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Life Sciences
2021 Year in Review

February 16, 2022

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Meet The Speakers

Anita Meiklejohn
Principal

Susan Morrison
Principal

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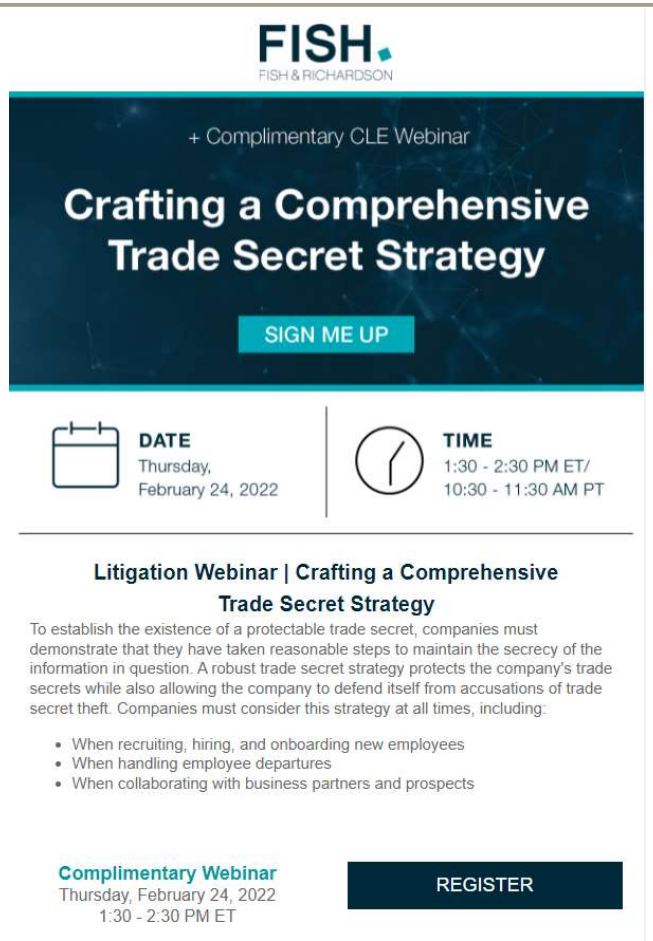
Overview

- **Housekeeping**
  - CLE
  - Questions
  - Materials
    - http://www.fr.com/webinars



Agenda

- **Enablement**
  - *Amgen v. Sanofi*
- **Written Description**
  - *Biogen v. Mylan*
  - *Indivior v. Dr Reddy's*
  - *Juno v. Kite Pharma*
- **Safe Harbor:** *Allele v. Pfizer*
- **Inducement:** *GSK v. Teva*
- **Doctrine of Equivalents:** *Jennewein v. ITC*
- **Reasonable Expectation of Success:** *Teva v. Corcept*

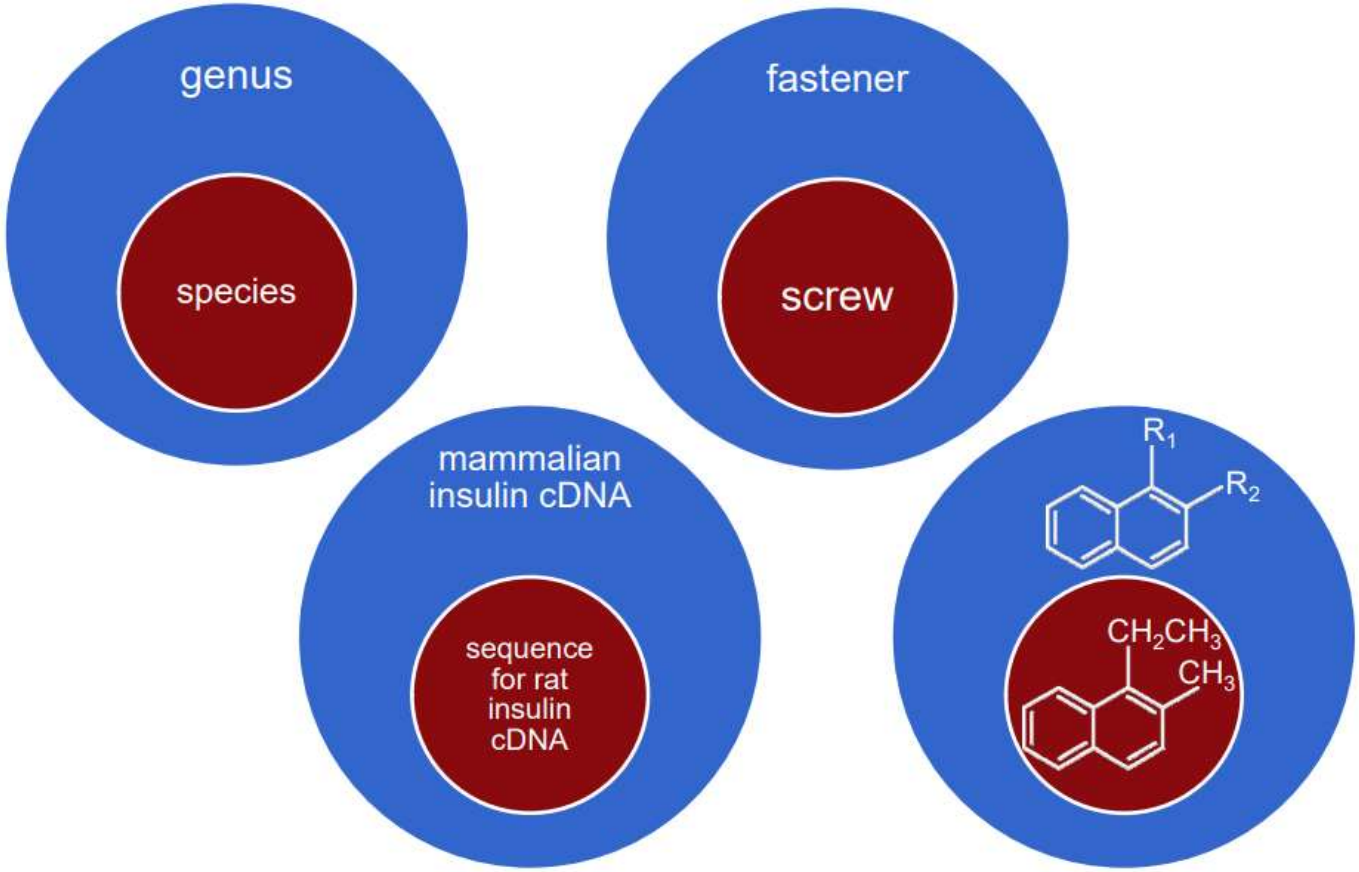
Enablement

35 U.S.C. § 112(a)

§ 112. Specification

(a) IN GENERAL.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

Genus Claims



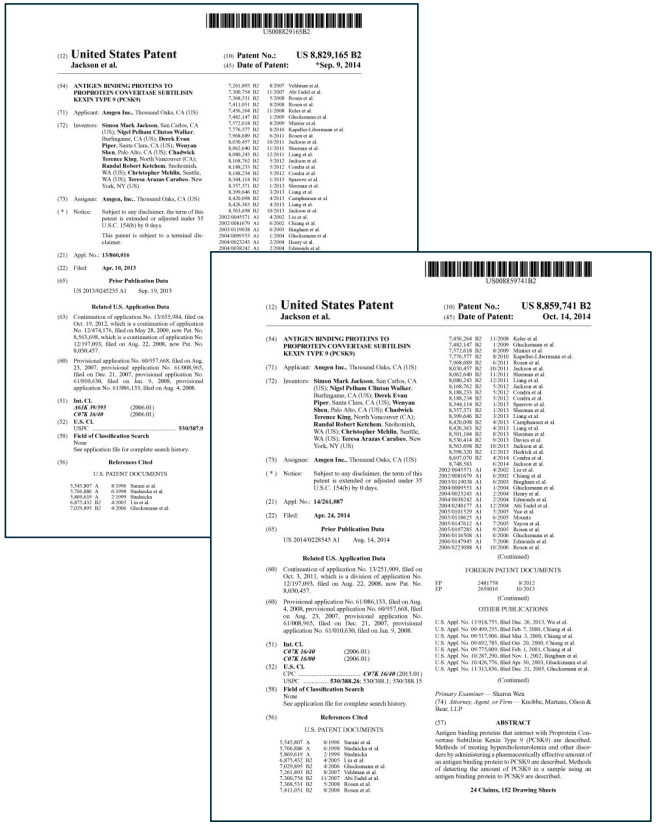
Genus Claims and Enablement

- **Genus sufficiently enabled if a skilled artisan would be able to practice the full scope of the claimed invention without 'undue experimentation.'" *In re Wands*, 858 F.2d 731, 736–37 (Fed. Cir. 1988).**
- **The Wands Factors:**
  - (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.
- **Although a specification does not need to "describe how to make and use every possible variant of the claimed invention, when a range is claimed, there must be reasonable enablement of the scope of the range." *McRO, Inc. v. Bandai Namco Games Am. Inc.*, 959 F.3d 1091, 1100 (Fed. Cir. 2020).**

Amgen v. Sanofi (Fed. Cir. 2021)

- Amgen's patents describe antibodies that purportedly bind to the PCSK9 protein and lower LDL levels.
- Common patent specification disclosed amino acid sequences for twenty-six antibodies, and included three dimensional structures of two antibodies (including Amgen's Repatha).
- Sanofi contended that there are millions of antibody candidates within the scope of the claims, antibody generation is unpredictable, and practicing the full scope of the claims requires substantial trial and error.

Amgen v. Sanofi (Fed. Cir. 2021)



US008829165B2

(12) **United States Patent**
Jackson et al.

(10) **Patent No.: US 8,829,165 B2**
(45) **Date of Patent: *Sep. 9, 2014**

(54) **ANTIGEN BINDING PROTEINS TO PROPROTEIN CONVERTASE SUBTILISIN KEXIN TYPE 9 (PCSK9)**

(71) Applicant: **Amgen Inc.**, Thousand Oaks, CA (US)

(72) Inventors: **Simon Mark Jackson**, San Carlos, CA (US); **Nigel Pelham Clinton Walker**, Burlingame, CA (US); **Derek Evan Piper**, Santa Clara, CA (US); **Wenyan Shen**, Palo Alto, CA (US); **Chadwick Terence King**, North Vancouver (CA); **Randal Robert Ketchem**, Snohomish, WA (US); **Christopher Mehlin**, Seattle, WA (US); **Teresa Arazas Carabeo**, New York, NY (US)

(73) Assignee: **Amgen, Inc.**, Thousand Oaks, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **13/860,016**

(22) Filed: **Apr. 10, 2013**

(65) **Prior Publication Data**

US 2013/0245235 A1 Sep. 19, 2013

Related U.S. Application Data

(63) Continuation of application No. 13/055,984, filed on Oct. 19, 2012, which is a continuation of application No. 12/476,176, filed on May 28, 2009, now Pat. No. 8,563,698, which is a continuation of application No. 12/197,895, filed on Aug. 22, 2008, now Pat. No. 8,030,457.

(60) Provisional application No. 60/957,668, filed on Aug. 23, 2007, provisional application No. 61/008,965, filed on Dec. 21, 2007, provisional application No. 61/010,630, filed on Jan. 9, 2008, provisional application No. 61/086,133, filed on Aug. 4, 2008.

(51) **Int. Cl.**
A61K 39/395 (2006.01)
C07K 16/40 (2006.01)

(52) **U.S. Cl.**
USPC **530/387.9**

(58) **Field of Classification Search**
None
See application file for complete search history.

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8,188,234	B2	5/2012	Cosdia et al.
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EP	2650016	10/2013

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U.S. Appl. No. 09/498,235, filed Feb. 7, 2000, Chiang et al.
U.S. Appl. No. 09/517,906, filed Mar. 3, 2000, Chiang et al.
U.S. Appl. No. 09/802,785, filed Dec. 20, 2001, Chiang et al.
U.S. Appl. No. 09/775,009, filed Feb. 1, 2001, Chiang et al.
U.S. Appl. No. 10/287,290, filed Nov. 1, 2002, Bingham et al.
U.S. Appl. No. 10/426,776, filed Apr. 30, 2003, Gluckmann et al.
U.S. Appl. No. 11/133,836, filed Dec. 21, 2005, Gluckmann et al.

(Continued)

Primary Examiner — Sharon Wen
(74) *Attorney, Agent, or Firm* — Knobbe, Martens, Olson & Bear, LLP

(57) **ABSTRACT**

Antigen binding proteins that interact with Proprotein Convertase Subtilisin Kexin Type 9 (PCSK9) are described. Methods of treating hypercholesterolemia and other disorders by administering a pharmaceutically effective amount of an antigen binding protein to PCSK9 are described. Methods of detecting the amount of PCSK9 in a sample using an antigen binding protein to PCSK9 are described.

24 Claims, 152 Drawing Sheets

US008859741B2

(12) **United States Patent**
Jackson et al.

(10) **Patent No.: US 8,859,741 B2**
(45) **Date of Patent: Oct. 14, 2014**

(54) **ANTIGEN BINDING PROTEINS TO PROPROTEIN CONVERTASE SUBTILISIN KEXIN TYPE 9 (PCSK9)**

(71) Applicant: **Amgen Inc.**, Thousand Oaks, CA (US)

(72) Inventors: **Simon Mark Jackson**, San Carlos, CA (US); **Nigel Pelham Clinton Walker**, Burlingame, CA (US); **Derek Evan Piper**, Santa Clara, CA (US); **Wenyan Shen**, Palo Alto, CA (US); **Chadwick Terence King**, North Vancouver (CA); **Randal Robert Ketchem**, Snohomish, WA (US); **Christopher Mehlin**, Seattle, WA (US); **Teresa Arazas Carabeo**, New York, NY (US)

(73) Assignee: **Amgen Inc.**, Thousand Oaks, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **14/261,087**

(22) Filed: **Apr. 24, 2014**

(65) **Prior Publication Data**

US 2014/0228545 A1 Aug. 14, 2014

Related U.S. Application Data

(60) Continuation of application No. 13/251,909, filed on Oct. 3, 2011, which is a division of application No. 12/197,895, filed on Aug. 22, 2008, now Pat. No. 8,030,457.

(60) Provisional application No. 61/086,133, filed on Aug. 4, 2008, provisional application No. 60/957,668, filed on Aug. 23, 2007, provisional application No. 61/008,965, filed on Dec. 21, 2007, provisional application No. 61/010,630, filed on Jan. 9, 2008.

(51) **Int. Cl.**
C07K 16/40 (2006.01)
C07K 16/00 (2006.01)

(52) **U.S. Cl.**
CPC ***C07K 16/40*** (2013.01)
USPC **530/388.22**; 530/388.1; 530/388.15

(58) **Field of Classification Search**
None
See application file for complete search history.

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Primary Examiner — Sharon Wen
(74) *Attorney, Agent, or Firm* — Knobbe, Martens, Olson & Bear, LLP

(57) **ABSTRACT**

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24 Claims, 152 Drawing Sheets

’165 Patent Claims:

1. An isolated monoclonal antibody, wherein, when bound to PCSK9, the monoclonal antibody binds to at least one of the following residues: S153, I154, P155, R194, D238, A239, 1369, S372, D374, C375, T377, C378, F379, V380, or S381 of SEQ ID NO:3, and wherein the monoclonal antibody blocks binding of PCSK9 to LDLR.

19. The isolated monoclonal antibody of claim 1 wherein the isolated monoclonal antibody binds to at least two of the following residues S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of PCSK9 listed in SEQ ID NO:3.

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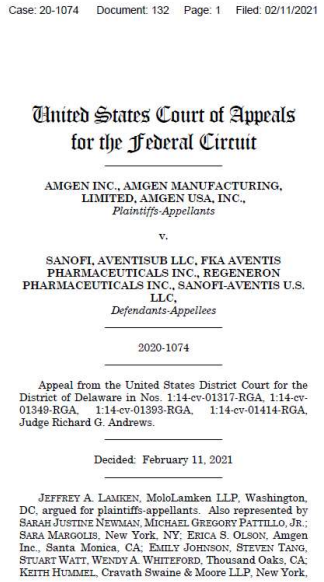
Amgen v. Sanofi (Fed. Cir. 2021)



Case: 20-1074 Document: 132 Page: 1 Filed: 02/11/2021

United States Court of Appeals
for the Federal Circuit

AMGEN INC., AMGEN MANUFACTURING, LIMITED, AMGEN USA, INC.,
Plaintiffs-Appellants

v.

SANOFI, AVENTISUB LLC, FKA AVENTIS PHARMACEUTICALS INC., REGENERON PHARMACEUTICALS INC., SANOFI-AVENTIS U.S. LLC,
Defendants-Appellees

2020-1074

Appeal from the United States District Court for the District of Delaware in Nos. 1:14-cv-01317-RGA, 1:14-cv-01349-RGA, 1:14-cv-01393-RGA, 1:14-cv-01414-RGA, Judge Richard G. Andrews.

Decided: February 11, 2021

JEFFREY A. LAMKEN, MoloLamken LLP, Washington, DC, argued for plaintiffs-appellants. Also represented by SARAH JUSTINE NEWMAN, MICHAEL GREGORY PATTILLO, JR.; SARA MARGOLIS, New York, NY; ERICA S. OLSON, Amgen Inc., Santa Monica, CA; EMILY JOHNSON, STEVEN TANG, STUART WATT, WENDY A. WHITEFORD, Thousand Oaks, CA; KEITH HUMMEL, Cravath Swaine & Moore LLP, New York,

- **Held: claim invalid for lack of enablement**
  - Claims broad both in number and in functional diversity
  - Unpredictable field of science with respect to satisfying functional limitations
  - Evidence only that a small subset of examples of antibodies can be predictably generated

- **"What emerges from our case law is that the enablement inquiry for claims that include functional requirements can be particularly focused on the breadth of those requirements, especially where predictability and guidance fall short. In particular, it is important to consider the quantity of experimentation that would be required to make and use, not only the limited number of embodiments that the patent discloses, but also the full scope of the claim."**

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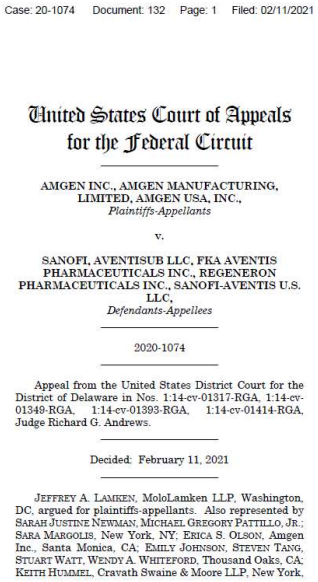
Amgen v. Sanofi (Fed. Cir. 2021)



Case: 20-1074 Document: 132 Page: 1 Filed: 02/11/2021

United States Court of Appeals
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AMGEN INC., AMGEN MANUFACTURING, LIMITED, AMGEN USA, INC.,
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SANOFI, AVENTISUB LLC, FKA AVENTIS PHARMACEUTICALS INC., REGENERON PHARMACEUTICALS INC., SANOFI-AVENTIS U.S. LLC,
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2020-1074

Appeal from the United States District Court for the District of Delaware in Nos. 1:14-cv-01317-RGA, 1:14-cv-01349-RGA, 1:14-cv-01393-RGA, 1:14-cv-01414-RGA, Judge Richard G. Andrews.

Decided: February 11, 2021

JEFFREY A. LAMKEN, MoloLamken LLP, Washington, DC, argued for plaintiffs-appellants. Also represented by SARAH JUSTINE NEWMAN, MICHAEL GREGORY PATTILLO, JR.; SARA MARGOLIS, New York, NY; ERICA S. OLSON, Amgen Inc., Santa Monica, CA; EMILY JOHNSON, STEVEN TANG, STUART WATT, WENDY A. WHITEFORD, Thousand Oaks, CA; KEITH HUMMEL, Cravath Swaine & Moore LLP, New York,

- **The Court noted that "[e]ach appealed claim in this case is a composition claim defined, not by structure, but by meeting functional limitations."**
  - Amgen's expert admitted that translating an antibody sequence into a 3D structure was not possible.
  - Amgen's expert conceded that testing would be required to ensure that amino acid substitutions did not alter antibody function.
- **"As the district court noted, the only ways for a person of ordinary skill to discover undisclosed claimed embodiments would be through either 'trial and error, by making changes to the disclosed antibodies and then screening those antibodies for the desired binding and blocking properties,' or else 'by discovering the antibodies De novo' according to a randomization-and-screening 'roadmap.' Either way, we agree with the district court that the required experimentation 'would take a substantial amount of time and effort.'"**
- **Enablement can be a high hurdle for broad, functionally defined genus claims.**
  - "We do not hold that the effort required to exhaust a genus is dispositive. It is appropriate, however, to look at the amount of effort needed to obtain embodiments outside the scope of the disclosed examples and guidance."
  - "While functional claim limitations are not necessarily precluded in claims that meet the enablement requirement, such limitations pose high hurdles in fulfilling the enablement requirement for claims with broad functional language."

Written Description

35 U.S.C. § 112(a)

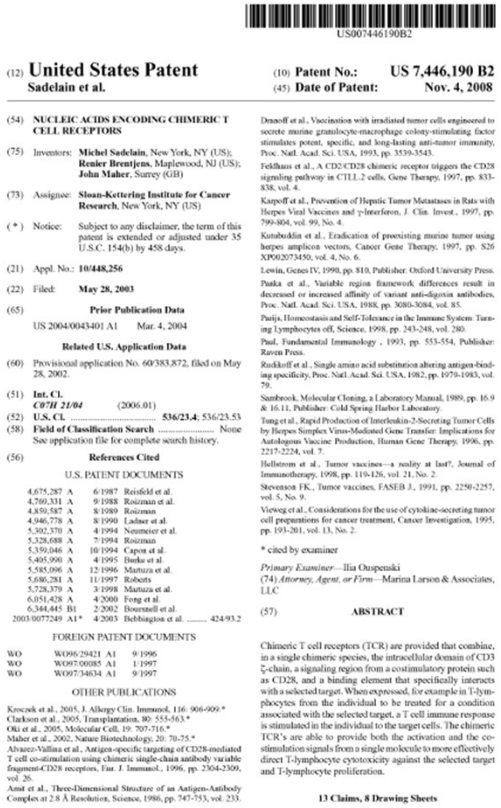
§ 112. Specification

(a) IN GENERAL.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

The test for adequate written description "is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date."

Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc)

Biogen v. Mylan (Fed. Cir. 2021)



US007446190B2

(12) **United States Patent**
Sadelain et al.

(10) **Patent No.: US 7,446,190 B2**
(45) **Date of Patent: Nov. 4, 2008**

(54) **NUCLEIC ACIDS ENCODING CHIMERIC T CELL RECEPTORS**

(75) Inventors: **Michel Sadelain**, New York, NY (US); **Renier Brentjens**, Maplewood, NJ (US); **John Maher**, Surrey (GB)

(73) Assignee: **Sloan-Kettering Institute for Cancer Research**, New York, NY (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 458 days.

(21) Appl. No.: **10/448,256**

(22) Filed: **May 28, 2003**

(65) **Prior Publication Data**

US 2004/0043401 A1 Mar. 4, 2004

Related U.S. Application Data

(60) Provisional application No. 60/383,872, filed on May 28, 2002.

(51) **Int. Cl.**
C07H 21/04 (2006.01)

(52) **U.S. Cl.** **536/23.4**; 536/23.53

(58) **Field of Classification Search** ..... None
See application file for complete search history.

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Primary Examiner—Ilia Ouspenski
(74) *Attorney, Agent, or Firm*—Marina Larson & Associates, LLC

(57) **ABSTRACT**

Chimeric T cell receptors (TCR) are provided that combine, in a single chimeric species, the intracellular domain of CD3 ζ-chain, a signaling region from a costimulatory protein such as CD28, and a binding element that specifically interacts with a selected target. When expressed, for example in T-lymphocytes from the individual to be treated for a condition associated with the selected target, a T cell immune response is stimulated in the individual to the target cells. The chimeric TCR's are able to provide both the activation and the co-stimulation signals from a single molecule to more effectively direct T-lymphocyte cytotoxicity against the selected target and T-lymphocyte proliferation.

13 Claims, 8 Drawing Sheets

1. A method of treating a subject in need of treatment for multiple sclerosis comprising orally administering to the subject in need thereof a pharmaceutical composition consisting essentially of

(a) a therapeutically effective amount of dimethyl fumarate, monomethyl fumarate, or a combination thereof, and

(b) one or more pharmaceutically acceptable excipients, wherein the therapeutically effective amount of dimethyl fumarate, monomethyl fumarate, or a combination thereof is about 480 mg per day.

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Biogen v. Mylan (Fed. Cir. 2021)

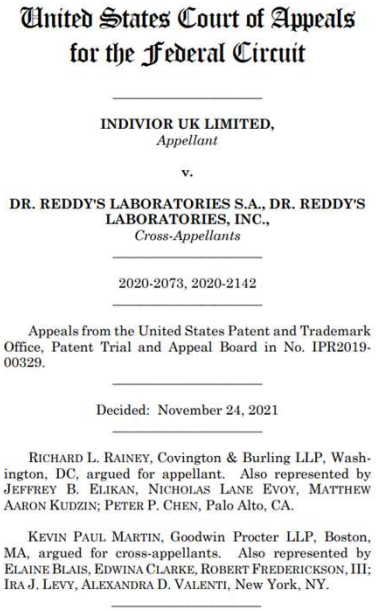
Court assumed disclosure of connection between treatment of MS and DMF

"Thus, assuming that a skilled artisan would understand the disclosure to be unambiguously focused on MS despite its inclusion among approximately three-dozen neurological disorders—a determination we need not reach in this case—the specification may arguably provide adequate information to convey to a skilled artisan that the invention supports method-of-treatment claims directed to MS and, perhaps, that the use of DMF may be therapeutically linked to MS treatment"

Court focused on the fact the 480 mg/day was mentioned only once

"[T]he district court did not clearly err in finding that a skilled artisan would not have recognized, based on the single passing reference to a DMF480 dose in the disclosure, that DMF480 would have been efficacious in the treatment of MS, particularly because the specification's only reference to DMF480 was part of a wide DMF-dosage range and not listed as an independent therapeutically efficacious dose."

Indivior v. Dr. Reddy's (Fed. Cir. 2021)



United States Court of Appeals
for the Federal Circuit

INDIVIOR UK LIMITED,
Appellant

v.

DR. REDDY'S LABORATORIES S.A., DR. REDDY'S LABORATORIES, INC.,
Cross-Appellants

2020-2073, 2020-2142

Appeals from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. IPR2019-00329.

Decided: November 24, 2021

RICHARD L. RAINEY, Covington & Burling LLP, Washington, DC, argued for appellant. Also represented by JEFFREY B. ELIKAN, NICHOLAS LANE EVOY, MATTHEW AARON KUDZIN; PETER P. CHEN, Palo Alto, CA.

KEVIN PAUL MARTIN, Goodwin Procter LLP, Boston, MA, argued for cross-appellants. Also represented by ELAINE BLAIS, EDWINA CLARKE, ROBERT FREDERICKSON, III; IRA J. LEVY, ALEXANDRA D. VALENTI, New York, NY.

Court considered WD support for a weight percent range of an ingredient in a drug containing film

There was a string of continuations, and because there was intervening anticipating reference, the issue was whether the first priority application provided WD support for the specified range

". . . a) about 40 wt % to about 60 wt % of a water soluble polymeric matrix . . ."

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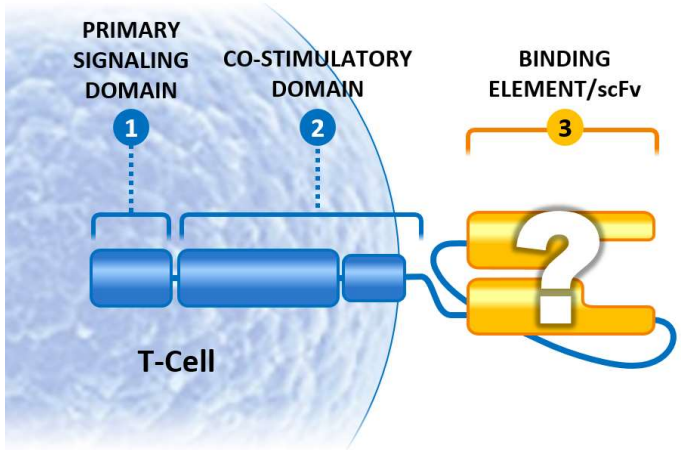
Indivior v. Dr. Reddy's (Fed. Cir. 2021)

- **What was not disclosed**
  - 40 wt % to 60 wt % was not mentioned, nor was 40% or 60%
- **What was disclosed**
  - In the examples, with some calculation, you could identify films where the amount of polymer was within the range, but the court said this is not a disclose of the range itself
  - For a different claim, there were examples at both ends of the claimed range (if you did some summing of percentages) but this is not a disclosure of the claimed range
- **What was not helpful**
  - Court noted that the variety of values disclosed and the statement that "[t]he film may contain any desired level of . . . polymer" contributed to the lack of clear support.
- **What did we learn**
  - "[W]ritten description cases are intensively fact oriented, and the cases vary, just as ranges vary"

Juno Therapeutics v. Kite Pharma (Fed. Cir. 2021)

YESCARTA



- Involved Kite's CAR-T therapy Yescarta®, indicated for treatment of certain blood cancers
- Juno inventors claimed to have invented a CAR with three explicit portions: (1) a primary signaling domain, (2) a costimulatory signaling domain, and (3) a binding element
- Claims specified the amino acid sequence for the two signaling portions
- But identified the binding element generically by its function: binding to a particular antigen, called CD19
- Specification had only one, vaguely disclosed example of a CAR that binds to CD19 and no amino acid sequence was provided for that example

Juno Therapeutics v. Kite Pharma (Fed. Cir. 2021)

US007446190B2

(12) **United States Patent**
Sadelain et al.

(10) **Patent No.: US 7,446,190 B2**
(45) **Date of Patent: Nov. 4, 2008**

(54) **NUCLEIC ACIDS ENCODING CHIMERIC T CELL RECEPTORS**

(75) Inventors: **Michel Sadelain**, New York, NY (US); **Renier Brentjens**, Maplewood, NJ (US); **John Maher**, Surrey (GB)

(73) Assignee: **Sloan-Kettering Institute for Cancer Research**, New York, NY (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 458 days.

(21) Appl. No.: **10/448,256**

(22) Filed: **May 28, 2003**

(65) **Prior Publication Data**

US 2004/0043401 A1 Mar. 4, 2004

Related U.S. Application Data

(60) Provisional application No. 60/383,872, filed on May 28, 2002.

(51) **Int. Cl.**
C07H 21/04 (2006.01)

(52) **U.S. Cl.** **536/23.4**; 536/23.53

(58) **Field of Classification Search** ..... None
See application file for complete search history.

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Vieweg et al., Considerations for the use of cytokine-secreting tumor cell preparations for cancer treatment, Cancer Investigation, 1995, pp. 193-201, vol. 13, No. 2.

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Primary Examiner—Ilia Ouspenski
(74) *Attorney, Agent, or Firm*—Marina Larson & Associates, LLC

(57) **ABSTRACT**

Chimeric T cell receptors (TCR) are provided that combine, in a single chimeric species, the intracellular domain of CD3 ζ-chain, a signaling region from a costimulatory protein such as CD28, and a binding element that specifically interacts with a selected target. When expressed, for example in T-lymphocytes from the individual to be treated for a condition associated with the selected target, a T cell immune response is stimulated in the individual to the target cells. The chimeric TCR's are able to provide both the activation and the co-stimulation signals from a single molecule to more effectively direct T-lymphocyte cytotoxicity against the selected target and T-lymphocyte proliferation.

13 Claims, 8 Drawing Sheets

1. A nucleic acid polymer encoding a chimeric T cell receptor, said chimeric T cell receptor comprising

(a) a zeta chain portion comprising the intracellular domain of human CD3ζ chain,

(b) a costimulatory signaling region, and

(c) a binding element that specifically interacts with a selected target,

wherein the costimulatory signaling region comprises the amino acid sequence encoded by SEQ ID NO:6.

2. The nucleic acid polymer of claim 1, wherein the binding element is an antibody.

3. The nucleic acid polymer of claim 2, wherein the antibody is a single chain antibody.

5. The nucleic acid polymer of claim 3, wherein the single chain antibody binds to CD19.

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Juno Therapeutics v. Kite Pharma (Fed. Cir. 2021)

- **Kite arguments on appeal**
  - Claims cover an enormous number (millions of billions) of scFv candidates
  - Only a fraction of which satisfy the functional binding limitation for any given target
  - Field is unpredictable since an scFv's binding ability depends on a variety of factors
  - The '190 patent discloses neither (1) representative number species or (2) common structural features of the claimed scFv genus adequate to identify which scFvs would function as claimed

- **Juno arguments on appeal**
  - scFvs and how to make them were well-known
  - The '190 patent describes two working scFv embodiments that are representative of all scFvs
  - scFvs had been incorporated in CARs well before the '190 patent's priority date
  - scFvs are interchangeable and have common structural features
  - *Ariad* was irrelevant because the real invention was the combination of the signaling domains, not the scFv portion

Juno Therapeutics v. Kite Pharma (Fed. Cir. 2021)

United States Court of Appeals
for the Federal Circuit

JUNO THERAPEUTICS, INC., SLOAN KETTERING INSTITUTE FOR CANCER RESEARCH,
Plaintiffs-Appellees

v.

KITE PHARMA, INC.,
Defendant-Appellant

2020-1758

Appeal from the United States District Court for the Central District of California in No. 2:17-cv-07639-PSG-KS, Judge Philip S. Gutierrez.

Decided: August 26, 2021

MORGAN CHU, Irell & Manella LLP, Los Angeles, CA, argued for plaintiffs-appellees. Also represented by ALAN J. HEINRICH, ELIZABETH C. TUAN; GREGORY A. CASTANIAS, JENNIFER L. SWIZE, Jones Day, Washington, DC; LISA LYNN FURBY, Chicago, IL; ANDREA WEISS JEFFRIES, Los Angeles, CA; MATTHEW J. RUBENSTEIN, Minneapolis, MN.

E. JOSHUA ROSENKRANZ, Orrick, Herrington & Sutcliffe LLP, New York, NY, argued for defendant-appellant. Also represented by MELANIE L. BOSTWICK, ROBBIE MANHAS, JEREMY PETERMAN, Washington, DC; GEOFFREY DONOVAN

While it is true that scFvs in general were known, and even known to bind, the record demonstrates that, for even the narrowest claims at issue, the realm of possible CD19-specific scFvs was vast and the number of known CD19-specific scFvs was small (five at most). The '190 patent, however, provides no details about which scFvs bind to CD19 in a way that distinguishes them from scFvs that do not bind to CD19. Without this guidance, under our controlling *Ariad* decision, no reasonable jury could find the '190 patent satisfies the written description requirement.

CONCLUSION

Substantial evidence does not support the jury's verdict in Juno's favor on the issue of written description. For the claimed functional scFv genus, the '190 patent does not disclose representative species or common structural features to allow a person of ordinary skill in the art to distinguish between scFvs that achieve the claimed function and those that do not. Accordingly, we reverse.

REVERSED

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Safe Harbor and Research Tools

Safe Harbor – 35 U.S.C. § 271(e)(1)

It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a **patented invention** (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques) solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

Two Unintended Distortions – *Eli Lilly v. Medtronic*

[T]he 1984 Act was designed to respond to two unintended distortions of the 17–year patent term produced by the requirement that certain products must receive premarket regulatory approval. First, the holder of a patent relating to such products would as a practical matter not be able to reap any financial rewards during the early years of the term. When an inventor makes a potentially useful discovery, he ordinarily protects it by applying for a patent at once. Thus, if the discovery relates to a product that cannot be marketed without substantial testing and regulatory approval, the "clock" on his patent term will be running even though he is not yet able to derive any profit from the invention.

Eli Lilly and Co. v. Medtronic, Inc., 496 U.S. 661, 669-70 (1990).

Two Unintended Distortions – *Eli Lilly v. Medtronic*

The second distortion occurred at the other end of the patent term. In 1984, the Court of Appeals for the Federal Circuit decided that the manufacture, use, or sale of a patented invention during the term of the patent constituted an act of infringement, see § 271(a), even if it was for the sole purpose of conducting tests and developing information necessary to apply for regulatory approval. *See Roche Products, Inc. v. Bolar Pharmaceutical Co.,* 733 F.2d 858, cert. denied, 469 U.S. 856, 105 S.Ct. 183, 83 L.Ed.2d 117 (1984). Since that activity could not be commenced by those who planned to compete with the patentee until expiration of the entire patent term, the patentee's *de facto* monopoly would continue for an often substantial period until regulatory approval was obtained. In other words, the combined effect of the patent law and the premarket regulatory approval requirement was to create an effective extension of the patent term.

Safe Harbor Scope

- In *Merck KGaA v. Integra Life Sciences,* 545 U.S.193, 206 (2005), the Supreme Court stated:
  - "[T]he statutory text [of § 271(e)(1)] makes clear that it provides a **wide berth** for the use of patented drugs in activities related to [FDA] approval." *Id*. at 202 (emphasis added)
  - ""[W]e think it apparent from the statutory text that § 271(e)(1)'s exemption from infringement extends to **all** uses of patented inventions that are **reasonably related** to the development and submission of any information to the [FDA]. This necessarily includes preclinical studies of patented compounds that are appropriate for submission to the FDA in the regulatory process." *Id*. (emphasis added)
  - "[The exemption] necessarily includes **preclinical** studies of patented compounds that are appropriate for submission to the FDA in the regulatory process." *Id.* (emphasis added).
  - "[T]he FDA requires that applicants include in an IND summaries of the **pharmacological, toxicological, pharmacokinetic, and biological qualities of the drug in animals**. . .The primary (and, in some cases, only) way in which a drug maker may obtain such information is through preclinical *in vitro* and *in vivo* studies." *Id.* at 203 (emphasis added).

What is Covered by The Safe Harbor

- **Applies To . . .**
  - ITC actions
  - Medical devices
  - Manufacture of patented items, most of which were used to generate data for the FDA
  - Submission of data to foreign regulatory agencies, where data are also submitted to the FDA
  - Use of patented product to develop alternative FDA approved manufacturing process
  - Use of FDA generated data to prepare patent applications

- **Does Not Apply To…**
  - Stockpiling — even for launch after patent expiry
  - Manufacturing patented products in the U.S. for shipment to foreign regulatory authorities
  - Use of product for foreign clinical trials where no indication that results would be submitted to the FDA
  - "Basic research"
  - Activity must in some way relate to potential FDA approval of drug (device), supplemental approval, or label modifications
  - Activities to support non U.S. approval are not protected

What about Research Tools?

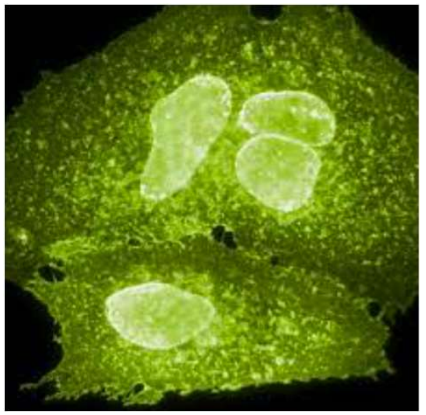
- *Proveris Sci. Corp. v. Innovasystems, Inc.*, 536 F.3d 1256 (Fed. Cir. 2008)
  - Innovasystems asserted Safe Harbor protection for its sales of optical spray machines used in analyzing the final product subject to FDA approval.
  - The Federal Circuit held that, although the devices were only used in developing data for FDA submissions, they were "not itself subject to FDA premarket approval process." *Id.* at 1265.
  - Thus, section 271(e)(1) did not apply.

What about Research Tools?

- *ISIS Pharms., Inc. v. Santaris Pharma A/S Corp., 2012 U.S. Dist. LEXIS 134107 (S.D. Cal. Sept. 18, 2012).*
  - Safe harbor **does not** cover "anti-sense" technology used to identify gene targets or screen targets for activity.
- *PSN Ill., LLC. v. Abbott Labs.,* 2011 U.S. Dist. LEXIS 108055 (N.D. Ill. Sept. 20, 2011).
  - Finds that the safe harbor **does not** apply to receptors used to screen drug candidates.
- *Teva Pharms. USA, Inc. v. Sandoz Inc.,* 2013 U.S. Dist. LEXIS 99121 (S.D.N.Y. July 16, 2013).
  - Finds that safe harbor **does** apply to polypeptide markers and methods of using them to analyze whether an active ingredient has particular molecular weight characteristics

Allele Biotechnology & Pharms., Inc. v. Pfizer, Inc., 2021 WL 1749903 (S.D. Cal. May 4, 2021)

- Allele sued Pfizer for infringement of its U.S. Patent No. 10,221,221 (“the ’221 patent”)
- Allele alleged Pfizer’s use of Allele’s mNeon Green product, in its research, development and testing of its SARS-COV-2 vaccine candidates, infringed the ‘221 patent
- Pfizer moved to dismiss complaint under Fed. R. Civ. P. 12(b)(6) arguing that it’s use was covered by The Safe Harbor
- Allele argued that mNeon Green – a research tool – was not a “patented invention” under section 271(e)(1).
- Pfizer responded that the Safe Harbor applied because the use was for developing information for FDA approval of its COVID-19 vaccine



Allele Court – No Safe Harbor for Research Tool

- **Court denied Pfizer's Motion to Dismiss, relying on *Proveris***
  - **Reason 1**: Allele's mNeon Green product was not subject to FDA premarket approval and thus was "not within the category of entities for whom the safe harbor provision was designed to provide relief." *See* 2021 WL 1749903, *4.
  - **Reason 2:** Because Allele's mNeon Green product was not subject to FDA premarket approval, it could not be extended under 35 U.S.C § 156(a), meaning it was not a "**patented invention**" within Section 271(e)(1). *See* 2021 WL 1749903, *4.

Safe Harbor Was a Hot Issue in 2021

- *UCB, Inc. v. Catalent Pharma Sols., Inc.*, 2021 U.S. Dist. LEXIS 90623 (E.D. Ky. May 12, 2021).
  - The patent in question covered a chemical compound that was an active pharmaceutical ingredient in the plaintiff's FDA-approved drug product. The Court found that the safe harbor applied to immunize the defendant from infringement.

- *Regenxbio, Inc. v. Sarepta Therapeutics, Inc.*, C.A. No. 20-1226-RGA (D. Del. Jan. 4, 2022).
  - The patent in question covered "cultured host cell containing a recombinant nucleic acid molecule encoding the capsid protein." The Court found that the cultured host cell was not subject to FDA approval, and therefore, the Defendants' use of it was not protected by the safe harbor.

Inducement – *GSK v. Teva*

Law for Induced Infringement

“Whoever actively induces infringement of a patent shall be liable as an infringer." 35 U.S.C. § 271(b).

"[I]nducement requires that the alleged infringer knowingly induced infringement and possessed specific intent to encourage another’s infringement.” *DSU Med. Corp. v. JMS Co.,* 471 F.3d 1293, 1306 (Fed. Cir. 2006) (en banc in relevant part) (citation omitted) (internal quotation marks omitted).

“Section viii” Carve Out – 505(j)(2)(A)(viii)

- **Permits a generic to “carve out” from the generic label indications included on the brand label**
- **Generic not seeking approval for carved out indications**
  - Generic product must still be safe and effective for remaining approved uses
- **ANDA with carved out label can be approved absent an unresolved PIV certification on another patent (e.g., a compound patent)**

Early Federal Circuit Decisions on Section viii Carve Outs

- **Two leading cases from 2003**
  - *Warner-Lambert v. Apotex* (2003)
  - *Allergan v Alcon* (2003)
- **Both cases were:**
  - Brought under 35 U.S.C. § 271(e) pre-launch
  - Both cases are for claims of induced infringement for off-label uses
- **Holdings**
  - Recognizes § 271(e) involves a hypothetical act of infringement: forced to analyze what will likely happen based on ANDA as opposed to analyzing direct evidence
  - Concludes cannot bring a claim for inducement for an off-label use
  - **Leaves open whether a claim for inducement can be brought post-launch**

Coreg® (carvedilol)

- **Three approved uses**
  - (#1) Heart Failure
  - (#2) Left ventricular dysfunction in patients post infarction (MI/LVD)
  - (#3) Hypertension
- **Hypertension patent expired with compound patent**
- **GSK only ever marketed for heart failure**
- **GSK obtained the ’000 re-issue patent, which covered heart failure, but only after generics had launched**

Teva's Carvedilol

- **Originally, pursued full-label, but launched as "skinny" label**
  - Sought indications for left ventricular dysfunction and hypertension
  - Attempted a section viii carve out for heart failure
- **After a few years, Teva put heart failure back on label**
- **Advertised that it was A-B rated for all uses**

GSK v Teva – District Court

- **Jury finds infringement for both skinny and full label periods**
  - Presented with evidence of full label, catalogs, websites and press releases as evidence of inducement
  - Found that Teva induced infringement
  - Awarded damages of $235 million

- **District Court grants Judgement as a Matter of Law (JMOL) centered on causation**
  - GSK had not shown "that any doctor was ever induced to infringe the patent by Teva's label (either skinny or full)"
  - Teva, on the other hand, had shown that other factors caused physicians to prescribe its generic for heart failure ("A reasonable factfinder could only have found that these alternative, non-Teva factors were what caused the doctors to prescribe generic carvedilol for an infringing use.")
    - Court found that other information available to prescribing physicians, including information provided by GSK, caused infringement

2020 Federal Circuit Decision

- **Majority:**
  - Jury verdict of infringement (and damages) re-instated
  - Labels, press releases, catalogs and other conduct indicated inducement
  - Attempt to shift blame to GSK not supported under the law of inducement

- **"Precedent makes clear that when the provider of an identical product knows of and markets the same product for intended direct infringing activity, the criteria of induced infringement are met."**

- **Strong dissent from Chief Judge Prost**
  - "Congress provided for skinny labels for exactly these circumstances, see 21 U.S.C. § 355(j)(2)(A)(viii), such that the lone method covered in the '000 patent would not foreclose access to more affordable carvedilol. And Teva acted exactly as Congress intended. Teva waited until GSK's patent covering the carvedilol compound expired to launch its product covering two unpatented indications—hypertension and post-MI LVD. So, when GSK's '000 reissue patent later issued—reciting a narrow method of treating a third indication, CHF—Teva's skinny label did not even suggest using its product according to the patented method."

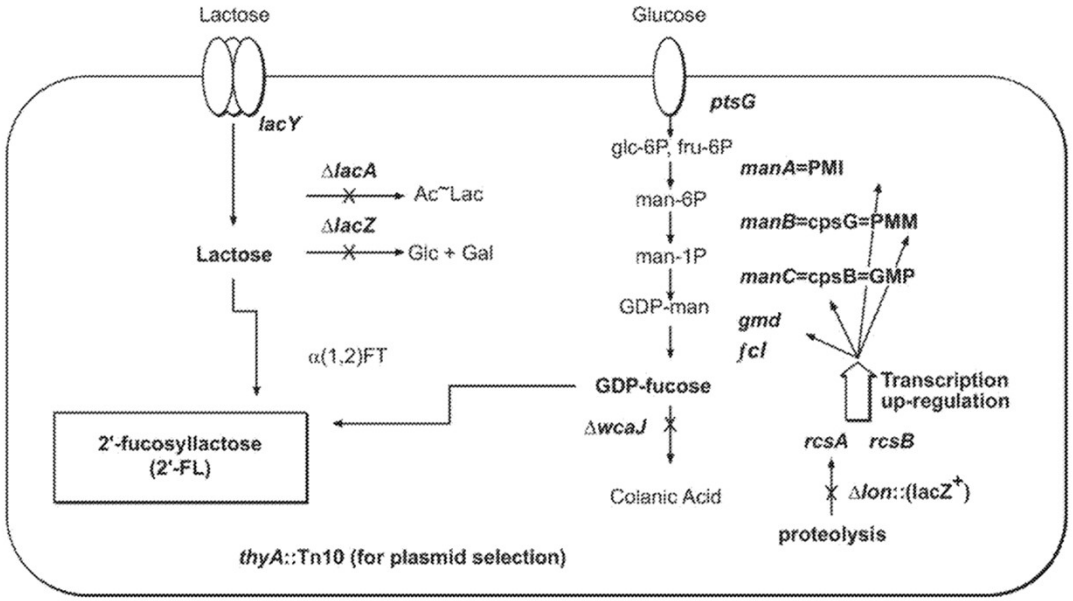
2021 Federal Circuit Decision

- **August 2021 decision focuses on Teva's failure to successfully carve out congestive heart failure**
  - "As this record reflects, in both time periods, substantial evidence supports that Teva actively induced by marketing a drug with a label encouraging a patented therapeutic use. They did not 'omit[] all patented indications' or 'merely note[] (without mentioning any infringing uses) that FDA had rated a product as therapeutically equivalent to a brand-name drug.'"
  - "This is a case in which substantial evidence supports a jury finding that the patented use was on the generic label at all relevant times and that, therefore, Teva failed to carve out all patented indications."
  - Causation can be inferred: "It was fair for the jury to infer that when Teva distributed and marketed a product with labels encouraging an infringing use, it actually induced doctors to infringe."

- **Another strong dissent from Chief Judge Prost**
  - "The evidence of inducement—i.e., that Teva had culpable intent to encourage infringement and that its skinny label or press releases caused doctors' prescribing practices—was thin to nonexistent. But a jury found Teva liable all the same. This sometimes happens. And when it does, there is a remedy: a court will reverse a jury's verdict if there is insufficient evidence to support it. The experienced trial judge sensibly did just that."

Doctrine of Equivalents - Jennewein Biotech GMBH v. ITC

Jennewein Biotech GMBH v. ITC



1. A method for producing a fucosylated oligosacharide in a bacterium, comprising providing an isolated E. coli bacterium comprising, … (ii) an **exogenous** functional β-galactosidase gene comprising a detectable level of β-galactosidase activity that is reduced compared to that of a wild-type E. coli bacterium, wherein the level of β-galactosidase activity comprises between 0.05 and 200 units;

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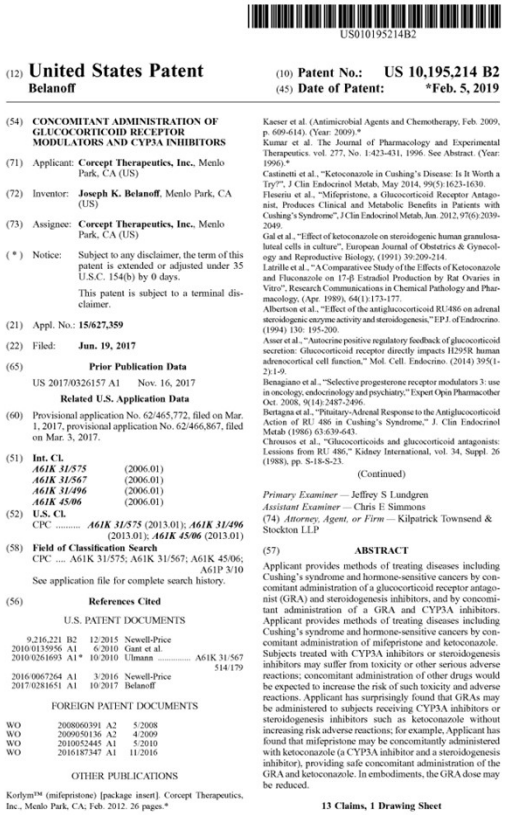
Doctrine of Equivalents - Jennewein Biotech GMBH v. ITC

Teva v. Corcept (Fed. Cir. 2021)



US010195214B2

(12) **United States Patent**
Belanoff

(10) **Patent No.: US 10,195,214 B2**
(45) **Date of Patent: *Feb. 5, 2019**

(54) **CONCOMITANT ADMINISTRATION OF GLUCOCORTICOID RECEPTOR MODULATORS AND CYP3A INHIBITORS**

(71) Applicant: **Corcept Therapeutics, Inc.**, Menlo Park, CA (US)

(72) Inventor: **Joseph K. Belanoff**, Menlo Park, CA (US)

(73) Assignee: **Corcept Therapeutics, Inc.**, Menlo Park, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **15/627,359**

(22) Filed: **Jun. 19, 2017**

(65) **Prior Publication Data**

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Related U.S. Application Data

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(51) **Int. Cl.**
A61K 31/575 (2006.01)
A61K 31/567 (2006.01)
A61K 31/496 (2006.01)
A61K 45/06 (2006.01)

(52) **U.S. Cl.**
CPC ***A61K 31/575*** (2013.01); ***A61K 31/496*** (2013.01); ***A61K 45/06*** (2013.01)

(58) **Field of Classification Search**
CPC A61K 31/575; A61K 31/567; A61K 45/06; A61P 3/10
See application file for complete search history.

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(Continued)

Primary Examiner — Jeffrey S Lundgren
Assistant Examiner — Chris E Simmons
(74) *Attorney, Agent, or Firm* — Kilpatrick Townsend & Stockton LLP

(57) **ABSTRACT**

Applicant provides methods of treating diseases including Cushing's syndrome and hormone-sensitive cancers by concomitant administration of a glucocorticoid receptor antagonist (GRA) and steroidogenesis inhibitors, and by concomitant administration of a GRA and CYP3A inhibitors. Applicant provides methods of treating diseases including Cushing's syndrome and hormone-sensitive cancers by concomitant administration of mifepristone and ketoconazole. Subjects treated with CYP3A inhibitors or steroidogenesis inhibitors may suffer from toxicity or other serious adverse reactions; concomitant administration of other drugs would be expected to increase the risk of such toxicity and adverse reactions. Applicant has surprisingly found that GRAs may be administered to subjects receiving CYP3A inhibitors or steroidogenesis inhibitors such as ketoconazole without increasing risk adverse reactions; for example, Applicant has found that mifepristone may be concomitantly administered with ketoconazole (a CYP3A inhibitor and a steroidogenesis inhibitor), providing safe concomitant administration of the GRA and ketoconazole. In embodiments, the GRA dose may be reduced.

13 Claims, 1 Drawing Sheet

1. A method of treating Cushing's syndrome in a patient who is taking an original once-daily dose of 1200 mg or 900 mg per day of mifepristone, comprising the steps of:

reducing the original once-daily dose to an adjusted once-daily dose of 600 mg mifepristone,

administering the adjusted once-daily dose of 600 mg mifepristone and a strong CYP3A inhibitor to the patient,

wherein said strong CYP3A inhibitor is selected from the group consisting of ketoconazole …

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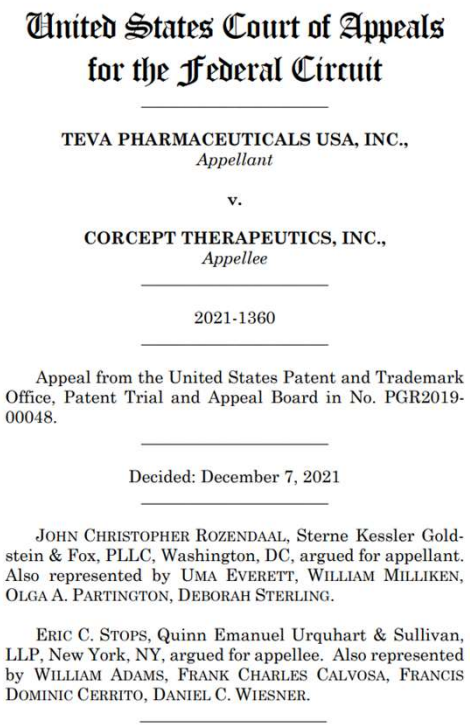


United States Court of Appeals
for the Federal Circuit

TEVA PHARMACEUTICALS USA, INC.,
Appellant

v.

CORCEPT THERAPEUTICS, INC.,
Appellee

2021-1360

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. PGR2019-00048.

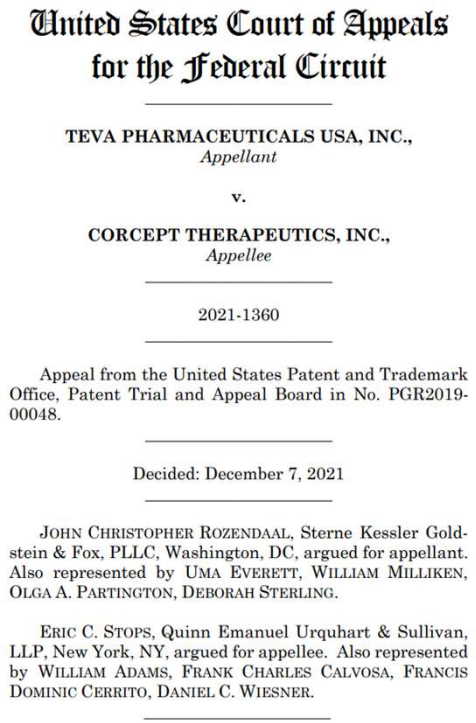
Decided: December 7, 2021

JOHN CHRISTOPHER ROZENDAAL, Sterne Kessler Goldstein & Fox, PLLC, Washington, DC, argued for appellant. Also represented by UMA EVERETT, WILLIAM MILLIKEN, OLGA A. PARTINGTON, DEBORAH STERLING.

ERIC C. STOPS, Quinn Emanuel Urquhart & Sullivan, LLP, New York, NY, argued for appellee. Also represented by WILLIAM ADAMS, FRANK CHARLES CALVOSA, FRANCIS DOMINIC CERRITO, DANIEL C. WIESNER.

- Claims were found to to be non-obvious in an IPR
- Teva argued that that claims were obvious based on the drug label in combination with FDA memorandum requiring the post marketing study
- The drug label said that administration of the drug should be limited to 300 mg/day in the presence of strong CYP3A inhibitors.

Teva v. Corcept (Fed. Cir. 2021)



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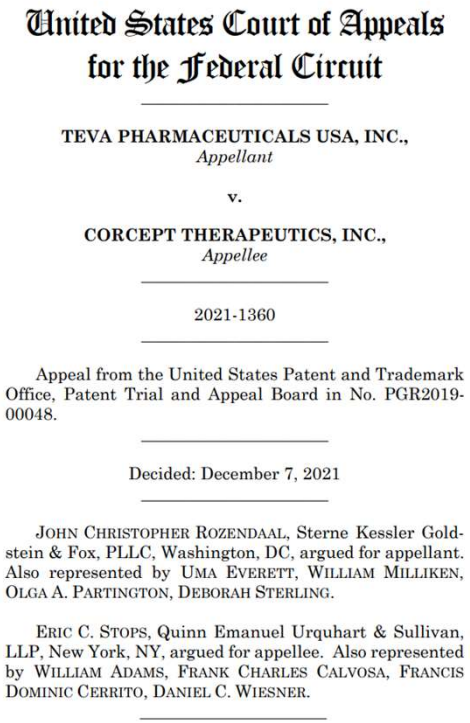
- Board construed the claims to require safe administration of mifepristone
- Board found that one would **not** have a reasonable expectation of success in administering a dose higher than 300 mg in combination with a CY3A inhibitor.
- Did not credit testimony of Teva's expert who said that "it was reasonably likely that 600 mg [per day of mifepristone] would be well tolerated and therapeutically effective when co-administered with a strong CYP3A inhibitor."

Teva v. Corcept (Fed. Cir. 2021)



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- The reasonable-expectation-of-success analysis must be tied to the scope of the claimed invention.
  - The 600 mg dose is what is in the claims
  - The Board found **no** expectation of success above 300 mg
- The claimed dosage was outside any range disclose in the prior art

Thank You!

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