IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

MERUS N.V.,	)	
	)	
Plaintiff,	)	
	)	C.A. No. _____
v.	)	
	)	
XENCOR, INC.,	)	
	)	
Defendant.	)	

COMPLAINT

Plaintiff Merus N.V. ("Merus"), for its Complaint against Defendant Xencor, Inc. ("Xencor" or "Defendant"), hereby alleges as follows.

INTRODUCTION

1. Merus brings this action for patent infringement against Xencor to protect Merus' pioneering inventions – which have enabled the creation and development of a new class of treatments for cancer and other serious diseases – and to hold Xencor accountable for the damages and other harms to Merus caused by Xencor's infringement.

THE PARTIES

2. Merus is a company organized and existing under the laws of the Netherlands, with a principal place of business at Uppsalalaan 17, 3584 CT Utrecht, the Netherlands. On May 19, 2016, Merus B.V., a private company with limited liability (besloten vennootschap met beperkte aansprakelijkheid) under Dutch law, converted into Merus N.V., a limited liability company (naamloze vennootschap) under Dutch law, and became publicly listed on the Nasdaq Global Market. As a B.V. and N.V, Merus has at all times been and remained the same company with the same ownership rights in its intellectual property, including the patents asserted in this Complaint.

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3. On information and belief, Xencor is a corporation organized and existing under the laws of Delaware, with a principal place of business at 465 North Halstead Street, Suite 200, Pasadena, California.

NATURE OF THE ACTION

4. This is a civil action for patent infringement involving three United States patents: U.S. Patent No. 9,944,695 ("the '695 patent" or "the Common Light Chain Patent") and U.S. Patent No. 9,358,286 ("the '286 patent") and U.S. Patent No. 11,926,859 ("the '859 patent") (the '286 and '859 patents, collectively, "the Heterodimerization Patents").

5. This action is based upon the Patent Laws of the United States, 35 U.S.C. § 1 *et seq.* It arises from, *inter alia*, Xencor's infringing manufacture, use, offer for sale, sale, and/or importation of common light chain antibodies in and/or into the United States, all before the expiration of the Common Light Chain Patent. This action also arises from Xencor's infringing manufacture, use, offer for sale, sale, and/or importation of heterodimeric antibodies in and/or into the United States, all before the expiration of the Heterodimerization Patents.

JURISDICTION AND VENUE

6. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

7. This Court has personal jurisdiction over Xencor because, *inter alia*, Xencor is a Delaware corporation.

8. Venue is proper in this Court pursuant to 28 U.S.C. § 1400(b) because, *inter alia*, Xencor is a Delaware corporation.

ASSERTED PATENTS

A. The Common Light Chain Patent

9. On April 17, 2018, the U.S. Patent and Trademark Office ("USPTO") duly and legally issued the '695 patent, titled "Antibody Producing Non-Human Mammals," to Merus as assignee. Merus has been, and continues to be, the sole owner of the '695 patent, including the right to sue and recover damages for any infringement of that patent. A copy of the '695 patent is attached hereto as Exhibit 1.

B. The Heterodimerization Patents

10. On June 7, 2016, the USPTO duly and legally issued the '286 patent, titled "Methods And Means For The Production Of Ig-Like Molecules," to Merus as assignee. Merus has been, and continues to be, the sole owner of the '286 patent, including the right to sue and recover damages for any infringement of that patent. A copy of the '286 patent is attached hereto as Exhibit 2.

11. On March 12, 2024, the USPTO duly and legally issued the '859 patent, titled "Methods And Means For The Production Of Ig-Like Molecules," to Merus as assignee. Merus has been, and continues to be, the sole owner of the '859 patent, including the right to sue and recover damages for any infringement of that patent. A copy of the '859 patent is attached hereto as Exhibit 3.

ACTS GIVING RISE TO THIS ACTION

A. Background

12. Antibodies are some of the most important treatments of cancer. Antibodies can target antigens that are either unique to, or overexpressed by, a tumor cell. Antibodies can cause tumor cell death through a variety of mechanisms. Among other things, antibodies are unique in

their ability to kill tumor cells directly while simultaneously engaging the host's own immune system to stimulate a long-lasting response against the tumor.

13. Antibody engineering innovations have made it possible to generate "human" antibodies through the use of either transgenic animals or *in vitro* "display" systems. The availability of such "human" antibodies has led to antibody-based therapeutics that carry a lower risk for inducing unwanted immune responses in humans.

14. A distinct advantage of antibody-based therapies is that they have the potential for high target specificity and a long half-life, while minimizing toxicity in the host. The targeted nature of antibody-based therapies is a feature that distinguishes them from conventional cancer treatments such as chemotherapy.

B. Merus' Pioneering, Patented Inventions

15. As naturally produced by the human immune system, and as historically developed as biopharmaceuticals, antibodies are monospecific, meaning the antibody binds to one particular target antigen. A number of monospecific antibody-based cancer therapies have been developed over the last twenty years. These therapies, however, are limited to binding to a single target. Bispecific and trispecific antibodies have garnered attention as the next generation of antibody-based therapies for treating cancers like hematologic malignancies and solid tumors. Bispecific antibodies are antibodies with two different binding domains, while trispecific antibodies contain three different binding domains. These therapeutics can be directed to two or three different epitopes of the same antigen or to different epitopes of different antigens.

16. Bispecific and trispecific antibodies offer important advantages over monospecific antibodies. For example, they can elicit superior cytotoxic effects due to the matched targeting of two or three different antigens, thereby eradicating tumor cells more precisely and effectively

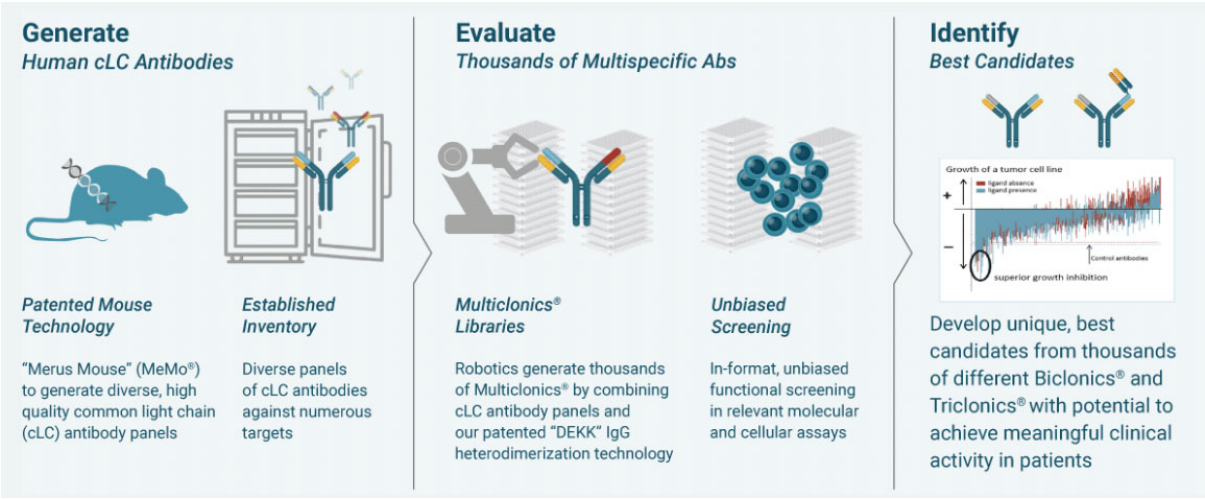
and/or by engaging the human immune system to bring it into contact with a tumor cell to kill in ways that a monospecific antibody cannot.

17. Merus is a clinical-stage oncology company committed to advancing leading-edge, targeted antibody treatments to address the unmet needs of patients with various types of cancer. In pursuit of this goal, Merus has pioneered multiple advances in the creation and development of novel bispecific and trispecific antibodies for therapeutic use.

18. As part of its pioneering advances, Merus invented, developed, and commercialized the ***Me***rus ***Mo***use, referred to as MeMo®, and technology to identify and use the biological products of MeMo® to create and develop novel bispecific and trispecific antibodies. Merus has used and continues to use these pioneering advances in, *inter alia*, the United States. Certain of these advances relate to Merus' Common Light Chain Patent.

19. MeMo® is a common light chain transgenic mouse useful in the process for generating novel, fully human bispecific and trispecific antibodies. Use of the patented MeMo® helps drive Merus' success in creating and developing novel bispecific and trispecific antibodies by using a single immunoglobulin light chain, combined with diversified heavy chains, to facilitate the creation of diverse collections of novel, high-affinity human antibodies.

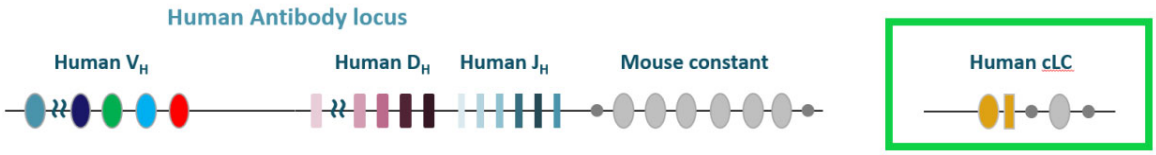
20. As reflected below, some of Merus' pioneering patented advances are summarized on the Merus website, which makes clear that Merus' MeMo® and related technology is patented.



See https://merus.nl/technology/multiclonics-platform/.

21. Merus' patented common light chain technology represents a significant advance in the field and allows for the efficient creation and development of superior therapeutics that combine the benefits of fully human immunoglobulin monoclonal antibodies with the ability to simultaneously bind multiple targets.

22. As depicted below, Merus' patented MeMo® integrates a common human immunoglobulin light chain, which combines with diversified heavy chains.



23. The common light chain format of the patented MeMo® is important in creating and developing novel multispecific antibodies because it allows single cell expression without mispairing of the variable regions of the heavy and light chains. Without a common light chain, a host cell with two different heavy chains and two different light chains will make ten different species of antibodies, with only one of those the desired outcome. With a common light chain, the

host cell makes three species of antibodies. To obtain essentially one species of bispecific antibody from two heavy chains and one light chain, Merus innovated the field still further.

24. As part of Merus' pioneering advances, Merus invented, developed, and commercialized an improved heterodimerization technology. Certain of these advances relate to Merus' Heterodimerization Patents.

25. Merus' patented heterodimerization technology allows for preferential and stable pairing of different antibody heavy chains to create a desired heterodimer, including as part of forming a multispecific antibody of interest. Merus' patented heterodimerization is achieved through certain electrical charge interactions, whereby opposite charges on antibody constant regions drive the preferential and stable pairing of the desired heavy chains.

26. For example, Merus' patented heterodimerization technology can comprise one Fc variant pair with substitution S364K in one heavy chain combined with substitution L368D in the other. The resulting domain yields a stable Fc conformation that is similar to that found in a wild-type IgG. Merus' patented heterodimerization technology can use these and other amino acid changes to generate bispecific antibodies that are stable and that can be readily produced and purified at industrial scale, with a standard mammalian cell culture platform and a routine purification protocol.

27. With its patented common light chain technology and patented heterodimerization technology, Merus has pioneered the field to develop, *inter alia*, diverse heavy chains paired to a common light chain, where the two heavy chains heterodimerize, such that a host cell can produce essentially a single multispecific antibody of interest, thus Merus' name, which in Latin means "pure."

C. Merus' Patented Inventions Are Commercially Valuable

28. Merus has used its pioneering, patented inventions to create and develop a broad pipeline of its own novel, fully human, common light chain heterodimeric bispecific and trispecific antibodies for cancer therapy, as well as those it has licensed. As one example, the U.S. Food & Drug Administration ("FDA") recently accepted for review a Biologics License Application ("BLA") for Merus' bispecific antibody zenocutuzumab ("Zeno") for the treatment of non-small cell lung and pancreatic cancers driven by NRG1 fusion. Prior to accepting the Zeno BLA for review, the FDA granted Zeno a Breakthrough Therapy Designation ("BTD") for two different indications. As another example, the FDA recently granted Merus' bispecific antibody petosemtamab ("Peto") a BTD for certain kinds of recurrent or metastatic head and neck squamous cell carcinoma.

29. Elements of Zeno and Peto, as well as their creation and production, are covered by Merus' Common Light Chain Patent and Heterodimerization Patents.

30. Merus' pipeline of novel, fully-human, common light chain heterodimeric bispecific and trispecific antibodies is extremely valuable and gives Merus a commercial advantage over competitors that do not have the benefit of using Merus' patented technologies to develop competing bispecific and trispecific antibody-based therapies.

31. Given the pioneering status of Merus' common light chain and heterodimerization technologies, leading pharmaceutical and biotechnology companies, as well as academic institutions, have sought to collaborate with Merus to create and develop novel bispecific and trispecific antibodies as treatment candidates. For example, in December 2016, Merus and Incyte Corporation entered into a strategic global collaboration agreement to use patented Merus technologies to create and develop novel bispecific antibodies. Similarly, in January 2021, Merus

and Eli Lilly and Company entered into a research collaboration agreement to use patented Merus technologies to create and develop novel bispecific antibodies. Most recently, in March 2024, Merus and Gilead Sciences, Inc. entered into a collaboration on the use of Merus' proprietary platform to develop trispecific antibody products. These and other collaborations are extremely valuable to Merus, both financially and otherwise. Among other things, such collaborations highlight Merus' status as a pioneer in the bispecific and trispecific antibody space and the sole non-infringing source of the common light chain and heterodimerization technologies covered by the Common Light Chain Patent and the Heterodimerization Patents.

D. Xencor's Infringement Of Merus' Common Light Chain Patent

32. Xencor has infringed Merus' Common Light Chain Patent, and continues to infringe the Common Light Chain Patent, by practicing the claimed methods for obtaining antibodies that bind to an antigen.

33. For example, 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.

34. On information and belief, Xencor has collaborated with Biocytogen Pharmaceuticals (Beijing) Co., Ltd. and Biocytogen Boston Corp. (collectively, "Biocytogen") to obtain and/or use the RenLite mouse.

35. On information and belief, Xencor entered into an agreement with Biocytogen on October 27, 2020, to license the RenLite mouse for Xencor's use. *See* Ex. 4, Biocytogen Enters

into RenMab™/RenLite™ Licensing Agreement with Xencor, https://biocytogen.com/biocytogen-enters-into-renmab-renlite-licensing-agreement-with-xencor/. Dr. John Desjarlais, Xencor's Chief Scientific Officer, stated that he "anticipate[d] the RenMab and RenLite platforms will extend [Xencor's] bispecific antibody discovery." *See id*.

36. On information and belief, Xencor entered into its agreement with Biocytogen with full knowledge that Merus' MeMo® was patented. On information and belief, Xencor also entered into its agreement with Biocytogen with full knowledge the RenLite mouse was a copy of Merus' MeMo® that infringed Merus' Common Light Chain Patent. For example, on information and belief, one or more scientists at Xencor was aware of the Common Light Chain Patent and that use of the RenLite mouse infringed that patent when Xencor entered into its agreement with Biocytogen.

37. According to Biocytogen, the RenLite mouse is a "platform for bispecific antibody discovery." *See* Ex. 5, Humanized Antibody Mice, https://web.archive.org/web/20211203231558/https://biocytogen.com/antibody-discovery/our-platform/humanized-antibody-mice/ ("Humanized Antibody Mice Website").

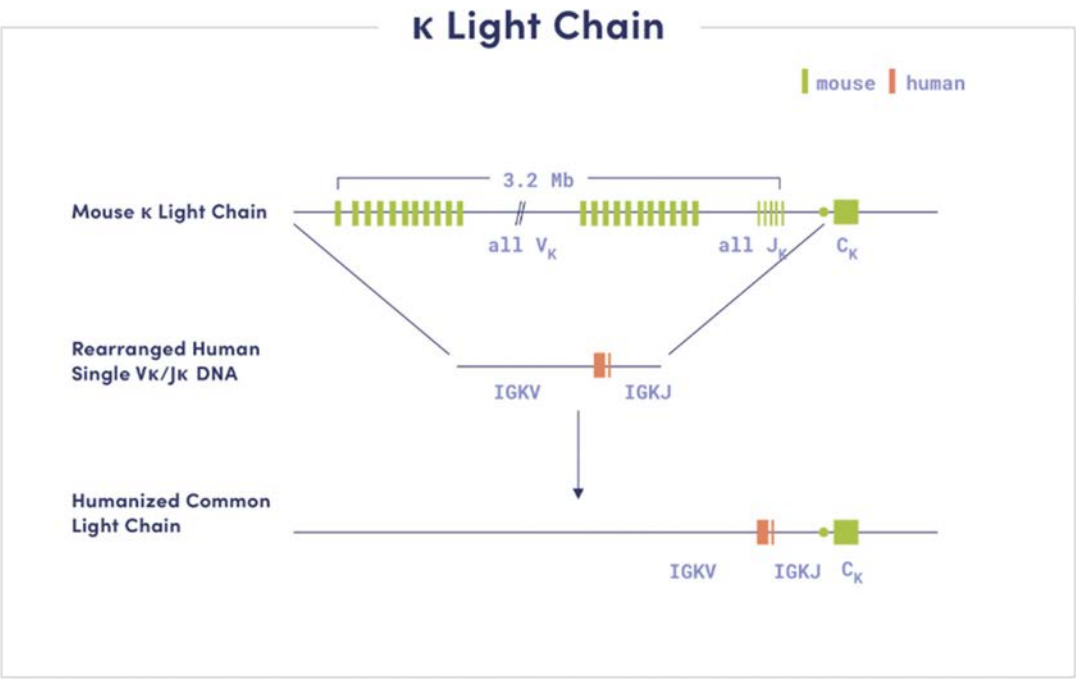
38. According to Biocytogen, the RenLite mouse is a transgenic mouse designed to be immunized with antigens and generate B cells that produce antibodies that bind to those antigens as part of a process to generate bispecific antibodies. *See* Ex. 6, WO 2021/244522 A1 ("the '522 Application").

39. According to Biocytogen, the "RenLite™ mouse carries full human heavy chain VDJ loci and a fixed common human light chain VJ gene." *See* Ex. 7, AACR 2021: Advancing Bispecific Antibody Discovery using a Common Light Chain Immunoglobulin Humanized Mouse, https://biocytogen.com/posters/aacr-2021-advancing-bispecific-antibody-discovery-

using-a-common-light-chain-immunoglobulin-humanized-mouse/ ("AACR 2021 Poster"). As a result, "[t]he derived antibodies share the same light chain with different heavy chain variable domain[s]." *See id.*

40. On information and belief, the genome of the RenLite mouse contains a transgene in which a human immunoglobulin light chain germline V gene segment is fused to a human immunoglobulin light chain germline J gene segment to encode a rearranged human immunoglobulin light chain variable region, with no mutation resulting from this fusion. *See, e.g.*, *id.* ("[The] RenLite™ mouse carries . . . a fixed common human light chain VJ gene."); Ex. 5, Humanized Antibody Mice Website ("[T]he RenLite™ model allows for fully human antibody production with maximum developability for the recognition of multiple antigens."); Ex. 6, '522 Application at Example 7.

41. Biocytogen depicts the fused human V/J gene segments of the RenLite mouse common light chain variable region on its website, a capture of which is shown below:



See Ex. 5, Humanized Antibody Mice Website; *see also* Ex. 8, RenLite Mouse, https://renmab.com/renlite ("RenLite Mouse Website").

42. Biocytogen provides further detail regarding the fused human V/J gene segments of the RenLite mouse common light chain variable region in the '522 Application. For example, SEQ ID NO: 38 in the '522 Application discloses an example of a human light chain variable region assembled by directly joining human IGKV3-39 (encoding protein segment in yellow) to human IGKJ4 (encoding protein segment in blue).

Amino acid sequence of common light chain VL encoded by human IGKV1-39/IGKJ4 (SEQ ID NO: 38)
DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTF
GGGTKVEIK

Ex. 6, '522 Application at Figure 32 (SEQ ID NO: 38) (highlighting added).

43. On information and belief, the transgene that contains the fused V/J gene segments in the RenLite mouse lacks an intronic light chain enhancer. For example, the '522 Application discloses SEQ ID NO: 35 (rearranged human IGKV1-39+J4), in which no intron enhancer is identified. *Id*. at 74. SEQ ID NO: 35 is stated to have 3012 base pairs. *Id*. The first 2000 base pairs are identified as "V1-39 Promoter" and are directly and sequentially followed by a directly joined VJ region, identified as "V1-39" and "J4", and then a region identified as "Human 3' UTR sequence."

Rearranged human IGKV1-39+J4 nucleic acid sequence 3012bp (SEQ ID NO: 35)

V1-39 Promoter	1-2000	
V1-39	2001-2475	(the last 2 nucleotides in V1-39 are deleted)
J4	2476-2512	(the first nucleotide in J4 is deleted)
Human 3' UTR sequence	2513-3012	

Id. No intron enhancer is identified, despite all of the base pairs being accounted for in SEQ ID NO: 35. *See id*.

44. A standard BLAST comparison confirms that there is no intron enhancer in SEQ ID NO: 35.

45. According to Biocytogen, the transgene that contains the fused V/J gene segments in the RenLite mouse is operatively linked to an endogenous mouse light chain constant region gene segment. *See, e.g.*, Ex. 7, AACR 2021 Poster ("The murine constant regions are retained for normal B cell development."); Ex. 8, RenLite Mouse Website; Ex. 5, Humanized Antibody Mice Website.

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.

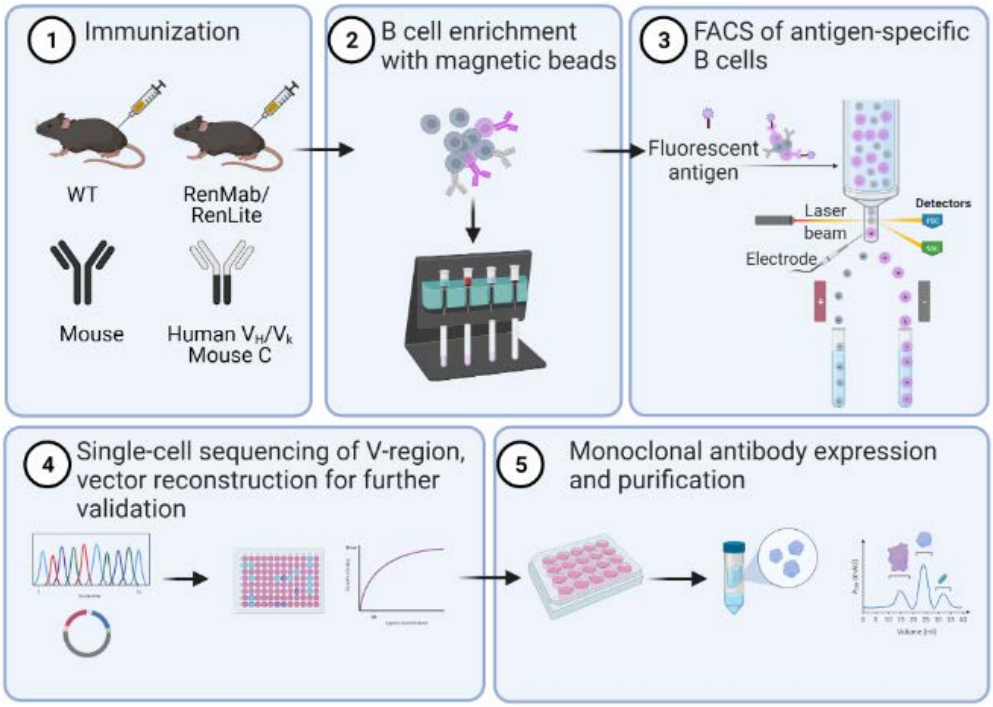
48. According to Biocytogen, antibodies generated by RenLite mice undergo natural selection, differentiation, and affinity maturation *in vivo* utilizing a human heavy chain repertoire. *See, e.g.*, Ex. 7, AACR 2021 Poster; Ex. 6, '522 Application at 63 ("The genetically engineered animal in various embodiments when immunized with an antigen of interest generates B cells that exhibit a diversity of rearrangements of human immunoglobulin heavy chain variable regions that express and function with a limited number (*e.g.*, 1, 2, 3, 4, 5) of rearranged light chains.").

49. On information and belief, Biocytogen provides instructions to its customers and licensees on how to create and obtain antigen-specific antibodies using RenLite mice. *See* Ex. 6, '522 Application; *see also* Ex. 9, Antibody Discovery Services, https://web.archive.org/web/20220331024554/https://biocytogen.com/antibody-discovery/.

50. For example, Biocytogen's website has described FACS-based B cell isolation, where antibody-producing B cells from the RenLite mouse are first screened for antigen binding. Biocytogen uses single-cell sequencing of the variable region and reconstructs vectors for further

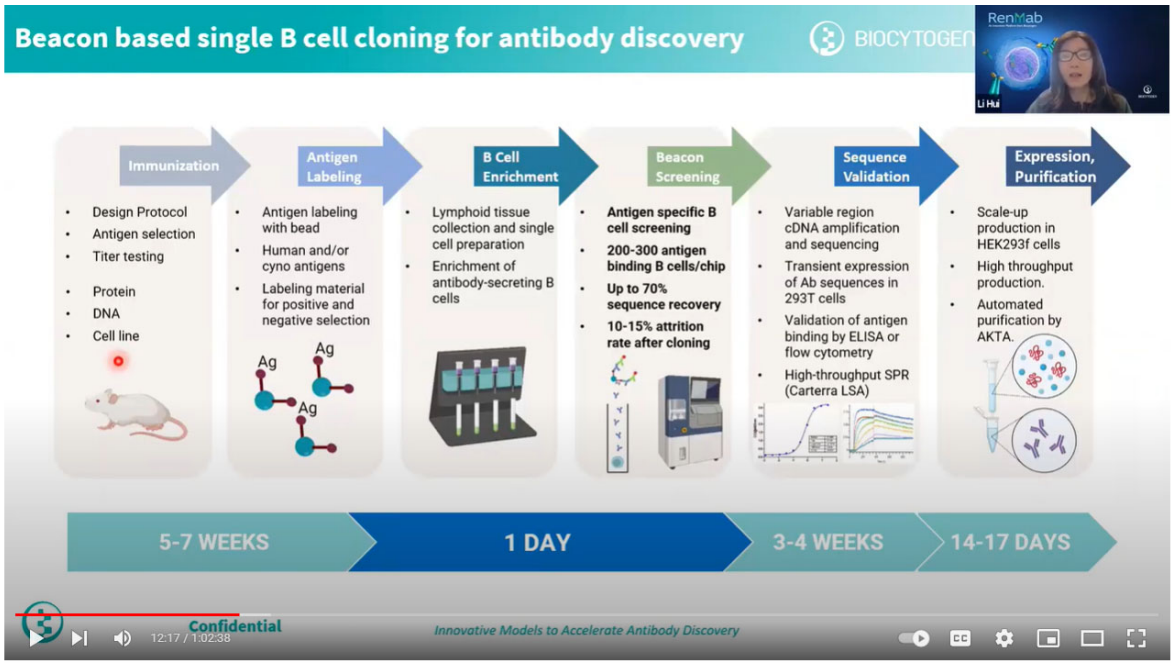
validation. The variable regions are then integrated into a recombinant cell, and the recombinant cell is then used to express the antigen-binding antibodies containing the variable regions identified from the RenLite mouse.

51. Biocytogen depicts the steps of this process on its website as follows:



See Ex. 10, FACS-based B Cell Isolation, https://web.archive.org/web/20230518065933/https://biocytogen.com/antibody-discovery/our-platform/facs/; *see also* Ex. 6, '522 Application.

52. On information and belief, Biocytogen provides additional information to its customers and licensees regarding how to create and obtain antigen-specific antibodies using RenLite mice. Biocytogen has included such instructions in, for example, webinars.



See Webinar: Generation and discovery of high affinity antibodies, https://www.youtube.com/watch?v=XLdHmSdz_cU ("Beacon System Webinar"); *see also* Ex. 11, Beacon Single B Cell Cloning, https://web.archive.org/web/20220520101617/https://biocytogen.com/antibody-discovery/our-platform/beacon-single-b-cell-cloning/.

53. On information and belief, Xencor uses the same or equivalent processes as those described by Biocytogen on its website and other publicly available sources to create and obtain antigen-specific antibodies using RenLite mice. For example, in the '012 Application, Xencor describes its use of RenLite mice and the biological products of RenLite mice to make multispecific antibodies that bind to, *inter alia*, PD-L1, PD-L2, and/or CD28. In doing so, Xencor has utilized Merus' patented common light chain technology and infringed Merus' Common Light Chain Patent.

54. 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.

55. Merus is entitled to damages and other relief for Xencor's infringing use of Merus' Common Light Chain Patent during its work to create and develop its own RenLite mouse-based common light chain antibodies.

56. Merus is also entitled to damages and other relief for Xencor's infringing use of Merus' Common Light Chain Patent during its work to create and develop RenLite mouse-derived common light chain antibodies with partners and/or collaborators, including with Biocytogen.

57. Each of Xencor's infringing uses of Merus' patented common light chain technology is a lost sale, lost licensing opportunity, or other damage to Merus, with resulting lost profits, lost royalties, and other damages to Merus. These lost profits, lost royalties, and other damages to Merus include lost future milestone and royalty payments on common light chain antibody products that would not exist but for Xencor's infringing use of Merus' Common Light Chain Patent.

E. Xencor's Infringement Of Merus' Heterodimerization Patents

58. In addition to infringing Merus' Common Light Chain Patent, Xencor has also infringed, and continues to infringe, Merus' Heterodimerization Patents, including during Xencor's independent and partnered or collaborative heterodimeric antibody creation and development work.

59. Xencor disclosed in its Form 10-K SEC filings for, *inter alia*, 2022 and 2023 that it was aware of Merus' patents and uses Merus' patented technology. *See* Exs. 12 and 13.

60. Specifically, Xencor stated in its Form 10-K filing for 2023 that: "For example, we are aware of issued patents owned by Merus B.V. (Merus) that may relate to and claim components of our bispecific antibody product candidates and partnered bispecific product candidates, including plamotamab, vudalimab and XmAb819 will putatively expire in 2033 . . . . We believe there exists reasonable arguments of invalidity for the Merus patents; however, we cannot assure that if challenged in litigation for infringement of these patents that we would prevail." Ex. 13, 2023 Xencor Form 10-K at 36.

61. The Merus patents referred to by Xencor in its Form 10-K SEC filings include Merus' Heterodimerization Patents.

62. In Merus' patented heterodimerization technology, certain opposite charges on antibody constant regions drive preferential pairing of different antibody heavy chains to create stable bispecific antibodies. *See* Merus Multiclonics, https://merus.nl/technology/multiclonics-platform/.

63. On information and belief, Xencor uses Merus' patented heterodimerization technology to take advantage of certain electrostatic interactions between the constant regions and make stable bispecific antibodies. *See* Ex. 14, Moore *et al.*, *A robust heterodimeric Fc platform engineered for efficient development of bispecific antibodies of multiple formats*, Methods 2019; 154:38 ("Moore Paper") at 48 ("Our own solution could be called a hybrid of these two approaches in that we introduce a modest change in both volume and charge."). 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 39 ("In this paper, we present a robust heterodimeric Fc, called the XmAb® bispecific platform, engineered for efficient development of bispecific antibodies and Fc

fusions of multiple formats."); *see also, e.g.*, https://xencor.com/pipeline/vudalimab/; https://xencor.com/pipeline/xmab819/.

64. Xencor describes the substitutions that are involved in its so-called XmAb technology: "Our E357Q/S364K-L368D/K370S variant results in a CH3 region that remained more stable than that of native IgG4." *See* Ex. 14, Moore Paper at 48. Xencor describes the variant pairing for this heterodimer and states that chain 1 has the E357Q/S364K substitution while chain 2 has the L368D/K370S substitution. *Id*. at 42, Table 1.

65. Many of Xencor's United States Patent Application Publications describe these same substitutions, including as used in early discovery and preclinical work. For example, U.S. Patent Application Publication No. 2022/0135684 (the "'684 Publication") at Figure 3B discloses Monomer 1 as including L368D/K370S and Monomer 2 as including S364K/E357Q.

66. The Xencor XmAb bispecific platform substitution at position 364 involves substituting a serine for a lysine, thereby changing the charge of the amino acid at this position from neutral to positive. The platform substitution at position 368 involves substituting a leucine for an aspartic acid, thereby changing the charge of the amino acid at this position from neutral to negative. 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.

67. 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.

68. Xencor highlights the importance and value of its use of Merus' patented heterodimerization technology on its website, stating that: "The plug-and-play nature of Xencor's

XmAb technology enables the rapid creation of more powerful, more effective antibodies and cytokines by simply changing a few amino acids in an antibody's Fc domain to the amino acids identified by our structure-based design." *See* Partnering, https://xencor.com/about-us/#partnering.

69. 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.

70. Merus is entitled to damages and other relief for Xencor's infringing use of Merus' Heterodimerization Patents during its work to generate and develop its own heterodimeric antibodies.

71. Merus is also entitled to damages and other relief for Xencor's infringing use of Merus' Heterodimerization Patents during its work to generate and develop heterodimeric antibodies with partners and/or collaborators.

72. Each of Xencor's infringing uses of Merus' patented heterodimerization technology and/or patented heterodimeric antibodies is a lost sale, lost licensing opportunity, or other damage to Merus, with resulting lost profits, lost royalties, and other damages to Merus. These lost profits, lost royalties, and other damages to Merus include lost future milestone and royalty payments on antibody products that would not exist but for Xencor's infringing use of Merus' Heterodimerization Patents.

73. On information and belief, Xencor has been aware of Merus' Heterodimerization Patents at all relevant times and has willfully infringed those patents. For example, Xencor has disclosed in multiple Form 10-K filings that it was aware of Merus' Heterodimerization Patents and is using Merus' technology. *See, e.g.*, Ex. 12, 2022 Xencor Form 10-K at 37. As a further

example, the Moore Paper, which was authored by Xencor's employees and published in 2019, identifies multiple infringing uses of Merus' Heterodimerization Patents. *See generally* Ex. 14, Moore Paper. The Moore Paper also cites a 2017 paper authored by Merus employees titled "A new approach for generating bispecific antibodies based on a common light chain format and the stable architecture of human immunoglobulin G1." *Id.* at 47.

74. Xencor lists Merus as a competitor in the field of cancer drug development and the development of multispecific antibody platforms in its Form 10-K SEC filings, and has done so for years. *See, e.g.*, Ex. 12, 2022 Xencor Form 10-K at 20; Ex. 13, 2023 Xencor Form 10-K at 20-21.

75. Xencor received written notice of the Heterodimerization Patents from Merus by letter on May 15, 2024. In that letter, Merus requested an IP meeting with Xencor, which meeting took place on July 2, 2024. During the IP meeting, Merus explained to Xencor how it was infringing the Heterodimerization Patents. Despite Merus' written notice of the Heterodimerization Patents and explanation of Xencor's infringement of those patents during the IP meeting, Xencor has made no effort to avoid further infringement of the Heterodimerization Patents.

76. Xencor's knowing infringement of the Heterodimerization Patents has been, and continues to be, extensive and egregious. For example, during the July 2, 2024, IP meeting, Xencor admitted that it uses the infringing S364K and L368D amino acid substitutions throughout its portfolio of antibodies, from its early discovery work through its lead clinical candidate vudalimab.

COUNT I
INFRINGEMENT OF U.S. PATENT NO. 9,944,695

77. Merus hereby realleges and incorporates by reference each and every allegation set forth in this Complaint.

78. Xencor has infringed one or more claims of the ’695 patent, including but not limited to Claim 1, literally or under the doctrine of equivalents, by practicing the claimed methods for obtaining antibodies, including by using the RenLite mouse and biological products of the RenLite mouse.

79. Claim 1 of the ’695 patent recites:

> 1. A method of obtaining an antibody that binds to an antigen, the method comprising
>
> (a) immunizing a transgenic mouse with the antigen, wherein the genome of the transgenic mouse comprises a transgene comprising a human immunoglobulin light chain germline V gene segment fused to a human immunoglobulin light chain germline J gene segment such that there is no mutation due to said fusion, wherein the fused human V/J gene segments encode a rearranged human immunoglobulin light chain variable region and
>
> wherein the transgene is inserted by site-specific integration in the murine Rosa locus or wherein said transgene lacks the intronic light chain enhancer MoEκi or comprises a truncation of the transgene 3′ kappa enhancer or combination of these,
>
> wherein the transgene comprises a murine light chain constant region gene segment or is operatively linked to an endogenous mouse light chain constant region gene segment; and
>
> wherein if the transgene is inserted by site-specific integration in the murine Rosa locus, the transgene comprises a murine light chain constant region gene segment;
>
> (b) obtaining a population of B cells producing antigen specific antibodies from the transgenic mouse, wherein said antibodies comprise the rearranged human light chain immunoglobulin variable region encoded by the fused human V/J gene segments and a murine constant region paired with a heavy chain variable region encoded by a rearranged and somatically hypermutated VH gene; and
>
> wherein the population of B cells producing antigen specific antibodies from the transgenic mouse comprise a diversity of clonally unrelated rearranged immunoglobulin heavy chain variable regions that bind to the antigen;
>
> (c) isolating nucleic acid encoding a rearranged immunoglobulin heavy chain variable region from a B cell in said population;

> (d) expressing nucleic acids encoding the rearranged immunoglobulin heavy chain variable region and at least the rearranged human immunoglobulin light chain variable region in a host cell; and
>
> (e) thus obtaining an antibody which binds to the antigen.

80. Xencor has infringed at least Claim 1 of the ’695 patent, either literally or under the doctrine of equivalents, by practicing the claimed method for obtaining antibodies in the United States, including by using the RenLite mouse as the claimed transgenic mouse and obtaining a population of B cells from the RenLite mouse, and/or by importing into the United States and/or using in the United States antibodies obtained by practicing the claimed methods outside of the United States, including by using the RenLite mouse as the claimed transgenic mouse and obtaining a population of B cells from the RenLite mouse.

81. Biocytogen provided the RenLite mouse to Xencor and provided instructions to Xencor, including on its website and other publicly available sources, on how to obtain a population of B cells producing antigen specific antibodies after immunizing the RenLite mouse and otherwise infringe the claimed methods of the ’695 patent.

82. On information and belief, Xencor uses the same or equivalent processes described on Biocytogen’s website and other publicly available sources to make antigen-specific antibodies by using the RenLite mouse and biological products of the RenLite mouse.

83. Evidence of Xencor’s infringement of the ’695 patent in connection with its use of the RenLite mouse and biological products of the RenLite mouse includes, without limitation, the following known aspects of the RenLite mouse platform.

84. According to Biocytogen, the RenLite mouse is immunized with antigens as part of a process to generate antibodies. *See* Ex. 6, ’522 Application.

85. The RenLite mouse genome comprises a transgene that comprises a human immunoglobulin light chain germline V gene segment fused to a human immunoglobulin light chain germline J gene segment and the fused human V/J gene segments encode a rearranged human immunoglobulin light chain variable region, with no mutation resulting from this fusion. *See, e.g.*, Ex. 7, AACR 2021 Poster ("[The] RenLite™ mouse carries . . . a fixed common human light chain VJ gene."); Ex. 5, Humanized Antibody Mice Website ("[T]he RenLite™ model allows for fully human antibody production with maximum developability for the recognition of multiple antigens."); Ex. 6, '522 Application at Example 7.

86. Biocytogen's '522 Application and a standard BLAST comparison confirm that the RenLite mouse transgene lacks an intronic light chain enhancer, and thus lacks the specific intronic light chain enhancer MoEκi.

87. The RenLite mouse contains an endogenous mouse light chain constant region gene segment, which is operatively linked to the transgene. *See, e.g.*, Ex. 7, AACR 2021 Poster ("The murine constant regions are retained for normal B cell development."); Ex. 8, RenLite Mouse Website; Ex. 5, Humanized Antibody Mice Website.

88. On information and belief, after being immunized, the RenLite mouse generates a population of B cells producing antigen-specific antibodies, which population can be obtained from the mouse for further work.

89. The antibodies produced by the population of B cells obtained from the RenLite mouse have a rearranged human light chain immunoglobulin variable region encoded by the fused human V/J gene segments. *See* Ex. 5, Humanized Antibody Mice Website; Ex. 6, '522 Application at Figure 32 (SEQ ID NO: 38).

90. The population of B cells producing antigen specific antibodies from the RenLite mouse comprise a diversity of clonally unrelated rearranged immunoglobulin heavy chain variable regions that bind to the antigen. *See* Ex. 7, AACR 2021 Poster; *see also* Ex. 6, '522 Application at 63 ("The genetically engineered animal in various embodiments when immunized with an antigen of interest generates B cells that exhibit a diversity of rearrangements of human immunoglobulin heavy chain variable regions that express and function with a limited number (*e.g.*, 1, 2, 3, 4, 5) of rearranged light chains.").

91. Biocytogen describes isolating the nucleic acids encoding the rearranged immunoglobulin heavy chain variable region from a RenLite mouse B cell and subsequently expressing those nucleic acids with nucleic acids encoding the rearranged human immunoglobulin light chain variable region together in a host cell to obtain antibodies that bind to the antigen. *See* Ex. 11, Beacon Single B Cell Cloning, https://web.archive.org/web/20220520101617/https://biocytogen.com/antibody-discovery/our-platform/beacon-single-b-cell-cloning/.

92. As a result of Xencor's infringement of the '695 patent, Merus has suffered and continues to suffer damages. Merus is entitled to recover from Xencor the damages sustained as a result of Xencor's wrongful and infringing acts.

93. Merus has also suffered, and will continue to suffer, irreparable harm for which there is no remedy at law. This irreparable harm to Merus will continue until Xencor's infringing activities are enjoined by this Court.

COUNT II
INFRINGEMENT OF U.S. PATENT NO. 9,358,286

94. Merus hereby realleges and incorporates by reference each and every allegation set forth in this Complaint.

95. Xencor has infringed, and continues to infringe, one or more claims of the ’286 patent, including but not limited to Claim 1, literally or under the doctrine of equivalents, by using the claimed methods for producing heterodimeric antibodies and/or by making, using, offering to sell, and/or selling in the United States, and/or importing into the United States, the claimed heterodimeric antibodies.

96. Claim 1 of the ’286 patent recites:

> 1. A method for producing a heterodimeric antibody from a single cell, wherein said antibody comprises two heavy chains with CH3 domains that are capable of forming an interface, said method comprising:
>
> (a) providing a host cell comprising
>
> (i) a first nucleic acid molecule encoding a 1st antibody heavy chain comprising at least one substitution of a neutral amino acid residue in the CH3 domain by a positively charged amino acid residue, and
>
> (ii) a second nucleic acid molecule encoding a 2nd antibody heavy chain comprising at least one substitution of a neutral amino acid residue in the CH3 domain by a negatively charged amino acid residue;
>
> (b) culturing said host cell and allowing for expression of said two nucleic acid molecules to produce said 1st antibody heavy chain and said 2nd antibody heavy chain, wherein the at least one positively charged amino acid residue substituted in the CH3 domain of said 1st antibody heavy chain interacts with the at least one negatively charged amino acid residue substituted in the CH3 domain of said 2nd antibody heavy chain in the interface between said 1st and 2nd antibody heavy chains to produce a heterodimeric antibody; and
>
> (c) harvesting said heterodimeric antibody from the culture.

97. On information and belief, Xencor’s infringement of the ’286 patent includes both Xencor’s own heterodimeric antibody generation and development work and Xencor’s “partnered” heterodimeric antibody generation and development work, for which it is jointly and severally liable.

98. Xencor has and continues to infringe at least Claim 1 of the ’286 patent, either literally or under the doctrine of equivalents, by, for example, producing a heterodimeric antibody from a single cell that has two heavy chains with CH3 domains that are capable of forming an interface. Evidence of this includes, without limitation, the following aspects of Xencor’s so-called XmAb technology.

99. Xencor’s “XmAb” antibodies contain a Fc heterodimer with heavy chain 1 having a S364K substitution and heavy chain 2 having a L368D substitution. Ex. 14, Moore Paper at 42; *see also* ’684 Publication, Figure 3B. The substitution at position 364 on chain 1 involves substituting a serine for a lysine, thereby changing the charge of the amino acid at this position from neutral to positive. The substitution at position 368 on chain 2 involves substituting a leucine to aspartic acid, thereby changing the charge of the amino acid at this position from neutral to negative.

100. To make this heterodimer, Xencor expresses in a host cell heavy chain regions with these specific substitutions in the Fc domain, thereby providing a host cell comprising a first nucleic acid molecule encoding a 1st antibody heavy chain comprising at least one substitution of a neutral amino acid residue in the CH3 domain by a positively charged amino acid residue, and a second nucleic acid molecule encoding a 2nd antibody heavy chain comprising at least one substitution of a neutral amino acid residue in the CH3 domain by a negatively charged amino acid residue. Ex. 14, Moore Paper at 39.

101. Xencor cultures said host cell, which allows for expression of said two nucleic acid molecules to produce said heavy chains, wherein the at least one positively charged amino acid residue substituted in the CH3 domain of said 1st antibody heavy chain interacts with the at least

one negatively charged amino acid residue substituted in the CH3 domain of said 2nd to produce a heterodimeric antibody. *See id.* at 39-40.

102. Xencor then harvests the heterodimeric antibody from the cell culture. *See id.* at 40.

103. As a result of Xencor's infringement of the '286 patent, Merus has suffered and continues to suffer damages. Merus is entitled to recover from Xencor the damages sustained as a result of Xencor's patent infringement.

104. Merus has also suffered, and will continue to suffer, irreparable harm for which there is no remedy at law. This irreparable harm to Merus will continue until Xencor's infringing activities are enjoined by this Court.

105. Xencor's infringement of the '286 patent has at all relevant times been, and continues to be, willful, deliberate, intentional, and egregious.

106. Merus is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT III
INFRINGEMENT OF U.S. PATENT NO. 11,926,859

107. Merus hereby realleges and incorporates by reference each and every allegation set forth in this Complaint.

108. Xencor has infringed, and continues to infringe, one or more claims of the '859 patent, including but not limited to Claim 1, literally or under the doctrine of equivalents, by making, using, offering to sell, and/or selling in the United States, and/or importing into the United States, the claimed heterodimeric antibodies.

109. Claim 1 of the '859 patent recites:

> 1. A heterodimeric antibody comprising a first human CH3 domain comprising a positively charged amino acid residue at position 364 according to the EU

numbering system, and a second human CH3 domain comprising a negatively charged amino acid residue at position 368 according to the EU numbering system.

110. On information and belief, Xencor's infringement of the '859 patent includes both Xencor's own heterodimeric antibody generation and development work and Xencor's "partnered" heterodimeric antibody generation and development work, for which Xencor is jointly and severally liable.

111. Xencor infringes at least Claim 1 of the '859 patent, either literally or under the doctrine of equivalents, by producing heterodimeric antibodies comprising the claimed human CH3 domains. Evidence of this includes, without limitation, the following aspects of Xencor's so-called XmAb technology.

112. Xencor's "XmAb" antibodies contain a first antibody heavy chain with a CH3 domain having a lysine at position 364. Ex. 14, Moore Paper at 42; *see also* '684 Publication, Figure 3B. Lysine is a positively charged amino acid.

113. Xencor's "XmAb" antibodies contain a second antibody heavy chain with a CH3 domain having an aspartic acid at position 368. *Id*. Aspartic acid is a negatively charged amino acid.

114. As a result of Xencor's infringement of the '859 patent, Merus has suffered and continues to suffer damages. Merus is entitled to recover from Xencor the damages sustained as a result of Xencor's patent infringement.

115. Merus has also suffered, and will continue to suffer, irreparable harm for which there is no remedy at law. This irreparable harm to Merus will continue until Xencor's infringing activities are enjoined by this Court.

116. Xencor's infringement of the '859 patent has at all relevant times been, and continues to be, willful, deliberate, intentional, and egregious.

117. Merus is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff Merus prays for a judgment in its favor and against Xencor and respectfully requests the following relief:

A. A judgment that Xencor has infringed each of the Heterodimerization Patents and Common Light Chain Patent;

B. An order enjoining Xencor and Xencor's officers, agents, servants, employees, attorneys, and all other persons in active concert or participation therewith, from any further infringement of the Heterodimerization Patents and/or the Common Light Chain Patent;

C. An award of damages adequate to compensate for Xencor's infringement of the Heterodimerization Patents and Common Light Chain Patent, together with pre- and post-judgment interest and costs;

D. A declaration that Xencor's infringement of the Heterodimerization Patents has been willful, deliberate, intentional, and egregious, and an increase of the relevant award of damages to three times the amount found or assessed by the Court, in accordance with 35 U.S.C. § 284;

E. A finding that this case is exceptional under 35 U.S.C. § 285, and an award of Merus' reasonable attorneys' fees and costs; and

F. Such further and other relief as this Court may deem just and proper.

DEMAND FOR JURY TRIAL

Pursuant to Federal Rule of Civil Procedure 38, Merus demands a trial by jury on all issues so triable.

MORRIS, NICHOLS, ARSHT & TUNNELL LLP

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