UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

No. 2014-1693

SANDOZ INC,

Plaintiff-Appellant,

v.

AMGEN INC. and
HOFFMANN-LA ROCHE INC.,

Defendants-Appellees.

APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA
IN CASE NO. 3:13-CV-02904
THE HONORABLE MAXINE M. CHESNEY

NONCONFIDENTIAL OPPOSITION BRIEF OF DEFENDANTS-APPELLEES, AMGEN INC. AND HOFFMANN-LA ROCHE INC.

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CERTIFICATE OF INTEREST

Counsel for the appellees, Amgen Inc. and Hoffmann-La Roche Inc., certifies the following:

1. The full name of every party represented by me is:

Amgen Inc.
Hoffmann-La Roche Inc.

2. The name of the real parties in interest represented by me is:

Amgen Inc.
Hoffmann-La Roche Inc.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are:

Amgen Inc.: none
Hoffmann-La Roche Inc. is a wholly owned subsidiary of Roche Holdings, Inc. Roche Holdings, Inc.'s ultimate corporate parent is Roche Holding Ltd. More than 10% of Roche Holding Ltd.'s voting shares are held either directly or indirectly by Novartis AG.

4. The names of all law firms and the partners, counsel or associates that appeared for the party represented by counsel for the appellee in the trial court or are expected to appear in this court are:

A. Sidley Austin LLP: David T. Pritikin; M. Patricia Thayer; Vernon M. Winters; Jeffrey P. Kushan; Samuel N. Tiu; James A. High Jr.; Fitz B. Collings; Kelly A. Krellner; and Sue Wang

B. Amgen Inc.: Wendy A. Whiteford; J Drew Diamond; and Gail A. Katz

Date: May 27, 2014

/s/ David T. Pritikin
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Pursuant to Federal Circuit Rule 28(d)(1)(B), defendants-appellees have prepared this public version of their brief in which they have redacted certain confidential information. Specifically, the material omitted on pages 12-14, 16-18, 24, 26-28, 36, 69, 71-72, 74, contains references to information that has been designated confidential by plaintiff-appellant, Sandoz Inc., in that each of the specific pages identified above contains information that was sealed by the district court and thus require continued confidential treatment in this Court.

STATEMENT OF RELATED CASES

There have been no other appeals in this suit from the court below to this or any other appellate court. The two patents-at-issue, U.S. Patents Nos. 8,063,182 and 8,163,522, have not been previously involved in any litigation or administrative proceeding. Counsel for defendants-appellees is not aware of any other cases pending in this or any other court that will directly affect or be directly affected by this Court's decision in this appeal.

JURISDICTIONAL STATEMENT

Plaintiff-appellant, Sandoz, Inc., alleged that the district court had jurisdiction over this civil action pursuant to 28 U.S.C. §§2201, 2202 and 28 U.S.C. §§1331, 1338(a). The district court determined that it lacked subject-matter jurisdiction in an Order issued on November 12, 2013, and on that basis entered final judgment on November 19, 2013.

Sandoz filed a notice of appeal on December 12, 2013. This Court has jurisdiction over the appeal pursuant to 28 U.S.C. §1295(a)(1).

COUNTER-STATEMENT OF THE ISSUES

1. Whether, having found that Sandoz had been developing and intended to submit (but had not yet submitted) its biological candidate for Food and Drug Administration licensure under the Biologics Price Competition and Innovation Act as a "biosimilar," the district court properly concluded that the BPCIA's prerequisites for invoking declaratory judgment—none of which Sandoz satisfied—prohibited Sandoz's declaratory judgment action.

2. Whether the district court properly concluded that no justiciable case or controversy existed, where (a) it was undisputed that Sandoz's proposed biological product had not undergone required clinical testing, had not been submitted for FDA approval, and might never receive FDA approval, and (b) neither Amgen nor Roche, through words or actions, had subjected Sandoz to actual injury or an imminent risk of injury.

INTRODUCTION

This is an appeal from a patent declaratory judgment case. The plaintiff-appellant, Sandoz Inc. ("Sandoz"), is developing a biological product that it may someday submit for approval by the Food and Drug Administration ("FDA"). But Sandoz has not yet done so, and it is uncertain when and if it will be in a position to do so. The outcome of FDA-required testing is uncertain, as Sandoz's witness acknowledged and as the FDA draft Guidance documents confirm. Indeed, when Sandoz filed its complaint, its biologic had not yet been tested for safety and efficacy on even a single afflicted patient.

Defendants-appellees, Amgen Inc. ("Amgen") and F. Hoffmann-La Roche Inc. ("Roche"), accordingly moved to dismiss for lack of subject-matter jurisdiction. The district court granted the motion on two separate bases. Both are correct, and each is an independently sufficient ground to affirm the district court's dismissal.

As an initial matter, the district court correctly held Sandoz to the limitations on declaratory judgment imposed by the Biologics Price Control and Innovation Act ("BPCIA"). In the proceedings below, Sandoz disclosed that it was developing and intended to seek approval

of its biologic as a "biosimilar"—a biologic that is similar to an earlier-approved biological product that has already undergone the full complement of clinical testing. Such "biosimilar" approval may only be sought through a specific approval procedure created by the BPCIA, a process that is designed to be faster and less expensive than the approval process for licensing the original biological medicine which the biosimilar references. Sandoz also explicitly invoked the BPCIA's "notice of commercial marketing" provisions to support its subject-matter jurisdiction arguments.

In these circumstances, the district court correctly concluded that Sandoz, having invoked the BPCIA's accelerated approval process to seek licensure of its candidate, was therefore also subject to the BPCIA's limitations on declaratory judgment. To hold otherwise would allow an end-run around the statutory framework that Congress passed to define the universe of patents in dispute and resolve or narrow that universe of patents through a series of private exchanges and negotiations between the parties, before involvement of the courts. That framework—established by the BPCIA—includes specific provisions to address patent declaratory judgment actions involving

biosimilars. As the district court noted, the Declaratory Judgment Act ("DJ Act") expressly provides that declaratory judgment actions regarding "drug patents" are subject to the BPCIA's limitations. The patents-in-suit are "drug patents."

Having determined that the BPCIA's limitations on declaratory judgment actions applied to Sandoz's lawsuit, the district court then examined the evidence in view of the statute's plain language to determine whether Sandoz had satisfied the necessary prerequisites to remove those limitations. The district court correctly found that Sandoz had not. Notably, the district court found as a matter of law that Sandoz's "notice of commercial marketing" was inoperative because it had no product "licensed under subsection (k)" on which to base its notice. Accordingly, the BPCIA's limitations on declaratory judgment actions required dismissal of Sandoz's lawsuit.

Second, and in any event, the district court correctly concluded that the parties did not have a dispute of sufficient immediacy and reality to confer jurisdiction under the Declaratory Judgment Act. In effect, Sandoz was seeking a declaratory judgment that ***if*** its Phase III testing succeeded and ***if*** it submitted an FDA application and ***if*** the

biologic finally submitted for FDA approval was the same as the biologic that Sandoz tested, and ***if*** the FDA approved the Sandoz's biologic, ***then*** that product would not infringe when Sandoz sold it. Based on the record that Sandoz presented, each of those outcomes was uncertain. On this record, the district court correctly concluded that the dispute lacked sufficient immediacy and reality.

The district court also found insufficient evidence to support jurisdiction on Sandoz's contention that Amgen or Roche had *caused* Sandoz to suffer real or immediate injury or threat of future injury. In the absence of anything further, public statements that the patents at issue here cover Amgen's own product and that Amgen generally defends its patents did not create any actual or threatened injury to Sandoz. Without such injury, Sandoz's complaint was properly dismissed.

This Court should affirm.

COUNTER-STATEMENT OF THE CASE

Sandoz brought this action in June 2013, with the stated goal of achieving patent 'certainty' before some hoped-for future launch of a biological candidate it designed to compete with Amgen's Enbrel® (etanercept).[1] Sandoz sued on two patents—patents owned by Roche and licensed to Amgen.[2] Sandoz's candidate, however, is still in clinical testing.[3] Sandoz started enrollment for Phase III trials concurrent with the filing of its suit.[4] Those clinical trials are not complete, and Sandoz is in no position to submit an application seeking FDA approval.[5]

In August 2013, defendants-appellees, Amgen and Roche, moved to dismiss under Federal Rule of Civil Procedure 12(b)(1) for lack of subject-matter jurisdiction.[6] Although Sandoz's complaint implied that Amgen's public statements regarding biosimilar competition were pertinent to its candidate, it did not show whether Sandoz was committed to the biosimilar pathway created by subsection (k) of the

[1] A2003:¶5.
[2] A2002:¶1; A2005:¶21; A2006:¶23.
[3] A002:5-6.
[4] *Compare* A2001(complaint) *with* A3030 (press release).
[5] *See* A002:6-8.
[6] A015 (showing docket entry).

BPCIA.[7] Accordingly, defendants' motion focused on Sandoz's failure to demonstrate a real and immediate dispute regarding the patents: Sandoz's recently-initiated Phase III testing was the first time its candidate would be tested for safety and efficacy in afflicted patients; it was uncertain whether those tests would permit Sandoz to seek FDA licensure; and it was uncertain whether FDA would grant such licensure, if Sandoz sought it.[8] Defendants' motion explained, however, that, even if a case or controversy existed, the possibility that Sandoz was preparing for approval under the BPCIA's subsection (k) pathway weighed in favor of discretionary dismissal, as the BPCIA's patent provisions reflect a congressional judgment that declaratory judgment actions regarding potential biosimilars should not be brought before an applicant has, at the least, submitted its biosimilar application.[9]

In opposition, Sandoz clarified that it was, in fact, developing "a biosimilar drug to compete with Amgen's Enbrel,"[10] and asserted that

[7] *E.g.*, A2002:¶3 (Sandoz began developing "a biologic drug containing etanercept to compete with Enbrel" years before the BPCIA passed).
[8] A1014-1025.
[9] A1026-1028.
[10] A2025:8-9; *see also, e.g.*, A2025:21-24 (lawsuit need to obtain pre-launch patent certainty).

use of the subsection (k) biosimilar pathway made the dispute more certain. Sandoz urged that development of its candidate as a "biosimilar" increased the likelihood of clinical success and eventual approval.[11] It further asserted that its pre-suit letter demanding a covenant-not-to-sue served as "notice of commercial marketing" under the BPCIA's patent provisions, purportedly removing the limitations on declaratory judgment that those provisions impose.[12]

The district court granted defendants' motion in November 2013. Having "read and considered the papers filed in support of and in opposition to the motion," the court concluded that no declaratory judgment jurisdiction existed.[13] Consistent with §2201(b) of the DJ Act, the court rejected Sandoz's efforts to claim the benefits of pursuing the BPCIA's abbreviated biosimilar approval pathway (e.g., comparative reduced costs and time) while avoiding the BPCIA's limitations on declaratory judgment actions.[14] Sandoz had satisfied none of the conditions that would remove those limitations.

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[11] A2028-2031.
[12] A2048:8-10.
[13] A001:21-24; A002:13-18.
[14] A002:13-003:24.

The district court correctly concluded that a biosimilar applicant like Sandoz could not provide operative "notice of commercial marketing" under 42 U.S.C. §262(*l*)(8)(A).[15] Because the phrase "biological product licensed under [§262] subsection (k)"—by its plain language—refers only to products FDA has *actually licensed*, and because it was undisputed that FDA had not licensed Sandoz's biologic, the court found that Sandoz neither had given nor could have given such notice.[16] The court found that even if Sandoz's biologic *had been licensed*, a "notice" could not have overcome the limitations of the BPCIA's patent provisions without Sandoz's having first fulfilled the statute's other obligations, none of which Sandoz had done.[17]

In any event, the district court concluded Sandoz had not established a dispute of sufficient immediacy and reality to confer jurisdiction.[18] The court found "no evidence" that Amgen or Roche could even begin to assess whether to bring suit unless and until Sandoz, at

[15] A003:16-24.
[16] A003:16-24 (brackets in original).
[17] A003:22-24.
[18] A003:25-004:24.

least, completed its clinical testing and prepared an FDA application.[19] The court likewise dismissed Sandoz's attempt to attach significance to Amgen's corporate statements and generalized observations about the importance of patents.[20] Finally, the court found that under this Court's precedent, Sandoz's future plans to submit an FDA application for its development candidate cannot confer jurisdiction under the DJ Act.[21]

COUNTER-STATEMENT OF THE FACTS

I. Sandoz's complaint concerns a development candidate for which it had only just begun critical safety and efficacy testing

Amgen and Roche are global biotechnology pioneers that discover, develop, manufacture, and deliver innovative human therapeutics.[22] Sandoz seeks to develop "biosimilars" of such innovative biologics.[23]

Amgen's FDA-approved ENBREL contains a recombinantly produced fusion protein called etanercept.[24] Sandoz is developing a biologic candidate it hopes to someday market as "biosimilar" to

[19] A004:3-7.
[20] A004:7-15.
[21] A004:16-23.
[22] A1075; A2003-2004.
[23] A2059:15-17.
[24] A1219.

ENBREL in both Europe and the U.S.[25] Before Sandoz can market or sell it in the U.S., that biologic must first succeed in FDA-mandated clinical trials, be submitted for licensure by FDA—and be approved.[26]

According to Sandoz's parent, Novartis, successful product development in the biotechnology industry is highly uncertain; very few development projects yield a commercial product.[27] Promising candidates may fail to reach the market for any number of reasons.[28] And regulatory agencies have substantial authority over the manufacture, marketing, and sale of human therapeutics.[29]

Sandoz has not yet submitted an application to FDA seeking to license its development candidate as a biosimilar.[30] Indeed, Sandoz announced the start of its FDA-mandated Phase III testing the same day (June 24, 2013) it filed its complaint.[31] Sandoz projected such testing to take more than [redacted] months.[32]

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[25] A2055:13-14; A2052:7-8.
[26] A002:5-8; A003:9-11.
[27] A3035; A3036.
[28] A3031.
[29] A3035.
[30] A003:9-11.
[31] *Compare* A3030 *with* A011.
[32] A3002 (estimated primary completion date of [redacted]).

Two Sandoz witnesses testified about the state of its testing, and each confirmed that it was uncertain. Its Head of Clinical Development for immunology, Dr. Roth, testified merely that: [redacted];[33] [redacted] [redacted][34] [redacted];[35] [redacted] [redacted][36]

The testimony of Dr. Jankowsky, Sandoz's Global Program Leader for biopharmaceutical development, reflected similar uncertainty. [redacted];[37] [redacted];[38] [redacted];[39] [redacted]

[33] A2061:17-18 (emphasis supplied).
[34] A2061:14-16 (emphasis supplied); *see also* A2062:12-13; A2062:16-17 [redacted]
[35] A2062:19 (emphasis supplied).
[36] A2063:6-7 (emphasis supplied).
[37] A2054:2-3 (emphasis supplied).
[38] A2055:4-6 (emphasis supplied).
[39] A2055:6-8 (emphasis supplied).

[redacted][40] [redacted]

[redacted]

[redacted][41] [redacted]

[redacted]

[redacted][42] [redacted]

[redacted]

[redacted][43] [redacted]

[redacted][44]

II. Sandoz does not face, and may never face, a dilemma from the patents

[redacted]

[redacted].[45] Sandoz chose to put only two of those patents at issue: U.S. Patent Nos. 8,063,182 ("'182 Patent") and 8,163,522 ("'522 Patent") relate to ENBREL. Roche owns both of them; Amgen

[40] A2055:10-11; *see also* A2056:20-21.
[41] A4061-4062; A4064; A4069.
[42] A4081; A4083-4084.
[43] A4073-4074.
[44] A4076-4077.
[45] A2007:17-22; A3129; A4090.

exclusively licensed them from Roche.[46] The '182 Patent's claims are directed to specified proteins and pharmaceutical compositions.[47] It issued in November 2011.[48] The '522 Patent's claims are directed to specified methods and polynucleotides.[49] It issued in April 2012.[50]

A. The patents' existence has not affected Sandoz's pursuit of preclinical and clinical studies for its development candidate

Sandoz's efforts to develop an ENBREL biosimilar for multiple countries have not been affected by the existence of the patents-at-issue. The patents did not affect Sandoz's decision or subsequent efforts to compare its candidate to ENBREL with respect to a limited set of physical characteristics—what Sandoz calls "characterization." [51] Nor did they affect Sandoz's decision or subsequent efforts to pursue its animal studies[52] or its Phase I studies.[53]

Nor has the existence of the patents-at-issue affected Sandoz's

[46] A002:3-4.
[47] A056-57.
[48] A025.
[49] A102-103.
[50] A058.
[51] A2053:10-21.
[52] A2053:10-27.
[53] A2054:9-13.

decisions or efforts to pursue further clinical testing. Skipping a Phase II study,[54] Sandoz began its current Phase III testing just before filing its complaint.[55] This testing, designed to support regulatory submissions not only in the U.S., but also in Europe,[56] is occurring exclusively outside the U.S.[57]

Sandoz makes its candidate at foreign facilities: the protein in [redacted],[58] which it combines with excipients in [redacted][59] [redacted][60]

The existence of the patents has not affected and will not affect Sandoz's decision to proceed with [redacted][61] [redacted];[62] [redacted]

[54] A2054:14-16.
[55] *Compare* A3030 *with* A011.
[56] A2061:3-7.
[57] A3019-3024.
[58] A4034-4035.
[59] A4037-4041.
[60] A4047:15-24.
[61] A4031-4032; A4034-4035; *see also* A2008-2009 (summarizing preclinical and clinical testing costs).
[62] A4056-4057; A2062:28-2063:7.

[redacted][63] not on the existence of the patents.

B. The patents have not affected, and will not affect, Sandoz's investment in expanding foreign production

In addition to clinical testing, Sandoz is investing in expanding its foreign production facilities. The existence of the patents has not affected its past efforts, and according to Sandoz, will not affect its future efforts either. According to Sandoz, in 2012 the European market for ENBREL was $1.8 billion.[64] [redacted][65] [redacted][66] [redacted],[67] [redacted].[68]

Toward that end, Sandoz [redacted]

[63] A4079:6-30; A2055:4-6.
[64] A2055:15-17.
[65] A4042:13-24.
[66] A2056:7-11.
[67] A2009:7-8.
[68] A4051-4052.

[redacted],[69] and has [redacted][70]—all without regard to any issue the patents might pose with respect to a U.S. launch. Indeed, Sandoz admitted this lawsuit [redacted][71] [redacted].[72]

C. Neither Amgen nor Roche had said or done anything that would have caused Sandoz a current or imminent threat of injury

The district court found no evidence that either Amgen or Roche had ever indicated an intent to sue Sandoz.[73] Sandoz's complaint alleged no such facts. As Amgen and Roche explained below, neither of them had ever "enforced the two attacked patents, or any of [their] Enbrel® patents, against any entity, at any time, against any product, in any jurisdiction."[74] The court further found that Sandoz submitted

[69] A2009:9-11.
[70] A2009:11-12.
[71] A4042:4-12; A4047:1-12.
[72] A4101:12-17.
[73] A004:3-7.
[74] A4016:23-26 (emphasis omitted).

no evidence that any actions by Amgen or Roche had subjected Sandoz to an imminent threat of injury.[75]

Instead, as to Amgen, Sandoz presented general corporate statements typical of biotechnology companies:

- the patents-at-issue were important and protected ENBREL,[76] and conferred exclusivity;[77]
- generalized statements, most of which did not concern the patents-at-issue, that Amgen would defend its patents;[78] and
- Amgen did not expect ENBREL competition from biosimilars,[79] although none of those statements suggested Amgen knew about Sandoz's biosimilar development program,[80] and Amgen's annual reports had identified many other kinds of (non-biosimilar) ENBREL competitors.[81]

As for Roche, Sandoz neither alleged nor provided evidence of any statement at any time or in any context with respect to the patents, Sandoz, or its candidate.[82] Rather, Sandoz's allegations with respect to Roche concerned a request for a covenant not to sue that Sandoz sent

[75] A003:25-A004:15.
[76] A2012:¶56.
[77] A2002:¶4.
[78] A2011:¶51.
[79] A2011:¶54.
[80] A4017:23-28.
[81] A3146.
[82] *See* A2014:3-9 (allegations against Roche).

jointly to Roche and Amgen days before filing this lawsuit. Sandoz complained that, like Amgen, Roche did not respond before Sandoz's filing.[83]

III. Sandoz's development candidate faces scientific uncertainty and regulatory risk before any eventual FDA approval

Innovative biological products typically go through three clinical development phases before their developers seek FDA approval: Phase I, which typically tests safety, tolerability, and pharmacologic properties on healthy human volunteers, and Phases II and III, which typically test safety and efficacy on, respectively, a small and then a larger group of afflicted patients.[84] If testing in each phase succeeds, the developer may be in a position to submit a Biologics License Application ("BLA").

In March 2010, the BPCIA was enacted and provided an abbreviated approval pathway, 42 U.S.C. §262(k), for licensing "biosimilars." As the BPCIA defines it, a "biosimilar" is a biological product that is (1) "highly similar to the reference product notwithstanding minor differences in clinically inactive components";

[83] A2014:6-9.

[84] A3040.

and (2) has "no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product."[85]

Starting in February 2012, FDA issued a series of draft Guidance documents to provide "an overview of FDA's approach to biosimilarity."[86] These were before the district court.[87] Those draft Guidance documents provide useful context for assessing the uncertain and contingent nature of the parties' dispute; Sandoz described one of them as "detailing precisely what will be required to show that a protein is 'highly similar,' . . . ."[88]

A. FDA's draft Guidance highlights that biosimilar hopefuls face significant clinical and regulatory uncertainties

FDA's 2012 draft Guidance documents recognized that even using then-current technology, a protein's three-dimensional structure can often be difficult to define precisely,[89] and further cautioned that

[85] 42 U.S.C. §§262(i)(2)(A), (B).

[86] A3057.

[87] A3052-3077 (Scientific Considerations Guidance); *see also* A1575-1592 (Quality Considerations Guidance); A3798-3818 (Q5E Comparability Guidance); A3843-3860 (Biosimilars Q & A Guidance).

[88] A2065:26-28.

[89] A1584:272-274.

characterization studies were unlikely to predict sufficient structural identity: "[u]nlike small molecule drugs, whose structure can usually be completely defined and entirely reproduced, proteins are typically more complex and are unlikely to be shown to be structurally identical to a reference product. Many potential differences in protein structure can arise."[90] Moreover, FDA cautioned that proteins generally exhibit "flexibility that enables dynamic, but subtle, changes in protein conformation over time, some of which may be absolutely required for functional activity."[91]

Such subtle differences could be important because, as FDA explained, "even minor structural differences . . . can significantly affect a protein's safety, purity, and/or potency."[92] The Guidance concluded that despite improvements in analytical techniques, "current analytical methodology may not be able to detect all relevant structural and functional differences between two proteins,"[93] and thus "a clinical study or studies are required to demonstrate biosimilarity unless FDA

[90] A3059:137-139.
[91] A1584:262-266.
[92] A3059:40-42.
[93] A3060:160-162.

determines an element unnecessary."[94]

The extent and scope of Phase III testing FDA requires in any particular circumstance turns on the uncertainty regarding the prospects for success in Phase III trials and, in particular, on the "extent of residual *uncertainty about the biosimilarity of the two products* after conducting structural and functional characterization and possible animal studies."[95]

Under the draft Guidance documents, FDA has indicated it will require Phase III testing if it has concluded that, as a scientific matter, uncertainties remain about whether a biologic clinical candidate is biosimilar, notwithstanding successful preclinical and Phase I testing: "[a]s a scientific matter, comparative safety and effectiveness data will be necessary to support a demonstration of biosimilarity if there are residual uncertainties about the biosimilarity of the two products based on structural and functional characterization, animal testing, human PK and PD data, and clinical immunogenicity assessment."[96]

[94] A3060:162-164.
[95] A3067:475-477.
[96] A3071:618-625.

B. The clinical and regulatory uncertainties highlighted in FDA's draft Guidance apply to Sandoz's biological candidate

Whether Sandoz's Phase III testing will succeed or fail is scientifically uncertain. [redacted] But the FDA's draft Guidance documents, issued three years later, recommended comparisons of other variables such as quaternary structure, post-translational modifications such as phosphorylation, and deamidation and oxidation.[97] Sandoz submitted no evidence [redacted][98]

Moreover, Sandoz's Phase I testing involved *healthy* patients and thus could not test efficacy.[99] [redacted][100] [redacted][101]

[97] A3064:333-343.
[98] *See generally* A2053.
[99] A4061-4062.
[100] A4066-4067.
[101] A4074.

Sandoz specifically cautioned investors and others in a press release that its then-just-begun clinical trials might yield unexpected results.[102] That release further referred readers to SEC filings of Sandoz's corporate parent, Novartis, *id.*, which regularly warn that "[d]ue to the risks and uncertainties involved in progressing through pre-clinical development and clinical trials, . . . we cannot reasonably estimate the timing[or] completion dates . . . of the development of any particular development compound."[103]

Consistent with those specific warnings about Sandoz's candidate, the district court had before it evidence that Phase III trials of biosimilars were expected to fail between 20% and 50% of the time,[104] and that Phase III trials of biologics generally failed between 21% and 58% of the time.[105]

Where there is sufficient certainty about a proposed biologic's safety and efficacy, the FDA can excuse Phase III testing. In particular, if an party believes that preclinical and Phase I studies have resolved

[102] A3031.
[103] A3043.
[104] A3080.
[105] A3082; A3086; A3089.

uncertainties about safety and efficacy, such that Phase III clinical studies are not required, it can request exemption from those studies.[106]

[redacted][107]

[redacted][108] [redacted]

[redacted][109]

[redacted]

[redacted][110]

[redacted]

[redacted][111] To the contrary, FDA has required that Sandoz test its candidate in Phase III clinical studies before it may even submit an application for licensure.[112]

Accordingly, [redacted]

[106] A3059:122-23 (citing 42 U.S.C. §262(k)(2)(A)(ii)).
[107] A2054.
[108] A2061.
[109] A4069:15-19.
[110] A4069:20-23.
[111] A4081:14-17; A4083:25 – A4084:2.
[112] A4069:2-19.

[redacted][113] Sandoz has not submitted an FDA application.[114] Nor is it in a position to do so; whether it will eventually be able [redacted][115] [redacted][116]

Sandoz did not disclose the excipients used in its formulation.[117] There was no evidence that they are the same as in Amgen's ENBREL. [redacted][118] The use of a different excipient may be critical: FDA has explained that "[p]roteins are very sensitive to their environment. Differences in excipients or primary packaging may affect product degradation and/or clinical performance."[119]

[113] A2061:¶11; A2062:¶14; A2062-2063:¶18; A2055:¶14.
[114] A003:9-11.
[115] A4079:6-13.
[116] A4076:24 – A4077:5.
[117] A2041:26-28.
[118] A2052:21-23.
[119] A1591:578-580.

C. If Sandoz's development candidate fails, it must re-start its process, creating greater uncertainty and taking more time

According to Sandoz, if its candidate fails, it cannot simply re-attempt Phase III testing. Instead, Sandoz would have to [redacted][120] That original process was inherently risk-fraught—and would be again, if repeated.

Even assuming success at every juncture, that "rewind" would take substantial time—as long as [redacted], using the timetable for Sandoz's current candidate as a guide.[121] And that does not account for the significant historical uncertainty of Phase III trials.[122]

SUMMARY OF THE ARGUMENT

The district court dismissed Sandoz's lawsuit on two separate grounds: first, that Sandoz was subject to, but had not satisfied, any of the BPCIA's limitations on declaratory judgment; and, second, that Sandoz had not presented a case or controversy. Each of the district court's two grounds of dismissal was correct.

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[120] A2029.

[121] A2040; A2052:¶2.

[122] A3082-3083.

The dismissal for failure to comply with declaratory judgment prerequisites. The district court found as a matter of fact that Sandoz had developed its biologic as a biosimilar and intended to submit it to the FDA as a biosimilar under 42 U.S.C. §262(k)—generally known as the "subsection (k)" abbreviated approval pathway.[123] That abbreviated pathway was created by the BPCIA, which also includes amendments to the Public Health Service Act ("PHSA"), the Declaratory Judgment Act, and the Patent Act, thereby putting into place a comprehensive framework to define and address related patent disputes. In 42 U.S.C. §262(*l*), immediately following the provisions creating the subsection (k) pathway, Congress established a specific framework that (1) requires the applicant to provide information to the reference product sponsor ("RPS"), (2) requires the parties to then exchange patent lists and positions and attempt to narrow the potential patents in dispute through license negotiation, and, if no resolution is reached, (3) requires the parties to identify a list of patents for litigation.

In particular, 42 U.S.C. §262(*l*)(9), entitled "Limitation on declaratory judgment action," provides in §262(*l*)(9)(C) that a biosimilar

[123] A002:5-11.

applicant cannot bring a declaratory judgment action with regard to *any* patent until, at the least, it has provided its FDA application and information about how its product is made to the RPS. The district court found as a matter of fact that Sandoz is still conducting the clinical studies required to prepare and file its biosimilar application with the FDA and accordingly has not carried out any of the requisite acts. In addition, and as the district court correctly noted, Sandoz invoked the BPCIA's notice of commercial marketing provisions to support its subject-matter jurisdiction arguments.[124]

In those circumstances, the district court was correct to apply the BPCIA's limitations on declaratory judgment to Sandoz's declaratory judgment action, because the other relevant statutory change that the BPCIA effected was to the DJ Act. In particular, the BPCIA amended 28 U.S.C. §2201(b) to require that in declaratory judgment actions involving drug patents with respect to biosimilars, courts must apply the BPCIA's limitations. This action involves drug patents. And Sandoz identifies no clear error in any of the district court's factual findings; indeed, it does not challenge them at all. Based on the facts as

[124] A003:11-14.

the court found them, the BPCIA precluded Sandoz's attempt to use the declaratory judgment remedy.

Sandoz contends that, notwithstanding that it has been working with the FDA to prepare an application to license its biologic as a biosimilar under the pathway expressly created for biosimilars by the BPCIA, it is exempt from BPCIA-created limitations on declaratory judgment actions. Sandoz's novel theory is that because it has not yet *submitted* its subsection (k) biosimilar application to the FDA and has thus not yet, in the language of the statute, "*fail[ed] to provide*" the requisite information, it can avoid those limitations. Not so. Sandoz cannot credibly argue that its prospective patent dispute is immediate and real because it is availing itself of the BPCIA's abbreviated regulatory pathway for biosimilars, yet avoid the BPCIA's limitations on declaratory judgment because it is merely a "prospective" (k) applicant. Congress created a single biosimilar approval pathway along with an integrated framework restricting when patent declaratory judgment litigation would be appropriate. Congress implemented that framework using precisely phrased conditions on when declaratory

judgment would or would not be authorized. Congress did not intend—or provide for—the absurd result that Sandoz seeks.

The district court likewise correctly dismissed Sandoz's argument that its declaratory judgment action could proceed because Sandoz had given Amgen and Roche what Sandoz deemed a "notice of commercial marketing" under the BPCIA. An applicant must provide such notice not later than 180 days before the date of the first commercial marketing of the "biological product licensed under subsection (k)."[125] But as a matter of law Sandoz could not have provided a "notice of commercial marketing" because its development candidate is not a "biological product licensed under subsection (k)."[126] In addition, even after an applicant has provided a "notice of commercial marketing," it cannot bring an action for declaratory relief until it has complied with the patent information disclosure and other obligations that the BPCIA imposes.[127] The district court's Order correctly explained this.[128]

[125] 42 U.S.C. §262(*l*)(8)(A).

[126] *Id*.

[127] 42 U.S.C. §262(*l*)(9)(A)–(C) (referring back to pre-suit disclosure obligations under the statute); *see also* 28 U.S.C. §2201(b).

[128] A003:11-24.

The dismissal for lack of a case or controversy. That Sandoz's suit is prohibited by the BPCIA's declaratory judgment limitations is not the only basis for the ruling below. The district court also correctly concluded that the parties' alleged dispute lacked the immediacy and reality required by *MedImmune, Inc. v. Genentech, Inc.,* 549 U.S. 118 (2007), and its progeny. Despite Sandoz's rhetoric that the district court "disagreed" with *MedImmune* and failed to cite it, the district court relied on this Court's decision in *Prasco, LLC v. Medicis Pharmaceutical Corp.*, 537 F.3d 1329, 1338-39 (Fed. Cir. 2008), which applied *MedImmune*. When it filed its complaint, Sandoz had just begun initial testing of its development candidate on afflicted human patients. As Sandoz's witness confirmed, the outcome of those tests was uncertain, as was the identity of the product, the timing of an FDA application, and FDA approval itself.

Further, according to Sandoz's evidence, neither of the two patents at issue has had, is having, or will have any effect on Sandoz's development activities. It began and completed its preclinical studies, began and completed Phase I studies, and began its Phase III testing—all without effect from the patents. And according to Sandoz's evidence,

no matter what happens in this lawsuit, it will proceed with its plans, as they are independently useful for Sandoz's ex-U.S. submission, approval, and hoped-for launch of its development candidate and are not subject to any interference by the patents because, as per Sandoz, they are all performed ex-U.S. Without any actual injury that had been caused by the patents, Sandoz attempted to establish a real and immediate threat of future injury. But the evidence was equally lacking. The court correctly found that public statements that the patents cover Amgen's ENBREL and that Amgen defends its patents were insufficient to show an imminent threat of injury to Sandoz.

In these circumstances, the district court correctly concluded that Sandoz's declaratory judgment was improper because of Sandoz's failure to comply with the prerequisites set forth in the BPCIA and that in any event the dispute lacked the requisite immediacy and reality. The district court properly dismissed this action.

STANDARDS OF REVIEW

The district court's dismissal may be affirmed on any ground the record supports.[129] Subject-matter jurisdiction is assessed as of the date the complaint was filed, and later events cannot cure its absence then.[130] Even absent a party's challenge, courts have an independent obligation to determine whether subject-matter jurisdiction exists.[131] Subject-matter jurisdiction must exist both when the complaint was filed and at all points in the case thereafter.[132]

Subject-matter jurisdiction is an issue of law reviewed *de novo*, but a district court's factual findings made in the course of a jurisdictional ruling are reviewed only for clear error.[133] A district court's statutory construction is reviewed *de novo*.[134]

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[129] *Wolfe v. Strankman*, 392 F.3d 358, 362 (9th Cir. 2004). Regional circuit law applies to this dispute. *Madey v. Duke Univ.*, 307 F.3d 1351, 1358 (Fed. Cir. 2002).

[130] *Dunmore v. United States*, 358 F.3d 1107, 1113 (9th Cir. 2004).

[131] *E.g., Arbaugh v. Y&H Corp.*, 546 U.S. 500, 506 (2006).

[132] *E.g., Benitec Australia, Ltd. v. Nucleonics, Inc.*, 495 F. 3d 1340, 1344 (Fed. Cir. 2007).

[133] *United States ex rel. Biddle v. Bd. of Trs. of Leland Stanford, Jr. Univ.*, 161 F.3d 533, 535 (9th Cir. 1998).

[134] *United States v. Cabaccang*, 332 F.3d 622, 625 (9th Cir. 2003).

ARGUMENT

I. The district court correctly concluded that the Declaratory Judgment Act forecloses Sandoz's patent action with respect to its biosimilar development candidate

A. Sandoz is developing its biologic candidate as a biosimilar and intends to submit it for FDA approval as a biosimilar

In the briefs it filed below, Sandoz made clear that it is developing its biologic as a biosimilar and intends to submit it to the FDA for approval on that basis. Sandoz's Global Program Leader testified that its development candidate [redacted];[135] [redacted];[136] [redacted][137] Sandoz characterized its development candidate as a "biosimilar drug to compete with Amgen's Enbrel" and represented that this lawsuit was its effort to clarify its rights before launching its "biosimilar version of Enbrel."[138] Sandoz disclosed that it "designed its Phase III study in close consultation with the FDA for the

[135] A2052:¶2.
[136] A2054:¶8.
[137] A2025:¶14.
[138] A2025.

purpose of showing biosimilarity under the FDA's regulations."[139] Sandoz's opening brief in this Court likewise represents that it intends to seek approval for its development candidate as "a biosimilar version of Amgen's Enbrel®."[140]

The benefit of Sandoz's pursuit of the subsection (k) pathway, it argued, is that evaluation of potential biosimilars is purportedly less rigorous, and potentially quicker, than the traditional subsection (a) pathway.[141] As a potentially abbreviated route to approval, Sandoz further argued, the subsection (k) pathway provided its dispute with more immediacy and reality.[142] Sandoz so embraced the BPCIA-created subsection (k) pathway that it even contended its pre-suit letter to Amgen and Roche satisfied its "notice of commercial marketing" obligations under the BPCIA's patent provisions.[143]

[139] A2030:16-18.
[140] *E.g.,* Opening Brief Heading §A.
[141] *E.g.*, A2065:10-17.
[142] *E.g.*, A2070:11-28.
[143] A2048:8-11.

B. Based on the record, the BPCIA, as incorporated by the Declaratory Judgment Act, foreclosed Sandoz's lawsuit

Based on the record that Sandoz itself established, the district court correctly held Sandoz to the limitations on declaratory judgment as set forth in the BPCIA's patent provisions.

Through the BPCIA, Congress amended the DJ Act to require that declaratory judgment be limited as described by the PHSA with respect to drug patents such as the two at issue.[144] The cross-reference in the DJ Act to the PHSA for limitations on actions came about through an amendment to the DJ Act introduced by the BPCIA. At the same time, and again through the BPCIA, Congress amended §351 of the PHSA, codified at 42 U.S.C. §262, to add, among other things, the new biosimilars regime at §262(k) and its patent provisions at §262(*l*).

Under the BPCIA-amended PHSA, when an applicant is pursuing FDA approval as a "biosimilar" under §262(k), declaratory judgment actions are subject to limitations unless and until certain events occur.

Under §262(*l*)(9), in order for a biosimilar applicant to bring a declaratory judgment action, it must do the following: (1) provide its

[144] 28 U.S.C. §2201(b).

FDA application and process information to the RPS, (2) comply with its obligations to provide patent lists and detailed positions thereon in exchanges with the RPS, (3) secure FDA approval for its biosimilar product, and (4) provide notice 180 days before the first commercial marketing of its licensed product. Until all of these requirements are met, the limitations of §262(*l*)(9)—as incorporated in 28 U.S.C. §2201(b)—apply here.

Sandoz argues that the BPCIA's patent provisions limit declaratory judgment actions only *after* (1) a biosimilar applicant has submitted a subsection (k) application to the FDA, (2) the FDA has accepted that application for review, and 20 days thereafter (3) the applicant "fails to provide" the application and additional manufacturing information to the RPS. Until such "failure" has occurred, Sandoz argues, the patent provisions of the BPCIA do not limit the prospective biosimilar applicant's ability to bring biosimilar-related declaratory judgment patent actions that would otherwise be restricted under the BPCIA. Sandoz's construction, however, eviscerates the statutory framework, is inconsistent with the BPCIA's cross-referencing within the PHSA and between it and the DJ Act,

furthers no logical public policy, undermines orderly access to the courts, and invites gamesmanship.

1. The BPCIA's patent provisions require an ordered exchange as a predicate to biosimilar-related lawsuits

In the BPCIA, Congress created a framework for resolving patent issues: Within 20 days of the date the FDA accepts a biologic license application for review under §262(k), the biosimilar applicant must "provide to the reference product sponsor a copy of the application submitted to the Secretary under subsection (k)," plus information sufficient to show how the proposed biosimilar is produced.[145] Once conveyed, this information enables the RPS and other relevant patent owners to identify those patents for which the RPS "believes a claim of patent infringement could reasonably be asserted"[146] and which, if any, the RPS would be prepared to license.[147]

In response, the biosimilar applicant can identify patents not listed by the RPS,[148] but it must take a position on each patent it or the RPS identifies—either stating that it will wait until that patent expires

[145] *Id.* §262(*l*)(2)(A).
[146] *Id.* §262(*l*)(3)(A)(i).
[147] *Id.* §262(*l*)(3)(A)(ii).
[148] *Id.* §262(*l*)(3)(B)(i).

to begin commercial marketing or providing a detailed basis for its belief that each patent is invalid, not infringed, or unenforceable.[149] The biosimilar applicant must also respond to any licensing proposals made by the RPS.[150] Next, the RPS must provide the biosimilar applicant a detailed response to the biosimilar applicant's invalidity, non-infringement and unenforceability contentions.[151] At this point, a preliminary set of disputed patents is known to each party.

The statute next mandates "patent resolution negotiations."[152] If negotiations fail, then, depending ultimately on the decision of the biosimilar applicant, all or a subset of these disputed patents become the subject of an "immediate" infringement action that can be brought by the RPS.

In order to facilitate the filing of a patent infringement action, Congress amended 35 U.S.C. §271(e)(2) to add subsection (C), which provides that the act of filing the biosimilar FDA application is patent infringement of those patents listed in the exchanges between the

[149] *Id*. §262(*l*)(3)(B)(ii).
[150] *Id*. §262(*l*)(3)(B)(ii).
[151] *Id*. §262(*l*)(3)(C).
[152] *Id*. §262(*l*)(4).

parties. In addition, 42 U.S.C.§262(*l*)(9) ("Limitations on declaratory judgment") places strict limitations, through 28 U.S.C. §2201(b), on the ability to bring patent declaratory judgment actions with respect to drug patents when the abbreviated regulatory pathway of 42 U.S.C. §262(k) is implicated.[153] This framework seeks to define, narrow, and focus patent disputes before the courts are involved.

Subsection §262(*l*)(9) is divided into three subparagraphs addressing access to declaratory judgment based on the biosimilar applicant's compliance with the statute's exchange and notice provisions. Taking the last first, if a subsection (k) applicant fails to provide a copy of its FDA application and the required process information to the RPS, §262(*l*)(9)(C) provides that "the reference product sponsor, *but not the subsection (k) applicant*, may bring an action under section 2201 of title 28 for a declaration of infringement, validity, or enforceability of *any patent* that claims the biological product or a use of the biological product."[154]

Even if the biosimilar applicant provides its application and process information to the RPS, §262(*l*)(9)(B) provides that if it fails to

[153] *Id.* §262(*l*)(9)(C).

[154] *Id.* (emphasis supplied).

carry out any of the other mandated actions it is required to perform by §262(*l*), "the reference product sponsor, *but not the subsection (k) applicant*, may bring an action under section 2201 of title 28 for a declaration of infringement, validity, or enforceability of *any patent* included in the list described in paragraph (3)(A), including as provided under paragraph (7)," *i.e.*, the list that the RPS provides in response to the applicant's provision of its application and manufacturing information—including relevant patents that are later licensed by or issued to the RPS.[155]

In contrast to §§262(*l*)(9)(C) and (B)—which lift only the restrictions placed on the RPS filing declaratory judgment actions—§262(*l*)(9)(A) sets out the only circumstances under which the applicant can file a declaratory judgment action. Specifically, §262(*l*)(9)(A) provides that in cases where the applicant timely provides a copy of its application and process information to the RPS, carries out all of its other required obligations in the patent exchanges under §262(*l*), and provides a "notice of commercial marketing" under §262(*l*)(8)(A), the applicant can bring a declaratory judgment action on those patents

[155] *Id*. §262(*l*)(9)(B) (emphasis supplied).

referenced in §262(*l*)(8)(B)—patents identified through the previous orderly exchanges. And by §262(*l*)(8)(A)'s plain language, such notice may only be provided once the product that was previously the subject of the subsection (k) application has been licensed by the FDA.

2. Sandoz's interpretation of the BPCIA's patent provisions creates internal inconsistencies

Sandoz asserts that the phrase "fails to provide" in the context of §262(*l*)(9)(C) means that a prohibition on declaratory judgment actions only arises as a consequence of a failure to act. Sandoz then argues that because one cannot "fail to act" until one is obligated to act, this means that any time before the applicant's deadline to provide the RPS with the biosimilar application, a biosimilar applicant is free to seek declaratory judgment. Sandoz's position, if accepted, would effectively abrogate each of the BPCIA's carefully defined provisions limiting that remedy and thereby disrupt the balance of incentives utilized by Congress through the BPCIA to drive behaviors.

Likewise, the precision with which Congress addressed the actions that the biosimilar applicant must take before it may file a declaratory judgment action under §262(*l*)(9)(A), and the BPCIA's integrated changes to the PHSA, the DJ Act and the Patent Act, cannot be

reconciled with Sandoz's theory that Congress intended the limitations of §262(*l*)(9) not to apply prior to the filing of the biosimilar application.

Rather, §262(*l*)(9)'s language reflects Congress's clearly stated intent to regulate precisely when a declaratory judgment remedy would be available to a party intending to seek approval of its biologic as a biosimilar. It is implausible that the statute could be read any other way. Sandoz cannot now circumvent Congress's intent to limit declaratory judgment actions by arguing that, even though it told a federal district court that it is seeking approval of its biologic as a biosimilar, it should not be treated as a biosimilar applicant for purposes of applying the limitations on seeking declaratory judgment.

It is a cardinal principle of statutory construction to give effect "'to every clause and word of a statute' . . . rather than to emasculate an entire section."[156] The amendments to §2201 mean that a declaratory judgment action is foreclosed to the applicant until all the statutorily required acts have either been carried out in the proper sequence and timing. Indeed, any other reading of the statute would produce illogical results. For example, under Sandoz's read of the statute (although

[156] *Bennett v. Spear*, 520 U.S. 154, 173 (1997).

Sandoz does not admit this), a biosimilar applicant is free to start a declaratory judgment action before the FDA's acceptance of its application. But the prohibition on such actions that §262(*l*)(9)(A) imposes would spring into effect at the twenty-day deadline for providing the biosimilar application and process information to the RPS, whether or not the biosimilar application and other information had been provided—and the earlier-filed declaratory judgment lawsuit would then have to be dismissed. Sandoz offers no conceivable rationale for interpreting the statute to create such an absurd result.[157]

Sandoz further argues that the BPCIA's limitations apply only to what it calls "artificial" acts of infringement under §271(e)(2) and not to what Sandoz calls "actual" infringement under §271(a). This cannot be correct. As a preliminary matter, the distinction that Sandoz seeks to draw is itself "artificial": the statute itself does not draw any distinction between "artificial" acts of infringement under §271(e) and other bases of infringement in §271. Section 262(*l*)(9) could easily have been drafted to preclude declaratory judgment based only on §271(e), but it

[157] Sandoz has developed and intends to submit its biologic under §262(k)'s abbreviated pathway. This appeal does not present issues regarding a biologic developed or intended for submission under §262(a).

was not. Instead, it was drafted unambiguously to include *any* patent declaratory judgment under §2201 of the DJ Act. And this makes sense. If the prohibitions of §262(*l*)(9) applied only to declaratory judgment actions under §271(e)(2)(C), biosimilar applicants in Sandoz's position could avoid the restrictions of the statute by simply bringing the same invalidity and unenforceability claims under §271(a), for example, instead.

Sandoz's reliance on *Caraco Pharmaceutical Laboratories, Ltd. v. Novo Nordisk A/S*, 132 S. Ct. 1670 (2012), borders on the ironic.[158] The Court there indeed held that "we are not inclined to interpret statutes as creating a jurisdictional bar when they are not framed as such."[159] Here, of course, the statutes are framed as such: in a section entitled "Limitation on declaratory judgment action," §262(*l*)(9) creates jurisdictional bars, and the DJ Act was amended specifically to incorporate those limitations on declaratory judgment for actions—like this one—that involve drug patents.[160]

[158] Opening Brief at 4, 38.
[159] *Caraco*, 132 S. Ct. at 1680.
[160] 28 U.S.C. §2201(b).

3. Sandoz did not provide, and cannot currently provide, a proper "notice of commercial marketing"

Sandoz has argued that it has, in any event, provided notice under §262(*l*)(8)(A) that was legally operative to remove any limitations that might exist with respect to its ability to bring a declaratory judgment action.[161] As the district court ruled, Sandoz is wrong.

Sandoz criticizes the district court for construing the term "biological product licensed under subsection (k)" in §262(*l*)(8)(A) to mean a biological product that the FDA has actually licensed rather than the development candidate that is still subject to the subsection (k) application process.[162] But the district court's construction of "product licensed" is consistent with the plain meaning of "licensed": "[t]o whom or for which a license has been granted; provided with a license."[163] That construction is also consistent with the statute's other uses of "product licensed,"[164] and stands in sharp contrast to the other

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[161] Opening Brief at 5.

[162] *Id.* at 40-41.

[163] 9 OXFORD ENGLISH DICTIONARY 245 (Oxford Univ. Press, 9th ed. 1971).

[164] *See, e.g.*, 42 U.S.C. §§262(d)(1), (i)(4) & (k)(5) (all using "product licensed" to refer to product that the FDA has licensed). Identical words used in different parts of the same statute presumptively have the same

provisions of §262(*l*), which refer merely to "a biological product that is the subject of an application under subsection (k)." In the other provisions of §262(*l*), which detail the exchange of information and patent lists, Congress chose to refer to the applicant's biological product by using the phrase "that is the *subject of an application under* subsection (k)."[165] But, in the context of the "notice of commercial marketing," Congress adopted the different phase "*licensed under* subsection (k)" when referring to the applicant's biological product. The rational conclusion is that Congress's adoption of the new phrase "product licensed" in the "notice of commercial marketing" of §262(*l*)(8)(A) was intentional and purposeful.

Given the BPCIA's statutory framework, in which the biosimilar applicant gets a significant say in controlling the order in which patents can be litigated, it makes sense that Congress intended the notice of commercial marketing to be triggered by licensure. When the FDA approves a biosimilar application, the RPS has the next six months—before the biosimilar product enters the market and the injury to the

meaning. *E.g.*, *Merrill Lynch, Pierce, Fenner & Smith, Inc. v. Dabit*, 547 U.S. 71, 86 (2006).

[165] 42 U.S.C. §§262(*l*)(2)(A), (*l*)(3)(A)(i), (*l*)(3)(B)(i), (*l*)(3)(B)(ii)(I), (*l*)(3)(C), (*l*)(7)(B).

RPS increases drastically (and before the harm caused by the biosimilar's entry perhaps becomes irreparable)—to seek a preliminary injunction on any patent that was included on the specified lists.[166] Maintaining the *status quo* for this limited time to permit the RPS to seek court intervention to prevent irreparable harm reflects a rational policy choice balancing competing public interests.

The district court was also correct to reject Sandoz's contention that the statute's "notice of commercial marketing"—even if it could be given prior to licensure—operates at any time to remove the BPCIA's limitations on the declaratory judgment remedy.[167] Subsection 262(*l*)(9)(A) spells out that the notice lifts the prohibition on the declaratory judgment remedy with respect to patents described by "clauses (i) and (ii) of (*l*)(8)(B)"—patents that cannot be ascertained until after all the exchanges have taken place. Indeed, if the biosimilar applicant fails to provide the RPS with its FDA application and manufacturing information, §262(*l*)(9)(C) prohibits biosimilar-applicant-initiated declaratory judgment actions and provides no basis for restoring such actions through a notice of commercial marketing.

[166] *Id.* §262(*l*)(8)(B).

[167] A003:16-24.

Sandoz's position, if accepted, would effectively delete these provisions from the statute.

C. Sandoz's three appeals to policy ring hollow

The statutory text leaves no room for Sandoz's statutory construction arguments, so Sandoz retreats to three policy arguments. Grounded in its one-sided notions of fairness, Sandoz's policy rationales do not withstand examination.

1. To hold Sandoz to the BPCIA does not "needlessly delay" the introduction of FDA-approved biosimilars

Sandoz first argues that to apply the statute as written "*needlessly* delays the availability of lower-cost biologic medicines" because a biosimilar would not be commercially available immediately upon FDA approval.[168] That argument assumes what it seeks to prove: that the statute's only goal is immediate introduction of biosimilars upon FDA approval.

The overall framework the BPCIA established affords the courts the opportunity to address the dispute in an orderly fashion, with the parties' reasonable cooperation in discovery and avoiding the types of

[168] Opening Brief at 41 (emphasis supplied).

emergency motions that happen in the absence of notice. The statute's plain language provides the RPS with 180 days to seek preliminary injunctive relief on the relevant listed patents. Timing the 180-day period to begin at licensure makes eminent sense against that background. Approval removes doubts about the final composition of the biosimilar product, as well as the approved formulation, indications and label that make up the commercial product at launch. The record for the injunction motion becomes more certain, and the RPS can seek injunctive relief without having prematurely expended judicial resources. And those motions can be addressed by the court before irreparable injury to the RPS is caused by the biosimilar's launch.

This is also not the first time Congress chose to weigh the interests of patent holders against market entry of lower-cost pharmaceutical products. The Hatch-Waxman ANDA framework includes a 30-month stay of FDA approval expressly to protect the legitimate interests of patent owners. Congress recognized the 30-month stay can delay market entry of a generic drug for some time after the FDA has determined it may be approved, but nonetheless expressly provided time to resolve patent litigation before the infringing generic

drug is allowed to enter the market.[169] Here too, Congress enacted a framework to allow patent disputes to unfold prior to market entry by a biosimilar. In both regimes, a copyist does not have an unfettered right to launch immediately upon FDA approval (or tentative FDA approval in the case of generics). Rather, having leveraged the innovator's prior demonstration of safety and efficacy to gain the benefit of a less expensive path to licensure, the copyist must yield to permit court intervention to enforce the exclusionary right of a patent, if such intervention proves justified.

2. The BPCIA provides Sandoz with tools to reduce or resolve "patent uncertainty" before commercial launch

Sandoz also contends that to hold it to the BPCIA deprives it of "any reasonable way to resolve its rights prior to commercial marketing."[170] But, with the limited exception of patents that might issue after the initial patent exchanges, the statute allows a subsection (k) applicant to force the RPS, at the risk of its damages

[169] 21 U.S.C. §355(j)(5)(B)(iii); *Eli Lilly & Co. v. Teva Pharms. U.S.*, 557 F.3d 1346, 1350-51 (Fed. Cir. 2009).

[170] Opening Brief at 44.

claim being otherwise limited to a reasonable royalty,[171] immediately to litigate all disputed patents that cause the (k) applicant concern, starting when the FDA begins its review of the application in earnest.[172] Although, practically speaking, court caseloads may not afford the subsection (k) applicant a full trial and appeal before FDA approval, the (k) applicant has tools, such as claim construction and summary judgment, to reach early resolution of dispositive issues. In total, the statutory framework achieves for the subsection (k) applicant the means significantly to reduce or resolve its "patent uncertainty" before commercial launch, and provides the RPS a modest opportunity to seek court intervention when commercial launch is certain—and achieves both without burdening the courts with premature cases.

Sandoz also can expedite the commencement of a lawsuit under the BPCIA framework: an applicant does not have to wait until expiration of every period applicable to it. For example, it can immediately forward its application and information to the RPS, and respond promptly after being provided a list of patents by the RPS,

[171] 35 U.S.C. §271(e)(6)(B).

[172] 42 U.S.C. §262(*l*)(3)–(7).

rather than waiting the full 20- and 60-day periods.[173] Sandoz thus inappropriately discounts its own conduct under the BPCIA regime as a vehicle to resolve expeditiously its purported concerns.

Sandoz's real complaint boils down to this: despite its pursuit of the biosimilar approval pathway, it wants the right to sue first, at the time and in the venue of its choosing, without engaging in exchanges to define the full scope of the potential disputes or the opportunity to resolve any of it. Nothing in the BPCIA reflects a preference for that outcome. Indeed, the statute reflects the opposite preference—several of its provisions expressly allow the RPS, but not the subsection (k) applicant, to initiate the suit.[174]

3. The complained-of six months of "additional exclusivity" results from the statute's plain text and reflects a rational policy choice

Finally, Sandoz complains that the district court's construction of §262(8)(A)'s 180-day notice provision "unwittingly" adds six months of "unjustifiable" exclusivity, with "no rational purpose" and in "def[iance of] Congress' policy judgment and the text of the statute."[175] Sandoz's

[173] *Id.* §§262(*l*)(2), (*l*)(3)(B).
[174] *Id.* §§262(*l*)(6), (*l*)(9)(B)-(C).
[175] Opening Brief at 46-47.

policy complaint lies with Congress, which created this framework, and not with the district court. The statutory text is clear, and it is the cardinal principle of statutory construction to give effect "'to every clause and word of a statute' . . . rather than to emasculate an entire section."[176]

In any event, Sandoz's argument that this framework is entirely illogical is wrong.

It was entirely rational for Congress to have allocated a short period—six months—for courts to resolve expedited requests for preliminary injunctive relief under disputed patents after licensure of the biosimilar product, at which point there is certainty as to the identity of the product and a higher degree of certainty about its imminent market entry. At that point, the possibility of non-approval—a significant risk for every biological product application—has been removed. And a six-month period is a reasonable balance for Congress to strike, weighing both the prospect of permitting infringement of valid and enforceable patents and the interests of the biosimilar manufacturer in marketing its licensed product.

[176] *E.g., Bennett*, 520 U.S. at 173 (ellipses in original).

Finally, this congressional choice is consistent with other statutory provisions, which tie the declaratory judgment rights of a party to the patent lists that have resulted from the back and forth exchanges—exchanges that are required to occur and lists that are not completely fixed in place until the very date of licensure.[177]

II. The district court correctly found Sandoz's declaratory judgment action to be inconsistent with *MedImmune* and its progeny

In addition to rejecting Sandoz's BPCIA-based arguments, the district court separately and properly concluded that Sandoz's suit was also prohibited because Sandoz failed as a matter of fact to establish a case or controversy of sufficient immediacy to invoke the court's jurisdiction under the DJ Act.[178] The DJ Act provides a conduit for the exercise of subject-matter jurisdiction; it does not independently create such jurisdiction.[179]

A. Sandoz failed to demonstrate the requisite immediacy and reality

For a court to have subject matter jurisdiction under the DJ Act, a

[177] *See* 42 U.S.C. §262(*l*)(3)-(*l*)(7).

[178] 28 U.S.C. §§2201-2202.

[179] *E.g.*, *Prasco, LLC v. Medicis Pharma. Corp.*, 537 F.3d 1329, 1335 (Fed. Cir. 2008).

declaratory judgment plaintiff must establish that there is a dispute between parties having adverse legal interests, "of sufficient *immediacy* and *reality* to warrant the issuance of a declaratory judgment."[180] As the district court found, Sandoz failed to establish these elements.

1. Because Sandoz is just beginning Phase III clinical trials, there is too much uncertainty on whether it will get FDA approval

When it filed this action, Sandoz was just beginning its Phase III clinical trial on its biosimilar product. This Phase III trial was the first time Sandoz's product was to be administered to patients (as opposed to healthy volunteers in Phase I). As such, it remains to be proven whether Sandoz's product will demonstrate the necessary safety and efficacy to be submitted to and approved by FDA. FDA's draft Guidance documents on biosimilars explain why this is so.

Those Guidance documents, promulgated by the agency with the duty to assess the safety and efficacy of proposed biologics, emphasize that:

[180] *MedImmune, Inc. v. Genentech, Inc.,* 549 U.S. 118, 127 (2007) (emphasis supplied); *see also Aetna Life Ins. Co. v. Haworth*, 300 U.S. 227, 240-41 (1937).

- even using then-current technology, a protein's three-dimensional structure can often be difficult to define precisely;
- small differences in structure can have significant effects on potency, purity, and safety; and
- because even current analytical techniques may not be able to detect all relevant structural and functional differences between two proteins, Phase III testing is necessary to address the uncertainty—unless FDA has reason to be convinced that such trials are not, in a particular circumstance, necessary.[181]

In other words, FDA's Guidance documents provide no basis to conclude that Phase III testing of a biosimilar product will succeed. To the contrary, they indicate that if Phase III trials are required, then uncertainty exists. Sandoz offers no basis for the courts to overrule that judgment and conclude that no uncertainty remains and thus that subject-matter jurisdiction is present. Instead, FDA's Guidance documents corroborate this Court's decisions (*Benitec* and *Telectronics*), which emphasize that Phase III clinical trials can help to resolve—or help to expose—whether an alleged dispute is sufficiently real or immediate to warrant the intervention of federal courts.

[181] *See* notes 89-96 & 106-112 and associated text, *supra*.

2. Sandoz's reliance on its "expectations" and "intentions" underscores the uncertain nature of any future dispute

Sandoz *argues* that its Phase III testing "will prove successful,"[182] that it "will" submit an FDA application,[183] and so on—as if its assurances were evidence. But on the questions critical for subject-matter jurisdiction purposes (whether its clinical testing will succeed; whether it will be able to submit an FDA application; whether its formulation will change; and whether the FDA will approve its candidate), the evidence confirmed the inherent uncertainty. Its witnesses were able to say merely that Sandoz "believe[s]," "intends" and "expects" it will succeed.

"Believes," "intends," and "expects" are not the blaze marks of a real and immediate dispute. To be sure, they indicate the possibility of a real and immediate dispute if facts develop as intended and expected. But they do not show that a real and immediate dispute existed when the complaint was filed.

This Court made that very point in *Benitec*, upon which the district court relied. There, as here, the declaratory judgment claimant

[182] Opening Brief at 13.

[183] *Id*. at 60.

offered testimony about its subjective expectations. There, this Court found that such a showing fails as a matter of law to "meet the immediacy and reality requirement of *MedImmune* necessary to support a justiciable controversy," because "to allow such a scant showing to provoke a declaratory judgment suit would be to allow nearly anyone who so desired to challenge a patent."[184] On that record, this Court affirmed dismissal for lack of declaratory judgment jurisdiction. This similar record calls for the same result.

3. Precedent emphasizes that Phase III success is a predicate to subject-matter jurisdiction

In the context of FDA-regulated products, this Court's declaratory judgment jurisprudence (*Teletronics* and *Benitec*) attaches great weight to two events that can resolve—or further expose—the scientific and regulatory uncertainty in developing FDA-regulated products: Phase III clinical trials and the filing of an FDA application.[185] Sandoz's opening

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[184] *Benitec Australia, Ltd. v. Nucleonics, Inc.*, 495 F.3d 1340, 1348-49 (Fed. Cir. 2007).

[185] *Benitec*, 495 F.3d at 1346 (holding that "[t]he fact that [declaratory judgment plaintiff] may file an [application for drug] in a few years does not provide the immediacy and reality required for a declaratory judgment"); *Telectronics Pacing Systems, Inc. v. Ventritex, Inc.*, 982 F.2d 1520, 1527 (Fed. Cir. 1992) (affirming dismissal of declaratory judgment action brought by patentee where accused "device had only recently

brief criticizes the district court's reliance on that precedent, arguing that it "ha[s] nothing to do with the facts here."[186] Quite the contrary: on this record, that precedent controls. In *Telectronics*, as here, FDA approval was required to market and sell the regulated research item at issue.[187] There, as here, the product was still undergoing clinical testing.[188] There, as here, although the product's sponsor had no plans to change the product, the product potentially could be modified prior to approval.[189] There, the Court affirmed the district court's dismissal for lack of subject-matter jurisdiction, determining that the matter lacked a "sufficient allegation of immediacy and reality" and emphasizing that, at the time the lawsuit was filed, the challenger's regulated device had "only recently begun clinical trials, and was years away from potential FDA approval."[190] *Telectronics* warrants the same result here.

Sandoz tried to avoid *Telectronics* below by arguing that the FDA-regulated device there was undergoing its very first clinical trial. But

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begun clinical trials, and was years away from potential FDA approval").

[186] Opening Brief at 59.

[187] *Telectronics,* 982 F.2d at 1521.

[188] *Id.* at 1526-27.

[189] *Id.*

[190] *Id.* at 1527.

so is Sandoz's candidate: the Phase III testing was the very first time that Sandoz's current development candidate was to be tested for efficacy and safety on afflicted patients rather than healthy human volunteers. Sandoz's declarant acknowledged that it cannot predict what those tests would show regarding injection site reactions or other safety and efficacy criteria, notwithstanding success in earlier preclinical and Phase I testing. Nor has the FDA assured or even suggested that Sandoz's current development candidate is safe and effective or biosimilar to ENBREL. In light of that record, *Telectronics'* teachings guide the analysis and outcome here, and the district court properly looked to it.

The district court likewise properly looked to *Benitec.*[191] There, the patentee sued for infringement; the accused infringer filed declaratory judgment counterclaims.[192] Two product markets were at issue: human applications and animal applications.[193] Both were FDA-regulated.[194]

[191] A004:16-23.
[192] *Benitec*, 495 F.3d at 1342.
[193] *Id.* at 1343.
[194] *Id.* at 1346, 1349.

Citing *Telectronics*, this Court held that the case lacked sufficient immediacy and reality with respect to the parties' claims regarding human applications because the activities of developing and submitting information to the FDA related to the human application were protected from infringement liability under §272(e)(1) and the infringer did not plan to file with the FDA for several years.[195] Here, it is likewise not sufficiently certain if or when Sandoz will complete Phase III testing or be in a position to submit an FDA application. Sandoz simply ignores these teachings from *Benitec*, and instead tries to escape only the decision's second holding: that the cased lacked sufficient immediacy and reality with respect to the animal applications because (1) the testimony about the declaratory judgment claimant's subjective intentions failed as a matter of law, and (2) "there may never be" a controversy between the parties on this issue, and the applicability of §271(e)(1)'s exemption was unclear based on the record.[196] But here, too, Sandoz's subjective testimony fails as a matter of law, and there may never be a controversy between these parties.

Sandoz tries to avoid this precedent by citing inapposite cases in

[195] *Id.* at 1346-47.

[196] *Id.* at 1349.

which declaratory judgment jurisdiction was found to exist. Citing *Glaxo, Inc. v. Novopharm, Ltd.*, Sandoz argues that its meaningful preparation supports declaratory judgment jurisdiction.[197] The *Glaxo* record was critically different. There, the declaratory judgment plaintiff had "indicated that it had [1] submitted an [FDA application] accompanied by [2] data sufficient to make FDA approval imminent,"[198] which necessarily meant that [3] the clinical trials had been finished successfully; and the declaratory judgment plaintiff had also [4] provided the declaratory judgment defendant with actual samples of the composition submitted for FDA approval.[199]

Only that constellation of facts provided the "meaningful preparations" from which this Court concluded that, unlike in *Telectronics*, "the threat of Novopharm entering the U.S. market was not 'years away' nor was there [any] doubt that Novopharm wished to sell [the composition submitted for FDA approval]."[200]

Sandoz also invokes *Cat Tech LLC v. TubeMaster, Inc.*, in support

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[197] Opening Brief at 58 (citing *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1571 (Fed. Cir. 1997)).

[198] *Glaxo*, 110 F.3d at 1571 (brackets supplied).

[199] *Id.* at 1569 n.2.

[200] *Id.* at 1571.

of its "meaningful preparations" argument.[201] But *Cat Tech* did not involve a product whose marketing and sale required FDA approval, and the record there showed that the sole impediment to marketing and selling the product in question was the patentee's threat of litigation.[202]

Here, in stark contrast, Sandoz cannot market or sell its biologic. Quite the opposite—it would be illegal for Sandoz to do so before FDA approval.[203] The impediments that Sandoz faces are those imposed by FDA and, as FDA has explained, the vagaries of science—not by the patents.

In *Cat Tech*, the patentee had sued the declaratory judgment claimant (the defendant) for infringement, but lost.[204] On appeal, and despite having initiated suit, the losing patentee switched positions, contending the court had lacked subject-matter jurisdiction to decide infringement.[205] This Court found the patentee's assertion on appeal

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[201] *Cat Tech LLC v. TubeMaster, Inc.*, 528 F.3d 871 (Fed. Cir. 2008); *see* Opening Brief at 57-60.

[202] *Cat Tech*, 528 F.3d at 882 ("[O]nce the threat of liability to Cat Tech has been lifted, it appears likely that [the declaratory judgment party] can expeditiously solicit and fill orders for" the accused device).

[203] 42 U.S.C. §262(a)(1)(A).

[204] 528 F.3d at 877-78.

[205] *Id.* at 883.

that the dispute it initiated was not sufficiently immediate and real to be decidedly unpersuasive.[206]

Sandoz urges that a nearly ten-year-old litigation in the District of Massachusetts, in which Amgen sought declaratory judgment, *Amgen Inc. v. Hoffmann-La Roche Ltd.*, 456 F. Supp. 2d 267 (D. Mass. 2006), somehow conferred declaratory judgment jurisdiction in the Northern District of California.[207] Sandoz does not disclose, however, two dispositive facts about that litigation. It did not involve a biosimilar subject to the BPCIA's limitations on the declaratory judgment remedy. Indeed, the case happened years before the BPCIA was passed. And in that case, the declaratory judgment plaintiff alleged past and current acts of infringement.[208] Sandoz, in sharp contrast, alleged no such thing.

Finally, in the proceedings below Sandoz urged (and may in reply urge here) that another district court decision, *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 3 F. Supp. 2d 104 (D. Mass. 1998), authorized

[206] *Id.*

[207] Opening Brief at 60-61.

[208] *Amgen*, 456 F. Supp. 2d at 271 ("On information and belief, [Roche/Hoffman is] currently importing into the United States a pharmaceutical composition containing a recombinant human EPO product . . . .") (brackets in original).

Sandoz's lawsuit. But there, too, the complaint alleged both present and future acts of infringement and did not involve a biosimilar subject to the BPCIA's limitations.[209] On dismissal of the counts for actual infringement, the court did not allow the case to proceed despite being only four month from the scheduled trial date, and instead placed the case on administrative hold, noting that "[n]ot only is FDA approval uncertain, but the process or the product itself may be altered during the interval in ways that are material to an infringement analysis. Any declaration issued by this Court now may be rendered moot by such alterations."[210]

B. Sandoz failed to demonstrate any injury-in-fact traceable to the defendants' conduct or capable of redress by the court

The lack of declaratory judgment jurisdiction can also be analyzed through the overlapping doctrine of standing.[211] To prove standing, the plaintiff must show (1) an injury-in-fact, *i.e.*, a harm that is concrete and actual or imminent, not conjectural or hypothetical, that is (2) fairly

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[209] *Amgen*, 3 F. Supp. 2d at 106 (also pleading future acts).

[210] *Id*. at 112.

[211] *MedImmune,* 549 U.S. at 128 n.8 (standing is coextensive with reality and immediacy); *Prasco,* 537 F.3d at 1338 (citing *Steel Co. v. Citizens for a Better Env't*, 523 U.S. 83, 102-03 (1998)).

traceable to the defendant's conduct, and which can be (3) redressed by a favorable judicial decision.[212]

1. There is nothing to redress because Sandoz faces no dilemmas that depend on the litigation of these patents

Sandoz asserts that the patents create a dilemma for three activities: (1) its present expansion of its [redacted] production facility—even though Sandoz admits it plans to continue that expansion; (2) its nascent Phase III testing in foreign sites—even though it admits it plans to finish that testing; and (3) its hoped-for future product launch—even though it admits that launch is contingent on success in the Phase III clinical trials, the submission of a subsection (k) application, and FDA approval. The evidence demonstrates that the patents do not create a real or immediate dilemma for Sandoz with respect to any of those activities.

The patents are directed to specified proteins and pharmaceutical compositions and specified methods and polynucleotides. Neither Amgen nor Roche has suggested that Sandoz's construction of a production facility outside of the U.S. that also has value for the

[212] *Id.*

European commercialization of its candidate per se invades the exclusive rights of the U.S. patents-in-issue. Similarly with respect to foreign clinical trials: neither Amgen nor Roche has suggested that their conduct, even to successful completion, per se invades these exclusive rights. As Sandoz itself admits, its foreign activities are not necessarily directed to products that will end up the U.S. market. Indeed, both its clinical trials and planned expansion are designed to create and address demand for its candidate (if it is ever approved) in whatever markets Sandoz can obtain approval—whether or not the U.S. market is one of them. Hence, in terms of the patents, and taking Sandoz's representations to the district court at face value, there is nothing about Sandoz's current or ongoing activities for a court to address at this time. Sandoz is free to pursue what it has represented as its multi-nationally-focused testing and development-related activities, is in fact pursuing them, and has no plans to stop pursuing them.

Which leaves Sandoz's last asserted dilemma: its hoped-for product launch. Sandoz alleges that it will "inevitably be required to choose between launching its product at risk or giving up what it

believes it has a right to do."[213] What "product"? The FDA has not approved any "product." Sandoz has not even submitted a product for approval. It merely has a development candidate, Phase III testing for which *began* just before the complaint was filed. At that point, Sandoz had not yet attempted to treat even a single afflicted patient with its development candidate.

Will that candidate be safe and effective? Perhaps—but perhaps not. For example, despite Sandoz's repeated argument that its biologic is "final," Sandoz's declarant conceded upon cross-examination that Sandoz [redacted]

Will the product for which Sandoz may one day seek approval be the same as its current development candidate? It *might* be the same. But it might not—at present, no one can say. The FDA certainly has not said so: despite many meetings with Sandoz, [redacted]

[213] Opening Brief at 55.

[redacted][214][redacted]

For all of these reasons, the launch of Sandoz's hoped-for biosimilar is highly contingent and uncertain. Sandoz's Phase III trials might fail. Its development candidate might change: any of the protein, the excipients, or the manner in which they are combined might be different. It might not be able to submit an FDA application. FDA might not grant approval. If FDA grants approval, what it approves might be different from what Sandoz is currently testing—Sandoz might have to under the "rewind" that its brief discusses.

The district court found as a matter of fact that Sandoz had submitted no evidence that either Amgen or Roche was in a position to evaluate a patent-infringement lawsuit against Sandoz. The record amply supports that conclusion. Indeed, in determining whether a dispute is actual or hypothetical, it can often be helpful to ask what claims the declaratory judgment defendant could have brought against

[214] 42 U.S.C. §262(k)(2)(A)(ii).

the declaratory judgment plaintiff.[215] What relief could Amgen and Roche have sought? Declaratory relief that ***if*** Sandoz's Phase III testing succeeded and ***if*** Sandoz submitted an FDA application and ***if*** the biologic at issue in the application was the same as the biologic that Sandoz tested, ***then*** that product would infringe when sold by Sandoz? On this record, such a complaint would have been seeking "an opinion advising what the law would be upon a hypothetical state of facts," contrary to the express teachings of *MedImmune* and *Aetna*.[216]

If, as Sandoz currently intends, Sandoz one day submits an FDA subsection (k) application concerning a biologic within the scope of the two patents in suit and/or other patents, the parties may then have a dispute. The law provides a process for resolving that possible dispute in timely fashion. Now is not that time.

2. There is no traceability, because there is no link between Amgen's or Roche's actions or words and Sandoz's actions

The facts, as Sandoz itself alleged, are that the patents have not moved Sandoz away from its actions or plans—and that they will not do so. Sandoz started and completed its preclinical testing and both of its

[215] *Benitec*, 495 F.3d at 1344.

[216] *MedImmune,* 549 U.S. at 127 (quoting *Aetna*, 300 U.S. at 240-41).

Phase I studies. It started its Phase III testing (all of it ex-U.S.) and "expects" to complete such testing. It "expects" to complete its planned expansion of its ex-U.S. protein production plant—albeit not until [redacted]. And it "intends" to file a subsection (k) application with the FDA. Sandoz has not [redacted]. Indeed, Sandoz's brief candidly admits that neither patent will affect it: "Sandoz, however, has no intention of abandoning its product in the face of Amgen's claims."[217] The district court's factual assessment of the record was correct, and certainly does not reflect clear error.

3. There is no injury-in-fact because neither Amgen nor Roche did anything before the complaint was filed to suggest that they would sue

Sandoz argues that the patents and Amgen's statements about them have "disrupted Sandoz's business" and that Sandoz's foreign facility expansion "stands to be wasted if Amgen ultimately prevails in their [sic] patent claims."[218] The district court correctly found that the facts are otherwise, and in particular that "as a factual matter, a

[217] Opening Brief at 16, 54.

[218] Opening Brief at 53-54.

cognizable case or controversy does not presently exist"[219] because Sandoz had not "submitted evidence demonstrating defendants[] . . . have subjected Sandoz to an 'immediate' threat of injury."[220]

An injury-in-fact does not arise merely because a party correctly "perceives such a patent to pose a risk of infringement"; instead, there still must be "some affirmative act by the patentee."[221] Sandoz neither alleged nor proved any such affirmative act by Amgen or Roche before Sandoz filed the complaint.

With respect to Roche, Sandoz argues only that Roche did not respond to Sandoz's request for a covenant not to sue it sent seven days before Sandoz filed the lawsuit. Sandoz argues that same point against Amgen. There are three defects, each separately fatal, in that argument.

As a threshold matter, Sandoz does not fairly argue the facts. The *only* pre-suit communication between Sandoz and Amgen or Roche regarding the patents was Sandoz's counsel's letter demanding a

[219] A002:17-18.

[220] A004:7-9.

[221] *Sandisk Corp v. STMicroelectronics, Inc.*, 480 F.3d 1372, 1381 (Fed. Cir. 2007); *see also Innovative Therapies, Inc. v. Kinetic Concepts, Inc.*, 599 F.3d 1377, 1382 (Fed. Cir. 2010) (affirming dismissal for lack of affirmative act); *Prasco,* 537 F.3d at 1338 (same).

covenant not to sue.[222] Sandoz sued a mere week later.[223] Sandoz's argument requires transforming that week-long silence into an affirmative refusal.

Second, as this Court has recently emphasized, refusal to grant a covenant not to sue does not "'create an actual controversy' because 'a patentee has no obligation to make a definitive determination, at the time and place of the competitor's choosing, that it will never bring an infringement suit.'"[224]

Third, neither Amgen nor Roche could have substantively assessed Sandoz's covenant demand, even leaving aside the uncertainty in Sandoz's Phase III studies and hoped-for FDA submission. Sandoz's covenant demand failed to include any information from which infringement could have been assessed, such as the amino acid sequence of its current development candidate (relevant to claims in the '182 Patent) or its production method (relevant to claims in the '522 Patent). Sandoz likewise failed to include validity analysis—or even

[222] A1556-1557.

[223] A2001.

[224] *Microsoft Corp. v. DataTern, Inc.*, __ F.3d __, No. 2013-1184, -1185, slip op. at 11 (Fed. Cir. May 5, 2014) (ellipses omitted) (quoting *Prasco*, 537 F.3d at 1341).

any reasons why validity might merit any inquiry. Instead the letter merely asserted that "Sandoz contests the validity and infringement of these patents."[225]

Sandoz fares no better in its other attempts to ensnare Amgen in this premature fight. Sandoz argues that Amgen has made a concrete claim of a specific right to exclude competition.[226] But the district court found as a factual matter that Sandoz submitted *no* "evidence demonstrating defendants[] . . . have subjected Sandoz to an 'immediate' threat of injury."[227] On appeal, Sandoz re-argues the facts, seeking a different outcome.[228] But it nowhere suggests, let alone shows, that the district court committed clear error.[229]

And the district court did not err. Sandoz neither argues nor submitted evidence that Amgen made any statements directly to it. Instead, Sandoz invokes a variety of bland Amgen statements made to broad audiences. Sandoz initially argues that Amgen has noted that patents are important. So has Sandoz's parent company, in SEC filings;

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[225] A1556.
[226] Opening Brief at 54.
[227] A004:7-9.
[228] Opening Brief at 52-53.
[229] *Biddle*, 161 F.3d at 535.

and the biotechnology industry has testified to that effect before Congress.[230] It is likewise true that Amgen has noted that patents protect a product within the scope of their claims and confer exclusivity. But that simply repeats basic statutory law.[231] Like many biotechnology companies (including Sandoz's parent), Amgen has also at various times said that it would defend its patents. That such a company would "state[] publicly in press releases or at industry meetings that it would defend its patents is unremarkable. The same could be said of many patent-holders."[232]

Sandoz attaches great weight to the fact that Amgen has noted that it did not expect ENBREL biosimilar competition. Sandoz fails to note, however, that Sandoz did not publicly announce its etanercept Phase III clinical trial until late June 2013, the day before it brought this suit, and as the record reflects, the Phase III clinical trial was not disclosed anywhere in the press until May 2013. Amgen can hardly be faulted for reporting that it did not expect ENBREL biosimilar competition when that potential competition had not been disclosed.

[230] A3041-3042; A3124.

[231] 35 U.S.C. §154(a)(1).

[232] A3168 (copy of *Bridgelux, Inc. v. Cree, Inc.,* No. C 06-6495 PJH, slip op. at 13 (N.D. Cal. Jul. 9, 2007) (unpublished)).

Sandoz also posits that "it is precisely the fact that Amgen ***will not*** sue immediately" that creates DJ jurisdiction for Sandoz's suit.[233] Indeed, Sandoz criticizes the district court for "focus[ing] myopically on an 'imminent' threat."[234] That does not fairly characterize the district court's analysis. After "having read and considered the papers," the district court found as a matter of fact that Amgen was "not in a position to consider the propriety of" a lawsuit "until after Sandoz has 'prepared an [application] for approval to launch a product in the U.S."—and that Sandoz "offered" "no evidence to the contrary."[235] The record amply supports that factual conclusion. As explained above, neither Amgen nor anyone else is currently in a position to know whether: Sandoz's current Phase III trial will succeed; the FDA will require more such testing; the FDA will approve Sandoz's foreign plant; or the development candidate that Sandoz is currently testing will be the same one that Sandoz submits for FDA approval, if it is ever in a position to submit its promised application.

In short, the district court correctly concluded as a matter of fact

[233] Opening Brief at 55 (emphasis in original).
[234] *Id.*
[235] A001:21-24; A004:3-7 (brackets in original).

that neither Amgen nor Roche had committed the requisite affirmative act. Sandoz thus failed to carry its burden of proof.[236]

CONCLUSION

The district court correctly concluded that this case cannot proceed without regard to the BPCIA's limitations on declaratory judgment. Based on the record, these limitations had not been removed. Furthermore, when Sandoz filed its complaint, there was no case or controversy between it and either of Amgen or Roche. The district court correctly entered a judgment of dismissal. Amgen and Roche respectfully request that this Court affirm that judgment.

Respectfully submitted,

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[236] *Prasco,* 537 F.3d at 1338-39; *see also Innovative Therapies,* 599 F.3d at 1382.

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CERTIFICATE OF SERVICE

I certify that on this 27th day of May, 2014, I caused this Nonconfidential Opposition Brief of Defendants-Appellees, Amgen Inc. and Hoffmann-La Roche Inc. to be filed electronically by using the Court's CM/ECF system and served by CM/ECF and electronic mail upon:

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CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limitations of Federal Rule of Appellate Procedure 32(a)(7)(B) and the Rules of this Court, because it contains 13,973 words (as determined by the Microsoft Word 2007 word processing system used to prepare the brief), excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(a)(7)(B)(iii).

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