Appeal decision

Appeal No. 2017-2373

Canada
Appellant TRANSLATUM MEDICUS INC

Tokyo, Japan
Patent Attorney TAKAOKA, Ryoichi

The case of appeal against the examiner's decision of refusal of Japanese Patent Application No. 2015-509271 "Methods for Treating and Diagnosing Blinding Eye Diseases" [international publication date on November 7, 2013, WO2013/163758 and nationally published on August 13, 2015, National Publication of International Patent Application No. 2015-523546] has resulted in the following appeal decision:

Conclusion

The appeal of the case was groundless.

Reason

No. 1 History of the procedures

The application was originally filed on April 30, 2013 as an International Patent Application (priority claim under the Paris Convention: May 1, 2012 (US), May 2, 2012 (US), August 24, 2012 (US), March 15, 2013 (US)), and the history of the further procedures is as follows:

April 25, 2016 written amendment
May 24, 2016 notification of reasons for refusal
August 30, 2016 written opinion, written amendment, and supplemental

statement

October 13, 2016 examiner's decision of refusal

February 17, 2017 request for appeal

February 17, 2017 written amendment

March 29, 2017 written amendment (formality)

June 9, 2017 reexamination report by Examiner before appeal

No. 2 Decision to Dismiss Amendment submitted on February 17, 2017

[Conclusion of Decision to Dismiss Amendment]

The amendment submitted on February 17, 2017 shall be dismissed.

[Reason]

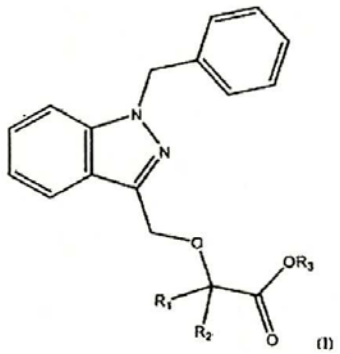
1. The details of the amendment submitted on February 17, 2017

The amendment submitted on February 17, 2017 (hereinafter referred to as "the Amendment") is to amend Claim 1 before the Amendment,

"[Claim 1]

Use of a compound of Formula I or a pharmaceutically acceptable salt thereof for manufacturing a medicament for reducing the rate of progression to dry age-related macular degeneration (AMD) in the hyaloid body,

[Chem. 1]



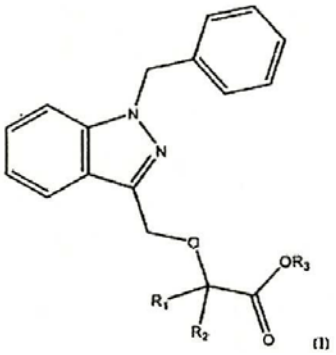
wherein each of R_1 and R_2 is independently H or C_1-C_6 alkyl, and R_3 is H or C_1-C_6 alkyl."

to

"[Claim 1]

Use of a compound of Formula I or a pharmaceutically acceptable salt thereof for manufacturing a medicament for reducing the rate of progression to dry age-related macular degeneration (AMD) in the hyaloid body,

[Chem. 1]



(I)

wherein each of R_1 and R_2 is independently H or C_1-C_6 alkyl, and R_3 is H or C_1-C_6 alkyl,

wherein the dry age-related macular degeneration (AMD) is diagnosed by detecting one or more of autofluorescent structures in the retinal pigment epithelium (RPE)."

2. Propriety of amendment

The amendment regarding Claim 1 is to limit "dry age-related macular degeneration (AMD)" before the amendment to dry age-related macular degeneration (AMD) "that is diagnosed by detecting one or more of autofluorescent structures in the retinal pigment epithelium (RPE)," and thus the amendment is applicable to restrict the scope of claims.

Whether the appellant shall be granted a patent for the invention described in Claim 1 after the Amendment (hereinafter referred to as "Amended Invention") independently at the time of filing the application (whether the Amended Invention falls under the provisions of Article 126(7) of the Patent Act which is applied mutatis

mutandis pursuant to the provisions of Article 17-2(6) of the Patent Act) will be examined.

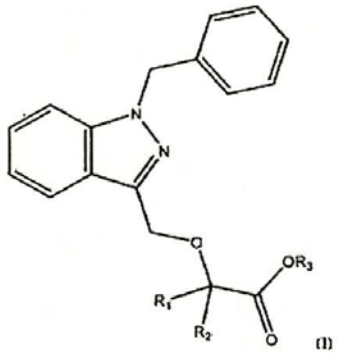
(1) Amended Invention

As described in the above 1., the Amended Invention is as follows.

"[Claim 1]

Use of a compound of Formula I or a pharmaceutically acceptable salt thereof for manufacturing a medicament for reducing the rate of progression to dry age-related macular degeneration (AMD) in the hyaloid body,

[Chem. 1]



(I)

wherein each of R_1 and R_2 is independently H or C_1-C_6 alkyl, and R_3 is H or C_1-C_6 alkyl,

wherein the dry age-related macular degeneration (AMD) is diagnosed by detecting one or more of autofluorescent structures in the retinal pigment epithelium (RPE)."

(2) Article 36(4)(i) of the Patent Act

A. Introduction

Article 36(4) of the Patent Act provides that "The statement of the detailed explanation of the invention as provided in item (iii) of the preceding Paragraph shall comply with each of the following items," and Article 36(4)(i) of the Patent Act requires that "in accordance with Ordinance of the Ministry of Economy, Trade and Industry, the statement shall be clear and sufficient in such a manner as to enable any person skilled

in the art to which the invention pertains to work the invention." (what is called enablement requirements)

In addition, the Amended Invention relates to "use for manufacturing a medicament for reducing the rate of progression to dry age-related macular degeneration (AMD) in the hyaloid body" and to medicinal use, and as it is generally difficult for medicinal use to predict the utility only from the name or chemical structure, even when the effective amount, method for administration, or matters for formulation are described in the detailed description of the invention, a person skilled in the art cannot understand whether the medicament actually has utility of the medicinal use, and thus there is need to describe pharmacological data or description equivalent to the pharmacological data in the detailed description of the invention for supporting utility of medicinal use, and if such description is not present, it should be said that the application does not meet enablement requirements.

This point will be examined as follows.

B. The detailed description of the invention

The following matters are described in the detailed description of the invention.

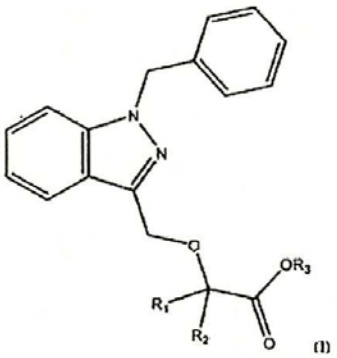
(a) "[0002]

This invention relates to methods and compositions that are useful for the diagnosis, treatment, or prevention of a blinding eye disease, including the discovery of drugs that are efficacious against these diseases." ([0002])

(b) "[0008]

In another aspect, the invention provides a method for treating or preventing dry AMD, comprising administering to a subject in need thereof an effective amount of a compound of Formula I:

[Chem. 1]



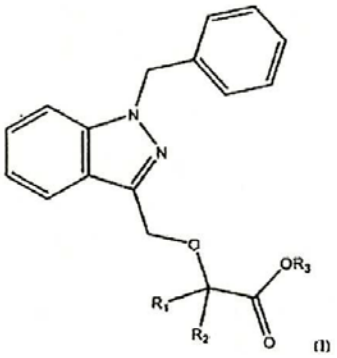
(I)

or a pharmaceutically acceptable salt thereof, wherein each of R_1 and R_2 is independently H or a C_1-C_6 alkyl and R_3 is H or a C_1-C_6 alkyl." ([0008])

(c) "[0031]

In another aspect, the invention provides a method for treating or preventing dry AMD, comprising administering to a subject in need thereof an effective amount of a compound of Formula I:

[Chem. 2]



(I)

or a pharmaceutically acceptable salt thereof, wherein each of R_1 and R_2 is independently H or a C_1-C_6 alkyl and R_3 is H or a C_1-C_6 alkyl. In one embodiment, the compound of Formula I is bindarit." ([0031])

(d) "[0207]

When ophthalmically administered to a human, for example, intravitreally, the

dosage of an agent of the invention, including, for example, Formula I, methotrexate or a pharmaceutically acceptable salt thereof and/or additional therapeutic agent is normally 0.003 mg to 5.0 mg per eye per administration, or 0.03 mg to 3.0 mg per eye per administration, or 0.1 mg to 1.0 mg per eye per administration. In one embodiment, the dosage is 0.03 mg, 0.3 mg, 1.5 mg, or 3.0 mg per eye. In another embodiment, the dosage is 0.5 mg per eye. The dosage can range from 0.01 mL to 0.2 mL administered per eye, or 0.03 mL to 0.15 mL administered per eye, or 0.05 mL to 0.10 mL administered per eye. In one embodiment, the administration is 400 μg of compound, monthly for at least three months.

[0208]

Generally, when orally administered to a mammal, the dosage of any agent described herein may be 0.001 mg/kg/day to 100 mg/kg/day, 0.01 mg/kg/day to 50 mg/kg/day, or 0.1 mg/kg/day to 10 mg/kg/day. When orally administered to a human, the dosage of any agent described herein is normally 0.001 mg to 1000 mg per day, 1 mg to 600 mg per day, or 5 mg to 30 mg per day. In one embodiment, oral dosage is 600 mg per day. In one embodiment, the oral dosage is two 300 mg doses per day. In another embodiment, oral dosage is 7.5 mg per week to 15 mg per week.

[0209]

For administration of any agent described herein by parenteral injection, the dosage is normally 0.1 mg to 250 mg per day, 1 mg to 20 mg per day, or 3 mg to 5 mg per day. Injections may be given up to four times daily. Generally, when orally or parenterally administered, the dosage of any agent described herein is normally 0.1 mg to 1500 mg per day, or 0.5 mg to 10 mg per day, or 0.5 mg to 5 mg per day. A dosage of up to 3000 mg per day can be administered.

[0210]

In some embodiments, it may be desirable to administer one or more of any agent described herein to the eye. Administration may be, by way of non-limiting example, intra-ocular, intra-vitreal, topical (including, but not limited to, drops and ointment), sub-conjunctival, sub-Tenon's, trans-scleral, suprachoroidal, subretinal, or via iontophoresis.

[0211]

Other routes of administration may also be used, such as, for example: intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, oral, sublingual, intranasal, intracerebral, intravaginal, transdermal, rectally, by inhalation, or topically, particularly to the ears, nose, eyes, or skin.

[0212]

The mode of administration can be left to the discretion of the practitioner, and depends in part upon the site of the medical condition. In most instances, administration results in the release of any agent described herein into the bloodstream.

[0213]

Any agent described herein can be administered orally. Such agents can also be administered by any other conventional route, for example, by intravenous infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral mucosa, rectal and intestinal mucosa, etc.), and can be administered together with another biologically active agent. Administration can be systemic or local. Various delivery systems are known, e.g., encapsulation in liposomes, microparticles, microcapsules, capsules, etc., and can be used for administration.

[0214]

Further methods of administration include but are not limited to intra-ocular, intra-vitreal, topical ocular (including but not limited to drops, ointments, and inserts), sub-conjunctival, sub-Tenon's, suprachoroidal, trans-scleral, intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, oral, sublingual, intranasal, intracerebral, intravaginal, transdermal, rectally, by inhalation, or topically, particularly to the ears, nose, eyes, or skin. In some embodiments, more than one of any agent described herein is administered to the eye. Administration may be, by way of non-limiting example, intra-ocular, intra-vitreal, topical (including, but not limited to, drops, and ointment), sub-conjunctival, sub-Tenon's, trans-scleral, or iontophoresis. The mode of administration can be left to the discretion of the practitioner, and depends in part upon the site of the medical condition. In most instances, administration results in release into the bloodstream.

[0215]

In specific embodiments, it may be desirable to administer locally to the area in need of treatment.

[0216]

In another embodiment, delivery can be in a vesicle, in particular a liposome (see Langer, 1990, Science 249:1527-1533; Treat et al., in Liposomes in the Therapy of Infectious Disease and Cancer, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 353-365 (1989)). In yet another embodiment, delivery can be in a controlled-release system. In one embodiment, a slow release intraocular device may be used. In some embodiments, this device consists of a locally delivered erodible or non-erodable liquid, gel, polymer, etc.

[0217]

In another embodiment, polymeric materials can be used (see Medical Applications of Controlled Release, Langer and Wise (eds.), CRC Pres., Boca Raton, Florida (1974); Controlled Drug Bioavailability, Drug Product Design and Performance, Smolen and Ball (eds.), Wiley, New York (1984); Ranger and Peppas, 1983, J. Macromol. Sci. Rev. Macromol. Chem. 23:61; see also Levy et al., 1985, Science 228: 190; During et al., 1989, Ann. Neurol. 25:351; Howard et al., 1989, J. Neurosurg. 71: 105). In another embodiment, a controlled-release system can be placed in proximity of the target area to be treated, e.g., the retina, thus requiring only a fraction of the systemic dose (see, e.g., Goodson, in Medical Applications of Controlled Release, supra, vol. 2, pp. 115-138 (1984)). Other controlled-release systems discussed in the review by Langer, 1990, Science 249: 1527-1533) may also be used.

[0218]

Administration of any agent described herein can, independently, be one to four times daily or one to four times per month, or one to six times per year, or once every two, three, four, or five years. Administration can be for the duration of one day or one month, two months, three months, six months, one year, two years, three years, and may even be for the life of the subject. Chronic, long-term administration will be indicated in many cases. The dosage may be administered as a single dose or divided into

multiple doses. In general, the desired dosage should be administered at set intervals for a prolonged period, usually at least over several weeks or months, although longer periods of administration of several months or years or more may be needed.
[0219]

The dosage regimen utilizing any agent described herein can be selected in accordance with a variety of factors, including type, species, age, weight, sex, and medical condition of the subject; the severity of the condition to be treated, the route of administration; the renal or hepatic function of the subject; the pharmacogenomic makeup of the individual; and the specific compound of the invention employed. Any agent described herein can be administered in a single daily dose, or the total daily dosage can be administered in divided doses of two, three, or four times daily. Furthermore, any agent described herein can be administered continuously rather than intermittently throughout the dosage regimen.
Methods of Treatment
[0220]

In various aspects, the present invention provides a method for treating or preventing dry AMD and/or RPD. In these aspects, the "agent of the invention" comprises compounds useful for both monotherapy and combination therapy (e.g. as an additional therapeutic agent). In general, monotherapy comprises the use of compounds of Formula I, methotrexate, or their pharmaceutically acceptable salts, while combination therapy comprises compounds of Formula I, methotrexate, or their pharmaceutically acceptable salts in combination with an additional therapeutic agent, including one or more of an anti-VEGF agent, an ACE inhibitor, a PPAR-γ agonist, a renin inhibitor, a steroid, an agent that modulates autophagy PPARγ modulator, semapimod, an MIF inhibitor, a CCR2 inhibitor, CKR-2B, a 2-thioimidazole, CAS 445479-97-0, CCX140, clodronate, a clodonate-liposome preparation, or gadolinium chloride." ([0207] to [0220])

(e) "[0250]

This invention is further illustrated by way of the following non-limiting

examples.

(Examples)

(Example 1): Systemic Injection of the RPE Toxin, $NaIO_3$, induces complex patterns of FAF similar to those of AMD and/or RPD.

(...Omitted...)

(Example 2): DNIRA of a rat eye after systemic ICG administration identifies the retinal pigment epithelial (RPE) layer in vivo.

(...Omitted...)

(Example 3): Discovery of compounds for the treatment of blinding eye diseases

(...Omitted...)

(Example 4): Assessing the activity of compounds for blinding eye diseases

(...Omitted...)" ([0250] to [0286])

(f) "(Example 5): Treatment of dry AMD with bindarit

[0287]

Human subjects, 56 to 100 years of age or more, presented with dry AMD, as diagnosed by one or more of the following clinical tests: clinical examination, FAF (at any wavelength), near infrared and/or red-free photography, fluorescein angiography, which allows for the identification and localization of abnormal vascular processes; OCT, which provides high-resolution, cross-sectional, or face images from within optical scattering media, such as the human retina and choroid; and structured illumination light microscopy, using a specially designed high resolution microscope setup to resolve the fluorescent distribution of small autofluorescent structures (lipofuscin granule) in retinal pigment epithelium tissue sections.

[0288]

The subjects were administered bindarit in two 300 mg oral doses once a day for 12 weeks. After an initial twelve-week treatment period, the subjects were evaluated for clinical outcomes. Alternatively, patients received intravitreal injection of a vehicle containing bindarit, with or without a drug delivery vehicle.

[0289]

A first clinical outcome is determined using a standard visual acuity test, as is well known in the art. The subjects are assessed for the ability to clearly see symbols and objects on a Snellen eye chart from a distance.

[0290]

A second clinical outcome assesses the rate of progression of geographic atrophy. To do so, the subjects' pupils are dilated with 1.0% tropicamide and 2.5% phenylephrine before retinal imaging. Imaging is carried out with an instrument (e.g., Spectralis HRA+OCT; Heidelberg Engineering, Heidelberg, Germany) that allows for simultaneous recording of cSLO and spectral-domain optical coherence tomography (SD-OCT) with two independent scanning mirrors, as described in Helb, et al. Acta Ophthalmol. 2010 Dec; 88(8):842-9. Five modes of operation are employed: white light, red-free light, near infrared, FAF, and OCT.

[0291]

cSLO images are obtained according to a standardized operation protocol that includes the acquisition of near-infrared reflectance (λ = 815 nm) and FAF (excitation at λ = 488 nm, emission 500-700 nm) images. Simultaneous SD-OCT imaging is carried out with an illumination wavelength of 870 nm, an acquisition speed of 40,000 A-scans, and a scan depth of 1.8 mm. Two SD-OCT scans, one vertical and one horizontal, per eye are performed through the approximate foveal center, or in the case of RPD, in proximity to the vascular arcades of the macula. Fluorescein angiography (λ = 488 nm, emission 500-700 nm, 10% fluorescein dye) is performed as needed. Color fundus photographs are obtained with a fundus camera (e.g. FF 450 Visupac ZK5; Carl Zeiss Meditec AG, Jena, Germany).

[0292]

Interpretation of clinical outcome data informs a decision for further treatment, if any." ([0286] to [0292])

(g) "(Example 6): Treatment of dry AMD with a combination therapy

[0293]

Human subjects, 56 to 100 years of age or more, presented with dry AMD, as

diagnosed by one or more of the following clinical tests: clinical examination, white-light fundus imaging, FAF at any wavelength, near infrared and/or red-free photography, blue-light illumination, and/or fluorescein or ICG angiography, which allows for the identification and localization of abnormal vascular processes; OCT, which provides high-resolution, cross-sectional, three-dimensional, and face images from within optical scattering media, such as the human retina and choroid; and structured illumination light microscopy, using a specially designed high resolution microscope or ophthalmoscope set up to resolve the distribution of small autofluorescent structures (lipofuscin, lipofuscin-like, or other granule) in the retinal pigment epithelium or other cells and cell layers.

[0294]

The subjects were administered bindarit in two 300 mg oral doses once a day for 12 weeks. The subjects were also administered ranibizumab injection once per month (roughly 28 days) in a dose of 0.5 mg per affected eye. After an initial twelve-week treatment period, the subjects were evaluated for clinical outcomes.

[0295]

A first clinical outcome is determined using a standard visual acuity test, as is well known in the art. The subjects are assessed for the ability to clearly see symbols and objects on a Snellen eye chart from a distance.

[0296]

A second clinical outcome assesses the rate of progression of geographic atrophy. To do so, the subjects' pupils are dilated with 1.0% tropicamide and 2.5% phenylephrine or a comparable agent before retinal imaging. Imaging is carried out with an instrument (e.g., Spectralis HRA+OCT; Heidelberg Engineering, Heidelberg, Germany) that allows for simultaneous recording of cSLO and SD-OCT, as described in Helb, et al. Acta Ophthalmol. 2010 Dec; 88(8):842-9. Multiple modes of operation can be employed: white light, red-free light, blue light, near infrared, and OCT. Similar analysis can be performed with a modified fundus camera.

[0297]

cSLO images are obtained according to protocols known in the art that may

include the acquisition of near-infrared reflectance (λ = 800-1000 nm) and FAF (excitation at λ = 280-550 nm, emission 350-700 nm) images. Simultaneous SD-OCT imaging is carried out with, for example, an illumination wavelength of 870 nm, an acquisition speed of 40,000 A-scans, and a scan depth of 1.8 mm. Multiple SD-OCT scans per eye are performed through the macula and additionally or in the case of RPD, in proximity to the vascular arcades of the macula. Other OCT imaging, such as, for example, time domain and swept domain, can also be used. Fluorescein angiography (λ = 488 nm, emission 500-700 nm, 10% fluorescein dye) is performed as needed. Color fundus photographs are obtained with a fundus camera (e.g. FF 450 Visupac ZK5; Carl Zeiss Meditec AG, Jena, Germany).

[0298]

Interpretation of clinical outcome data informs a decision for further treatment, if any. Illustrative data analysis includes macular cube analysis and 5 line raster." ([0292] to [0298])

(h) "(Example 7): Detection and/or prediction of a blinding eye disease subject response to an agent

(...Omitted...)

(Example 8): DNIRA of a rat eye after systemic ICG administration labels immune cells in vivo

(...Omitted...)

Example 9: Clinical in vivo imaging of RPD and Diffuse trickling AMD:

(...Omitted...)" ([0298] to [0328])

C. Judgment

Regarding methods and compositions that are useful for the diagnosis, treatment, or prevention of a blinding eye disease, including the discovery of drugs that are efficacious against these diseases (summarized matter (a)), a method for treating or preventing dry AMD, comprising administering to a subject in need thereof an effective amount of the compound of Formula I or a pharmaceutically acceptable salt thereof ("a

compound of Formula I or a pharmaceutically acceptable salt thereof" may be hereinafter collectively referred to as "a compound of Formula I") is described in the detailed description of the invention (summarized matter (b)), and the effective amount and method for administration are also described to some extent (summarized matter (d)); however as described in the above "A," it cannot be understood whether the compound of Formula I of the Amended Invention is actually useful in "use for manufacturing a medicament for reducing the rate of progression to dry age-related macular degeneration (AMD) in the hyaloid body."

In addition, examining whether pharmacological data supporting the utility or description equivalent to the pharmacological data are described in the detailed description of the invention, it is described in Examples 5 and 6 in the detailed description of the invention that human subjects with dry AMD were administered bindarit in two 300 mg oral doses once a day for 12 weeks or received intravitreal injection of a vehicle containing bindarit, and a method for evaluating the administration is also described (summarized matters (f) and (g)), and thus it can be said that a method for administering bindarit, which is a compound of Formula I (summarized matter (c)), to a subject with dry AMD and evaluating the administration is described in the detailed description of the invention.

However, it is not described that the evaluation method has actually been performed, and there is no description whether the compound of Formula I has been found capable of "reducing the rates of progression to dry age-related macular degeneration (AMD) in the hyaloid body" from the result of evaluation.

That is, it cannot be said that Examples 5 and 6 are pharmacological data actually supporting the utility of "use of the compound of Formula I for manufacturing a medicament for reducing the rates of progression to dry age-related macular degeneration (AMD) in the hyaloid body," and there is no description equivalent to the pharmacological data supporting the utility.

Further, Examples other than Examples 5 and 6 are "(Example 1): Systemic Injection of the RPE Toxin, $NaIO_3$, induces complex patterns of FAF similar to those of AMD and/or RPD, (Example 2): DNIRA of a rat eye after systemic ICG administration

identifies the retinal pigment epithelial (RPE) layer in vivo, (Example 3): Discovery of compounds for the treatment of blinding eye diseases, (Example 4): Assessing the activity of compounds for blinding eye diseases, (Example 7): Detection and/or prediction of a blinding eye disease subject response to an agent, (Example 8): DNIRA of a rat eye after systemic ICG administration labels immune cells in vivo, (Example 9): Clinical in vivo imaging of RPD and Diffuse trickling AMD" (summarized matters (e) and (h)), and these Examples are not related to the compound of Formula I, and thus these Examples are not pharmacological data actually supporting the utility of "use of the compound of Formula I for manufacturing a medicament for reducing the rates of progression to dry age-related macular degeneration (AMD) in the hyaloid body," and there is no description equivalent to the pharmacological data supporting the utility.

In addition, examining the other detailed description of the invention, there is no description of pharmacological data actually supporting the utility of "use of the compound of Formula I for manufacturing a medicament for reducing the rates of progression to dry age-related macular degeneration (AMD) in the hyaloid body," and there is no description equivalent to the pharmacological data supporting the utility.

As described above, since pharmacological data supporting the utility or description equivalent to the pharmacological data is not described in the detailed description of the invention, the detailed description of the invention is not clear and sufficient to enable a person skilled in the art to carry out the Amended Invention of "use of the compound of Formula I for manufacturing a medicament for reducing the rates of progression to dry age-related macular degeneration (AMD) in the hyaloid body."

D. Summary

Therefore, the detailed description of the invention of the invention does not comply with the provision of Article 36(4)(i) of the Patent Act, and thus the Amended Invention should not be independently patentable at the time of patent application.

(3) Article 36(6)(i) of the Patent Act

A. Introduction

Article 36(6) of the Patent Act provides "The statement of claims as provided in paragraph (2) shall comply with each of the following items," and Article 36(6)(i) of the Patent Act provides "The invention for which a patent is sought is stated in the detailed description of the invention." Whether the statement in the claims satisfies the requirement stipulated in Article 36(6)(i) of the Patent Act (what is called support requirements) is determined by comparing the claimed invention and the detailed description of the invention, and by determining whether the claimed invention is the invention described in the detailed description of the invention and is within the extent in the description to which a person skilled in the art would recognize that a problem to be solved by the invention would actually be solved, or is within the extent in the description to which a person skilled in the art would recognize that a problem to be solved by the invention would actually be solved by taking into account common general technical knowledge at the time of filing the application even if the problem is not described or indicated, and thus this point will be examined.

B. Judgment

It is described in the detailed description of the invention that the invention provides a method for treating or preventing dry AMD, comprising administering to a subject in need thereof an effective amount of a compound of Formula I (summarized matters (b) and (c)), and taking into account the matters specifying the Amended Invention, it can be said that the problem to be solved by the Amended Invention is to provide "use for manufacturing a medicament for reducing the rate of progression to dry age-related macular degeneration (AMD) in the hyaloid body."

However, as described in the above (2)C., there is no description, in the detailed description of the invention, of pharmacological data actually supporting the utility of the compound of Formula I in "use for manufacturing a medicament for reducing the rate of progression to dry age-related macular degeneration (AMD) in the hyaloid body" or description equivalent to the pharmacological data, it cannot be said that a person skilled in the art would recognize that the problem is to be solved with the detailed

description of the invention.

In addition, even if pharmacological data or description equivalent to the pharmacological data is not described the detailed description of the invention, there was no common general technical knowledge at the time of filing the application that a person skilled in the art was capable of "use of a compound of Formula I for manufacturing a medicament for reducing the rate of progression to dry age-related macular degeneration (AMD) in the hyaloid body," and would recognize that the problem is to be solved.

Thus, there is no description in the detailed description of the invention that a person skilled in the art would recognize that the problem is to be solved by the Amended Invention, and there is no description that a person skilled in the art would recognize that the problem is to be solved by taking into account common general technical knowledge at the time of filing the application even if the problem is not described or indicated, and the Amended Invention is not described in the detailed description of the invention.

C. Summary

Therefore, since the description of claims according to the Amended Invention does not comply with the provision of Article 36(6)(i) of the Patent Act, the Amended Invention should not be independently patentable at the time of patent application.

(4) Appellant's allegation

The appellant alleges in the written opinion submitted on August 30, 2016 that the detailed description of the invention is clear and sufficient to enable a person skilled in the art to carry out the Amended Invention, and the Amended Invention is described in the detailed description of the invention, pointing out the following points.

"As described in Example 5 of the application, on the basis of the evaluation in animal models for dry age-related macular degeneration (AMD) (Examples 1-2), intravitreal injection of bindarit is used to treat a subject with dry AMD. As evidence

showing surprising effect of bindarit on treatment of dry AMD, including reducing the rate of progression to dry AMD and the rate of progression of geographic atrophy, the appellant submits experimental data (US written oath (Evidence A No. 1)) by Doctor Boyd, who is the inventor of this application.

As is clear from the experimental data, monotherapy by intravitreal injection of bindarit surprisingly and significantly reduced progression of patch of geographic atrophy indicating blinding complication and disease progression after dry AMD. At Time 1 (left panel) of both Figures A and B of the experimental data, patch of geographic atrophy is present in a rat's eye. Figure A shows treatment of patch present in an animal model of the present invention with negative control (saline). As shown at Time 2 of Figure A, the patch treated with saline was expanded (arrow in right panel). In contrast, as shown at Time 2 of Figure B, the patch treated with bindarit was not expanded (no arrow in right panel). These data are summarized in Figure C. There is no progression of geographic atrophy in all animals receiving bindarit in eye.

Pharmacological effect of a compound of the Invention can be evaluated by using the animal model described in Examples 1 and 2 and performing the method described in Examples 5 and 6, and thus a person skilled in the art can obtain the above data easily. Therefore, the appellant considers that the detailed description of the invention is clear and sufficient to enable a person skilled in the art to carry out the Invention, and the Invention is described in the detailed description of the invention."

However, the above data are not described in the detailed description of the invention and were not common general technical knowledge at the time of filing the application, and thus if the detailed description of the invention meets the requirement stipulated in Article 36(4)(i) of the Patent Act and the claimed invention meets the requirement stipulated in Article 36(6)(i) of the Patent Act by submitting the above data after filing the application, the submission violates the object of Patent Act employing the so-called first-to-file system and the submission is not accepted.

Therefore, any of the appellant's allegation cannot be accepted.

In addition, the appellant alleges in the grounds for the appeal amended on March 29, 2017 that the detailed description of the invention is clear and sufficient to enable a person skilled in the art to carry out the Amended Invention, and the Amended Invention is described in the detailed description of the invention, pointing out the following points.

"According to the above amendment, 'dry age-related macular degeneration (AMD)' described in Claims 1 and 6 is limited to the dry age-related macular degeneration (AMD) 'diagnosed by detecting one or more of autofluorescent structures in the retinal pigment epithelium (RPE).' The amendment is to reflect the matters described in the detailed description of the invention of the application. Namely, the amendment is to reflect the matters for specifically evaluating the effect of a compound of the invention by detecting one or more of autofluorescent structures in the retinal pigment epithelium (RPE) in use of the compound and a method for reducing the rate of progression to dry age-related macular degeneration according to the invention, to the claimed invention 1 and 6. For example, this method is disclosed in Examples 1, 2, 8 and Figures 3A, 3B, 3C, 4A, 4B, 4C, 5, 6, 7A, 7B, 8A, 8B, 8C, 9A, 9B, 10 of the application. Detecting one or more of autofluorescent structures in the retinal pigment epithelium (RPE) is specifically described in Example 1. In addition, on the basis of the evaluation in dry age-related macular degeneration (AMD) disclosed in Example 1, as described in Example 5, it is thought that a person skilled in the art can use intravitreal injection of bindarit for treating patients with dry AMD.

Therefore, the appellant believes that the claimed inventions after the Amendment are described in the detailed description of the invention of the application to be clear and sufficient to enable a person skilled in the art to carry out the claimed inventions after the Amendment."

Examining the above allegation, even though a method for detecting one or

more of autofluorescent structures in the retinal pigment epithelium (RPE) is described in Examples 1, 2, 8 and Figures 3A, 3B, 3C, 4A, 4B, 4C, 5, 6, 7A, 7B, 8A, 8B, 8C, 9A, 9B, 10, there is no relationship between a method for detecting an autofluorescent structure and the actual utility of the compound of Formula I in "use for manufacturing a medicament for reducing the rate of progression to dry age-related macular degeneration (AMD) in the hyaloid body," and on the basis of the description, in the detailed description of the invention, of the method for detecting an autofluorescent structure, it cannot be said that there is description of pharmacological data actually supporting the utility of the compound of Formula I in "use for manufacturing a medicament for reducing the rate of progression to dry age-related macular degeneration (AMD) in the hyaloid body" or description equivalent to the pharmacological data.

In addition, even though an animal model is described in Example 1 and a method for evaluation is described in Example 5, as described in the above (2)C, it cannot be said that there is description of pharmacological data actually supporting the utility of the compound of Formula I in "use for manufacturing a medicament for reducing the rate of progression to dry age-related macular degeneration (AMD) in the hyaloid body" or description equivalent to the pharmacological data.

Thus, the detailed description of the invention is not clear and sufficient to enable a person skilled in the art to carry out the Amended Invention, and the Amended Invention is not described in the detailed description of the invention.

Therefore, any of the appellant's allegations cannot be accepted.

3. Closing regarding the Amendment

As described above, since the Amended Invention should not be independently patentable at the time of patent application, the Amendment regarding Claim 1 violates the provisions of Article 126(7) of the Patent Act which is applied mutatis mutandis pursuant to the provisions of Article 17-2(6) of the Patent Act.

Therefore, the Amendment shall be dismissed under the provisions of Article 53(1) of the Patent Act applied mutatis mutandis by replacing certain terms pursuant to

Article 159(1) of the Patent Act.

No. 3 The Invention

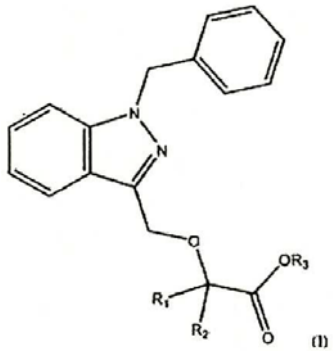
1. The Invention

As described above, since the Amendment shall be dismissed, the inventions of the application are inventions specified by the matters described in Claims 1 to 10 amended by written amendment submitted on August 30, 2016, and the invention according to Claim 1 (hereinafter referred to as "the Invention") is as follows.

"[Claim 1]

Use of a compound of Formula I or a pharmaceutically acceptable salt thereof for manufacturing a medicament for reducing the rate of progression to dry age-related macular degeneration (AMD) in the hyaloid body,

[Chem. 1]



(I)

wherein each of R_1 and R_2 is independently H or C_1-C_6 alkyl, and R_3 is H or C_1-C_6 alkyl."

2. Reasons for refusal stated in the examiner's decision

Refusal stated in the examiner's decision is "The application should be rejected based on Reasons 2 and 3 described in the notification of reasons for refusal issued on May 24, 2016," and the "Reasons 2 and 3" described of reasons for refusal are as follows.

"2. (enablement requirements) For the following reasons, the detailed description of the invention of this application does not meet the requirement stipulated in Article 36(4)(i) of the Patent Act.
3. (support requirements) For the following reasons, the claimed invention of this application does not meet the requirement stipulated in Article 36(6)(i) of the Patent Act.

Note

(...Omitted...)
* Regarding Reason 2 (enablement requirements) and Reason 3 (support requirements)

- Claims 1 to 10

The inventions according to Claims 1 to 10 are regarded as inventions relating to medicinal use of a compound of Formula (I).

However, regarding a pharmacological test supporting the medicinal use, although methods for the pharmacological test are described in Examples 5 and 6 in the detailed description of the invention (paragraphs [0287] to [0298]), the result of pharmacological test is not specifically disclosed.

Meanwhile, in the field of pharmaceutical compounds, it is difficult in common general technical knowledge to predict pharmacological effect of a compound from only a structure of the compound, and there is no explanation in the detailed description of the invention based on technical evidence of a relationship between a structure of the compound of Formula (I) and therapeutic activity in dry age-related macular degeneration, and it cannot be said that use of the compound as an agent for treating dry age-related macular degeneration can be predicted with common general technical knowledge at the time of filing the application, and thus it cannot be said that use of the compound as the therapeutic agent is described in the detailed description of the invention.

Thus, it cannot be said that the detailed description of the invention of the application is clear and sufficient to enable a person skilled in the art to carry out the inventions according to the claims.

In addition, taking into account the detailed description of the invention and common general technical knowledge, it cannot be said that the detailed description of the invention of the application can be understood by a person skilled in the art such that the problem of the invention to provide a compound of Formula (I) as an agent for treating dry age-related macular degeneration is to be solved.

Therefore, since the claimed inventions are beyond the range supported by the detailed description of the invention, it cannot be said that the claimed inventions are described in the detailed description of the invention."

3. Judgment by the body

As described in the reasons for refusal stated in the examiner's decision, since the detailed description of the invention is not clear and sufficient to enable a person skilled in the art to carry out the Invention, the detailed description of the invention does not comply with provision of Article 36(4)(i) of the Patent Act, and since the Invention is not described in the detailed description of the invention, the claimed invention does not comply with the provision of Article 36(6)(i) of the Patent Act. Thus, the application should be rejected.

The reasons are as follows.

The Invention does not include the matters that "the dry age-related macular degeneration (AMD) is diagnosed by detecting one or more of autofluorescent structures in the retinal pigment epithelium (RPE)," which is the matters specifying the Amended Invention, and it is obvious that the Invention includes a method "wherein the dry age-related macular degeneration (AMD) is diagnosed by detecting one or more of autofluorescent structures in the retinal pigment epithelium (RPE)."

In addition, as described in the above "No. 2 2. (2)," the detailed description of the invention is not clear and sufficient to enable a person skilled in the art to carry out the Amended Invention, and based on a similar reason, the detailed description of the invention is not clear and sufficient to enable a person skilled in the art to carry out the Invention, and thus the detailed description of the invention does not comply with the

provision of Article 36(4)(i) of the Patent Act.

Further, as described in the above "No. 2 2. (3)," the Amended Invention is not described in the detailed description of the invention, and based on a similar reason, the Invention is not described in the detailed description of the invention, and thus the claimed invention does not comply with the provision of Article 36(6)(i) of the Patent Act.

No. 4 Closing

As described above, the application should be rejected, since the detailed description of the invention does not comply with provision of Article 36(4)(i) of the Patent Act, and the claimed invention does not comply with the provision of Article 36(6)(i) of the Patent Act.

Therefore, the appeal decision shall be made as described in the conclusion.

September 11, 2017

Chief administrative judge: NAITO, Shinichi

Administrative judge: INOUE, Chiyako

Administrative judge: ASANO, Mina