No. 2020-1037

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

IMMUNEX CORP., AMGEN MANUFACTURING, LTD.,

Plaintiffs-Appellees,

HOFFMANN-LA ROCHE INC.,

Plaintiff,

v.

SANDOZ INC., SANDOZ INTERNATIONAL GMBH, SANDOZ GMBH,

Defendants-Appellants.

Appeal from the United States District Court for the District of New Jersey
Civil Action No. 16-1118-CCC (Cecchi, J.)

APPELLANTS' CORRECTED OPENING BRIEF

George C. Lombardi
Maureen L. Rurka
Julia Mano Johnson
Dan H. Hoang
Loren G. Rene
WINSTON & STRAWN LLP
35 W. Wacker Drive
Chicago, IL 60601-9703
Tel.: 312.558.5600
Fax: 312.558.5700

Counsel for Appellants Sandoz Inc., Sandoz International GmbH, and Sandoz GmbH

William M. Jay
Brian T. Burgess
GOODWIN PROCTER LLP
1900 N Street, N.W.
Washington, DC 20036
Tel.: 202.346.4000
Fax: 202.346.4444

David J. Zimmer
Gerard J. Cedrone
GOODWIN PROCTER LLP
100 Northern Ave.
Boston, MA 02210
Tel.: 617.570.1000
Fax: 617.523.1231

Cindy Chang
GOODWIN PROCTER LLP
The New York Times Building
620 Eighth Ave.
New York, NY 10018
Tel.: 212.813.8800
Fax: 212.355.3333

CERTIFICATE OF INTEREST

Counsel for Appellants, William M. Jay, certifies the following:

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

   Sandoz Inc.
   Sandoz International GmbH
   Sandoz GmbH

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:

Sandoz Inc.:	None
Sandoz International GmbH:	None
Sandoz GmbH:	None

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:

Sandoz Inc.:	Novartis AG
Sandoz International GmbH:	Novartis AG
Sandoz GmbH:	Novartis AG

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in the court (and who have not or will not enter an appearance in this case) are:

   James Richter, Merritt Westcott, Karalena Guerrieri, Noorossadat Torabi, and Thomas Melsheimer of Winston & Strawn LLP

   James Hilmert, Melinda Lackey, Michael Meneghini, and Tyler Johannes, formerly of Winston & Strawn LLP

   Eric I. Abraham of Hill Wallack LLP

   Yevgenia Kleiner and Christina Saveriano, formerly of Hill Wallack LLP

5. The title and number of any case known to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal.

Immunex Corporation et al. v. Samsung Bioepis Co., Ltd., No. 19-cv-11755 (D.N.J.)

/s/ William M. Jay
William M. Jay
Goodwin Procter LLP
901 New York Avenue NW
Washington, DC 20001
Tel.: 202.346.4000
Fax.: 202.346.4444

December 23, 2019

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STATEMENT OF RELATED CASES

No appeal in or from the same district court proceeding was previously before this or any other appellate court.

Counsel is aware of one case pending in this or any other court or agency that will be directly affected by this Court's decision in the pending appeal: *Immunex Corporation et al. v. Samsung Bioepis Co., Ltd.*, No. 19-cv-11755 (D.N.J.).

TABLE OF ABBREVIATIONS

’182 Patent	Asserted U.S. Patent No. 8,063,182 (Appx12684-12718)
’522 Patent	Asserted U.S. Patent No. 8,163,522 (Appx12719-12766)
’029 Patent	U.S. Patent No. 5,808,029 (Appx30905-30923)
’225 patent	U.S. Patent No. 7,915,225 (Appx27246-27261)
’690 Patent	U.S. Patent No. 5,605,690 (Appx27295-27321)
2004 Agreement	Accord and Satisfaction Agreement between Roche, Wyeth, Amgen, and Immunex (Appx25836-25864)
aBLA	Abbreviated biologics license application
CH2, CH3	Immunoglobulin constant region heavy chain domain 2; constant region heavy chain domain 3
Fc	Crystallizable fragment of immunoglobulin
GATT	General Agreement on Tariffs and Trade, implemented by the Uruguay Round Agreements Act
IgG	Immunoglobulin G (IgG_1: immunoglobulin G, subclass 1)
ODP	Obviousness-type double patenting
p55 receptor	TNF receptor subtype weighing approximately 55 kilodaltons
p75 receptor	TNF receptor subtype weighing approximately 75 kilodaltons
Psoriasis patents	U.S. Patent Nos. 7,915,225, 8,119,605, and 8,722,631 (Appx27246-27261; Appx27262-27277; Appx27278-27294)

Smith	Smith et al., "A Receptor for Tumor Necrosis Factor Defines an Unusual Family Of Cellular and Viral Proteins," Science 248:1019-1023 (1990) (Appx26978-26982)
TNF	Tumor necrosis factor
TNFR	Tumor necrosis factor receptor
TNFR:Fc	Fusion protein comprising TNFR and Fc

INTRODUCTION

At the heart of patent law is a bargain: a limited period of statutory exclusivity in exchange for disclosing innovation. 35 U.S.C. §154. Once the patent term expires, the invention "covered by the patent becomes public property." *Singer Mfg. Co. v. June Mfg. Co.*, 163 U.S. 169, 185 (1896). In the face of this rule, Plaintiff-Appellee Immunex and its corporate parent Amgen (collectively, "Immunex") are now well into their *third decade* of exclusivity for claims covering the protein etanercept, the active ingredient in Immunex's biologic product Enbrel®. On the market since 1998, Enbrel captures close to $5 billion in annual U.S. sales (Appx5791), yet it still faces no biosimilar competition. Under the decision below, that exclusivity will extend until 2029.

How did Immunex attempt such an extraordinary extension of its patent term? Another company, Plaintiff-Appellee Roche, had been working to develop proteins that would compete with Enbrel. When Roche's clinical trials for its protein failed, Immunex—anticipating the end of its lucrative exclusivity when its own etanercept patents expired—struck a deal with Roche. Their "Accord and Satisfaction" (the "2004 Agreement") gave Immunex control of the "pre-GATT" patent applications that Roche had filed in 1995. Although Immunex insisted on calling it a license, the 2004 Agreement functioned as an assignment by providing Immunex with all substantial rights to the applications—including complete control over prosecution,

the exclusive right to commercial use, the ability to sue for infringement and control infringement litigation, and the right to grant royalty-free sublicenses. Though Roche did not develop, describe, or claim etanercept, Immunex used its exclusive prosecution authority to amend the claims *and* specifications to shoehorn etanercept into the Roche applications.

The reworked applications issued to Immunex in 2011 and 2012 as U.S. Patent Nos. 8,063,182 (the "'182 patent"), and 8,163,522 (the "'522 patent"), respectively—each for a term of 17 years from issuance. These patents, through the irrevocable 2004 Agreement, give Immunex the exclusive right to commercial use of etanercept for 15 years after its original patent claiming etanercept expired and 31 years since Enbrel was first marketed—until 2029.

The FDA approved Sandoz's etanercept biosimilar in 2016, but this litigation has kept Sandoz off the market. The patents Immunex asserted here to keep Sandoz's biosimilar from the public are invalid for three reasons.

First, the patents violate the equitable prohibition on obviousness-type double patenting ("ODP"), which "forbids an individual from obtaining more than one patent on the same invention" and its obvious variants. *AbbVie Inc. v. Mathilda & Terence Kennedy Inst. of Rheumatology Tr.*, 764 F.3d 1366, 1372 (Fed. Cir. 2014). Immunex cannot evade ODP by mislabeling the 2004 Agreement with Roche as a "license" rather than an assignment. The bar against ODP "prevent[s] unjustified

timewise extension of the right to exclude … *no matter how the extension is brought about*." *In re Hubbell*, 709 F.3d 1140, 1145 (Fed. Cir. 2013) (emphasis added) (quotation marks omitted).

Second, the patents-in-suit fail to satisfy the written-description requirement of 35 U.S.C. §112. Etanercept is a fusion protein combining a tumor necrosis factor receptor ("TNFR") with a molecular weight of approximately 75 kilodaltons (the "p75 receptor"), and an immunoglobulin molecule ("IgG_1"). The Roche applications were focused on a shorter "p55 receptor" invented at Roche; they were not directed toward etanercept until Immunex repurposed them. The Roche priority application does not disclose the full-length p75 receptor, much less the p75-IgG_1 etanercept protein claimed by the patents-in-suit.

Third, the asserted claims are obvious. All elements of the claimed invention were in the prior art, and Immunex concedes there was a reasonable expectation that they would work if combined. Moreover, the prior art clearly encouraged the combination, as illustrated by parallel work that created similar fusion proteins—including by Immunex itself, which actually invented etanercept.

The district court's contrary decision rested on basic legal errors. The Court should reverse the judgment below, dissolve the injunction, and allow the public to *finally* enjoy the benefits of biosimilar competition.

STATEMENT OF JURISDICTION

The district court had jurisdiction under 28 U.S.C. §§1331 and 1338, and entered final judgment for Plaintiffs on October 8, 2019. Sandoz noticed this appeal the same day. This Court has jurisdiction under 28 U.S.C. §1295(a).

STATEMENT OF ISSUES

1. Whether the patents-in-suit are invalid for ODP, where Immunex—which owns all substantial rights in those patents, including the ability to control patent prosecution—had already obtained earlier-expiring patents claiming obvious variants of the same inventions.

2. Whether the claims-in-suit are invalid for lack of written description, where the original specification did not disclose the key claimed features of etanercept and Immunex had to amend the specification to add them.

3. Whether the district court's ruling on obviousness was infected by legal error.

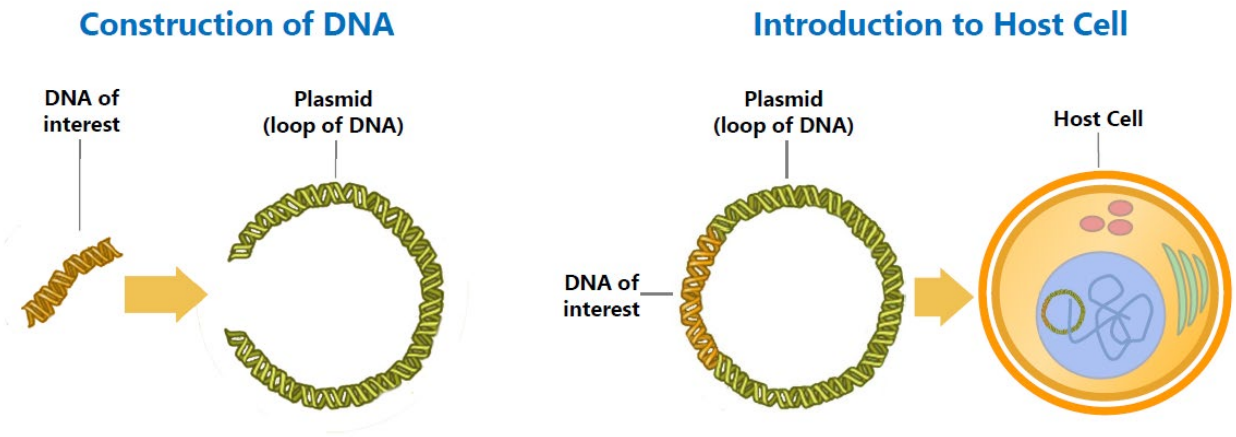
STATEMENT OF THE CASE

I. Immunex obtains patents that give it control over the etanercept franchise for more than two decades.

A. Fusion proteins.

Proteins are made up of a series of smaller molecules called amino acids. Appx4107. A protein consists of dozens to hundreds of amino acids. *Id.* Human DNA provides the code for constructing these amino acids. Appx4109-4110. As of

the priority date in 1990, scientists had learned how to use cells to make proteins from a given piece of DNA. Scientists could introduce a specific sequence into a loop of DNA, insert that DNA into a cell, and have the cell make the protein of interest (Appx4109-4110):

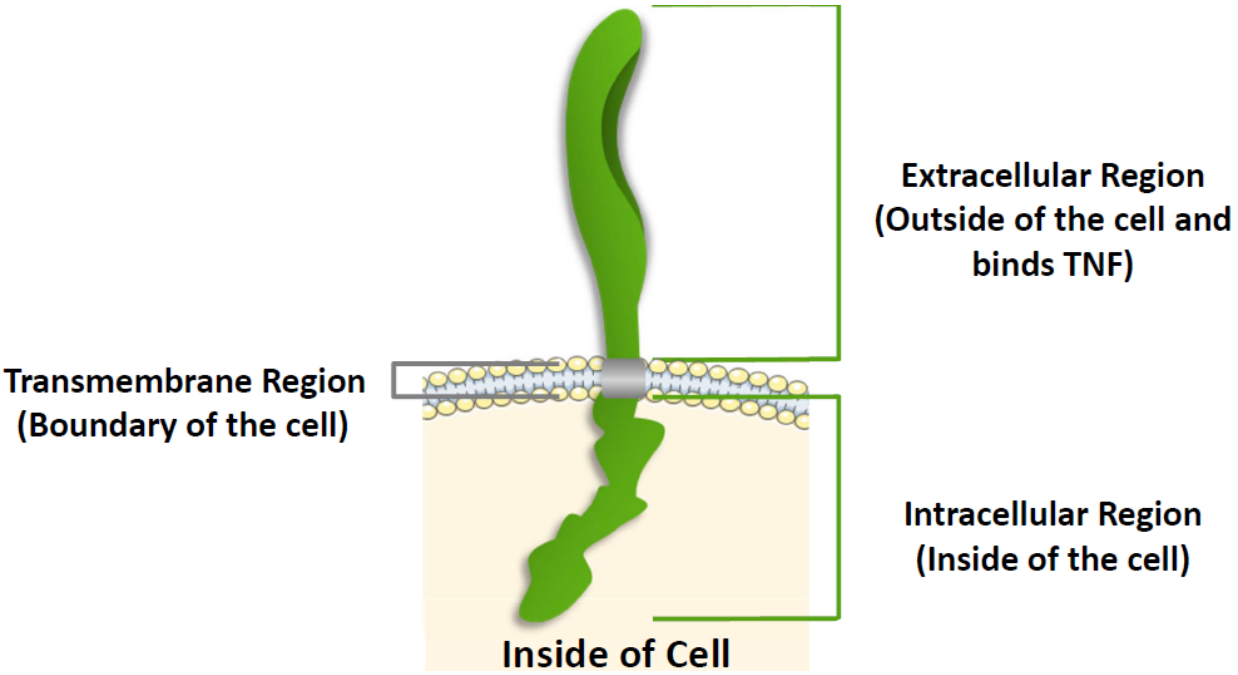


Appx7002; Appx4110-4111. This technique can also be used to combine desired parts of *different* proteins, creating new "fusion" proteins that do not occur naturally.

B. TNF and TNFRs.

Tumor necrosis factor ("TNF") is a messenger protein that helps initiate an immune response when it binds to receptors on the surface of human cells. Appx5; Appx4112-4113. While TNF is beneficial, too much TNF can trigger several known autoimmune disorders, including rheumatoid arthritis. Appx4112-4114; Appx4151-4154.

The TNFR has three parts, the most significant of which is the extracellular region, which is outside the cell and binds to TNF:



Appx7003; Appx4114-4115.

In the late 1980s to 1990, there was tremendous interest in studying whether blocking TNF from binding to its cell-surface receptors would provide a therapeutic effect. Appx4116-4117; Appx7. By the priority date, major biotech institutions were focused on using portions of the body's own TNFRs to remove TNF from the body. Appx4155-4159. At least two different TNFRs were known: a smaller p55 TNFR (weighing approximately 55 kilodaltons), and a larger p75 TNFR. Appx4115-4116.

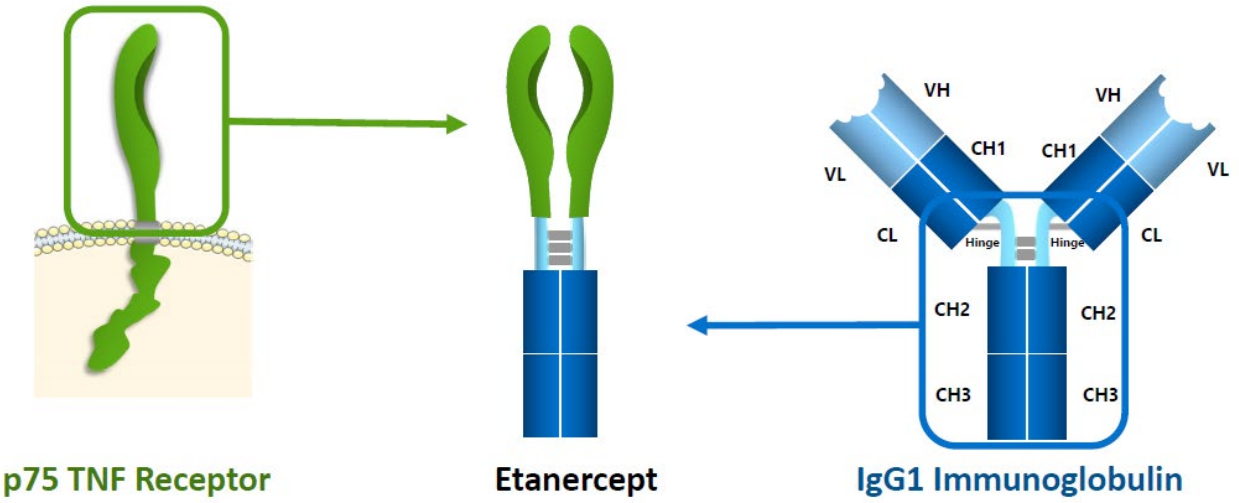
Much of the institutional research focused on cloning (*i.e.*, isolating and identifying the DNA sequence for) "soluble" forms of these TNFRs, which are portions of the extracellular region that, when cut off from the cell surface, would still bind TNF in *in vitro* assays. Appx5; Appx4116-4117. By 1990, several

researchers were also studying means to enhance the properties of soluble receptors, including TNFRs, by creating TNFR-based fusion proteins. Appx4176-4177; Appx10602. These fusion proteins were considered useful for studying TNF *in vitro*, as potential diagnostic assays, and as potential treatments for various conditions, from HIV/AIDS to rheumatoid arthritis. Appx4161-4162; Appx4209-4211; Appx4832; Appx28349; Appx28150-28151.

C. Immunex wins the race to sequence the full p75 receptor and invents etanercept.

Immunex led the work on TNFRs and TNFR fusion proteins, focusing on the p75 receptor. By October 1989, Immunex became the first to clone the full-length p75 receptor, publishing its full-length sequence in *Science* in May 1990 ("Smith"). Appx26978; Appx10602; Appx28264.

Shortly thereafter, in late 1990, Immunex became the first to make the p75 TNFR-IgG_1 fusion protein now known as etanercept. Appx28266; Appx5269. Etanercept combines the extracellular portion of a p75 receptor with the hinge-CH2-CH3 portion of a human IgG_1 protein:



Appx7000; Appx4105-4106.

The Roche inventors of the patents-in-suit played *no* role in Immunex's development of etanercept. Appx28254; Appx28260; Appx5169; Appx4794.

D. Immunex obtains the reference patents.

Etanercept became the active ingredient in Immunex's product Enbrel. Appx11496. Immunex obtained a series of patents directed to etanercept and methods of using etanercept, the last expiring in 2019.

1. The '690 patent.

U.S. Patent No. 5,605,690 (the "'690 patent") was filed in 1995, issued in 1997, and expired in 2014. Appx27295. Claim 3 recites, in pertinent part, administering "a TNF-lowering amount of a chimeric antibody comprising a TNFR comprising the sequence of amino acids 3-163 of SEQ ID NO:1 fused to the constant domain of an immunoglobulin molecule." Appx27320. As described in detail below, that claim covers etanercept. *See* pp. 42-46, *infra*; Appx4145-4146.

Until its expiration, Immunex listed the '690 patent on Enbrel's label as covering Enbrel. Appx11504.

2. The psoriasis patents.

Immunex also obtained three patents on methods of treating psoriasis using etanercept. The earliest, U.S. Patent No. 7,915,225 (the "'225 patent"), issued in 2011, and all three expired on August 13, 2019. Appx27246; Appx27262; Appx27278. Claim 1 of each patent recites methods of treating psoriasis by administering a therapeutically effective dose of "TNFR:Fc," which has been defined to mean etanercept. Appx27261; Appx27277; Appx27294; *see* Appx4123-4125. These claims would have directed a skilled artisan, using routine steps, to produce etanercept. Appx4131; Appx4133-4134; *see also* Appx4110-4112.

II. Roche invents different fusion proteins.

A. The Roche inventors developed different TNFR sequences and different fusion proteins.

The Roche inventors were also interested in using TNFR fusion proteins. Appx4831-4832. But their work differed from Immunex's in two key ways.

First, the Roche inventors' efforts focused on the p55 receptor, which they cloned in October 1989. Appx26957; Appx4802; Appx4834; Appx28234. This research led to Roche's development and testing of a p55-IgG_1 fusion protein in clinical trials, starting in 1993, but those trials failed. Appx28353; Appx5752-5753.

Second, the Roche inventors tried, but failed, to clone the full-length p75 receptor. Appx4824; Appx4868-4869; Appx5070; Appx5074; Appx28415. Rather than isolating the whole p75 receptor, Roche scientists isolated only a partial p75 cDNA clone with several key mutations (the "truncated/mutated p75 receptor") Appx4824; Appx4866.

The inventors' truncated/mutated p75 receptor differed from Immunex's full-length p75 receptor. Most importantly, as compared to the sequence of 235 amino acids comprising the full p75 extracellular region, Roche's truncated/mutated p75 receptor does not include the first 48 amino acids. Appx4450; Appx4453; Appx5036; Appx4855. This accounts for a substantial portion—20 percent—of the extracellular region. Appx4453-4454; Appx5037. Roche's sequence also omits the first 22 amino acids comprising the signal sequence, which is essential to protein secretion from the cell. Appx4453-4454. In addition, that truncated/mutated p75 receptor contains four differences in amino acids. Three of those are mutations from the full-length p75 sequence that would have significantly affected the protein's properties. Appx4456-4461; Appx4855. For instance, Roche's receptor substitutes the amino acid arginine for methionine at the 196th position, which leads to a different shape and function and is associated with susceptibility to lupus. *See* Appx4458-4459. The fourth difference is that Roche's receptor has one extra amino

acid at residue 369, which leads to significant structural differences. Appx4460-4461.

Having failed to sequence the full-length p75 receptor, Roche did not seriously pursue p75 fusion proteins. Appx4794; Appx4845; Appx4848-4849. Indeed, when Roche sought to use etanercept in a study to compare its efficacy against Roche's p55-IgG_1 protein, Roche had to *borrow the protein from Immunex*. Appx10611.

B. Roche sought to patent its own TNFR, representing that it was patentably distinct from Immunex's receptor.

Roche sought and received U.S. Patent No. 5,808,029 (the "'029 patent") covering its truncated/mutated p75 receptor. Appx30923. During prosecution, Roche insisted to the PTO that its truncated/mutated p75 receptor was patentably distinct from Immunex's full-length p75 receptor. Appx31502-31503. Roche represented that Immunex's full-length p75 receptor, disclosed in Smith, is "a cDNA sequence encoding a human TNF-R of about 80 kD, whereas applicants' claim a purified and isolated polynucleotide encoding an insoluble protein which has an apparent molecular weight of about 75 kilodaltons." *Id.*; *see* Appx31500. And Roche emphasized that its truncated/mutated TNFR contains the three mutations and one extra amino acid, described above. Appx31501-31502.

C. Roche's priority application for the patents-in-suit discloses fusion proteins based on *Roche's* TNFR sequences.

By April 1990, the Roche inventors had cloned the p55 receptor and the truncated/mutated p75 receptor and filed for a Swiss patent describing and claiming those proteins. Appx27350. The inventors' subsequent filings, including U.S. patent applications in the same family as the patents-in-suit, disclosed only the two TNFR sequences the Roche inventors had discovered—the p55 receptor (Figure 1) and the truncated/mutated p75 receptor (Figure 4)—and fusion proteins based on those sequences. Appx24589-24590; Appx24593-24594; Appx25139-25140; Appx25143-25144; Appx24476-24477; Appx24480-24481. Roche's priority application did not discuss the full-length p75 receptor, or a fusion protein using that receptor.

1. Roche's original specification does not disclose the full-length p75 receptor.

Given Immunex's publications, the Roche inventors could have described Immunex's full-length p75 receptor in the specification. Appx5063-5064. They did not. Instead, they chose to describe the truncated/mutated p75 receptor that they had obtained. Appx5061; Axxp5064-5065; Appx4863.

Specifically, the priority application is based on two disclosed sequences for TNFRs: Figure 1, disclosing the full p55 sequence, and Figure 4, disclosing the "[n]ucleotide sequence and deduced amino acid sequence for cDNA clones derived

from 75/65 kD TNF-BP." Appx25084. The rest of the application rests *entirely* on these sequences, and close variants thereof. There is no dispute that Figure 4 is the only p75 receptor sequence disclosed in the specification. Appx4448; Appx4961-4962. Figure 4, and smaller fragments of it, is the only p75 receptor mentioned in the Summary of the Invention. Appx25083-25084; Appx5050. The Detailed Description of the Invention likewise defines Figure 4 as *the* p75 portion of the invention, Appx25085; Appx25090; Appx4462-4463, and describes the "present invention" as TNF-binding proteins "containing the amino acid sequence depicted in Figure l or in Figure 4," Appx25085; *see also* Appx25090; Appx4464-4465. None of the examples describe a full-length p75 receptor. Example 8, for instance, describes only Roche's cloning of the truncated/mutated p75 leading up to filing the priority application. Appx25113-25114; Appx4469-4470.

2. The priority application does not disclose a p75-IgG$_1$ fusion protein that incorporates the p75 receptor.

Fusion proteins combine specific proteins (or parts thereof) at a specific place. Appx4492-4493; Appx4496-4497; Appx4515. Roche's original specification does not disclose the claimed p75-IgG$_1$ protein because it does not describe *any* of the requisite parts or how to arrange them. Appx4492-4493.

The specification describes the immunoglobulin portion of the invention as a "partial sequence encoding all domains except the first domain of the constant region of the heavy chain of human immunoglobulin IgG, IgA, IgM, or IgE." Appx25083-

25084; Appx4483. A skilled artisan understood that there were 11 potential immunoglobulins within these classes. Appx28617-28618; Appx27869-27870. Moreover, even after selecting a particular immunoglobulin, the specification statement encompasses a pantheon of potential hinges and a universe of variations, and does not describe the specifically-claimed exon-encoded hinge-CH2-CH3 of IgG_1. Appx4483-4484.

The specification provides only one example of DNA that could be used to make a p55-IgG_3 fusion protein. Appx4495; Appx4514; Appx4515. It was undisputed that: (1) the p55 is a very different gene product than the p75, Appx4495, and (2) IgG_3 is a different immunoglobulin from IgG_1, with a hinge four times as long and a different sequence compared to the IgG_1 hinge, *id.* Because of these differences, a skilled artisan could not have used Example 11 to make a p75-IgG_1 fusion protein. Appx4496-4497.

3. During its prosecution, Roche consistently pursued claims directed to the p55 receptor.

In May 1995, Roche filed divisional applications that led to the patents-in-suit. Appx12686; Appx12721. By filing these applications days before the Uruguay Round Agreements Act ("GATT") went into effect, Roche obtained patent terms running 17 years from issuance. Appx28330.

The divisional applications focused on the p55 receptor. Under Roche's control from May 1996 until late 2004, all claims in the '182 patent application

related only to the p55 receptor. Appx13060-13061; Appx13077-13078; Appx13098-13099; Appx13253-13255; Appx13379-13381; Appx28329-28330; Appx28331; Appx28331-28332; Appx28332-28333. Roche sought six extensions, adding over a year to the prosecution. Appx13046; Appx13058; Appx13087; Appx13108; Appx13397; Appx13416. Moreover, on three occasions between 1996 and 1998, Roche prevented the patent from issuing by ignoring communications from the PTO. Appx13056; Appx13076; Appx13096.

Similarly, the '522 patent application was filed with a preliminary amendment, in which all claims related to the p55 receptor. Appx19150; Appx19156-19158; Appx28337-28338. In August 2000, Roche amended the claims to relate to both the p55 and its truncated/mutated p75 receptor. Appx19159-19161. In response, the examiner issued a restriction, and Roche again elected the p55 receptor. Appx19528; Appx28341; Appx19575. While Roche controlled prosecution, it added almost one year to the process by requesting four extensions. Appx19580; Appx19607; Appx19761; Appx19778.

III. Immunex and Roche enter into a transaction allowing Immunex to extend its patent control over etanercept.

A. The 2004 Agreement transferred all substantial rights in the patents-in-suit to Immunex.

In 1998, after Immunex obtained FDA approval for Enbrel, Roche and Immunex entered into an agreement to cross-license their respective patents and

applications involving TNF receptors. Appx25865-25891. This agreement, which extended to the applications that became the patents-in-suit, provided Immunex with all it needed to market Enbrel. Appx5754; Appx28280; Appx25879.

Subsequently, Roche and Immunex entered into the 2004 Agreement, which turned Immunex into the *de facto* owner of the applications from which the patents-in-suit issued. Appx25836-25864. That Immunex paid Roche only $45 million—just nine days of Enbrel revenue—is consistent with the fact that Roche's applications were not directed to etanercept. Appx5790-5792.

The stated purpose of the 2004 Agreement was for Immunex "to *acquire all rights* licensed pursuant to the [1998] Roche-Immunex Agreement and to eliminate the continuing obligations to pay royalties to Roche" under the 1998 Agreement. Appx25836. The 2004 Agreement further stated that "Roche is willing to *sell such rights* in accordance with the terms of" the 2004 Agreement. *Id.* (emphasis added).

Among other things, the 2004 Agreement gave Immunex:

- The exclusive right to make, use, sell, offer for sale, and import the claimed inventions. Appx25839; Appx25839.
- The absolute right to exclude anyone, including Roche, from commercializing the claimed inventions. Appx25839.
- The complete, unfettered right to sublicense the patents. Appx25839; Appx28335; Appx5762-5763.
- The first right to sue for infringement and to then control litigation it initiated, including unilateral authority to settle and the right to collect

all damages. Appx25840; Appx5769-5770; Appx5771; Appx5775; Appx28336; Appx28337.

- The complete, unfettered right to control the prosecution of the patent applications. Appx25840; Appx28335-28336; Appx5763-5765; Appx5772.

Roche could not terminate the agreement for any reason. Appx25848.

Roche had expected to receive "an offer from [Immunex] to purchase [the] patents covering Enbrel." Appx11494; Appx28321-28322; Appx28324. But Roche "couldn't get [Immunex] to agree to have [the patents] assigned" to Immunex because Immunex "preferred a license." Appx28324-28325. Immunex had ample reason for that preference. Immunex's lead negotiator testified that he recognized that the ODP doctrine could apply to patents that became commonly owned through assignments. Appx5784. Notably, ODP law does not apply outside the United States, and the transfer of patent rights outside of North America to Wyeth in the same agreement—which are the same as the rights provided to Immunex for the U.S. patents in every material respect—was straightforwardly called an "assignment." Appx25838. Underscoring the fiction of the parties' label, Immunex could convert the "license" into a formal assignment for just $50,000. Appx25840. That clause was included at Immunex's insistence, as Roche was willing to formally assign the patent applications at no additional cost. Appx28335.

B. Immunex repurposes the patents-in-suit to focus on the p75 receptor.

In October 2004, Roche transferred its powers of attorney for the '182 and '522 patent applications to Immunex's attorneys. Appx28333-28334; Appx28341-28342; Appx13641-13648; Appx19782-19789. Immunex then repurposed the claims to cover etanercept.

In January 2005, Immunex amended the '182 application to claim either a p55 *or* a p75 TNFR:Fc fusion protein. Appx13659; Appx13665-1366. Then, in October 2005, Immunex amended the claims to remove all references to the p55 receptor, so for the first time, all claims related exclusively to the p75 TNFR:Fc fusion protein. Appx15931; Appx15933-15938; Appx5582.

In November 2006, Immunex amended the specification to include a reference to an October 2006 deposit of a plasmid related to the p75 receptor. Appx16424-Appx16425; Appx5788. This was the first time the full-length p75 receptor was incorporated into the specification. Appx24. While rewriting the '182 patent, Immunex obtained five extensions, adding 16 months to prosecution. Appx13764, Appx15932, Appx16236, Appx16720.

Immunex similarly changed the claim scope of the '522 patent. In December 2004, Immunex filed an amendment cancelling all pending claims, and filed amended claims related solely to the p75 receptor. Appx19798-19802. In August 2007, Immunex amended the specification to, for the first time, incorporate by

reference an article (Smith) showing the correct amino-acid sequence for the full p75 TNFR. Appx22640; Appx5788. Additionally, Immunex amended the specification to include a reference to the plasmid deposit it made in October 2006. Appx22641. During prosecution of the '522 patent, Immunex obtained seven additional extensions, adding 18 months to prosecution. Appx19824; Appx22240; Appx22488; Appx22493; Appx23047; Appx24076; Appx24421.

The '182 patent issued in 2011 and expires on November 22, 2028. Appx12686. The '522 patent issued in 2012 and expires on April 24, 2029. Appx12721.

C. Immunex's ultimate claims focus on the etanercept compound never disclosed in the priority application.

Immunex asserts claims 11, 12, 35, and 36 of the '182 patent, all of which depend partly from claim 1, which recites a protein comprising part (a) (directed to a portion of the p75 receptor) and part (b) (directed to a portion of an IgG immunoglobulin consisting of the hinge and the CH2 and CH3 domains). Appx12717-12718. Claims 11, 35, and 36 all depend from claim 1, which limit the portion of the p75 receptor to the extracellular region and the portion of the immunoglobulin to the exon-encoded "hinge-CH2-CH3" of IgG_1, per the parties' agreed claim construction. *Id*. Claim 12 is directed to a pharmaceutical composition containing the protein of claim 11.

Immunex also asserts claims 3, 8, and 10 of the '522 patent, which are directed to a process for making the fusion protein claimed by the '182 patent. The '522 patent requires "culturing a host cell comprising a polynucleotide" that consists of only the two parts—the p75 extracellular region and the IgG_1 immunoglobulin portion—and "purifying an expression product of the polynucleotide [*i.e.*, the protein] from the cell mass or culture medium." Appx12765.

IV. The district court blesses Immunex's end-run around established patent terms.

In 2005-2006, Sandoz began to develop a biosimilar version of etanercept, now called Erelzi. Appx28383. Based on the existing patents covering etanercept, Sandoz expected that it could launch Erelzi globally in 2015. Appx4677-5678. In 2011, however, Immunex announced the issuance of the '182 patent, which would not expire until 2028. Appx12607.

In 2015, Sandoz submitted an abbreviated biologics license application ("aBLA") under 42 U.S.C. §262(k), seeking authorization to market Erelzi and designating Enbrel as the reference product. After Immunex and Sandoz completed the exchange of patent lists under §262(*l*), Immunex, Amgen, and Roche filed suit against Sandoz in the District of New Jersey, alleging that Sandoz's submission of an aBLA referencing Enbrel was an act of infringement under 35 U.S.C. §271(e)(2)(C). Sandoz argued that the asserted claims were invalid on several

grounds, including ODP, lack of written description, and obviousness. Following a bench trial, the district court concluded that the patents-in-suit are not invalid.

With respect to ODP, the court first held that the patents held by Immunex could not be used as reference patents on the theory that Roche still owned the patents-in-suit. Appx68-73. The court relied primarily on Immunex's characterization of the agreement as a license, and concluded that Roche had not transferred all substantial rights to the patents-in-suit. *Id.*

In the alternative, the district court concluded that the Immunex patents are patentably distinct from the patents-in-suit. Appx74-84. As to the psoriasis patents, the court's conclusion turned on its application of the "two-way test," which "is appropriate only in the unusual circumstance where the PTO is *solely* responsible for the delay in causing the second-filed application to issue prior to the first." *Hubbell*, 709 F.3d at 1149 (emphasis added) (quotation marks omitted). As to the '690 patent, the court rejected Sandoz's proposed construction that the fusion protein claimed by the patent is etanercept. Appx76-77.

The district court also concluded that the priority application provides adequate written-description support. Appx11-28. The court recognized that the application fails to disclose the full-length p75 sequence as part of the invention, but concluded that the disclosure of that sequence in the art, combined with oblique references to that disclosure, was enough. Appx8-19. The district court then

concluded that the application disclosed the p75-IgG_1 etanercept protein. The court reasoned that the application disclosed each part of that protein, and that a skilled artisan would have been directed by *the claims themselves* to combine those parts to create the claimed protein. Appx19-21.

Finally, the district court rejected Sandoz's argument that the asserted claims of the patents-in-suit were obvious under §103. Appx28-59.

SUMMARY OF ARGUMENT

I. The asserted claims are invalid for ODP because they are obvious over Immunex's earlier-issued patents. The district court's contrary conclusion rested on several legal errors.

A. The district court concluded that the patents-in-suit are exempt from ODP, on the theory that the 2004 Agreement did not transfer formal title to Immunex. Appx67-73. That holding was legally incorrect. The rule against ODP for commonly-owned patents applies with full force to applications acquired by assignment during prosecution. *See In re Longi*, 759 F.2d 887, 893 (Fed. Cir. 1985). And the 2004 Agreement is an assignment in all but name, because it irrevocably conveys all substantial rights in the patents-in-suit to Immunex. The meager rights retained by Roche—to practice the patents for private, research uses and to bring an infringement suit if Immunex does not sue first or grant a sublicense—are insubstantial.

The district court's alternative holding that the patents-in-suit were patentably distinct (Appx74-84) was likewise infected with legal errors. The court's conclusion as to the psoriasis patents depended *entirely* on applying the two-way test—a test that is inapplicable because both Immunex and Roche contributed to the PTO's delay in issuing the patents-in-suit through multiple extensions and major claim amendments. As to the '690 patent, the district court's conclusion that it does not claim etanercept misconstrues the claims and contradicts both the specification and prosecution history.

II. The priority application does not provide written-description support for etanercept for two reasons.

A. First, it does not describe the full-length p75 sequence, and hence does not disclose a fusion protein based on that sequence. The priority application was based entirely on the sequences identified in Figures 1 and 4 and close variants thereof—*i.e.*, the full p55 sequence and the truncated/mutated Roche p75 sequence. *Every* discussion of the p75 receptor, and *every* reference to a fusion protein based on that receptor, refers to the Roche sequence in Figure 4, *not* to the full-length p75 sequence previously discovered and used by Immunex in etanercept. The Smith reference that discloses the full-length sequence is mentioned only once in the priority application, and the parties' experts *agreed* that this passing reference

neither incorporated Smith by reference nor instructed a skilled artisan to use Smith as a substitute for Roche's Figure 4 sequence.

The district court could only find disclosure of the p75 sequence through the type of hindsight- and obviousness-based approach to written description that this Court has rejected. *See, e.g.*, *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1352 (Fed. Cir. 2010) (en banc).

B. Second, the priority application failed to disclose the specific p75-IgG_1 etanercept protein Immunex claimed. A specification disclosing a genus of compounds only discloses a species within that genus if it provides "blaze marks" that would lead a skilled artisan to the later-claimed species. *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1326-27 (Fed. Cir. 2000). The priority application does not provide "blaze marks" to the full-length p75 sequence. Moreover, the application identifies a range of potential immunoglobulins, with an accompanying range of potential hinges. *Nothing* points a skilled artisan to the *specific* combination of features of etanercept.

The district court disputed none of this, but held that a skilled artisan would have been directed to etanercept *by the claims themselves*. That is blatant legal error. *See, e.g.*, *Novozymes A/S v. DuPont Nutrition Biosciences APS*, 723 F.3d 1336, 1349 (Fed. Cir. 2013).

III. The district court's obviousness analysis similarly rested on fundamental legal errors. In concluding that a skilled artisan would not have been motivated to combine the p75 receptor with an immunoglobulin to create etanercept, the court relied on the premise that the potential to stimulate inflammation would have taught away from this combination by making the fusion protein a poor candidate for treating autoimmune diseases like rheumatoid arthritis. But the asserted claims are *not* directed to a method of treatment, and it was legal error for the district court to discount evidence showing a motivation to create etanercept for *other* purposes. The district court likewise erred in assessing secondary considerations, disregarding the history of etanercept's conception and patenting *by Immunex*.

ARGUMENT

I. The patents-in-suit are invalid for ODP.

The rule against ODP enforces a fundamental bargain: a patentee receives exclusivity for an invention subject to the condition that "on the expiration of a patent the monopoly created by it ceases to exist." *Singer*, 163 U.S. at 185; *AbbVie*, 764 F.3d at 1372. Although ODP has been "described as a court created doctrine," it is "grounded in the text of the Patent Act," and in particular on §101's instruction that no one may "obtain[] more than one patent on the same invention." *AbbVie*, 764 F.3d at 1372. ODP doctrine implements this statutory policy by preventing

"separate applications or patents" from "claim[ing] inventions so alike that granting both exclusive rights would effectively extend the life of patent protection." *Hubbell*, 709 F.3d at 1145 (quotation marks omitted).

The patents-in-suit represent just such an invalid life-extension. The district court's ruling allowed Immunex to continue its patent protections after expiration of its own patents rested on several legal errors.

A. Standard of review.

ODP is a question of law, reviewed de novo. *UCB, Inc. v. Accord Healthcare, Inc.*, 890 F.3d 1313, 1324 (Fed. Cir. 2018). Underlying factual findings are reviewed for clear error. *Id.*

B. Patents owned by Immunex are proper reference patents, because Immunex is the effective owner of the patents-in-suit.

"[C]ommonly-owned applications by different inventors" are subject to the rule against ODP. *Longi*, 759 F.2d at 893. Under the 2004 Agreement, the applications that resulted in the patents-in-suit, the psoriasis patents, and the '690 patent were all "commonly-owned" by Immunex. The district court's contrary holding conflicts with precedent recognizing that an agreement that transfers all substantial rights to the patent is an assignment for purposes of federal patent policy.

1. An agreement that conveys all substantial rights to a patent is tantamount to an assignment of ownership.

Immunex has argued that its patents are not ODP references for the patents-in-suit because the 2004 Agreement supposedly conveyed only an exclusive license to the patents without formally transferring ownership. But an agreement *labeled* as a license "may be tantamount to an assignment" for purposes of federal patent law. *Aspex Eyewear, Inc. v. Miracle Optics, Inc.*, 434 F.3d 1336, 1340 (Fed. Cir. 2006). Thus, although only "[a] patentee" may sue for infringement, 35 U.S.C. §281, if an agreement "transfers 'all substantial rights' to the patent, this amounts to an assignment or a transfer of title" that provides standing for the transferee to sue in its "own name alone." *Morrow v. Microsoft Corp.*, 499 F.3d 1332, 1340 (Fed. Cir. 2007). The transferee "becomes the effective patentee," *id.* at 1340 n.6, with "effective title" to the patents-in-suit, *Keranos, LLC v. Silicon Storage Tech., Inc.*, 797 F.3d 1025, 1031 (Fed Cir. 2015). The same logic applies to the ODP context.

a. The district court questioned whether this Court's "all substantial rights" test should apply outside "the 'standing to sue' context." Appx70. Tellingly, however, the court did not suggest *any other way* to decide whether a purported licensee, whose license transaction is an assignment in every way that matters, should be treated like a patent owner for purposes of federal law.

Nor did the district court consider the textual links between the ownership inquiries in the ODP and standing contexts, which strongly support a common test.

As noted, only "[a] patentee" has statutory authorization to sue for infringement. 35 U.S.C. §281. This Court's decisions recognizing that some exclusive licensees nonetheless may sue in their own name rely on the definition of "patentee" in §100(d) to include "successors in title" to the patent. *See Karanos, LLC v. Silicon Storage Tech.*, 797 F.3d 1025, 1031 (Fed. Cir. 2015). As the Court has reasoned, when a party acquires all substantial rights to the patent, it becomes the "successor" under §100(d). *See id.* Similarly, even though only a "patentee or applicant" may file a terminal disclaimer to overcome an ODP objection, 35 U.S.C. §253(b), §100(d)'s definition of "patentee" establishes that a successor acquires authority to file a terminal disclaimer. *See In re Bowers*, 359 F.2d 886, 889 (C.C.P.A. 1966) (cited with approval in *Longi*, 759 F.2d at 894); *accord In re Borg*, 392 F.2d 642, 644 (C.C.P.A. 1968).

If anything, the argument for following the "all substantial rights" test is *stronger* in the ODP context. ODP comes from the fact that "§101 forbids an individual from obtaining more than one patent on the same invention." *AbbVie*, 764 F.3d at 1372. If Immunex would "become the effective patentee" for standing purposes, then Immunex has surely "obtained" that patent for ODP purposes.

b. Immunex argued below that courts should decide whether a party owns an application or patent for purposes of ODP by reference to *state* law. That approach is unworkable. The question of patent ownership in this context, as in the

context of statutory standing, directly implicates issues of *federal* patent policy that demand a "uniform national rule." *Rhone Poulenc Agro, S.A. v. DeKalb Genetics Corp.*, 284 F.3d 1323, 1328 (Fed. Cir. 2002).

Immunex's position also produces absurd results, because it offers an easy path for companies to circumvent ODP. On Immunex's account, a company that would face a certain ODP objection under *Longi* could avoid that objection merely by reclassifying the assignment as a license but *without changing anything of substance*. It would not matter, under this theory, whether the putative license is "tantamount to an assignment." *Alfred E. Mann Found. for Sci. Research v. Cochlear Corp.*, 604 F.3d 1354, 1358-59 (Fed. Cir. 2010). According to Immunex, if the relevant state law would accept the parties' label, then ODP cannot apply.

Immunex has no viable response to the relabel-an-assignment-as-a-license scenario because *that is this case*. As discussed, p. 17, *supra*, the executive who negotiated the 2004 Agreement for Immunex knew that commonly-owned patents are subject to ODP scrutiny under U.S. patent law. Appx5784. Whereas Roche executed a formal assignment of patent rights outside North America to Wyeth—a label that carried no invalidity risk, because ODP is not recognized outside the United States—Immunex insisted on characterizing its own substantively indistinguishable agreement as a "license," even though Roche had offered an assignment for the same price. Appx28324-28325. According to Immunex, this

strategic gambit allows it to avoid ODP while still enjoying complete control over the reference patents *and* the patents-in-suit, even during prosecution. But ODP "prevent[s] unjustified timewise extension of the right to exclude … *no matter how the extension is brought about*." *Hubbell*, 709 F.3d at 1145 (emphasis added). The Court should reject Immunex's easy-to-manipulate approach to determining ODP common ownership and instead apply the well-developed "all substantial rights" test.

2. The 2004 Agreement provided Immunex with all substantial rights to the patents-in-suit.

a. While this Court has "never established a complete list of the rights that must be examined to determine whether a patentee has transferred away sufficient rights to render another party the owner of a patent," it has described "the exclusive right to make, use, and sell" the patented invention as "*vitally important*." *Diamond Coating Techs., LLC v. Hyundai Motor Am.*, 823 F.3d 615, 619 (Fed. Cir. 2016) (quotation marks, brackets, and ellipses omitted). Likewise, the Court has identified "the nature and scope of the patentee's retained right to sue accused infringers and license the patent" as perhaps "the most important factors." *Id.* (quotation marks and brackets omitted). Those critical factors overwhelmingly support recognizing that the 2004 Agreement "transfer[s] away sufficient rights."

The 2004 Agreement granted Immunex all the classic indicia of ownership, including the two critical rights identified in *Diamond Coating*. Under Paragraph

3.1, Immunex obtained "a paid-up, irrevocable, exclusive license, with the sole right to grant sublicenses, under the [patents-in-suit] to make, have made, use, sell, offer for sale and import [the claimed inventions] for the life of such patents." Appx25839. As to litigation rights, Paragraph 3.5 provides Immunex with the first right to rectify any alleged infringement by, *e.g.*, suing the infringer or sublicensing the patents-in-suit. Appx25840-25841. Moreover, if Immunex exercises its right to sue, it has the complete rights to control the litigation—including to settle the claim on whatever terms it considers appropriate—and to pocket all proceeds from the lawsuit. *Id.*

The flip side is that Roche has been stripped of any of the traditional attributes of ownership. Here, Roche not only lost any ability to commercialize the claimed invention, but also did not "retain[] control of licensing" for the patents-in-suit. *Diamond Coating*, 823 F.3d at 620; *see* Appx25839. Likewise, Roche did not "retain[] control" of "litigation activities." *Diamond Coating*, 823 F.3d at 620. The Agreement provides Immunex with the unilateral right to initiate infringement litigation, which is then "solely within" Immunex's "control." Appx25840. Roche only has a back-up right to sue for infringement if Immunex declines to do so within 180 days of Roche's written request. Appx25841. That highly circumscribed right is "illusory" because Immunex "can render [it] nugatory by granting the alleged infringer a royalty-free sublicense." *Speedplay, Inc. v. Bebop, Inc.*, 211 F.3d 1245,

1251 (Fed. Cir. 2000). Specifically, Paragraph 3.5 authorizes Immunex "to rectify any infringement by sublicense." Appx25840. The Agreement does not place any limits on how Immunex exercises its licensing discretion, nor does it require Immunex to collect any royalties on a sublicense.

These factors alone show that the 2004 Agreement transferred all substantial rights in the patents-in-suit to Immunex. *See, e.g.*, *Diamond Coating*, 823 F.3d at 619; *Aspex*, 434 F.3d at 1342; *Alfred E. Mann*, 604 F.3d at 1360-61. But there is more. Under Paragraph 3.3, Immunex obtained the sole right to control the prosecution of the patents-in-suit—Roche did not even retain a right to review PTO submissions. Appx25840; Appx28335-28336; Appx5763-5765; Appx5768. That factor is highly significant in the ODP context, since ODP's purpose is to prevent applicants from receiving new patents that "extend the life" of their existing patents. *Hubbell*, 709 F.3d at 1145. This case shows why. Immunex used its control over prosecution to amend the applications that became the patents-in-suit in order to claim an invention—etanercept—that Roche never possessed or disclosed, but which Immunex itself had already claimed in its own patents.

b. The district court's contrary conclusion—reviewed de novo, *Lone Star Silicon Innovations LLC v. Nanya Tech Corp.*, 925 F.3d 1225, 1230 (Fed. Cir. 2019)—relied primarily on the fact that the 2004 Agreement's transfer of rights to Immunex was "expressly called a license," which the court contrasted with the

"[a]ssignment" label given to the transfer of Roche's corresponding patent rights outside of North America to Wyeth. Appx71. The court similarly looked to testimony by Immunex's lead negotiator, which reinforced that Immunex required Roche to retain formal ownership of the patents. Appx72. But the district court's reasoning runs headlong into this Court's precedent: "labels given by the parties do not control" the substantial-rights inquiry, *A123 Sys., Inc. v. Hyrdo-Quebec*, 626 F.3d 1213, 1218 (Fed. Cir. 2010), which is supposed to turn on "substance" "rather than formalities or magic words," *Lone Star*, 925 F.3d at 1229.

The need for courts to look beyond labels is especially pronounced in the ODP context, where assignees will have clear incentives to recharacterize agreements transferring patent ownership as licenses. Certainly Immunex had such an incentive here. *See* p. 17, *supra*.

Beyond its focus on the 2004 Agreement's labels, the district court identified just two rights that Roche supposedly maintained, neither of which comes close to establishing Roche's continued patent ownership.

First, the district court emphasized Roche's secondary right to sue for infringement. Appx71-72. But, as discussed, pp. 31-32, *supra*, that right was "illusory" because Immunex could undercut Roche's ability to sue by granting a royalty-free sublicense to an alleged infringer. *Speedplay*, 211 F.3d at 1251. Resisting that conclusion, the district court asserted that "Immunex could *not* end a

Roche-initiated lawsuit by granting a sublicense on its own." Appx73. But nothing in the 2004 Agreement supports the court's declaration, which conflicts with Paragraph 3.5's express grant of authority for Immunex "to rectify any … infringement" of the patents-in-suit "by sublicense." Appx25840.

Without referencing Paragraph 3.5, the district court instead relied on Paragraph 3.6, which states that Immunex "will cooperate with Roche" in a Roche-initiated suit," including by "participating as a party in the suit to the extent required by the court in order to bring suit." Appx25841. That provision, however, merely requires Immunex's participation in litigation. It does not qualify Immunex's express authority to eliminate the predicate for suit by granting a sublicense. The only other provision cited by the district court—the 2004 Agreement's mutual restrictions on further assignments without the counterparty's consent (Appx25849)—does not fill this gap. Immunex does not need *to assign* the patents-in-suit to an alleged infringer in order to vitiate Roche's ability to sue; a non-exclusive license would do. *See Carborundum Co. v. Molten Metal Equip. Innovations, Inc.*, 72 F.3d 872, 878 (Fed. Cir. 1995).[1]

[1] Roche's ability "to veto the assignment of Immunex's rights to a third party" also does not "suggest[] that the parties envisioned the agreement to be a license." Appx73. Paragraph 11.4, on which the district court relied, appears in a global section of the Agreement that also applied to Roche's agreement with Wyeth, and even Immunex recognizes that Wyeth received an assignment. Moreover, the

Even if Paragraph 3.6 could be read to implicitly restrict Immunex's otherwise unlimited right to grant sublicenses *during* a "Roche-initiated lawsuit," Appx73, Roche's secondary right to sue would remain illusory because it would still exist purely as a matter of Immunex's grace. Before Roche can file a lawsuit, Paragraph 3.5 requires Roche to make a written request to Immunex and to wait at least 180 days. Appx25841. There is no question that if Immunex grants a sublicense to the alleged infringer on day 179, Roche would lose any right to sue. Thus, just as in *Speedplay*, Immunex's sublicensing rights render Roche's secondary right to sue "illusory." 211 F.3d at 1251.

By contrast, in *Alfred E. Mann*, the patent owner's secondary right to sue was meaningful because sublicensing rights were "fettered" by the licensee's obligation to charge pass-through royalties on any sublicenses, which would flow back to the patent owner. *See* 604 F.3d at 1361-62; *see also Abbott Labs. v. Diamedix Corp.*, 47 F.3d 1128, 1132 (Fed. Cir. 1995) (similarly attributing significance to a retained right to sue, because any sublicense granted had to include royalties). No similar royalty requirement applies here.

Second, the district court pointed to Roche's reserved right "to practice the invention." Appx73. More specifically, Paragraph 3.2 allows Roche and its

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Agreement gives Immunex the same right to veto the assignment of *Roche's* rights to a third party. Appx25849.

affiliates "to practice under the [patents-in-suit] for internal, non-clinical research only." Appx25839. As this Court has explained, however, "this is not a substantial right" since it is the same right that any non-exclusive licensee might possess. *Luminara Worldwide, LLC v. Liown Elecs. Co.*, 814 F.3d 1343, 1351 (Fed. Cir. 2016). "The retained right to practice a patent is not the same as a retained right to exclude others from doing so." *Id.*

In short, Roche transferred all of its substantial rights to Immunex—which already owned multiple other etanercept patents.

C. The patents-in-suit are not patentably distinct from the '225 patent.

In conducting an ODP analysis after identifying the reference patents, the Court first "construes the claims in the earlier patent and the claims in the later patent and determines the differences." *AbbVie*, 764 F.3d at 1374 (quotation marks and brackets omitted). The Court then asks "whether those differences render the claims patentably distinct." *Id.* (quotation marks omitted). The "general rule" for deciding whether claims are patentability distinct is to apply a "one-way test," which asks whether the asserted patent claim is obvious over or anticipated by the reference-patent claim. *Hubbell*, 709 F.3d at 1149.

Under that "general rule," the obviousness of the asserted claims of the patents-in-suit over the claims of the psoriasis patents is clear beyond reasonable dispute. The patents-in-suit claim the etanercept protein (the '182 patent) and a

method of manufacturing etanercept (the '522 patent) using routine steps that were well known in the art. *See* pp. 18-20, *supra*. The psoriasis patents claim methods of using a therapeutically effective dose of etanercept to treat psoriasis. *See* p. 9, *supra*. The '225 patent, issued before both of the patents-in-suit, is unquestionably a proper ODP reference. *See Novartis Pharms. Corp. v. Breckenridge Pharm. Inc.*, 909 F.3d 1355, 1359 (Fed. Cir. 2018).[2] Thus, the issue here is whether patents claiming etanercept (the '182 patent) and a method for manufacturing etanercept (the '522 patent) were anticipated by or obvious over previously issued patent claims that presupposed etanercept's existence and described how to use etanercept to treat a specific condition. That question answers itself: because the psoriasis patent claims are effectively species of the asserted genus claims in the patents-in-suit, they are invalid for ODP. *See Perricone v. Medicis Pharm. Corp*., 432 F.3d 1368, 1374 (Fed. Cir. 2005).

The district court did not conclude otherwise, but rather reached a different result because it employed the far more lenient (and rarely applied) "two-way test." Appx78. Under that test, "the order of issuance is, in effect, ignored," and a patentee will escape ODP if its earlier patent claims are distinct from later-issued claims. *In*

[2] The district court's extended discussion of the "[i]mpact of GATT on the Patents-in-Suit" is accordingly irrelevant to this appeal because the court acknowledged that the '225 patent could serve as a proper reference based on its date of issuance. Appx82.

re Janssen Biotech, Inc., 880 F.3d 1315, 1325 (Fed. Cir. 2018). Reversing the district court's decision to apply the two-way test—which this Court "review[s] without deference," *In re Fallaux*, 564 F.3d 1313, 1316 (Fed. Cir. 2009)—compels the conclusion that the asserted claims are invalid for ODP.

1. The district court committed legal error by applying the "two-way" test.

The two-way test is reserved for "unusual circumstances," and the standard for invoking it is strict. *Janssen*, 880 F.3d at 1325. The test is "only appropriate where (1) a second-filed application issues prior to a first-filed application, and (2) the PTO is *solely* responsible for the delay in the issuance of first-filed application." *Id.* (emphasis added) (quotation marks omitted). And "solely" really means "solely": a patentee does *not* get the benefit of the test merely by showing that "on … balance" the PTO was more responsible for the sequencing of patent issuance. *Hubbell*, 709 F.3d at 1149. If an applicant's "actions, or inactions, had a direct effect on the prosecution," then "the two-way test … *does not apply*." *In re Basell Poliolefine Italia S.P.A.*, 547 F.3d 1371, 1376 (Fed. Cir. 2008) (emphasis added); *see also Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, n.7 (Fed. Cir. 2001) (rejecting the two-way test because continuation requests filed by the applicant showed that the delay in patent issuance "was not solely caused by the PTO"); *In re Emert*, 124 F.3d 1458, 1461 (Fed. Cir. 1997) (two-way test did not apply where actions taken by the applicant, including receiving "numerous time

extensions in various filings," showed that the PTO "did not dictate the rate of prosecution").

a. The undisputed facts show that the PTO was not "solely responsible" for the delayed issuance of the patents-in-suit: Roche and Immunex unquestionably contributed to the fact that those patents issued after the '225 patent. Immunex obtained five extensions for the '182 patent and seven extensions for the '522 patent, adding at least 16 months and 18 months to the prosecutions of those patents, respectively. Appx13764; Appx15932; Appx16236; Appx16720; Appx19824; Appx22240; Appx22488; Appx22493; Appx23047; Appx24076; Appx24421. Moreover, before Immunex took control of prosecution, Roche also sought numerous extensions for both the '182 and '522 patent applications, adding another year to their prosecutions. Appx13046; Appx13058; Appx13087; Appx13108; Appx13397; Appx13416; Appx19580; Appx19607; Appx19761; Appx19778. And between 1996 and 1998, Roche repeatedly ignored communications from the PTO regarding the '182 patent, further delaying issuance. Appx13056; Appx13076; Appx13096.

Roche and Immunex also repeatedly amended the patent applications, which delayed their issuance. As discussed, Immunex made radical changes following the 2004 Agreement by shifting the focus of the claims from the p55 to the p75 receptor and amending the specifications. *See* pp. 18-19, *supra*. For example, in December

2004, Immunex filed an amendment that cancelled all pending claims of the '522 application, which Roche had prosecuted for a decade, in order to file amended claims related to the p75 receptor. Appx19798-19802. Likewise, in 2005, Immunex filed a series of amendments to the '182 patent to add claims related to the p75 receptor and then remove all references to the p55 receptor. Appx13659; Appx13665-13669; Appx15931; Appx15933-15938. Immunex also made substantial amendments to the patent specifications in 2006 and 2007 in an effort to add belated descriptions of etanercept. *See* pp. 18-19, *supra*.

The upshot of Immunex's efforts was to render much of Roche's previous decade of prosecution irrelevant, substantially delaying issuance. Immunex's contribution to the delay is underscored by the fact that Immunex did not add the asserted claims to the respective applications until *late 2010*—15 years after Roche filed the applications. Appx 18227; Appx18234; Appx18778; Appx23323-23324; Appx23362; Appx24440.

b. The district court's decision to apply the two-way test focused almost exclusively on *instances* of delay that it concluded were attributable to the PTO. Appx80. But even accepting the court's findings as to those examples, they do not support applying the two-way test. Unless the PTO was "*solely* responsible for any delays associated with [the] claims" asserted here, the one-way test applies. *Hubbell*, 709 F.3d at 1149 (emphasis added).

Although the district court purported to find "as a matter of fact" that the PTO "was solely responsible for the delay" in issuance of the patents-in-suit (Appx80), the court's analysis reveals that it applied the wrong legal standard—so the factual findings that rest on that wrong legal standard are not entitled to deference. *Pullman-Standard v. Swint*, 456 U.S. 273, 287 (1982). Specifically, the district court acknowledged that Roche and Immunex made "*several* … requests" for extensions, but it discounted those repeated extensions on the ground that they supposedly were made "in good faith." Appx80-81 (emphasis added). But an applicant's purported "good faith" is legally irrelevant. The one-way test is not a sanction; it is the *default* rule that applies outside of the "unusual circumstance" in which the PTO *alone* is responsible for the fact that an earlier-filed patent issued after the reference patent. *Janssen*, 880 F.3d at 1325.

In any event, the district court's decision to apply the two-way test could not survive even clear-error review. No possible view of the record supports a finding that Roche's and Immunex's actions and inactions during prosecution had *nothing* to do with the patents-in-suit issuing after the '225 patent.

2. The patents-in-suit are not patentably distinct from the '225 patent under the one-way test.

Applying the one-way test resolves ODP as to the '225 patent. As noted, p. 9, *supra*, claim 1 of the '225 patent recites methods of treating psoriasis by administering a therapeutically effective dose of etanercept. Those claims would

have directed a skilled artisan to produce etanercept (Appx4131), thus rendering the asserted claims of the '182 patent obvious. Moreover, to produce etanercept, a skilled artisan would have taken all of the steps described in the asserted claims of the '522 patent—*i.e.*, performing the routine steps of culturing a host cell encoding the DNA for etanercept and purifying etanercept from parts of the cell. Appx4133-4134; Appx4110-4112. Clear and convincing evidence thus establishes that the asserted claims of the patents-in-suit are obvious over claim 1 of the '225 patent when the one-way test is applied.

D. The asserted claims in the patents-in-suit are not patentably distinct from claim 3 of the '690 patent.

Claim 3 of the '690 patent covers a method of administering etanercept, and is thus not patentably distinct from the asserted claims of the patents-in-suit.

Specifically, claim 3 recites "a method for lowering the levels of active TNF-α in a mammal in need thereof which comprises administering to said mammal a TNF-lowering amount of a chimeric antibody comprising *a TNFR comprising the sequence of amino acids 3-163 of SEQ ID NO:1 fused to the constant domain of an immunoglobulin molecule*." Appx27320 (emphasis added). That claim describes etanercept: the etanercept molecule fuses the extracellular region of the TNFR ("a TNFR comprising the sequence of amino acids 3-163 of SEQ ID NO:1") to the hinge-CH2-CH3 region of IgG_1 (the constant domain of an immunoglobulin molecule"). Appx4105-4106, Appx4136-4137, Appx4145-4146.

Below, both parties agreed that claim 3 covers a protein consisting of the extracellular region of the p75 receptor fused to a portion of a human IgG_1. So the only dispute concerns the proper construction of the phrase "fused to the constant domain." Immunex argued, and the district court agreed, that that phrase describes a protein in which the TNFR is fused to "a *completely unchanged and unmodified* constant region domain for the light chain *and* for the heavy chains." Appx5272 (emphasis added). That construction is incorrect.

"Claim interpretation requires the court to ascertain the meaning of the claim to one of ordinary skill in the art at the time of invention." *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1338 (Fed. Cir. 2005). "The intrinsic evidence, *i.e.*, the patent itself, including the claims, the specification and, if in evidence, the prosecution history is the most significant source of the legally operative meaning of disputed claim language." *Id.* (quotation marks omitted). Here, evidence from the '690 patent's specification and prosecution history shows that the phrase "fused to the constant domain" in claim 3 covers the fusion of etanercept's TNFR to the hinge-CH2-CH3 region of IgG_1.

1. First, consider the '690 patent's specification. An interpretation of a patent's claims that excludes "a preferred … embodiment in the specification … is rarely, if ever, correct." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583 (Fed. Cir. 1996). But that is precisely what the district court has done.

Figure 1 presents a schematic representation of a "recombinant human TNFR/Fc fusion protein." Appx27297-27298; Appx27304. Both sides' experts recognized that "[t]his Figure 1 … *is* etanercept": it combines "the soluble portion, the extracellular domain of the p75 TNF receptor" with "the hinge-CH2 and CH3 domain of a human IgG." Appx4137 (emphasis added); *accord* Appx5392. A comparison of Figure 1 (Appx27297) to the schematic of etanercept in the district court's opinion (Appx6) underscores the point:

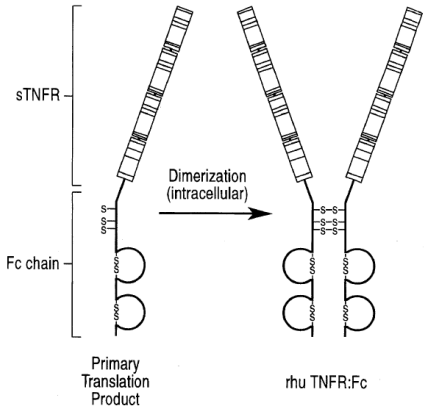

Figure 1

Etanercept

The '690 patent's examples are of similar effect. Example 2 describes the production of etanercept—referred to as a "TNFR/Fc fusion protein." Appx27310-27311 (14:55-15:60); Appx4138; Appx5392-5393. Example 4 describes the use of the p75 extracellular region and etanercept to suppress the effects of arthritic conditions, while Examples 5 and 6 describe further testing with just etanercept. Appx27312 (7:16-20:43); Appx4138-4139; Appx5393-5394.

Finally, the single paragraph in the '690 patent specification that discusses a "chimeric antibody" describes etanercept:

> A recombinant chimeric antibody molecule may also be produced having TNFR sequences substituted for the variable domains of either or both of the immunoglobulin molecule heavy and light chains and having unmodified constant region domains…. One specific example of a TNFR/Fc fusion protein is disclosed in SEQ ID NO:3 and SEQ ID NO:4.

Appx27307 (7:42–58). As both parties' experts confirmed, the TNFR/Fc fusion protein disclosed in SEQ ID NO:3 and SEQ ID NO: 4 is etanercept. Appx4139; Appx5391.

2. The prosecution history of the '690 patent points in the same direction, though Plaintiffs' expert failed even to consider it. Appx5390. The applicants amended their claims to specify that one example of a "chimeric antibody comprising a TNF receptor and the constant domain of an immunoglobulin molecule" (the phrase that now appears in claim 3) was a "soluble human TNFR is fused to the Fc region of the human immunoglobulin molecule"—*i.e.*, etanercept. Appx10016; Appx10172; Appx10219. Moreover, the applicants relied upon a declaration reporting clinical data from administering etanercept to demonstrate the utility of the claimed chimeric antibody. Appx20223; Appx10236-10237; Appx10230-10252; Appx4139-4141. At no point did the applicants disavow that the chimeric antibody includes etanercept.

3. The district court failed even to address the specification language and prosecution history discussed above. *See* Appx76-77. Instead, the court relied on a single fact: "the specification of the '690 Patent describes a chimeric antibody as a molecule 'having TNFR sequences substituted for the variable domains of either or both of the immunoglobulin heavy and light chains and having *unmodified* constant region domains.'" Appx77 (quoting Appx27307).

But etanercept *does* have unmodified constant region domains: the molecule consists of a TNFR fused to the *unmodified* hinge-CH2-CH3 region of IgG_1. *See* pp. 7-8, *supra*. According to the district court, that was not enough: *each and every constant region domain* (including CH1) must remain unmodified. Appx76-77. But that interpretation places more weight on a single passage in the specification—"having unmodified constant region domains"—than it can reasonably bear. Considering the intrinsic record as a whole, the only reasonable interpretation is that the phrase requires *some* unmodified constant region domains. Indeed, Plaintiff's own expert conceded that he did not know whether the phrase "fused to the constant domain of an immunoglobulin molecule" precludes fusing the TNFR to the hinge-CH2-CH3 portion of an immunoglobulin. Appx5400-5401.

Thus, the district court erred in holding that Claim 3 of the '690 patent does not cover etanercept. That resolves the ODP analysis, because none of Immunex's

experts disputed the obviousness of the asserted claims under this construction of claim 3.

II. The district court erred in concluding that the priority application disclosed possession of the claimed invention.

The asserted claims, added by Immunex in 2010—15 years after Roche filed the priority application—are also invalid because they lack written-description support in "the original priority application." *Novozymes*, 723 F.3d at 1344.

Roche did not have possession of etanercept. It did not invent etanercept, never even *made* etanercept, and was never even able to clone the full p75 receptor. Roche's application thus, unsurprisingly, did not describe etanercept—or any other fusion protein with the full p75 receptor.

Immunex's late-added etanercept claims survived only because the district court erroneously applied an obviousness framework to the written-description inquiry. The court looked not to the invention *actually disclosed*, but to what might have been obvious to a skilled artisan in light of those disclosures—a far lower bar than what this Court's law requires. *See Idenix Pharms. LLC v. Gilead Sci. Inc.*, 2019 WL 5583543, at *8-10 (Fed. Cir. Oct. 30, 2019) (reversing the district court's denial of JMOL on written description, where the court relied on obviousness-based arguments as a substitute for the specification's failure to describe the compound claimed).

A. Standard of review.

This Court reviews a district court's "compliance with legal standards" de novo. *Veritas Technologies LLC v. Veeam Software Corp.*, 835 F.3d 1406, 1411 (Fed. Cir. 2016). In addition, "if a district court's findings rest on an erroneous view of the law, they may be set aside on that basis." *Pullman-Standard*, 456 U.S. at 287. Absent legal error, whether a patent's specification adequately demonstrates possession of the claimed subject matter is a question of fact, reviewed for clear error. *Ariad*, 598 F.3d at 1351.

B. The district court legally erred by repeatedly looking outside the "four corners of the specification."

The written-description requirement "limits patent protection to those who actually perform the difficult work of 'invention'—that is, conceive of and complete the final invention." *Billups-Rothenberg, Inc. v. Associated Reg'l & Univ. Pathologists, Inc.*, 642 F.3d 1031, 1036 (Fed. Cir. 2011). A patent's description of the invention "must clearly allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed" by demonstrating "possession of the claimed subject matter as of the filing date." *Ariad*, 598 F.3d at 1351 (quotation marks and alterations omitted). Holding the inventors to their originally-disclosed invention is particularly important for "claims added during prosecution" to ensure that they are not used to "expand the scope of [the] invention or to complete an idea." *Novozymes*, 723 F.3d at 1343-44.

Moreover, because "the hallmark of written description is disclosure," the written-description "test requires an objective inquiry into the four corners of the specification." *Ariad*, 598 F.3d at 1351. "[A] description that merely renders the invention obvious does not satisfy the [written-description] requirement." *Id.* at 1352. Similarly, a description is not adequate simply because it is later possible, "[w]orking backward from a knowledge of the claims," to put together "an amalgam of disclosures" that, "plucked selectively from the … application," can be combined together and with the prior art to create the later-claimed invention. *Novozymes*, 723 F.3d at 1349. Nor can a patentee expand an invention by initially disclosing a broad genus of compounds or characteristics, and then later claiming one species that is nowhere highlighted in the disclosure. Instead, the original disclosure must include "blaze marks" leading from the genus to the later-claimed species. *E.g.*, *Idenix*, 2019 WL 5583543, at *9.

The district court's decision flouts these basic principles. Roche's priority application never even identified each individual *piece* of the later-claimed etanercept fusion protein, let alone the "blaze marks" necessary to identify that particular protein. The district court repeatedly used hindsight to piece together what Immunex ultimately claimed—*not* what the specification describes.

C. Roche's priority application does not include written-description support for the etanercept-based claims Immunex later added.

The asserted claims all require a fusion protein with two parts: the full extracellular region of the p75 receptor and specific portions of human IgG_1, connected at a specific point. The priority application therefore must disclose a fusion protein with those specific attributes. But Roche's priority application only discloses fusion proteins that include *some* receptor portion and *some* immunoglobulin portion. Appx25091. It does *not* describe the specific combination of elements that result in etanercept.

1. The priority application described a fusion protein based on the truncated/mutated p75 DNA sequence disclosed in Figure 4, *not* the full p75 DNA sequence used in etanercept.

a. The TNFR portion of the fusion proteins disclosed in Roche's priority application was based on the DNA and amino-acid sequences disclosed in Figure 1 and Figure 4. Figure 1 discloses the p55 receptor. Appx25084. Figure 4 discloses the "[n]ucleotide sequence and deduced amino acid sequence for cDNA clones derived from 75/65 kD TNF-BP." *Id*.

All of the TNFR portions of the fusion proteins in the priority application rest on these specific DNA and amino-acid sequences, and close variations thereof. For instance, the application stated that its DNA coding for TNF-binding proteins should be "selected from the following: (a) DNA sequences as given Figure 1 or Figure 4 as well as their complementary strands, or those which include these sequences."

Appx25089. The application also identified similar DNA sequences that "hybridize" with those in Figure 1 or Figure 4, or that "code for polypeptides having exactly the same amino acid sequence." *Id*. It explained that the invention encompasses "those DNA sequences which result from deletions, substitutions and additions from one or more nucleotides of the sequences given in Figure 1 or Figure 4." Appx25090.

In discussing preferred embodiments, the specification again focused on Figures 1 and 4. It stated that "preferred first of all [are] those DNA sequences which code for such a protein having an apparent molecular weight of about 55 kD, whereby the sequence given in Figure 1 is especially preferred"; fragments of the Figure 1 sequence could also be used. *Id*. The application then disclosed that "[t]here are also preferred DNA sequences which code for a protein of about 75/65 kD, whereby those which contain the partial cDNA sequences shown in in Figure 4 are preferred." *Id.* The application never identified any DNA sequence—other than Figure 1 or 4, or close variants thereof—from which to draw the TNF-receptor portion of the fusion protein.

There is no dispute that truncated/mutated Figure 4 is *not* the full sequence for the extracellular portion of the p75 receptor that Immunex ultimately claimed. Most importantly, of the sequence of 235 amino acids that ultimately made part of the claimed fusion protein, the Figure 4 disclosure omits 20%—the first 48 amino

acids—which comprise the N-terminus of the p75 extracellular region as incorporated into etanercept. Appx4454; Appx5037. Figure 4 also omits the 22-amino-acid signal sequence, which is essential to protein secretion. Appx4453-4454. Moreover, Roche's Figure 4 sequence includes *different* amino acids than the Smith sequence in three important positions, and includes one amino acid that is not in Smith. Appx7004; Appx4456-4461. Plaintiffs' expert thus had to admit that the actual DNA or amino acid sequence ultimately used in the etanercept fusion protein Immunex later claimed "is not recited in the patent as a simple matter of fact." Appx5054-5055.

The closest the priority application comes to disclosing a fusion protein with the full p75 extracellular region is its vague reference to Smith. Specifically, after discussing how the invention encompasses "deletions, substitutions and additions" from Figure 1 or Figure 4, the application stated that "[o]ne sequence which results from such a deletion is described, for example, in Science 248, 1019-1023, (1990)," *i.e.*, Smith. Appx25090.

This vague reference to Smith as an example of a "deletion" from Figure 4 does not come close to disclosing a fusion protein that incorporates that *different* sequence for the p75 receptor, rather than the sequence repeatedly referenced in the priority application itself. Most importantly, the application does not incorporate Smith generally, or Smith's full p75 sequence specifically. It simply gives Smith as

an example of a "deletion." As Sandoz's expert explained, Smith provides such an example because Roche's Figure 4 sequence includes an alanine amino acid at residue 369 that the Smith sequence lacks. Appx4460-4461.

Plaintiffs' expert disputed this explanation, but had to acknowledge that the priority application did *not* "incorporate Smith by reference," and did *not* instruct a skilled artisan to "use Smith to complete the sequence of Figure 4." Appx5062-5063. Moreover, he agreed that if the Roche applicants had wanted to describe as their invention a fusion protein that included the p75 sequence in Smith—rather than the Figure 4 sequence that they possessed—"[n]othing stopped … the applicants from saying … our preferred sequence is Smith or we incorporate Smith by reference." Appx5064. Ultimately, Plaintiffs' expert described the priority application's reference to Smith as an example of a deletion as "making no sense": "I can't make sense of it as it says because it's on its face ridiculous." Appx5061-5062. The best he could do was to describe this reference as "refer[r]ing a person of skill in the art to Smith," and identifying it as a "landmark paper" that a skilled artisan should "go and read." Appx5063; Appx5091-5092. That is a far cry from *describing* a DNA sequence contained in Smith as part of Roche's invented fusion protein. At most, it would make such a protein-portion obvious, which is not the standard. *See Indenix*, 2019 WL 5583543, at *10.

b. Roche characterized its invention as a fusion protein that used the Figure 4 sequence, rather than the sequence disclosed in Smith, as the TNFR portion. That was no accident—Roche knew it had described a sequence that was different than Smith, and chose to include its own as the basis for its fusion protein. This is perhaps most clear from Roche's prosecution of the '029 patent, which was directed to the TNFR sequence disclosed in Figure 4. *See* p. 11, *supra*. During that prosecution, Roche distinguished its sequence from the prior-art Smith sequence precisely because its sequence was shorter and included important variations. Roche told the PTO that the Smith sequence is "a cDNA sequence encoding a human TNF-R of about 80 kD, whereas applicants claim[ed] a purified and isolated polynucleotide encoding an insoluble protein which has an apparent molecular weight of about 75 kilodaltons." Appx31502-31503; *see* Appx31500. Roche further distinguished its p75 receptor from Immunex's full-length p75 receptor because Roche's receptor contains the three amino-acid mutations and one extra amino acid described above. Appx31501-31502.

Roche's decision to focus on the distinct Figure 4 sequence was perfectly understandable. As explained, pp. 10-11, *supra*, Roche had failed to clone the full sequence disclosed in Smith, but had only identified smaller sequences, including the Figure 4 sequence and the much smaller SEQ IDs described in the priority application. *E.g.*, Appx4857. Accordingly, in describing the "final invention" that

Roche "conceive[d] of and complete[d]," *Billups-Rothenberg*, 642 F.3d at 1036, Roche naturally focused on a fusion protein with the TNFRs that Roche itself had developed, which was *not* etanercept. Indeed, when Roche needed etanercept—a fusion protein based on the full Smith sequence—for its own clinical trials, it had to *ask Immunex for it*. Appx10611.

Immunex *itself* evidently recognized that Roche had not described a fusion protein with the full p75 receptor sequence. As explained, pp. 18-19, *supra*, after Immunex took over prosecution, it amended the specifications to reference Immunex's own Smith publication—serving to highlight that Roche had *failed* to do just that in the priority application. Most blatantly, Immunex amended the specification to add the Smith sequence as Figure 5 in what ultimately became the '522 patent; to state that Smith was "incorporated by reference" into that specification; and to reference, in both patent specifications, a 2006 plasmid deposit of the full sequence never mentioned in the priority application (because it took place a decade after the priority application was filed). Appx22640-22641. These amendments to the specification do not change the written-description analysis, which focuses on "the written description of the *original priority application*." *Novozymes*, 723 F.3d at 1344 (emphasis added). But they are highly revealing as to how Immunex itself read Roche's specification: If Roche's priority application *already* described an invention that encompassed a fusion protein with the Smith

sequence, Immunex would have had no need to amend the specification to incorporate that same sequence.

c. Without even acknowledging many of Sandoz's arguments, the district court found adequate written-description support largely by concluding that a skilled artisan could have deduced the later-added claims by combining the application's disclosures with other prior-art references. That obviousness-based approach to written description was legally and factually flawed.

The district court most clearly went beyond the "four corners of the specification," *Ariad*, 598 F.3d at 1351, in concluding that a skilled artisan could have uncovered the full p75 sequence based on two small fragments of that sequence described in the priority application as SEQ ID NO: 10 and SEQ ID NO: 7. Appx14-15; Appx18-19. These two sequences disclose only 36 of the 235 amino acids that make up the full p75 sequence. Appx18. But the court nonetheless suggested that a skilled artisan could have taken these two sequences, submitted them to a third-party depository, received back the full p75 sequence, and then used the extracellular portion of *that* sequence in the fusion protein instead of the Figure 4 sequence actually described. Appx18-19. The court held that this was enough to "sufficiently describe the subject fusion protein using the known full p75 sequence." Appx19.

Even if a skilled artisan could have used these fragments to deduce the full p75 sequence in this way and then used that sequence in a fusion protein, at best that

would show that the priority application rendered the later-added claims directed to etanercept *obvious*, not that the *application itself* described a fusion protein that included the full p75 sequence. Notably, Plaintiffs' expert admitted that there is no teaching directing a skilled artisan to combine SEQ ID 10 and 7 together to get the p75 portion to use in a fusion protein. Appx5070.

The district court also relied heavily on the fact that the p75 amino acid sequence supposedly "was well known to a POSA at the time of the invention." Appx16. Again, that misses the point. The written-description problem here is not that the art was silent on p75 sequences; it is that the priority application specified *exactly* what p75 sequence Roche had in its possession, which was the sequence Roche itself had discovered and described in Figure 4. While the priority application did not need to "re-descri[be]" invoked and known prior-art concepts, *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005), it cannot incorporate every *un*-invoked prior-art concept related to the described invention; otherwise, this Court's repeated instruction that the inquiry is limited to the "four corners of the specification" would have no meaning. *Ariad*, 598 F.3d at 1351.

Finally, the district court similarly missed the point in concluding that the specification's reference to Smith as a "deletion" would not have "deterred" a skilled artisan from looking to Smith. Appx17-18. Merely *looking* to Smith is not enough. Rather, the passage describing Smith *only* as an example of a deletion made clear

that (as Plaintiffs' expert conceded) the Roche inventors were aware of Smith and yet were *not* incorporating Smith—or the DNA sequence it disclosed—as part of Roche's invented fusion protein. Appx5063.

2. The priority application did not adequately demonstrate possession of the claimed p75-IgG$_1$ fusion protein.

Describing a broad genus of compounds is insufficient to provide written-description support for a claim directed to a specific compound. Rather, the original disclosure must provide enough direction to lead skilled artisans to "single out" the invention from the various alternatives discussed in the disclosure. *Purdue*, 230 F.3d at 1326; *see also Boston Sci. Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1367-68 (Fed Cir. 2011). As this Court explained, "one cannot disclose a forest in the original application, and then later pick a tree out of the forest and say here is my invention. In order to satisfy the written description requirement, the blaze marks directing the skilled artisan to that tree must be in the originally filed disclosure." *Purdue*, 230 F.3d at 1326. The district court's decision flouts this basic principle.

a. The priority application did not provide *any* indication that Roche had invented the *specific* p75-IgG$_1$ fusion protein that Immunex later claimed. First, it did not provide "blaze marks" suggesting that the Smith p75 sequence should be chosen for a fusion protein. To the contrary, for a skilled artisan to arrive at a fusion protein with the Smith sequence, she would have had to ignore the Figure 4 sequence repeatedly identified in the specification as "preferred"; ignore Examples 1-8 that

use Figure 4; and select the never-referenced full Smith sequence, even though many other soluble fragments of that sequence would have bound TNF.

Second, after selecting the Smith sequence, a skilled artisan would have had to select both IgG_1 and the exon-encoded version of the hinge. The specification mentioned 5 different immunoglobulin classes, associated with a wide range of potential hinges. Appx4483-4484. Indeed, Immunex argued below that "[a] POSA selecting an IgG would not have selected an exon-encoded hinge-CH2-CH3 of IgG1." Appx60334. Thus, even if the IgG_1 and the exon-encoded hinge were *described* as *possible* options within the broad genus of fusion proteins disclosed, the priority application provided no "blaze marks" that would have led a skilled artisan to their selection.

Third, to the extent the priority application provided blaze marks, they went to *different* proteins than etanercept. Example 11, the only example in the priority application directed to making a fusion protein, is directed to a p55-IgG_3 protein. As one of the Roche inventors admitted, a skilled artisan would need to alter the Example 11 method in many ways to make a p75-IgG_1 protein. Appx4844-4845; *see also* Appx4495-4497.

b. The district court's discussion of Roche's possession of Immunex's later-claimed fusion protein ignored these governing legal principles and impermissibly relied on "hindsight," "working backward from a knowledge of [the

claims] … to derive written description support from an amalgam of disclosures plucked selectively from the application." *Novozymes*, 723 F.3d at 1349.

Most blatantly, the district court relied on *the claims themselves* as evidence of the required "blaze marks." For instance, in discussing why Example 11 provided written-description support, the court stated that a skilled artisan would have modified that example to use p75 to create etanercept "based on *the claims in the Patents-in-Suit* and the specification." Appx20 (emphasis added). The court similarly found possession because "*the claim language* identifies the requisite elements of the subject invention …. and, in conjunction with the specification, provides support of possession." Appx21 (emphasis added). And the district court's ultimate finding of possession was "based on the specifications …, including the examples within the specifications, *and the claims*." Appx22 (emphasis added).

This repeated reliance on *the claims themselves* as written-description support is a flagrant use of improper hindsight. This Court held in *Ariad* that even claims in *the original application* need their own written-description support. 598 F.3d at 1349. Using claims added many years *after* the original disclosure to demonstrate possession is even more impermissible. *E.g.*, *Purdue*, 230 F.3d at 1326-27.

III. The district court's obviousness analysis was infected by legal error.

A. Standard of review.

"[W]hether a claimed invention would have been obvious is a question of law reviewed de novo." *Bayer Pharma AG v. Watson Labs, Inc.*, 874 F.3d 1316, 1321 (Fed. Cir. 2017).

B. The district court's motivation analysis disregarded the asserted claims' objective reach and instead focused on the inventors' motivation.

As of the priority date, the components of etanercept were well known and actively studied. The district court found that the prior art taught the DNA sequences of the p75 receptor and hinge-CH2-CH3 of the IgG_1, both of which are required to construct etanercept. Appx16, Appx20, Appx26. The court also found that a skilled artisan could construct etanercept and would reasonably expect etanercept to bind TNF. Appx26; Appx49. The court nevertheless held that the asserted claims were nonobvious because a skilled artisan would not have been motivated to either select the p75 receptor or combine it with an immunoglobulin based on a concern that it could stimulate inflammation and thus would be ineffective to treat inflammatory conditions like rheumatoid arthritis.[3]

[3] *See, e.g.*, Appx32-39 (addressing only whether a skilled artisan, seeking to treat rheumatoid arthritis or another pro-inflammatory disease, would be motivated to select the p75 receptor and IgGs), Appx40 ("[T]he prior art … taught that Ig fusion proteins activated effector functions leading to inflammation in the body.… Given this prior art, a POSA would have expected a fusion protein combining TNFR and IgG_1 to lead to autoimmune damage caused by effector functions."); Appx41 ("[T]he

That was legal error: the asserted claims are not directed to the treatment of any disease or condition, let alone rheumatoid arthritis or other inflammatory conditions. The sole limitation requiring any specific activity is contained in the asserted claims of the '182 patent, which only require the construct to "specifically bind TNF"—a function that, without dispute, a person of skill would have fully expected the claimed TNFR/IgG fusion protein to produce. Appx48-49. Indeed, the specification does not even mention rheumatoid arthritis, nor does it contain any data concerning the treatment of any disease.

By nonetheless centering its analysis on whether a skilled artisan would have been motivated to develop etanercept as an autoimmune-disease treatment, the district court adopted a "narrow conception of the obviousness inquiry" that precedent rejects. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 419 (2007). "[N]either the particular motivation nor the avowed purpose of the patentee controls. What matters is the objective reach of the claim." *Id.*

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prior art actually taught away from using an Ig fusion protein, such as the one proposed in Smith '760, to treat auto-immune diseases because such a construct would have likely elicited an inflammatory response in the body."); Appx44-45 (a skilled artisan would have disregard the prior-art's teaching to modify the Smith '760 protein by removing the CH1 and light chains, because the prior art would have "dissuaded a POSA from making these modifications … based on their proven increase in effector functions," which could increase inflammation).

Narrowing the motivation inquiry to exclude the full scope of the claim is reversible error here because the district court ignored the undisputed evidence that several groups working in the field at the time *were* making TNFR/IgG fusion proteins. Appx4176-4177; Appx4155-4156; Appx5170-5171; *see* Appx10602; Appx28205; Appx28199. Moreover, it was undisputed that TNFRs and TNFR/IgG fusion proteins were considered useful, not just as potential therapeutic compounds, but, importantly, as potential diagnostic and research tools. Appx4161-4162; Appx4832; Appx28349. Yet the district court did not address these potential uses, instead focusing exclusively on whether a person of skill would be motivated to make a TNFR/IgG fusion protein to treat autoimmune diseases. That is a glaring error. *See Nalpropion Pharms., Inc. v. Actavis Labs., FL, Inc.*, 934 F.3d 1344, 1354 (Fed. Cir. 2019) (rejecting patentee's motivation argument that contradicted "[t]he inescapable, real-world fact … that people of skill in the art *did combine*" two medical treatments).

C. The district court's analysis of secondary considerations was legally erroneous.

The district court also committed legal error in its decision on certain objective indicia of nonobviousness—specifically on praise, "clinical success," long-felt need, and failure of others—by incorrectly analyzing the required nexus between the claims and these asserted objective indicia. Appx52; Appx54. The court then compounded that legal error by improperly dismissing the evidence of Immunex's

simultaneous invention of etanercept (Appx57-58), resulting in a peculiar ruling that evidence of *Immunex's* success led to a finding of failure of others, when in fact Immunex—an "other"—succeeded where the inventors actually failed.

"For objective evidence to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention." *In re GPAC Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995). Where objective evidence relates to "something other than what is both *claimed and novel* in the claim, there is no nexus to the merits of the claimed invention." *Merck & Cie v. Gnosis S.P.A.*, 808 F.3d 829, 837 (Fed. Cir. 2015).

Most particularly, the court failed to consider earlier patents claiming etanercept, including the '690 patent, and to define what was novel about the patents-in-suit compared to those earlier patents. With no evidence that objective indicia are "a result of the novel features in the … patent[s], as opposed to the other patents involved," any such indicia are "not sufficiently connected with the novel elements of the asserted claims" and thus "carry little weight." *Id.* at 838-39.

The court further legally erred in dismissing the evidence of simultaneous invention, especially by Immunex. Appx56-58. In fact, *only* Immunex combined the specific pieces set forth in the claims—the inventors never did. All the benefits etanercept allegedly offered were attributable to Immunex's work, and Immunex's patents. The court misread this Court's cases to establish a rule that one instance of

simultaneous invention is insufficient. Appx58. In the case cited, the alleged simultaneous inventors had collaborated on or seen the patented invention. *Lindemann Maschinenfabrik GmbH v. Am. Hoist & Derrick Co.,* 730 F.2d 1452, 1460 (Fed. Cir. 1984). Here, by contrast, Immunex invented etanercept independently of the inventors.

Likewise, the court legally erred in concluding that there was a "failure of others," while relying on the work of others—*i.e.*, Immunex—and ignoring the failure of the Roche inventors. Appx53-54.

CONCLUSION

This Court should reverse the district court's decision and hold that the asserted claims of the patents-in-suit are invalid.

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Respectfully submitted,

/s/ William M. Jay

William M. Jay
Brian T. Burgess
GOODWIN PROCTER LLP
1900 N Street NW
Washington, DC 20036
Tel.: 202.346.4000
Fax: 202.346.4444

David J. Zimmer
Gerard J. Cedrone
GOODWIN PROCTER LLP
100 Northern Ave.
Boston, MA 02210
Tel.: 617.570.1000
Fax: 617.523.1231

George C. Lombardi
Maureen L. Rurka
Julia Mano Johnson
Dan H. Hoang
Loren G. Rene
WINSTON & STRAWN LLP
35 W. Wacker Drive
Chicago, IL 60601-9703
Tel.: 312.558.5600
Fax: 312.558.5700

Cindy Chang
GOODWIN PROCTER LLP
The New York Times Building
620 Eighth Ave.
New York, NY 10018
Tel.: 212.813.8800
Fax: 212.355.3333

Counsel for Appellants Sandoz Inc., Sandoz International GmbH and Sandoz GmbH

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