

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

XENCOR, INC.,
Petitioner

v.

MERUS N.V.,
Patent Owner

Case IPR2025-00604
Patent No. 9,358,286

**PETITIONER'S OPPOSITION TO
PATENT OWNER'S DISCRETIONARY DENIAL BRIEF**

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I. INTRODUCTION

Institution is strongly favored under the traditional discretionary considerations of *Fintiv* and *Advanced Bionics*. The district court case is in its infancy—there has been no Rule 16 conference, and no case schedule has been entered. Also, a stay is likely here based on statistics for the district court. But even without a stay, a final written decision in this proceeding would likely precede trial by many months (if not longer). And for the original prosecution, Xencor’s Petition showed how the Examiner clearly erred by mistakenly accepting Merus’s incorrect statement that the prior art did not teach the claimed neutral-to-positive and neutral-to-negative mutations. That error should be corrected, and correcting that error will not lead to any redundant work with the district court. Thus, *Fintiv* and *Advanced Bionics* favor institution.

Contrary to Merus’s arguments, policy also strongly favors institution. Xencor is a U.S.-based biopharmaceutical company that is developing and testing novel bispecific antibodies for treating cancer and autoimmune diseases. Although Xencor has developed an extensive pipeline of antibody drug *candidates*, that development is still in the preclinical and clinical stages. Xencor does not currently market any drug products. Development of such candidate drug products takes a long time and is very expensive. Xencor has spent many years focusing its time and money on the critical development for its candidate drug products.

Congress has recognized the value in promoting this sort of resource-intensive development activity and has created a safe harbor from infringement in 35 U.S.C. § 271(e)(1). Xencor publicly expressed its expectation that its pre-commercialization work would be covered by this safe harbor as early as 2017—eight years ago—which Merus apparently has been aware of. And Merus itself expressed the same expectation in its own 10-K filings for its own work, referencing the safe harbor.

Instead of acting early to challenge Xencor’s expectations, Merus sat back and waited, allowing Xencor to continue investing hundreds of millions of dollars in this development activity year-over-year. Then, in 2024, Merus filed suit, seeking to cut off Xencor’s statutorily protected “safe harbor” activities and demanding damages.

This IPR is the result of Merus’s surprising infringement assertion of a patent that issued only due to Examiner error (which was induced by Merus’s incorrect characterization of the prior art), and is not an attempt by Xencor to upset Merus’s settled expectations, since there are none. In fact, Merus’s 10-K filings evidence an expectation that Merus’s patents would be subject to AIA challenges, even for pre-AIA patents. Public policy, public health, and settled expectations all favor instituting Xencor’s IPRs and allowing Xencor to continue conducting its

protected pre-commercialization development activities unobstructed by Merus's late-arising infringement assertions.

II. BACKGROUND

A. District of Delaware Litigation

On August 5, 2024, Merus N.V. ("Merus") filed a patent infringement complaint in the District Court of Delaware, alleging Xencor, Inc. ("Xencor") infringed three of Merus's patents—U.S. Patent No. 9,944,695 ("the '695 patent"), U.S. Patent No. 9,358,286 ("the '286 patent"), and U.S. Patent No. 11,926,859 ("the '859 patent"). (EX1052, ¶4.) The '286 and '859 patents are similarly directed to methods of heterodimerization of antibodies, whereas the '695 patent is different, relating to a method of manufacturing antibodies containing a human common light chain. (EX1052, ¶¶9-11.) Merus's case was originally assigned to Chief Judge Connolly. (EX1053.)

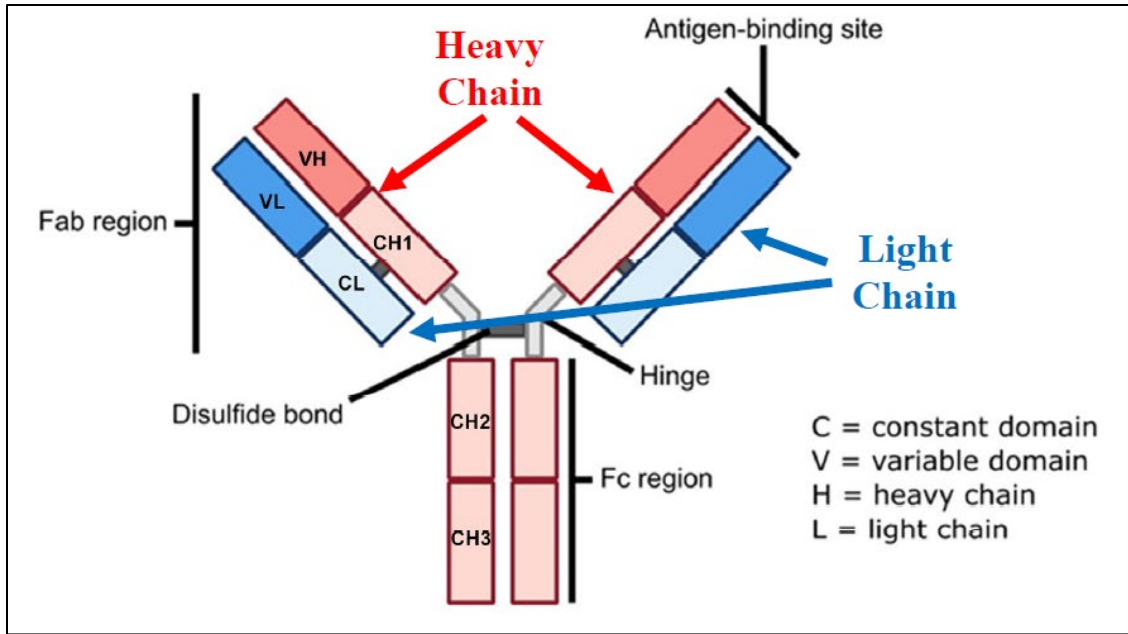
Recognizing the weakness in Merus's complaint targeting activity covered by the safe harbor provision in 35 U.S.C. § 271(e)(1), Xencor filed a motion to dismiss Merus's complaint on October 10, 2024. (EX1054.) Although Xencor does not currently have any drug products on the market, Merus seeks monetary damages from certain "developmental" activities. (EX1054, 3-5.) Xencor has been focused on developing novel therapies that utilize bispecific antibody platforms, with the eventual goal of submitting those therapies for FDA approval.

(EX1054, 3.) At present, Xencor has multiple therapies undergoing various stages of clinical trials but has yet to receive permission from the FDA to market any therapy under Xencor’s developmental direction. (EX1054, 3-5, 8-9.)

Xencor’s motion to dismiss was fully briefed before the district court by November 14, 2024. (EX1053, 5.) Then, on May 6, 2025, the case was reassigned to Judge Barker of the Eastern District of Texas. (*Id.*) Other than ministerial filings by the parties, no further activity in the case has occurred—there has been no Rule 16 conference and there is currently no case schedule. The motion to dismiss remains pending.

B. Technology Background

The technology at issue involves methods for making antibodies from two different parts (“heterodimeric” antibodies). One common antibody type is human IgG, which is composed of several portions, as shown below:



(Pet., 5-6; EX1013, 112-13; EX1002, ¶¶23-30.) This antibody comprises a left and a right half of the “Y,” with the antigen binding sites being on the two top sides of the “Y.” If the two halves are the same, this is known as a homodimeric antibody. (Pet., 7; EX1002, ¶26.) If they are different, it is a heterodimeric antibody. (Pet., 7-8; EX1002, ¶32.) One example of a heterodimeric antibody is shown below:

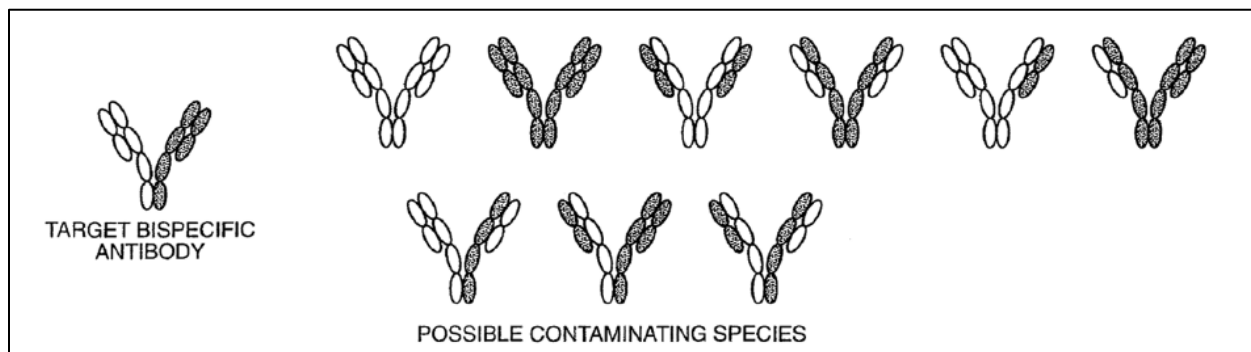


(EX1006, Fig. 1A; Pet., 8.)

One reason to make a heterodimeric antibody is to allow the antibody to be bispecific, meaning it can bind to two different antigens (or two different epitopes

on the same antigen). (Pet., 7-8; EX1002, ¶¶31-34.) This allows new and more-effective treatment options for certain diseases. (Pet., 8; EX1013, 182-84; EX1004 ¶¶3, 6; EX1006, 1-2.) The black-and-white figure above shows an example of a heterodimeric, bispecific antibody, since the two halves are different and because the two antigen binding sites are different. (Pet., 7; EX1002, ¶32.)

Bispecific antibodies have been known for a long time. However, their use as therapeutic agents has been hampered by low yield caused by mismatching of the heavy and light chains (which are created separately in the cell that generates the antibody). (Pet., 9.) An example of such mismatching is shown below.

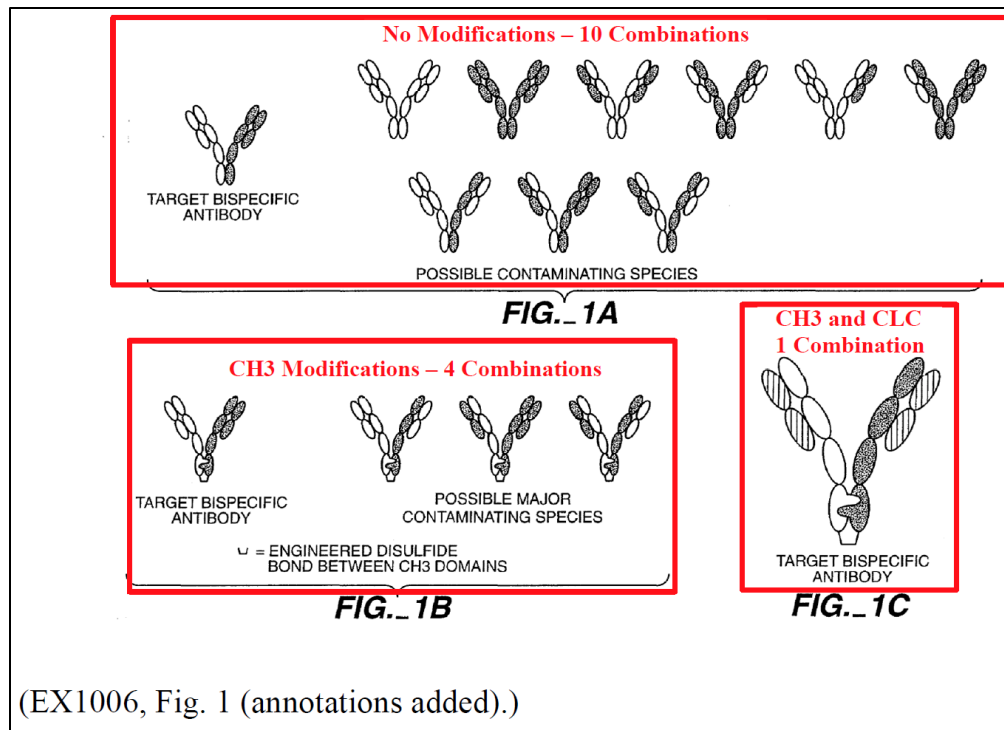


(EX1006, Fig. 1A.)

For this reason, several techniques have been developed to reduce mismatching to improve yield of the desired antibody. (Pet., 9-10; EX1002, ¶¶40-59.) Merus's '286 patent claims are directed to one such method for encouraging proper matching of the heavy chains—making substitutions in the

CH3 domain¹ to introduce a charge interaction. That is, by introducing a positively charged amino acid in the CH3 domain on one heavy chain and a negatively charged amino acid in the CH3 domain on the other, heterodimers (positive-to-negative) are favored, and homodimers (positive-to-positive and negative-to-negative) are disfavored. This is called “electrostatic steering,” and was a known technique. (Pet., 10; EX1016, 188-190; EX1007, 2:33-3:7; EX1012, 19637; EX1002, ¶¶53-59.) In fact, other heterodimerization techniques were known and common in the art well before Merus’s patents, such as “knob-into-hole” (or “protuberance-into-cavity”), using a “common light chain,” and creating non-natural (or “engineered”) disulfide bonds. (Pet., 9-10; EX1002, ¶¶40-59.) And the prior art expressly taught that these types of techniques could be combined to improve yield, as in Fig. 1C below:

¹ As shown in the human IgG graphic above, the CH3 domain is at the bottom of the “Y.” (Pet., 6.) The CH3 domains play a critical role in the pairing of the two heavy chains. (*Id.*)



(Pet., 40 (annotating EX1006, Fig. 1); *see also* EX1002, ¶¶57, 60-93, 155, 311; EX1006, 42-44, 48-55; EX1017, 678.)

Merus’s ’286 patent expressly recognized some of these prior art techniques. (E.g., EX1001, 2:64-3:59 (describing “bispecific antibodies” and “common light chain”), 4:29-5:52 (describing “knob-into-hole,” and “electrostatic engineering”).) In describing the point of novelty of the “present invention,” however, Merus incorrectly narrowed and characterized the prior art electrostatic steering approach as being limited to a “charge reversal” strategy—where “charged contact amino acids of CH3 domains that[] were known to be involved in the CH3-CH3 pairing were substituted by amino acids of opposite charge.” (EX1001, 17:67-18:3.) Based on this incorrect framing, Merus argued its claimed mutations “are an

inventive approach” because they change “non-charged or neutral” amino acids with “charged residues”—a neutral-to-charged approach. (*Id.*, 18:4-10.) But this neutral-to-charged approach was clearly taught in the prior art that Xencor presented in its Petition:

TABLE 1	
Preferred CH3 domain variants that favor Fc heterodimerization.	
Variant 1	Variant 2
F405A	T394F
S364D	Y349K
S364E	L368K
S364E	Y349K
S364F	K370G
S364H	Y349K
S364H	Y349T
S364Y	K370G
T411K	K370E
V397S/F405A	T394F
K370R/T411K	K370E/T411E
L351E/S364D	Y349K/L351K
L351E/S364E	Y349K/L351K
L351E/T366D	L351K/T366K
P395T/V397S/F405A	T394F
S364D/K370G	S364Y/K370R
S364D/T394F	Y349K/F405A
S364E/F405A	Y349K/T394F
S364E/F405S	Y349K/T394Y
S364E/T411E	Y349K/D401K
S364H/D401K	Y349T/T411E
S364H/F405A	Y349T/T394F
S364H/T394F	Y349T/F405A
Y349C/S364E	Y349K/S354C
L351E/S364D/F405A	Y349K/L351K/T394F
L351K/S364H/D401K	Y349T/L351E/T411E
S364E/T411E/F405A	Y349K/T394F/D401K
S364H/D401K/F405A	Y349T/T394F/T411E
S364H/F405A/T411E	Y349T/T394F/D401K

(Pet., 26 (annotating *Lazar* showing neutral-to-positive and neutral-to-negative substitutions).)

Table 1: CH3 domain amino acid modifications for the generation of Fc variant heterodimers.								
Variant	Chains	Fc Mutations						
AZ34	A	L351Y	S400E	F405A	Y407V	-	-	-
	B	T366I	N390R	K392M	T394W	-	-	-

(Pet., 62 (annotating *Cabrera* showing neutral-to-positive and neutral-to-negative substitutions).) Thus, in contrast to Merus’s erroneous statements, engineering charge pairs—whether by starting with a positive charge and changing to a negative one (or vice versa), or starting with a neutral amino acid and changing to charged amino acid—was known in the art. This fact was overlooked by Merus (and the Examiner) even though the *Kannan* prior art expressly teaches that their electrostatic steering strategy can be used to modify “uncharged residues to charged residues at the CH3 domain interface.” (EX1007, 10:16-18; *See* EX1002, ¶57.)

C. ’286 Patent Prosecution

The ’286 patent should have never issued. During prosecution, Merus argued that the prior art does not disclose the claimed neutral-to-positive and neutral-to-negative mutation strategy. (EX1008, 244-46.) But as shown above, that simply was not true.

The Examiner issued only one office action rejecting the claims as anticipated by *Carter*² and, separately, as being anticipated by *Kannan*.³ (EX1008, 217-219.) In response to the Examiner’s rejection, Merus argued that the cited prior art “does not disclose a heterodimeric antibody in which the CH3 domain of the first heavy chain contains a substitution of a neutral amino acid with a positively charged amino acid, and the CH3 domain of the second heavy chain contains a substitution of a neutral amino acid with a negatively charged amino acid.” (EX1008, 244-46; Pet., 14.) The Examiner accepted Merus’s rationale and allowed the claims, determining that “the prior art does not teach or suggest replacing a neutral amino acid (considered to be any amino acid other than R, K, H, E or D) with a positively charged amino acid in the CH3 domain.” (EX1008, 274-75; Pet., 14-15.) This was an incorrect conclusion for *Kannan*, and it overlooks *Lazar*’s and *Cabrera*’s clear teaching of this feature for the reasons described in Xencor’s Petition. (Pet., 23-28, 61-62.)

² U.S. Patent No. 7,642,228 to Carter *et al.*, issued January 5, 2010.

³ The Examiner cited patent application publication US 2010/0286374, while *Kannan* (EX1007) is International Patent Application Publication No. WO 2009/089004 A1. But the relevant disclosures are identical in each.

For *Kannan*, although it describes a so-called “charge reversal” strategy (as described in the ’286 patent background), its teachings are not *limited* to reversing charges. In fact, *Kannan* expressly teaches that their electrostatic engineering strategy can be used to modify “uncharged residues to charged residues at the CH3 domain interface.” (EX1007, 10:16-18; *see* EX1002, ¶57.) Thus, *Kannan* taught the very aspect that Merus argued was its point of novelty. Unfortunately, the Examiner overlooked this clear teaching in *Kannan*, which led the Examiner to accept Merus’s incorrect argument and allow the claims.

The Examiner also apparently overlooked the clear teachings in *Lazar* and *Cabrera* shown above which also disclose the neutral-to-positive and neutral-to-negative mutations emphasized as novel by Merus during prosecution. (EX1004, Table 1; EX1005, 39.) Had the Examiner been aware of these teachings, they would not have allowed the ’286 patent claims to issue and would have rejected this neutral-to-charged aspect that Merus argued as novel and continues to push today.

III. ARGUMENT

The Director should decline Merus’s request for discretionary denial. Merus is attempting to stifle and penalize pre-commercialization development activities by Xencor that are covered under the § 271(e)(1) safe harbor based on a patent that is demonstrably unpatentable. Xencor’s Petition challenging the ’286 patent

should be considered on the merits to clear the cloud that Merus has put over Xencor's protected activity.

Xencor has done everything it can to treat these IPRs⁴ as an alternative to district court litigation for the unpatentability challenges presented herein. Xencor did not wait until its statutory bar date, and instead swiftly prepared these petitions in half of the statutorily allotted time. And even though the parallel district court case has laid dormant, with virtually no activity occurring thus far, Xencor has agreed to *Sotera* stipulations to avoid any doubt of Xencor's intent to treat this proceeding as an alternative to district court litigation. Furthermore, this petition is not redundant with original prosecution. Instead, Xencor has shown in its Petition how the point of novelty that Merus stressed during prosecution (neutral-to-negative and neutral-to-positive mutations in the CH3 domain) were disclosed long ago in multiple pieces of prior art—including art that was never before the Examiner. Thus, Xencor's Petition is not redundant with prosecution.

The Director should deny Merus's request for discretionary denial and refer the Petition to the Board for an institution decision.

⁴ Xencor has filed a concurrent IPR petition challenging the '859 patent—IPR2025-00605.

A. Xencor’s Petition Is Not Redundant with Prosecution under 35 U.S.C. § 325(d) or *Advanced Bionics*

Under § 325(d) and the *Advanced Bionics* framework, Xencor’s Petition is not redundant with prosecution. *Advanced Bionics, LLC v. MED-EL Elektromedizinische Gerate Ges.m.b.H*, IPR2019-01469, Paper 6 at 8 (Feb. 13, 2020). Discretionary denial is inappropriate because *Cabrera* was not considered at all, and for *Lazar*, even though it was cited in an IDS, the Examiner expressly erred in the notice of allowance, likely due to having been misinformed by Merus, stating that “the prior art does not teach or suggest” the claim feature that is, in fact, expressly taught in *Lazar*—neutral-to-positive substitutions in the CH3 domain. (Pet., 75-76 (quoting EX1008, 274).)

During prosecution, the Examiner issued rejections based on two pieces of prior art, *Kannan* and *Carter* (EX1008, 217-220), neither of which are related to the prior art Xencor used in its present petition. And Merus does not even argue that the prior art used in the Petition is substantially the same as either *Kannan* or *Carter* (or any other art mentioned by the Examiner). Instead, Merus merely points out that *Lazar* and *Arathoon* were cited in relatively large IDSs. (DDB,⁵ 13-15; EX1008, 252-258 (57 references), 263-269 (66 references).) The Director should consider this “volume of the references submitted to the Office” in Merus’s

⁵ Merus’s Request for Discretionary Denial, Paper 6, is cited as “DDB” herein.

IDSs and find it weighs against discretionary denial. *Ecto World LLC v. RAI Strategic Holdings, Inc.*, IPR2024-01280, Paper 13 at 6-7 & n.3 (May 19, 2025) (pointing out “[m]ost IDS submissions contain fewer than 25 references”). But even if the Director considers this IDS citation sufficient to render the references to have been individually “considered,” Xencor explained exactly how the Examiner erred regarding *Lazar*.

In the notice of allowance, the Examiner determined that “the prior art does not teach or suggest replacing a neutral amino acid ... with a positively charged amino acid in the CH3 domain.” (EX1008, 274.) But as Xencor explained, that is just incorrect—both *Lazar* and *Cabrera* expressly teach this. (Pet., 26 (annotating *Lazar*), 62 (annotating *Cabrera*), 75-76.)

In light of these teachings in the prior art, the Examiner clearly erred in his rationale for allowing the claims that the prior art did not teach or suggest neutral-to-positive substitutions in the CH3 domain. *See Ecto World* at 5-6 (explaining that an examiner errs where “previously presented art teaches the limitations of the challenged claims, and that no reasonable examiner could have found otherwise”). As the Director explained in *Ecto World*, both *Lazar* and *Arathoon* “[were] not a basis for rejection during examination, [are] not substantially the same as prior art the Examiner applied, and include[] specific teachings that ‘impact patentability of the challenged claims.’” *Id.* at 5 (quoting *Advanced Bionics* at 8 n.9).

For *Cabrera*, Merus does not contest that *Cabrera* was not considered during prosecution, and thus it does not even get past the first step of *Advanced Bionics*. And Merus does not assert that *Cabrera* is similar to or redundant with the prior art the Examiner applied during prosecution (*Kannan and Carter*). Instead, Merus argues *Cabrera* is similar to *Lazar*. (DDB, 14-15.) But as shown above, the relied-upon teachings are different, relying on different mutations at different locations. The fact that they have the same overall general strategy of encouraging heterodimerization and discouraging homodimerization, on its own, does not render them “substantially the same,” as Merus argues. (*Id.*) Instead, it merely shows that multiple pieces of prior art were investigating the subject matter of the challenged claims before Merus, and even disclosed Merus’s claimed solution before Merus. And in any case, as Xencor explained in its Petition, the Examiner’s conclusion that the prior art does not teach neutral-to-charged CH3 modifications is erroneous over the teachings of *Cabrera* as well. (Pet., 75-76.)

Merus also argues that the teachings of *Lazar* and *Cabrera* are, in Merus’s view, deficient. (DDB, 14-15, 17-18.) But Merus’s arguments are cryptic and deficient for the reasons explained in the merits section (Section III.C.3), which shows that this really is a merits dispute, ideal for IPR resolution, rather than a discretionary consideration.

For all of these reasons, the Director should not discretionarily deny the Petition based on supposed redundancy with prosecution. These are new challenges that the Office has never considered and Xencor expressly identified where and how the Examiner erred.

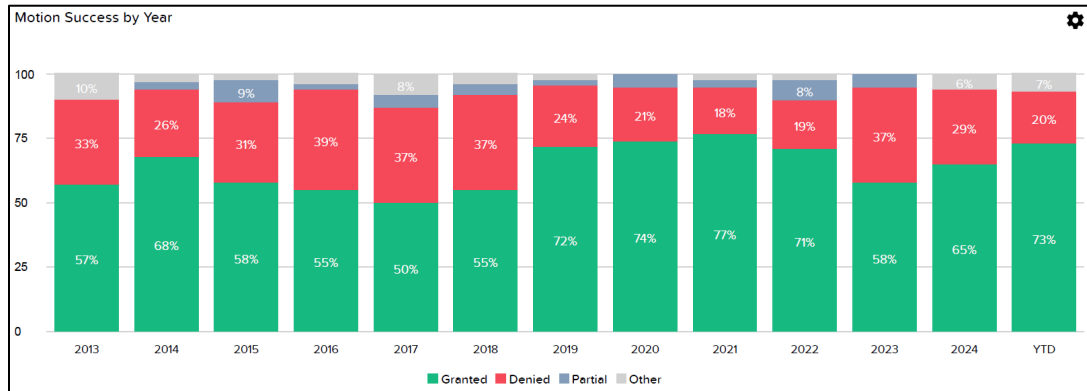
B. Early Stage of Parallel Litigation Favors Institution Under *Fintiv*

The *Fintiv* factors weigh strongly in favor of institution. The parallel district court case is in its infancy—meaning both that there has been practically no investment of resources, and that, due to Xencor’s *Sotera* stipulation, there will be no redundant work between the forums. In fact, the parallel case is so early in its life that a case schedule or even a trial date has not yet been contemplated by the court. For these reasons, and in light of the District of Delaware’s stay statistics, a stay is likely if these proceedings are instituted. The Director should decline Merus’s request for discretionary denial and refer the case to a panel for a determination on the merits.

1. Factor 1 – Whether the court granted a stay or evidence exists that one may be granted if a proceeding is instituted

Factor 1 favors institution because a stay is likely based on district-wide statistics and the current early stage of the litigation. Merus’s analysis of this factor is deficient, labeling the chances that a stay will be granted a “coin-toss,” without any substantiating statistics or evidence. (DDB, 19.) The statistics show a

different story—that stays in favor of IPR proceedings are commonly granted in the District of Delaware, being well above 50% in recent years:



(EX1055.) This high grant rate is sufficient evidence to show to a preponderance of the evidence that a stay is likely if this proceeding is instituted—particularly in light of Merus’s failure to provide any support for its contrary argument.

Merus argues the fact Xencor only challenged two of the three asserted Merus patents influences the chance of obtaining a stay. (DDB, 2, 20.) But Merus provides no statistics or evidence-based analysis for this particular dispute. Merus has long been aware, even before filing its complaint, that Xencor’s work with the RenLite® mice that Merus accused of infringing the ’695 patent was limited and quickly discontinued. (EX1054, 8&n.4, 20.) This limited activity that terminated long ago would not be a sufficient justification to deny a stay if the other two asserted patents are instituted in IPRs. Indeed, the District of Delaware has frequently stayed cases even where not all asserted patents were instituted for review. *See, e.g., Cleveland Medical Devices, Inc. v. ResMed Inc.*, No. 1-22-cv-

00794, D.I. 300 (D. Del. June 21, 2024) (granting stay despite some asserted patents not being instituted due to those patents making up a small amount of the damages claims); *Monterey Research, LLC v. Nanya Tech. Corp.*, No. 1-19-cv-02090, D.I. 84 (D. Del. June 25, 2021) (granting stay where four of six asserted patents were instituted because litigation “would be ‘simplified’ because it would be concluded as to four of the six asserted patents” if found unpatentable); *NEC Corp. v. Peloton Interactive, Inc.*, No. 22-987-CJB, 2024 WL 1533952 (D. Del. Apr. 9, 2024) (granting stay where one asserted patent was not at issue in the IPR); *Speyside Med., LLC v. Medtronic CoreValve LLC*, No. 1-20-cv-00361, D.I. 155 (D. Del. Sept. 30, 2021) (granting stay where IPR instituted on three of five asserted patents).

2. Factor 2 – Proximity of the court’s trial date to the Board’s projected statutory deadline for a final written decision

Factor 2 strongly favors institution because no trial date has been set in the parallel district court litigation and trial would likely be well after the projected September 2026 final written decision date for this proceeding. Because essentially no activity has occurred in the district court thus far, getting through fact discovery, expert discovery, dispositive motions, and trial within 15 months from the date of filing of this paper is utterly unrealistic.

Merus speculates, without citing to any evidence, that it expects trial to be in August 2026, roughly two years from the filing of its complaint. (DDB, 19.) But

that is contrary to the most recent average time to trial statistics for the District of Delaware and ignores the current status of the case. As published on the U.S. Courts website, median time to trial in the District of Delaware is 33 months. (EX1056, 14; *see also* Pet., 76 (citing EX1046, 14 (32.2 month median time as of September 2024))).) Even ignoring the fact that the case has not even begun and simply applying the above District of Delaware median time to trial, because Merus's complaint was filed in August 2024, trial would be May 2027—months after the projected final written decision here (September 30, 2026).

Additionally, the case was recently transferred from Chief Judge Connolly to Judge Barker (a visiting judge in the District of Delaware that ordinarily sits in the Eastern District of Texas), adding an unknown amount of additional time to the case. (EX1053.) Judge Barker recently was assigned eleven cases from the District of Delaware (one of which being Merus's case). Furthermore, the average time to trial from the initial disclosures date (the first item in a case schedule) in patent cases before Judge Barker (although a limited data set) is 552 days, or around one-and-a-half years. (EX1057.) Thus, even if initial disclosures were made today and no stay were granted, according to Judge Barker's track record, trial would not be until December 2026—again, months after the projected final written decision here (September 30, 2026).

Attempting to distract from the merits, Merus accuses Xencor of being responsible for the “lack of progress in the parallel district court litigation.” (DDB, 20-21.) But Merus provides no support for this accusation, only arguing Xencor’s motion to dismiss is—in Merus’s view—meritless. (DDB, 21.) Clearly the District Court does not think so, as it has been considering Xencor’s motion for quite some time. And Merus cannot fairly blame Xencor for the timing of the district court’s decision on Xencor’s motion to dismiss—Merus, as the plaintiff, chose to litigate in the District of Delaware, which has a busy docket.

3. Factor 3 – Investment in the parallel proceeding by the court and the parties

Factor 3 strongly favors institution because the district court and the parties have invested minimally in the district court litigation. This *Fintiv* factor serves to gauge potential efficiencies—where substantial investment has already been made in the parallel district court proceeding, it would be less efficient to institute an *inter partes* proceeding which would only increase litigation costs. *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 11, 9-10 (Mar. 20, 2020) (“Specifically, if, at the time of the institution decision, the district court has issued substantive orders related to the patent at issue in the petition, this fact favors denial.”)

The only activity by the parties has been Merus’s filing of its complaint and the briefing of Xencor’s motion to dismiss based on the 35 U.S.C. § 271(e)(1) Safe Harbor, with the court’s activity only being referring the case to another judge.

Merus attempts to inflate the investment by pointing to its own required pre-suit review of “thousands of pages of documents” (DDB, 20), but this fact on its own, in view of what *Fintiv* Factor 3 aims to assess, is inconsequential. What is consequential is that the district court has yet to issue any substantive orders related to the patents at issue. Given the minimal investment by the parties and the court, efficiency favors institution.

**4. Factor 4 – Overlap between issues raised
in the petition and in the parallel proceeding**

Factor 4 strongly favors institution due to the early stage of litigation and Xencor’s *Sotera* stipulation, which Merus fails to mention, even though it was served a month before Merus’s discretionary denial brief. (EX1058.) The submission of a *Sotera* stipulation serves to bind a petitioner to the full scope of estoppel under 35 U.S.C. § 315(e)(2), eliminating the possibility of any substantive overlap between the proceedings should an *inter partes* review proceed to a final written decision. *See Sotera Wireless, Inc. v. Masimo Corp.*, IPR2020-01019, Paper 12, 18-19 (Dec. 1, 2020) (precedential as to §II.A). Because Xencor, as the defendant in the district court litigation, has yet to file an answer to Merus’s complaint and because Xencor’s motion to dismiss regards the issue of non-infringement under the 35 U.S.C. § 271(e)(1) Safe Harbor (not invalidity), no potentially overlapping substantive arguments have been made to the district court.

Thus, Xencor's *Sotera* stipulation prevents any duplicative arguments in the two forums.

Merus argues that factor 4 favors discretionary denial (DDB, 20), but Merus misunderstands the "overlap" factor. Under factor 4, "if the petition includes the same or substantially the same claims, grounds, arguments, and evidence as presented in the parallel proceeding, this fact has favored denial." *Fintiv*, Paper 11, 12-13. Merus argues that this factor favors denial because the district court proceeding "includes three asserted patents" and thus this IPR would not fully "dispose of that parallel proceeding." (DDB, 20.) But this factor does not automatically favor denial any time a plaintiff asserts more than one patent (*i.e.*, where the district court proceeding could potentially cover more patents and issues than the IPR). The relevant question is whether the IPR proceeding would be redundant with the litigation due to overlap of the issues and arguments already made during the parallel proceeding, not whether the IPR alone would dispose of the case. Here, Xencor's swift filing of its IPR early in the district court proceeding combined with its *Sotera* stipulation means that this factor favors institution because there will be no overlapping issues.

Furthermore, the third asserted patent covers a distinct technology from the two patents at issue in Xencor's IPRs, with Merus arguing infringement for that third patent based on different allegedly infringing activity. (EX1052, ¶9.) This

also minimizes the likelihood of litigating overlapping issues in Xencor’s IPRs and in the district court.

5. Factor 5 – Whether the petitioner and the defendant in the parallel proceeding are the same party

Factor 5 favors institution because, even though Xencor is the defendant in the parallel proceeding, this IPR is likely to proceed to final written decision before that parallel litigation would go to trial, meaning estoppel under 35 U.S.C.

§ 315(e)(2) would apply (not to mention Xencor’s *Sotera* stipulation). *Fintiv* itself explained that where the petitioner is “unrelated to a defendant,” that factor weighs against denying an IPR petition for discretionary reasons. *Fintiv*, Paper 11, 13-14.

Merus assumes the opposite is true—that the petitioner being the defendant in a parallel district court case weighs in favor of discretionary denial—but *Fintiv* did not hold that. And the Board has held that where the final written decision would precede trial, the fact that the defendant is the petitioner weighs *in favor of*

institution (not denial) because estoppel would apply. *See, e.g., BMW of N. Am., LLC v. Mich. Motor Techs. LLC*, IPR2023-01234, Paper 11, 14-15 (Jan. 26, 2024); *Huawei Tech. Co. v. WSOU Inv., LLC*, IPR2021-00225, Paper 11 at 13-14 (June 14, 2021); *Google LLC v. Parus Holdings, Inc.*, IPR2020-00846, Paper 9 at 20-21 (Oct. 21, 2020). Because a final written decision here would precede trial, *see* Section III.B.2, factor 5 favors institution.

6. Factor 6 – Other circumstances that impact the Board’s exercise of discretion, including the merits

Factor 6 favors institution because Xencor’s unpatentability merits are strong. *See* Section III.C.3. Other than the merits, Merus identifies no “other circumstances” for the *Fintiv* analysis. (*See* DDB, 20.)

* * *

Considering all the *Fintiv* factors collectively, the balance weighs in favor of institution. Accordingly, the Director should reject Merus’s request to discretionarily deny institution based on *Fintiv*.

C. Interim Process Memo Rationales Do Not Justify Denial

1. The District Court Case Is in Its Infancy and Has Not Adjudicated Validity of the Challenged Claims

Merus ignores the first consideration in the Director’s Interim Process Memo, which favors institution here. (EX2005, 2.) Because there have been no previous PTAB challenges to the ’286 patent and because the district court case is in its infancy, this IPR would be the first opportunity to “adjudicate[] the validity or patentability of the challenged patent claims.” (*Id.*) This consideration favors institution.

2. Merus’s “Candor” Accusations Fail for the Reasons Explained in the Parallel IPR Proceeding—IPR2025-00605 (’859 patent)

Merus’s argument in the parallel IPR (IPR2025-00605) is a red herring thrown into that proceeding in an attempt to distract from the clear unpatentability

of Merus’s ’859 patent. That argument has no bearing on this IPR. Moreover, as explained in Xencor’s briefing for IPR2025-00605, Merus argues that Xencor concealed the fact that Xencor has “shockingly similar” claims to Merus’s claims in the ’859 patent. But that argument makes no sense for two reasons.

First of all, Xencor’s Ground 1 is anticipation over the very patent that Merus argues Xencor “was careful not to draw the Acting Director’s and the Board’s attention to.” (IPR2025-00605 DDB, 14.) And that ground expressly mentions the claims of that prior-art patent. (IPR2025-00605 Pet., 41 (referring to “the *Desjarlais* patent claims”).)

Secondly, Merus confusingly suggests that two parties with completely different specifications and similar claims should be treated identically by the USPTO. This makes no sense, as each party must individually face the statutory requirements based on its unique specifications, which, particularly in the case of § 112, will necessarily be different (as is the case here). To suggest otherwise is disingenuous.

Merus’s arguments on this topic should be rejected as even further afield in this proceeding.

3. The Petition’s Unpatentability Merits Are Strong

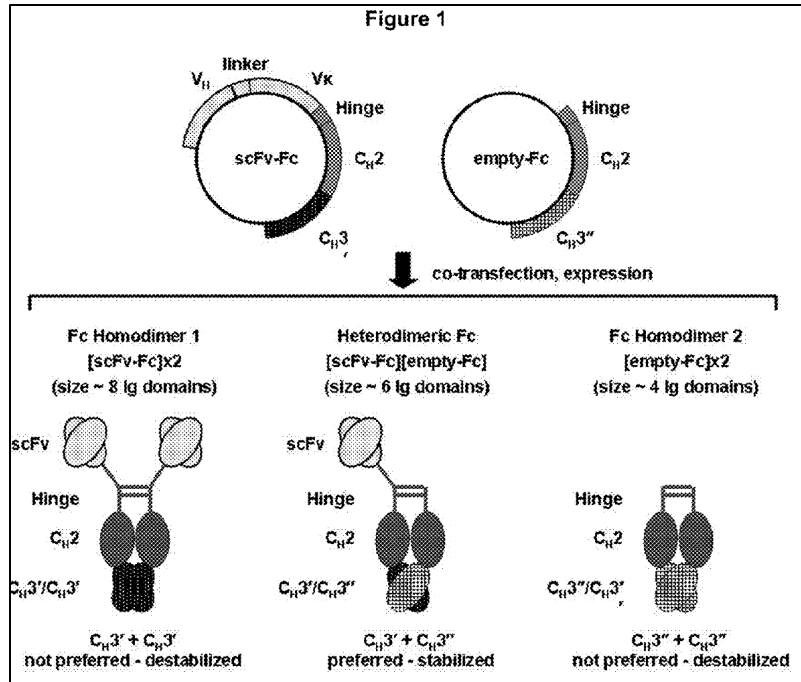
Merus’s conclusory and confusing arguments fail to undermine the strength of Xencor’s unpatentability grounds. And the skeletal and cryptic nature of

Merus's merits-based arguments stifle Xencor's ability to meaningfully respond. This should cut against any merits-based discretionary denial and weigh in favor of referring Xencor's petition to a Board panel for a decision on the merits.

a) Ground 1 (*Lazar*) Is Strong

Merus only makes a vague assertion that *Lazar* supposedly does not disclose modifications on “two heavy chains.” (DDB, 23.) Tellingly, even though Merus argues “it is beyond legitimate dispute that *Lazar* does not disclose” certain features, Merus does not cite *Lazar* once in this section or point to any evidence, other than a supposed definition of “heavy chain” in the '286 patent. (DDB, 23-24.) The Director should reject this intentionally opaque and confusing argument.

To the extent Merus is criticizing *Lazar*'s testing of “empty-Fc” and “scFv-Fc” constructs (shown below) to find desirable mutations for heterodimerization, such an argument ignores the purpose of *Lazar*'s testing, which was to apply those preferential mutations to its bispecific antibody constructs.



(EX1004, Fig. 1.) As *Lazar* explains, this testing was “to screen for Fc variants that favor heterodimerization,” and this “empty-Fc/scFv-Fc system was developed as a test system.” (EX1004, ¶238.) This testing resulted in several “[p]referred CH3 domain variants that favor Fc heterodimerization,” which Xencor relied on in its Petition. (Pet., 26 (annotating EX1004, ¶241 (Table 1)).)

Lazar describes these “Fc Modifications that Favor Heterodimerization” as being applied “within *each heavy chain* that forms the Fc region.” (EX1004, ¶120 (emphasis added); see also *id.*, ¶¶80 (describing an “IgG heavy chain” as being “composed of four immunoglobulin domains linked from N- to C-terminus in the order VH-CH1-CH2-CH3”), 119-125.) And when describing its antibody constructs, *Lazar* explains that they “incorporate[] hetero-Fc variants that favor heterodimerization” (e.g., EX1004, ¶244; see also *id.*, ¶¶42, 107), which clearly

are pointing at the CH3 domain modifications that were discovered with the test system (*id.*, ¶236). Merus’s vague argument thus appears to be improperly reading *Lazar*’s teachings narrowly and in isolation, rather than considering *Lazar*’s teachings as a whole.

b) Ground 2 (*Lazar & Arathoon*) Is Strong

Merus again relies on an unexplained and unsupported argument that “*Lazar* does not teach a POSA to make two heavy chains that each have a substitution of a neutral to charged residue that interact with each other across the CH3 region interface to produce a heterodimeric antibody” (DDB, 24)—which appears to be the same faulty argument it was making for Ground 1. But for Ground 2, Merus also asserts “*Lazar* teaches away from introducing neutral to charged substitutions into the CH3 regions of the heavy chains.” (DDB, 24.) Merus includes no citations whatsoever, and this assertion makes no sense in light of *Lazar*’s Table 1, disclosing “[p]referred CH3 domain variants that favor Fc heterodimerization” that list several pairs of mutations swapping neutral amino acids with charged ones. (*See* Pet., 26 (annotating EX1004, ¶241 (Table 1)).)

For the combination of *Lazar* and *Arathoon*, Merus argues a lack of motivation to combine and a supposed teaching away. (DDB at 24-25.) Regarding motivation to combine, Merus completely ignores the rationales given in the Petition (Pet., 34-36), instead demanding an express suggestion in the references themselves,

(DDB, 24-25), but that is not required. *See KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) (“[T]he analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.”). For teaching away, Merus cites nothing and provides no explanation. (DDB, 24-25.)⁶ Thus, this argument should be rejected out of hand.

Merus’s arguments additionally do not address the combination of the references, where *Arathoon* teaches heterodimerization methods that can be combined and shows one type of bispecific antibody (one with a full heavy chain) and *Lazar* teaches the relevant CH3 domain modifications that favor heterodimerization, which are broadly applicable to antibody constructs with CH3 domains (*e.g.*, those with full heavy chains). (Pet., 34-38.)

⁶ Proving teaching away is a high burden: “a reference does not teach away if it ‘merely expresses a general preference for an alternative invention but does not criticize, discredit or otherwise discourage investigation into the invention claimed.’” *UCB, Inc. v. Actavis Laby’s UT, Inc.*, 65 F.4th 679, 692 (Fed. Cir. 2023) (quoting *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314, 1327 (2009)).

c) Ground 3 (*Cabrera*) Is Strong

As Merus did with *Lazar* and Ground 1, it again makes impossibly opaque arguments as to why *Cabrera* supposedly “does not disclose all of the claim elements,” this time citing absolutely nothing at all. (DDB, 25.) To the extent Merus is faulting *Cabrera* for supposedly not disclosing “data” showing the substitutions “interact,” the fact that the positions of the amino acid substitutions in the relied-upon AZ34 example are made at the known interface between the two CH3 domains is sufficient. (*See* Pet., 62 (citing EX1007, Table 1).)

d) Ground 4 (*Lazar, Arathoon, & Cabrera*) Is Strong

For Ground 4, other than relying on its previous faulty arguments regarding the individual references, Merus also criticizes motivation to combine. (DDB, 26.) Merus argues Xencor’s motivation is merely a “vague generality” that ““the same is true of *Cabrera*.”” (DDB, 26 (quoting Pet., 70).) But Merus’s argument blatantly ignores the motivations expressly described in this section of Xencor’s Petition, which explain that *Cabrera*, like *Lazar* and *Arathoon*, “teaches techniques for boosting heterodimer yield through CH3 domain modifications ... envisions combination modifications ... and applies its modifications to a variety of antibody structures.” (Pet., 70-71.) Additionally, Merus ignores all of the explanation provided in the prior section of Xencor’s Petition regarding the combination of

Lazar and *Arathoon*, which is what Xencor’s Petition was referring to where it said “the same is true of *Cabrera*.” (Pet., 70 (citing Pet., 34-36 (Section X.B.1)).)

Furthermore, Merus’s arguments should not be credited in light of its arguments elsewhere that *Cabrera* is “substantially the same as *Lazar*.” (DDB, 1, 13-16 (calling them “nearly identical”).) Assuming *arguendo* that *Cabrera* and *Lazar* are “substantially the same” as Merus argues, in such circumstances, motivation to combine is apparent. *See, e.g., iRobot Corp. v. SharkNinja Operating LLC*, No. 2023-1398, 2024 WL 3687981, at *5 (Fed. Cir. Aug. 7, 2024) (affirming motivation to combine based on the Board’s reliance on “the similarities between the two references’ teachings”). Merus cannot have it both ways.

4. Xencor’s Reliance on Dr. Presta’s Declaration Does Not Favor Denial

Dr. Presta’s declaration was appropriate in both length and content. The Director should reject Merus’s conflicting arguments that Dr. Presta’s declaration was somehow both too little (“parroting”) and too much (not “focused”). (DDB, 26-29.) To the contrary, this factor weighs against discretionary denial. First, Merus does not identify any portions of the expert testimony that suggest Xencor is using its expert to fill gaps in the prior art.

Second, for “parroting,” the only portion of Dr. Presta’s declaration Merus identifies is a screenshot of paragraphs 274-277, which it argues is “copying and pasting.” (DDB, 28.) But as is clear from Merus’s own screenshots, these

paragraphs are not copy pasted from the Petition. Instead of relying on gap-filling or parroting, Xencor appropriately relies on Dr. Presta to explain the background knowledge of a person of ordinary skill in the art, which Dr. Presta supports with citations to evidence. (*See, e.g.*, EX1002, ¶¶19-59 (including additional context and scientific detail).)

It is unsurprising that Xencor's Petition and the expert declaration supporting the Petition's unpatentability arguments point to the same portions of the prior art references and come to similar conclusions. The Director should not discretionarily deny on this basis.

5. Settled Expectations Favor Xencor, not Merus

Although the '286 patent issued in 2016 and Xencor's 2017 10-K filing acknowledges "a recently issued patent owned by Merus," the Director should not discretionarily deny institution here due to the settled expectation (evidenced in the same 10-K) that Xencor's pre-commercialization activities would be protected under the 35 U.S.C. § 271(e)(1) safe harbor. It was Merus that upset this settled expectation by suing Xencor, alleging such pre-commercialization activities infringe their patents, thus triggering this IPR challenge. And Merus has no settled expectation that its own patents would be immune from IPRs, having expressly contemplated such proceedings (even for pre-AIA patents) in its own 2024 10-K. (EX1059, 87.) Settled expectations should not be used to deny institution here.

Merus cites Xencor's 2017 10-K as showing Xencor's knowledge of an unnamed Merus patent. (DDB, 29-30.) But Merus completely ignores the surrounding context in Xencor's 10-K submission that explains Xencor's expectations at that time. (*Id.*) In the same paragraph that Merus quotes, Xencor noted that "we believe that our current development of [Xencor's bispecific product candidates] currently falls into the 'safe harbor' of non-infringement under 35 U.S.C. § 271(e)(1)," noting that "this protection terminates upon commercialization." (EX2007, 46.) Xencor is not alone in this expectation that the § 271(e)(1) safe harbor would protect their pre-commercialization activities—Merus expressed the same expectations for their own candidates in their own 2024 10-K submission. (EX1059, 83.) Additionally, Xencor's 10-K expressly noted that, based on Xencor's preliminary analysis, "there exists reasonable argument[s] of invalidity and/or [non-]infringement" for Merus's patent. (EX2007, 46.)

In other words, Xencor's 10-K evidences an expectation that Merus's patent is invalid and/or not infringed, but in any case, Xencor's pre-commercialization activity would be protected from infringement by the § 271(e)(1) safe harbor, so there was no need to challenge Merus's patent before commercialization. Xencor still is in the pre-commercialization phase. (EX1054 at 3-4 ("Xencor does not currently market any drug products," explaining that its "antibody therapeutics are currently in various stages of clinical and preclinical development").) Even though

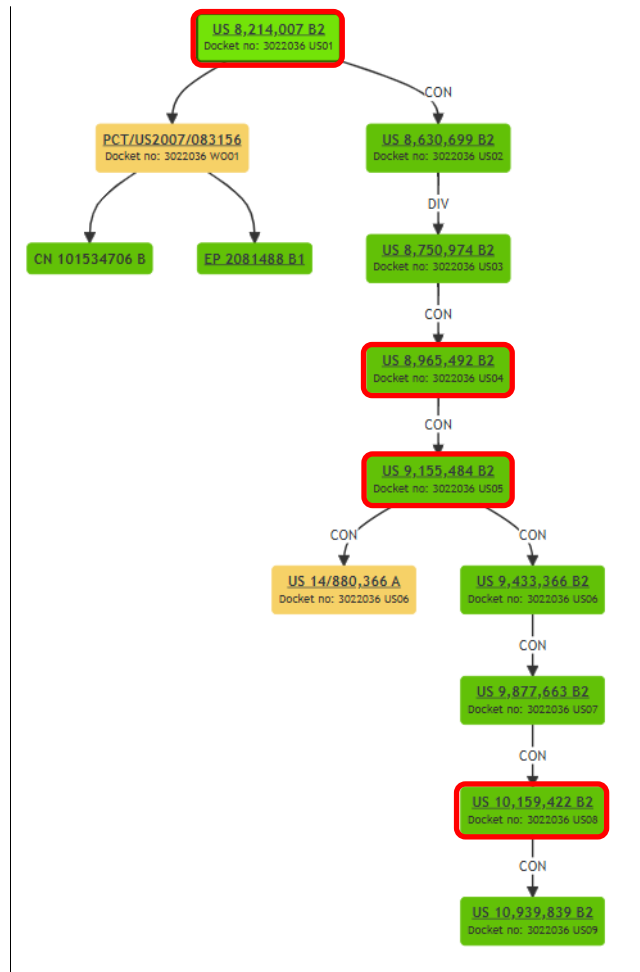
Merus apparently was aware of Xencor's public 10-K filing evidencing an expectation of the § 271(e)(1) safe harbor coverage, Merus sat idly by for more than six years before suing Xencor, despite being aware of Xencor's antibody development activities. (EX1060, 19.) And Merus's lawsuit is based on Xencor's continuing pre-commercialization activity that is covered by the safe harbor—something Xencor certainly did not expect and should not have had to divert resources away from its development activities in order to defend. Thus, it was Merus's years of inaction followed by aggressive assertion of infringement against pre-commercialization work that led to this IPR filing at the very outset of the district court litigation, not any belated attempt to upset settled expectations by Xencor.

The Director recently issued two decisions denying institution based on “settled expectations.” *iRhythm Tech., Inc. v. Welch Allyn, Inc.*, IPR2025-00374, Paper 10, 3 (June 6, 2025); *Dabico Airport Solutions Inc. v. AXA Power ApS*, IPR2025-00408, Paper 21, 2-3 (June 18, 2025). In *iRhythm*, the Director discretionarily denied five IPR petitions based on a petitioner's citation of one of the four challenged patents in an IDS. *iRhythm* at 3. The Director considered the IDS citation to be evidence of “settled expectations” that “outweigh[ed]” every other factor that favored institution. *Id.* In *Dabico*, the Director relied on the fact that the patent had “been in force almost eight years,” also denying institution.

Dabico at 2. But settled expectations do not favor denial here, and instead favor institution.

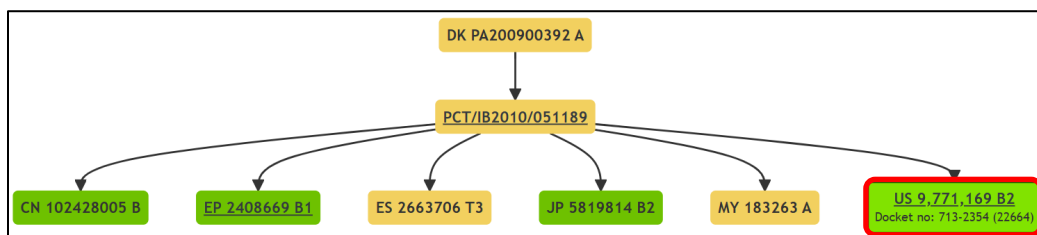
First, as described above, the evidence Merus points to as showing prior knowledge is less specific than that in *iRhythm* (not even naming any particular patents by number) and evidences Xencor’s expectations at the relevant time. As explained above, Xencor’s public 10-K filing shows expectation of invalidity/non-infringement as well as safe harbor coverage—none of which Merus contested, thus allowing Xencor’s expectations to become settled.

Second, the patent families in *iRhythm* and *Dabico* are distinguishable for settled expectations purposes because their continuation chains had terminated long before the IPRs challenging those patents. That is, since there were no pending continuation applications, there could be no additional future claims to “unsettle” the analysis. For example, *iRhythm* involved a set of relatively older patents with no active continuations, with the youngest challenged patent in *iRhythm* being U.S. Patent No. 10,159,422 from 2018.



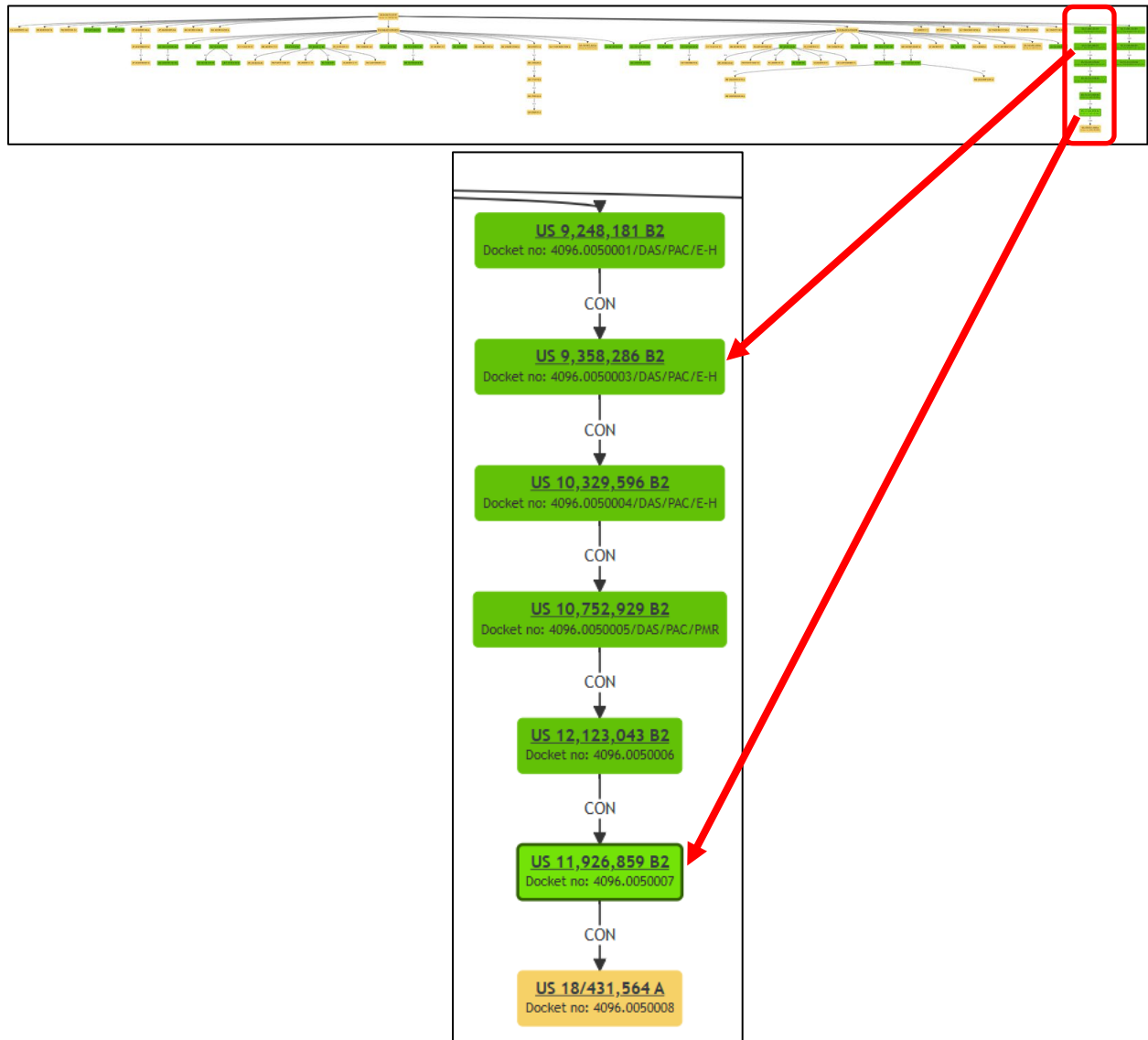
(Boxing the challenged patents in *iRhythm* in red.) Thus, the *iRhythm* patent family was relatively tight-knit and had been solidified (no pending continuations) well before the petitioner in *iRhythm* brought its challenges.

Similarly, the *Dabico* family involved a single U.S. Patent that issued in 2017 with no continuations to date.



(Boxing the challenged patent in *Dabico* in red.)

In contrast, here, Merus has asserted a far-reaching patent family that strings together continuations (which are still ongoing), attempting to retroactively capture Xencor's public disclosures.



It would be unfair to read “settled expectations” into the Xencor 10-K’s vague reference to Merus’s patents when Merus has turned its family into a

moving target that covers even Xencor's disclosures made years before Merus's claims (as with the '859 patent in the parallel proceeding).

6. Public Health

Public health would be benefitted by instituting Xencor's Petitions, rather than discretionarily denying them. Xencor's development activities relate to therapies for cancer and autoimmune diseases. This activity has been pre-commercial, yet Merus is attempting to shut it down through a lawsuit based on a patent that should have never been issued. Discretionarily denying IPRs in these circumstances would be bad policy, as it would increase risk and costs for entities conducting early drug discovery. For instance, even if one were to assume that pre-commercialization development activities were not covered by the § 271(e) safe harbor, requiring companies that are early in their development to file IPR challenges to all suspect patents that might potentially apply, before suitable candidates are even identified or sufficiently advanced, would be wasteful and expensive. This added risk and cost would lead to fewer new drug products being developed, which would be bad for public health.

For Merus's part, they fail to explain how discretionarily denying Xencor's Petition would benefit public health. Merus's argument seems to be that the '286 patent claims are beneficial because they relate to the creation of bispecific antibodies for therapeutic uses. (DDB, 30-31.) But such a general tether would

apply to any patents directed to any pharmaceutical or therapeutic agent or method.

The genericness of such an argument precludes it from being a reasoned application of the Director's discretion to the specific facts of this case.

IV. CONCLUSION

For these reasons, Xencor respectfully requests that the Director reject Merus's request for discretionary denial and refer Xencor's Petition to a panel for an institution decision on the merits.

Respectfully submitted,

Dated: June 30, 2025

By: /Naveen Modi/
Naveen Modi (Registration No. 46,224)
Counsel for Petitioner

CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. § 42.24(d), the undersigned certifies that the foregoing Petitioner's Opposition to Patent Owner's Discretionary Denial Brief contains, as measured by the word-processing system used to prepare this paper, 7,471 words. This word count does not include the items excluded by 37 C.F.R. § 42.24.

Respectfully submitted,

Dated: June 30, 2025

By: /Naveen Modi/
Naveen Modi (Registration No. 46,224)
Counsel for Petitioner

CERTIFICATE OF SERVICE

I hereby certify that on June 30, 2025, I caused a true and correct copy of the foregoing Petitioner's Opposition to Patent Owner's Discretionary Denial Brief to be served via email on Patent Owner at the following addresses:

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Respectfully submitted,

Dated: June 30, 2025

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