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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

U.S. Patent No. 5,670,373

Issued: September 23, 1997

Inventors: Tadamitsu KISHIMOTO

Applicant: Chugai Seiyaku Kabushiki Kaisha

Product: Actemra® (tocilizumab), humanized anti-human IL-6R monoclonal antibody

APPLICATION FOR PATENT TERM EXTENSION UNDER 35 U.S.C. §156

Mail Stop: Hatch Waxman PTE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir or Madam:

Applicant Chugai Seiyaku Kabushiki Kaisha ("Applicant") hereby applies for patent term extension of U.S. Patent No. 5,670,373 under 35 U.S.C. § 156(d) and 37 C.F.R. § 1.740.

U.S. Patent No. 5,670,373 issued in the named of the sole inventor, Tadamitsu Kishimoto ("Kishimoto"). No assignment has been made or recorded in the U.S. Patent and Trademark Office. Applicant is an agent of the patent owner and is authorized to act on behalf of Kishimoto.

This application is based on the approval by the United States Food and Drug Administration ("FDA") of a Biologics License Application (BLA # 125276/0) on January 8, 2010, for Actemra® (tocilizumab), a humanized monoclonal antibody that is an interleukin-6 receptor (IL-6R) inhibitor, for the treatment of adult patients with rheumatoid arthritis.

For convenience, the information contained in this application will be presented according to the format set forth in 37 C.F.R. § 1.740(a).

03/02/2010 SSANDARA 00000004 5670373

01 FC:1457 1120.00 OP
02 FC:1999 90.00 OP

(1) A Complete Identification Of The Approved Product As By Appropriate Chemical And Generic Name, Physical Structure Or Characteristics

The approved product is a recombinant humanized anti-human Interleukin-6 Receptor (IL-6R) monoclonal antibody of the immunoglobulin IgG_1 subclass, formulated for intravenous (iv) infusion. The approved product has the trade name Actemra®, and established name of "tocilizumab."

Actemra® (tocilizumab) is an IgG1κ (gamma 1, kappa) antibody with a typical H_2L_2 structure. The amino acid sequence of the light chain is shown in Figure 1.

Figure 1: Amino Acid Sequence of the L Chain

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  1    DIQMTQSPSS LSASVGDRVT ITCRASQDIS SYLNWYQQKP GKAPKLLIYY  50
 51    TSRLHSGVPS RFSGSGSGTD FTFTISSLQP EDIATYYCQQ GNTLPYTFGQ 100
101    GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
151    DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
201    LSSPVTKSFN RGEC                                       214
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The amino acid sequence of the heavy chain is shown in Figure 2.

Figure 2: Amino Acid Sequence of the H Chain

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  1   pEVQLQESGPG LVRPSQTLSL TCTVSGYSIT SDHAWSWVRQ PPGRGLEWIG  50
 51    YISYSGITTY NPSLKSRVTM LRDTSKNQFS LRLSSVTAAD TAVYYCARSL 100
101    ARTTAMDYWG QGSLVTVSSA STKGPSVFPL APSSKSTSGG TAALGCLVKD 150
151    YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY 200
201    ICNVNHKPSN TKVDKKVEPK SCDKTHTCPP CPAPELLGGP SVFLFPPKPK 250
251    DTLMISRTPE VTCVVVDVSH EDPEVKFNWY VDGVEVHNAK TKPREEQYNS 300
301    TYRVVSVLTV LHQDWLNGKE YKCKVSNKAL PAPIEKTISK AKGQPREPQV 350
351    YTLPPSRDEL TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL 400
401    DSDGSFFLYS KLTVDKSRWQ QGNVFSCSVM HEALHNHYTQ KSLSLSPG   448
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(2) A Complete Identification Of The Federal Statute Including The Applicable Provision Of Law Under Which The Regulatory Review Occurred

Regulatory review of the approved product occurred under § 505(i) of the Federal Food, Drug, and Cosmetic Act ("FFDCA"), 21 U.S.C. § 355(i) (*see also* 21 C.F.R. Part 312)

and § 351(a) of the Public Health Service Act ("PHSA"), 42 U.S.C. § 262(a) (*see also* 21 C.F.R. Part 314 and 601).

(3) An Identification Of The Date On Which The Product Received Permission For Commercial Marketing Or Use Under The Provision Of Law Under Which The Applicable Regulatory Review Period Occurred

The approved product, Actemra® (tocilizumab), received permission for commercial marketing on January 8, 2010, when the FDA approved BLA # 125276/0 for the treatment of adults with rheumatoid arthritis, under § 351(a) of the PHSA.

(4) In The Case Of A Drug Product, An Identification Of Each Active Ingredient In The Product And As To Each Active Ingredient, A Statement That It Has Not Been Previously Approved For Commercial Marketing Or Use Under The Federal Food, Drug And Cosmetic Act, The Public Health Service Act, Or The Virus-Serum-Toxin Act, Or A Statement Of When The Active Ingredient Was Approved For Commercial Marketing Or Use (Either Alone Or In Combination With Other Active Ingredients), The Use For Which It Was Approved, And The Provision Of Law Under Which It Was Approved

The approved product contains only one active ingredient, tocilizumab. Tocilizumab (Actemra®) has not been previously approved for commercial marketing or use under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act.

(5) A Statement That The Application Is Being Submitted Within The Sixty Day Period Permitted For Submission Pursuant To 37 C.F.R. § 1.720(F) And An Identification Of The Date Of The Last Day On Which The Application Could Be Submitted

The Application is being submitted within the sixty day period permitted under 37 C.F.R. § 1.720(f) .

The last day on which the application can be submitted is March 8, 2010, i.e., sixty days from the date (January 8, 2010) the approved product first received permission for commercial marketing or use under the PHSA.

(6) A Complete Identification Of The Patent For Which An Extension Is Being Sought By The Name Of The Inventor, The Patent Number, The Date Of Issue, And The Date Of Expiration.

The patent for which an extension is being sought is:

Inventors:	Tadamitsu Kishimoto
Patent No:	U.S. Patent No. 5,670,373
Title:	Antibody to Human Interleukin-6 Receptor
Issue Date:	September 23, 1997
Current Expiration Date:	January 2, 2013 (the expiration date of Jan. 2, 2013 is based upon a terminal disclaimer over US 5,480,796, which expires on January 2, 2013.)

The '373 patent has not previously been extended.

(7) A Copy Of The Patent For Which An Extension Is Being Sought, Including The Entire Specification (Including Claims) And Drawings

A copy of U.S. Patent No. 5,670,373 is attached hereto as Exhibit 1.

(8) A Copy Of Any Disclaimer, Certificate Of Correction, Receipt Of Maintenance Fee Payment, Or Reexamination Certificate Issued In The Patent.

No certificates of correction or reexamination certificates have been issued in the patent. A terminal disclaimer, however, was filed over US Patent No. US 5,480,796, a copy of which is attached hereto as Exhibit 2. Copies of the 4th, 8th and 12th year maintenance fee payment receipts is attached hereto as Exhibit 3.

(9) A Statement That The Patent Claims The Approved Product, Or A Method Of Using Or Manufacturing The Approved Product, And A Showing Which Lists Each Applicable Patent Claim And Demonstrates The Manner In Which At Least One Such Patent Claim Reads On The Approved Product

Actemra® (tocilizumab) is a monoclonal antibody that binds an interleukin-6 receptor and specifically, a human interleukin-6 receptor. Actemra® is approved for use in treating "adult patients with moderately - to severely – active rheumatoid arthritis who have had an inadequate response to one or more TNF antagonist therapies." See Full Prescribing Information for Actemra®, section 1 (Exhibit 4). Rheumatoid arthritis is a chronic systemic disease primarily of the joints, marked by inflammatory changes in the synovial membranes and articular structures and by atrophy and rarefaction of the bones.

U.S. Patent No. 5,670,373 claims an isolated antibody that specifically binds to human interleukin-6 receptor, which reads on the approved product Actemra®. Accordingly, applicable claims of the '373 patent for patent term extension which claim the approved product include claims 1 and 3:

1. An isolated antibody to human interleukin-6 receptor, wherein said antibody specifically binds to said human interleukin-6 receptor.

3. An antibody according to claim 1, wherein said antibody is monoclonal.

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