for relief. *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 545 (2007). This involves a two-part analysis. "First, the factual and legal elements of a claim are separated," with all well-pleaded facts accepted as true (but any legal conclusions are disregarded). *Bishop v. J.P. Morgan Chase & Co.*, No. 13-001, 2013 WL 4007508, at *2 (D. Del. Aug. 5, 2013) (citing *Fowler v. UPMC Shadyside*, 578 F.3d 203, 210 (3d Cir. 2009)). Second, courts determine "whether the facts alleged in the [pleading] are sufficient to show that the plaintiff has a 'plausible claim for relief.'" *Id*. (citing *Fowler*, 578 F.3d at 211); *see also Twombly*, 550 U.S. at 545 ("Factual allegations must be enough to raise a right to relief above the speculative level on the assumption that all of the [pleading's] allegations are true."). "To decide a motion to dismiss, courts generally consider only the allegations contained in the complaint, exhibits attached to the complaint and matters of public record." *Schmidt v. Skolas*, 770

F.3d 241, 249 (3d Cir. 2014) (cleaned up). Courts may also consider "a document integral to or explicitly relied upon in the complaint." *Id.*

Following *Twombly*, the Third Circuit and this District have further explained that "a complaint must do more than simply provide 'labels and conclusions' or 'a formulaic recitation of the elements of a cause of action.'" *Davis v. Abington Mem'l Hosp.*, 765 F.3d 236, 241 (3d Cir. 2014) (citation omitted). Courts are "not required to credit bald assertions or legal conclusions improperly alleged in the complaint." *In re Rockefeller Ctr. Props., Inc. Sec. Litig.*, 311 F.3d 198, 216 (3d Cir. 2002); *see also DiStefano Patent Tr. III, LLC v. LinkedIn Corp.*, 346 F. Supp. 3d 616, 620 (D. Del. 2018) (courts need not accept "bald assertions," "unsupported conclusions, and unwarranted inferences," or "self-evidently false" allegations).

B. The 35 U.S.C. § 271(e)(1) Safe Harbor

The Section 271(e)(1) safe harbor excepts certain activities from alleged infringement. The relevant portions of the statute are set forth below:

> It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs.

35 U.S.C. § 271(e)(1).

The Supreme Court has explained that "[t]he statutory text makes clear that § 271(e)(1) provides a wide berth for the use of patented drugs in activities related to the federal regulatory process, including uses reasonably related to the development and submission of any information under the [Federal Food, Drug, and Cosmetic Act]." *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 193 (2005). "The use of the word 'under' in the statute is expansive. . . . 'Under a federal law' extends beyond just the 'most barebones information' required by the FDA, and instead encompasses all 'materials the FDA demands in the regulatory process.'" *Momenta Pharms., Inc. v. Amphastar Pharms., Inc.*, 686 F.3d 1348, 1356 (Fed. Cir. 2012) (citation omitted); *see also Edwards Lifesciences Corp. v. Meril Life Scis. Pvt. Ltd.*, 96 F.4th 1347, 1351 (Fed. Cir. 2024) (holding that Section 271(e)(1) exempted "importation of two demonstration samples of its transcatheter heart valves to a medical conference" for purposes of "recruiting investigators for a clinical trial to support FDA approval").

This "wide berth" of exempted activities applies to both clinical and preclinical studies. *Merck*, 545 U.S. at 202 ("This necessarily includes preclinical studies of patented compounds that are appropriate for submission to the FDA in the regulatory process. There is simply no room in the statute for excluding certain information from the exemption on the basis of the phase of research in which it is developed or the particular submission in which it could be included."). "Congress

did not limit § 271(e)(1)'s safe harbor to the development of information for inclusion in a submission to the FDA . . . . Rather, it exempted from infringement *all* uses of patented compounds 'reasonably related' to the process of developing information for submission under *any* federal law regulating the manufacture, use, or distribution of drugs." *Id.* at 206 (emphasis in original); *see also Momenta*, 686 F.3d at 1356 (courts have "expressly rejected the notion that the safe harbor only applies to information developed during a clinical trial"). As the Supreme Court has explained, the protection applies when a drug maker "has a reasonable basis for believing that a patented compound may work, through a particular biological process, to produce a particular physiological effect, and uses the compound in research that, if successful, would be appropriate to include in a submission to the FDA." *Merck*, 545 U.S. at 207.

C. The Section 271(e)(1) Safe Harbor Can Serve as a Basis for Dismissal

"The safe harbor provision in 35 U.S.C. § 271(e)(1) may properly be considered at the motion to dismiss stage, even if it is viewed as an affirmative defense." *Classen Immunotherapies, Inc. v. Shionogi, Inc.*, 993 F. Supp. 2d 569, 575 (D. Md. 2014) *aff'd*, 586 F. App'x 585 (Fed. Cir. 2014) (dismissing complaint based on safe harbor and stating "the Court may consider affirmative defenses on a motion to dismiss where they are clear from the face of the complaint"). Indeed, courts have dismissed patent infringement complaints due to

the allegedly infringing activities falling within the Section 271(e)(1) safe harbor. *See, e.g.*, *Galderma Labs., L.P. et al. v. Medinter US, LLC et al.*, No. 18-1892, 2020 WL 871507, at *3 (D. Del. Feb. 14, 2020) (dismissing allegations covered by the safe harbor pursuant to Rule 12(b)(6)); *Classen Immunotherapies, Inc. v. Somaxon Pharm.*, No. 12-06643, 2013 WL 9947386, at * 6 (C.D. Cal. Apr. 11, 2013) *aff'd*, 550 Fed. App'x. 897 (Fed. Cir. 2014) (dismissing complaint with prejudice pursuant to Rule 12(b)(6) because allegedly infringing activity fell within the safe harbor); *see also Icon Laser Sol's., LLC v. Abercrombie & Fitch, Co.*, No. 3:15-03308, 2016 WL 7379138, at *4 (N.D. Tex. July 13, 2016) (granting motion to dismiss based on § 287(b)(2) innocent seller exemption and noting that, "[s]ince the safe harbor provision relieves the Defendant of patent liability, the Plaintiff has no viable claim in these cases because it is not entitled to any relief, unless the Plaintiff could plead facts showing that this did not apply").

V. ARGUMENT

The Court should dismiss the Complaint because Merus's allegations are directed to Xencor's research and development work—all of which involves the generation of information for potential submission to the FDA—and thus fall squarely under the Section 271(e)(1) safe harbor. Merus has simply not pleaded any cause of action that would allow the Court to draw any reasonable inference that Xencor is liable for alleged patent infringement.

A. The Section 271(e)(1) Safe Harbor Protects the Activities Accused of Infringing the '286 and '859 Patents

The '859 and '286 patents (referred to by Merus as the "Heterodimerization Patents") are directed to a "heterodimeric antibody" and a "method for producing a heterodimeric antibody," respectively. Federal law requires FDA approval of all drugs, including "heterodimeric antibody" drugs. (*See* D.I. 1, Ex. 13 at 22.) These patents are therefore subject to potential safe harbor protection. *Shire LLC v. Amneal Pharms., LLC*, 802 F.3d 1301, 1304 (Fed. Cir. 2015) (patents covering active ingredients are safe harbor-eligible); *Amgen Inc. v. Hospira, Inc.*, 944 F.3d 1327, 1338 (Fed. Cir. 2019) (patents covering methods of making active ingredients are safe harbor-eligible). Indeed, Merus's Complaint alleges that its own antibodies in development, called "Zeno" and "Peto," are covered by the '859 and '286 patents. (D.I. 1 at ¶ 29 ("Elements of Zeno and Peto, as well as their creation and production, are covered by Merus' . . . Heterodimerization Patents.").) The Complaint also explains that both Zeno and Peto antibody products are subject to FDA review (*see id.* at ¶ 28), as are Xencor's clinical candidates. Accordingly, Xencor's accused activities relating to the '859 and '286 patents clearly qualify for the Section 271(e)(1) safe harbor.

As explained below, all of the accused activities are reasonably related to the development of information for submission (or potential submission) to the FDA

for the purpose of obtaining approval for drugs utilizing Xencor's XmAb® platform.

1. Any Specific Allegations of Infringement Are Protected by the Safe Harbor

The only specific Xencor products identified in Merus's Complaint are plamotamab, vudalimab, and XmAb819.[5] (D.I. 1 at ¶¶ 60; 63.) Exhibits to the Complaint, however, show that each of these candidates are currently in clinical trials:

- "We conducted a Phase 1 study of plamotamab in patients with non-Hodgkin's lymphomas."
- "We are conducting two Phase 2 clinical studies of vudalimab in patients with [metastatic castration-resistant prostate cancer], a study of vudalimab as a monotherapy in the clinically defined high-risk patient population and a study of vudalimab in combination with chemotherapy, in the aggressive variant patient population."
- "We are conducting a Phase 1 study evaluating XmAb819 in patients with advanced clear cell [renal cell carcinoma]."

(D.I. 1, Ex. 13 at 8.) As such, these accused activities clearly fall within the safe harbor. *See, e.g.*, *Galderma*, 2020 WL 871507, at *3 ("[C]linical trials for FDA

[5] Merus does not expressly allege that plamotamab is infringing (*see* D.I. 1 at ¶ 60), but that antibody is nonetheless addressed out of an abundance of caution.

approval fall within Section 271(e)(1)'s protection.") (citing *Merck*, 545 U.S. at 202).

Merus alleges that "Xencor uses Merus' patented heterodimerization technology to take advantage of certain electrostatic interactions between the constant regions and make stable bispecific antibodies. . . . Xencor refers to its use of Merus' patented heterodimerization technology as its 'XmAb® bispecific platform' and uses it in many of its antibodies." (D.I. 1 at ¶ 63; *see also id.* at ¶¶ 63-67, 98-102, 112-13.) The alleged "patented heterodimerization technology," however—and more specifically the claims at issue—are directed to either a "heterodimeric antibody" or a "method for producing a heterodimeric antibody." (*Id*. at ¶¶ 25, 67, 95, 96, 108, 109.) The subject matter encompassed by these claims is what the safe harbor is designed to protect: the use of patented compounds (and methods of making them) to further the generation of data for possible submission to the FDA (*supra* at IV.B).

The relevant inquiry is whether the accused Xencor antibodies made utilizing the "XmAb®" technology are protected by the safe harbor. They are. All of Xencor's XmAb® antibodies in development are (1) directed to a particular biological target implicated in a disease and (2) being evaluated for potential submission to the FDA for approval, whether in connection with preclinical or clinical studies. (*See* D.I. 1, Ex. 13 at 5 ("Our business, research, and clinical

efforts are to develop and advance our Fc technologies and our portfolio of XmAb drug candidates in oncology and other serious diseases."); *id.* at 7-10 (listing biological targets).) Under Supreme Court and Federal Circuit precedent, this is safe harbor-protected activity. *Integra Lifesciences I, Ltd. v. Merck KGaA*, 496 F.3d 1334, 1341 (Fed. Cir. 2007) (holding that the safe harbor applies whenever there is a "reasonable basis for identifying the compounds as working through a particular biological process to produce a particular physiological effect"); *cf. Merck*, 545 U.S. at 205-06 (excluding from safe harbor "basic scientific research on a particular compound, performed without the intent to develop a particular drug or a reasonable belief that the compound will cause the sort of physiological effect the researcher intends to induce").

2. Merus's Bald "Early Discovery" Assertions Cannot Save Its Complaint

Merus's remaining allegations center on its contention that certain alleged activities constitute "early discovery and preclinical generation of antibodies." (D.I. 1 at ¶ 66; *see also id.* at ¶ 69 (referring to "use during the antibody generation and discovery process, which occurs long before any antibody is selected as a possible candidate for regulatory review and/or approval").) This transparent attempt to sidestep the safe harbor fails.

As an initial matter, Merus does not identify any support for these naked assertions. For example, Merus does not identify a single example of any such

"early discovery and preclinical" activities by Xencor (*id.* at ¶ 65), let alone articulate how such activities could infringe the '859 and '286 patents.[6] Because this Court is "not required to credit bald assertions or legal conclusions improperly alleged in the complaint," these allegations should be disregarded. *See, e.g.*, *Rockefeller*, 311 F.3d at 216.

Even if the Court were to consider these allegations, they do not amount to a plausible claim of infringement because the underlying activities are protected by the safe harbor. As explained above, the Supreme Court has made clear that a broad range of preclinical and clinical studies—both of which are required for FDA approval (D.I. 1, Ex. 13 at 22)—is covered by the safe harbor. *Merck*, 545 U.S. at 202-03 (holding that safe harbor "includes preclinical studies of patented compounds that are appropriate for submission to the FDA in the regulatory process," and that such preclinical data includes "pharmacological, toxicological, pharmacokinetic, and biological qualities of the drug in animals"). The Court held that even "preclinical *in vitro* and *in vivo* studies" that are reasonably related to an FDA submission are covered. *Id.* at 203. Accordingly, it does not matter whether a compound is actually "selected as a possible candidate for regulatory

[6] These allegations are also repeated verbatim with respect to the '695 patent, discussed below, which further evinces their conclusory nature.

review" (D.I. 1 at ¶ 69), as Merus alleges. *See, e.g.*, *Integra*, 496 F.3d at 1341 (explaining that safe harbor applies to "experiments with rejected candidates").

This is because the safe harbor applies whenever there is a "reasonable basis for identifying the compounds as working through a particular biological process to produce a particular physiological effect." *Id.* As noted in Merus's Complaint, Xencor's antibodies are designed for specific targets, including "PD-L1, PD-L2, and/or CD28." (D.I. 1 at ¶ 53.) Each are known targets for cancer therapeutics. (D.I. 1 at ¶ 33 (citing U.S. Patent Publication No. 2023/0383012).) As noted above (*supra* at III.B), Xencor is also investigating antibodies targeting "ENPP3," "B7-H3," "CLDN6," "CD20," "STEAP1," "Claudin-18.2," and "PSMA" as cancer therapeutics. (D.I. 1, Ex. 13 at 7-10.) In short, Merus has not adequately pleaded that Xencor has undertaken any allegedly infringing activities that do not involve "identifying . . . compounds as working through a particular biological process to produce a particular physiological effect." *Integra*, 496 F.3d at 1341. Accordingly, its infringement allegations relating to the '859 and '286 patents should be dismissed.

B. The Section 271(e)(1) Safe Harbor Protects the Activities Accused of Infringing the '695 Patent

The same is true with respect to Merus's infringement allegations concerning the '695 patent. The claims of that patent (referred to by Merus as the "Common Light Chain Patent") are likewise directed to "method[s] of

obtaining an antibody" (D.I. 1 at ¶ 79), and thus are also safe harbor-eligible. *Amgen*, 944 F.3d at 1338 (finding safe harbor protection for method of making drug substance). And all of the accused activities relating to the '695 patent are reasonably related to the submission of information to the FDA.

Merus's allegations regarding the '695 patent concern third-party Biocytogen's RenLite® mouse. (D.I. 1 at ¶ 36.) As explained above (*supra* at III.C), Xencor's work with this technology was limited and quickly discontinued. Merus's only specific allegation concerns Xencor's supposed use of the RenLite® mouse (as allegedly described in U.S. Patent Application Publication No. 2023/0383012) "to make multispecific antibodies that bind to, *inter alia*, PD-L1, PD-L2, and/or CD28." (D.I. 1 at ¶ 33; *see also* at ¶ 49 (acknowledging that the RenLite® mouse was used to generate "antigen-specific antibodies"), ¶ 53 (same), ¶ 46 ("Xencor has immunized RenLite mice with antigens and obtained from the RenLite mice populations of B cells that produce antibodies specific to those antigens.").) As with the '859 and '286 patents, these activities directed towards antibodies with specific therapeutic targets qualify for the Section 271(e)(1) safe harbor. *See, e.g.*, *Integra*, 496 F.3d at 1341 (protecting activity involving "reasonable basis for identifying the compounds as working through a particular biological process to produce a particular physiological effect").

Merus's remaining allegations are, once again, unsupported and should not be credited by this Court. Specifically, Merus alleges that "Xencor's infringing use of Merus' Common Light Chain Patent includes use during the antibody generation and discovery process, which occurs long before any antibody is selected as a possible candidate for regulatory review and/or approval." (D.I. 1 at ¶ 54.) This is the identical language Merus included with respect to the '859 and '286 patents. For the same reasons explained above (*supra* at V.A.2), this conclusory allegation does not avoid the safe harbor.

C. The Court Should Dismiss Merus's Complaint with Prejudice Because Any Amendment Would Be Futile

The Court should dismiss the Complaint with prejudice rather than allow any proposed amendment. Leave to amend a complaint may be denied where amendment would be "futile," Fed. R. Civ. P. 15(a), which occurs where the complaint, even if amended, would fail to state a claim on which relief could be granted, *see Grayson v. Mayview State Hosp.*, 293 F.3d 103, 113 (3d Cir. 2002).

This is precisely the case here, as there are no facts Merus could plead that would avoid dismissal. For instance, even if Merus were to assert 28 U.S.C. § 2201 declaratory judgment claims based on potential future product sales, its Complaint would still be subject to dismissal pursuant to Rule 12(b)(1). *Juno Therapeutics, Inc. v. Kite Pharma, Inc.*, No. 16-1243, 2017 WL 2559735, at *1-3

(D. Del. June 13, 2017) (explaining that, in addition to "conflict[ing] with the purpose of the Safe Harbor Provision of the Patent Act," such a claim would fail the immediacy prong of declaratory judgment jurisdiction given uncertain FDA approval); *Clarus Therapeutics, Inc. v. Lipocine, Inc.*, No. 15-1004, 2016 WL 5868065, at *4 (D. Del. Oct. 6, 2016) (declining to exercise declaratory judgment jurisdiction "where Defendant is not currently infringing, has not engaged in any product marketing, and has not solicited orders," which "would . . . allow Plaintiff to circumvent the Safe Harbor Provision"). Nor is there any basis to allege that Xencor is stockpiling products for eventual sale. *See Amgen Inc. v. Hospira, Inc.*, 336 F. Supp. 3d 333, 345 (D. Del. 2018), *aff'd*, 944 F.3d 1327 (Fed. Cir. 2019) (holding that certain commercial use batches were not safe harbor-protected).

Here, Xencor is not engaged in any potentially infringing activity, but only research and development activities that are protected by the Section 271(e)(1) safe harbor.

VI. CONCLUSION

Even taking the allegations in Merus's Complaint as true, the alleged infringing conduct falls squarely within the statutory safe harbor exemption. For the reasons explained above, Xencor respectfully requests that the Court dismiss the Complaint with prejudice pursuant to Rule 12(b)(6).

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WORD COUNT CERTIFICATION

The undersigned hereby certifies that Defendant Xencor Inc.'s Opening Brief in Support of its Motion Dismiss Pursuant to Federal Rule of Civil Procedure 12(b)(6) contains 4,951 words (exclusive of the title, tables of authorities and contents, caption, and signature block) in Times New Roman 14-point font, counted using Microsoft Word's word count feature.

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CERTIFICATE OF SERVICE

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