

18-02987-E

March 5 2018

US Securities & Exchange Commission
Office of FOIA and Privacy Act Operations
100 F Street, NE Mail Stop 5100
Washington, DC 20549-5100



Dear FOIA Office:

Under the Freedom of Information Act (FOIA), please send a copy of the following:

A copy of: Exhibit 10.1 to the form 8-K/A filed by ISTA PHARMACEUTICALS INC on December 28, 2004

In the event confidential treatment has not expired provide the specific date for which confidential treatment is still in effect. I do not need a copy of the order. We authorize up to \$61.00 in processing fees. Thank You,

Paul D'Souza
Managing Editor - Deals

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Phone: +44-2074334789
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
STATION PLACE
100 F STREET, NE
WASHINGTON, DC 20549-2465

Office of FOIA Services

April 25, 2018

Mr. Paul D'Souza
Clarivate Analytics
160 Blackfriars Road
London, UK SE18EZ

RE: Freedom of Information Act (FOIA), 5 U.S.C. § 552
Request No. 18-02987-E

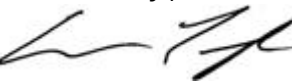
Dear Mr. D'Souza:

This letter is in response to your request, dated and received in this office on March 05, 2018, for Exhibit 10.1 to the form 8-K/A filed by Ista Pharmaceuticals, Inc., on December 28, 2004.

The search for responsive records has resulted in the retrieval of 26 pages of records that may be responsive to your request. They are being provided to you with this letter.

If you have any questions, please contact me at johnsonee@sec.gov or (202) 551-8350. You may also contact me at foiapa@sec.gov or (202) 551-7900. You also have the right to seek assistance from Aaron Taylor at (202) 551-7900 as a FOIA Public Liaison for this office, or contact the Office of Government Information Services (OGIS) for dispute resolution services. OGIS can be reached at 1-877-684-6448 or Archives.gov or via e-mail at ogis@nara.gov.

Sincerely,

For 

Everene Johnson
FOIA Research Specialist

Enclosure

LICENSE AGREEMENT

This LICENSE AGREEMENT (hereinafter called this "License Agreement") is made and effective as of the 17th day of November, 2004 by and between:

SENJU Pharmaceutical Co., Ltd., a legal entity duly organized and existing under the laws of Japan, having its principal office of business at 5-8, Hiranomachi 2-chome, Chuo-ku, Osaka 541-0046, Japan (hereinafter called "SENJU") and;

ISTA Pharmaceuticals, Inc., a legal entity duly organized and existing under the laws of Delaware, having its principal office of business at 15279 Alton Parkway, Suite 100, Irvine, CA 92618, U.S.A. (hereinafter called "ISTA");

WITNESSETH THAT;

WHEREAS, SENJU is an exclusive licensee, in certain countries or areas of the world including U.S.A., of certain rights to the human ophthalmic pharmaceutical specialty ecabet sodium in topical preparations for topical ophthalmic applications by way of an agreement (*Kaigaimuke Raisennsu Keiyaku*) entered into as of March 6, 2002 (revised as of August 26, 2004) by and between SENJU on one hand; and Tanabe Seiyaku Co., Ltd., a Japanese corporation having its principal place of business at 2-10, Dosho-machi 3-chome, Chuo-ku, Osaka 541-8505, Japan (hereinafter referred to as "TANABE") on the other hand (hereinafter referred to as "SENJU-TANABE License Agreement"); and

WHEREAS, SENJU has a sub-license right under the SENJU-TANABE License Agreement and desires to grant ISTA a license to develop, manufacture and sell topical ophthalmic formulations of ecabet sodium in ISTA Territory as hereinafter defined, according to the terms and conditions set forth herein and ISTA wishes to receive such license.

NOW THEREFORE, in consideration of the foregoing, the mutual covenants contained herein and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, SENJU and ISTA (SENJU and ISTA collectively called "Parties" and/or individually called "Party") hereby agree as follows:

Article 1. - Definitions

The following terms used in this License Agreement shall have the meanings set forth in this Article 1 unless the context clearly requires otherwise, and the singular shall include the plural and vice versa.

1.01 "Compound" shall mean a certain chemical compound having its chemical structure of (+)-(1R,4aS,10aR)-1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-6-sulfo-1-phenanthrenecarboxylic acid 6-sodium salt pentahydrate, which is commonly named ecabet sodium.

1.02 "Development Activity" shall mean ISTA's activities to perform all tests, studies, and other activities necessary to develop the Preparation and obtain and maintain Government Approval of the Preparation in ISTA Territory.

1.03 “Effective Date” shall mean the date first above written on which this License Agreement shall become effective.

1.04 “First Commercialization” shall mean the date of the first commercial sale by ISTA or ISTA Marketing Agent of the Preparation in commercial quantities to a Third Party in ISTA Territory under this License Agreement.

1.05 “Governmental Approval” shall mean any kind of approvals by USFDA (U. S. Food and Drug Administration) or equivalent future governmental authority, necessary to commercialize the Preparation in ISTA Territory, including, without limitation, any approvals necessary for the manufacture, distribution, and sale of the Preparation in ISTA Territory.

1.06 “ISTA Developer” shall mean any developer appointed by ISTA who develops the Preparation in ISTA Territory on behalf of ISTA.

1.07 “ISTA Manufacturer” shall mean any manufacturer appointed by ISTA who manufactures the Preparation in ISTA Territory on behalf of ISTA.

1.08 “ISTA Marketing Agent” shall mean any agent or other party appointed by ISTA who sells, markets, distributes, promotes and offers to sell the Preparation in ISTA Territory on behalf of ISTA.

1.09 “ISTA Trademark” shall mean trademark to be used by ISTA in connection with the marketing of the Preparation in ISTA Territory other than **TANABE** Trademark.

1.10 “ISTA Technical Information & Know-How” shall mean any Technical Information & Know-How owned or controlled by ISTA.

1.11 “ISTA Territory” shall mean United States of America as well as Puerto Rico, Guam, the U.S. Virgin Islands and any other U.S. territories and possessions.

1.12 “Net Sales” shall mean the gross invoiced amount charged by ISTA or ISTA Marketing Agent to sell the Preparation to Third Parties in ISTA Territory less (a) all normal and customary deductions of any type or nature (such as, e.g., returns, credits, refunds, discounts, allowances, rebates, chargebacks and adjustments); and (b) freight, shipping, insurance costs, customs, duties, taxes and other governmental charges and surcharges imposed upon the sale or distribution of the Preparation. Net Sales shall be determined in accordance with generally accepted accounting principles in ISTA Territory, applied on a basis consistent with ISTA’s annual audited financial statements, with interim Net Sales calculations in any year subject to adjustment pending completion of ISTA’s annual audit for that year.

1.13 “Patent Rights” shall mean U.S. Patent No. 5,830,913, reissues, re-examinations, and any patent term extensions thereto.

1.14 “Preparation” shall mean any pharmaceutical product for human use containing the Compound as an active ingredient in topical ophthalmic form (i) having a stimulating action of mucin secretion or (ii) for the treatment of (A) cornea or conjunctival diseases or disorders or (B) dry eye syndrome or any other ophthalmic diseases or disorders caused from dry eye syndrome.

1.15 “Secrecy Agreement” shall mean the secrecy agreement dated November 19, 2003 between SENJU and ISTA on the Preparation and letter agreement dated February 18, 2004 from SENJU to ISTA.

1.16 “SENJU Licensee” shall mean a third party who will be granted by SENJU to develop, manufacture, use, market and sell the Preparation outside ISTA Territory.

1.17 “SENJU Technical Information & Know-How” shall mean any Technical Information & Know-How owned or controlled by SENJU, or by SENJU and TANABE jointly and licensed to SENJU under SENJU-TANABE License Agreement. SENJU Technical Information & Know-How shall include any and all technical information and know-how disclosed by SENJU to ISTA under Secrecy Agreement.

1.18 “Senju Territory” shall mean the any and all countries or areas throughout the world, which are not included in ISTA Territory and TANABE Territory.

1.19 “Semi-Annual Period” shall mean each of the six (6) months period commencing April 1st and October 1st and ending respectively on the following September 30th and March 31st. And, “Financial Year” shall be the twelve months period from April 1st to March 31st.

1.20 “Subsidiary” shall mean any legal entity which, whether de jure or de facto, directly or indirectly owns, is owned by or is under common ownership with SENJU, ISTA or TANABE, respectively, to the extent of at least more than fifty percent (50%) of the equity (or such lesser percentage which is the maximum allowed to be owned by a foreign corporation in a particular jurisdiction) having the power to vote on or direct the affairs of the entity and any person, firm, partnership, corporation, or other entity actually controlled by, controlling or under common control with SENJU, ISTA or TANABE, respectively.

1.21 “TANABE Licensee” shall mean third party who is granted the right now or hereafter will be granted by TANABE the right to develop, manufacture, use, market and sell the Preparation outside the SENJU and ISTA Territories.

1.22 “TANABE Territory” shall mean People’s Republic of China (including Hong Kong and Macao), Republic of China, Republic of Korea, Democratic People’s Republic of Korea, Republic of Indonesia, Republic of Philippines, Islamic Republic of Pakistan, Kingdom of Thailand, India, Malaysia, Socialist Republic of Viet Nam, Union of Myanmar, Kingdom of Cambodia, Democratic Socialist Republic of Sri Lanka, People’s Republic of Bangladesh and Republic of Singapore.

1.23 “TANABE Trademark” shall mean trademark to be registered by TANABE in ISTA Territory corresponding to the trademark registered in Japan that TANABE now or hereafter owns, controls and offers ISTA to use for the Preparation and ISTA selects and desires to use for the commercialization of the Preparation in ISTA Territory.

1.24 “Technical Information & Know-How” shall mean any and all technical information and know-how which relates to the Preparation or the Compound, which is necessary or useful for the practice of the Patent Rights, including without limitation, the development of the Preparation, obtaining Government Approval and manufacture and sale of the Preparation in ISTA Territory.

1.25 “Third Party” shall mean any party other than SENJU, SENJU-Licensee, SENJU Subsidiary, ISTA, ISTA Manufacturer, ISTA Developer, ISTA Marketing Agent, **TANABE, TANABE Licensee and TANABE Subsidiary.**

Article 2. - Grant

2.01 SENJU hereby shall grant by way of sub-license and license to ISTA, and ISTA shall hereby accept, a sole and exclusive, running royalty-bearing license under the Patent Rights and the SENJU Technical Information & Know-How to make, have made, offer to provide and provide, develop, manufacture, use, market, sell and offer to sell the Preparation in ISTA Territory. Except as provided in Paragraph 2.02 below, the license granted to ISTA herein shall not include the right to grant further licenses to any Third Party or to any SENJU Licensee, SENJU Subsidiary, ISTA Developer, ISTA Manufacturer, ISTA Marketing Agent, **TANABE, TANABE Subsidiary and TANABE Licensee.** SENJU hereby represents that it has the full right and authority to enter into this License Agreement, to grant the licenses provided herein and to perform its obligations hereunder. In addition, SENJU shall be responsible for the complete performance of all obligations of SENJU Licensee, SENJU Subsidiary, **TANABE, TANABE Licensee and TANABE Subsidiary** described hereunder.

2.02 ISTA’s license granted under Paragraph 2.01 of this License Agreement shall include the right to appoint ISTA Developers and ISTA Manufacturers to practice or use the Patent Rights and the SENJU Technical Information & Know-How to develop and manufacture, respectively, the Preparation on behalf of ISTA and ISTA Marketing Agents to sell, market, distribute, promote and offer to sell the Preparation on behalf of ISTA in ISTA Territory. ISTA hereby acknowledges and confirms that by appointing ISTA Developer, ISTA Manufacturer and ISTA Marketing Agent to develop, manufacture, market, sell and offer to sell the Preparation hereunder it shall not be released from any of its contractual obligations under this License Agreement and that it shall remain fully responsible for the complete performance of such obligations under this License Agreement. Promptly after the Effective Date and from time to time if ISTA renews, ISTA shall provide SENJU with a list of each existing and currently proposed ISTA Developer, ISTA Manufacturer and ISTA Marketing Agent, for SENJU’s approval. Any such list submitted by ISTA shall be deemed approved by SENJU **fifteen (15) days** after its submission, unless ISTA receives from SENJU written objections to such list within such **fifteen (15) day** period, in which case, the list will not be approved by SENJU only to the extent of such objections.

2.03 SENJU agrees that during the term of this License Agreement, SENJU, SENJU Licensee, SENJU Subsidiary, **TANABE, TANABE Licensee or TANABE Subsidiary** shall not, directly or indirectly (a) develop the Preparation for use or sale in ISTA Territory or manufacture, use, offer to sell, market, distribute, or sell the Preparation for commercial purpose in ISTA Territory or (b) grant any license to the Patent Rights or the Technical Information and Know-How in ISTA Territory that would entitle any Third Party to develop, manufacture, use, offer to sell, market, distribute or sell during the term of this License Agreement, any product utilizing the Patent Rights or SENJU Technical Information and Know-How in ISTA Territory. Provided, however, that SENJU shall retain the right to develop, have developed, make, have made the Preparation in ISTA Territory for the sole purpose of commercialization of the Preparation outside ISTA Territory.

2.04 Prior to the first administration of the Preparation in ISTA Territory to a human in accordance with this License Agreement, and for a period during the commercialization of the Preparation by ISTA, ISTA shall obtain and/or maintain, at its sole cost and responsibility, product

liability insurance in an amount known in the pharmaceutical industry to be reasonably sufficient to meaningfully protect SENJU and **TANABE** consistent with ISTA's indemnification obligations hereunder. Such product liability insurance shall insure against all liability for personal injury, physical injury and property damage, subject to the scope and limits customarily required of such insurance. ISTA shall, upon SENJU's request, submit the evidence of the existence and sufficiency of any and all such product liability insurance to SENJU.

Article 3. Technical Information & Know-How

3.01 Immediately after Effective Date, SENJU agrees to provide ISTA with a listing of all documentation of SENJU Technical Information & Know-How and SENJU Technical Information & Know-How already translated into English language, and with copies of any and all patents and patent applications, now owned or controlled by SENJU as of the Effective Date covering the Patent Rights or SENJU Technical Information & Know-How, including all patent office actions received and amendments filed, if any, relative thereto. During the term of this License Agreement, SENJU agrees to continue to provide ISTA with any additional SENJU Technical Information & Know-How and patents and patent applications as described above, hereafter owned or controlled by SENJU after the Effective Date, promptly after SENJU's receipt thereof. The list of SENJU Technical Information & Know-How shall be renewed by SENJU and provided to ISTA whenever SENJU Technical Information & Know-How, which did not appear on a former list, is available to SENJU and hereafter owned or controlled by SENJU. From time to time during the term of this License Agreement and if ISTA desires access to SENJU Technical Information & Know-How written in Japanese language which is appearing on the list, SENJU agrees to translate such SENJU Technical Information & Know-How into English language under its sole expense and responsibility and provide ISTA with it at the timing discussed and agreed between SENJU and ISTA. SENJU Technical Information & Know-How translated into English language shall be certified as being an accurate translation of the original document, if requested by ISTA. SENJU Technical Information & Know-How provided by SENJU to ISTA shall include information in possession of or under the control of SENJU, which is necessary or useful for the practice of the Patent Rights and for the Development Activities and obtaining the Governmental Approval.

3.02 From time to time during the term of this License Agreement, and subject to the terms hereof (including without limitation Article 15), the Parties shall exchange Technical Information & Know-How which has not been provided to the other Party concerning any new finding relevant to the safety, efficacy, dosage formulation and new indications of the Preparation when they become available to either Party (including any process improvements which relate solely to the Preparation) (hereinafter called "Improvements"). SENJU shall provide **TANABE** with the Improvements provided by ISTA.

3.03 SENJU may freely, use or have SENJU Licensee, SENJU Subsidiary, **TANABE, TANABE Licensee and TANABE Subsidiary** use, without compensation to ISTA, Improvements made by ISTA under Paragraph 3.02 for any purpose in any countries outside ISTA Territory. Provided, however, that if the Improvement is a patentable new invention or discovery, such Improvement shall be subject to Article 15. ISTA may freely use or have ISTA Developer, ISTA Manufacturer and ISTA Marketing Agent use, without compensation to SENJU, all Improvements made by SENJU under Paragraph 3.02 for the Preparation in ISTA Territory. Provided, however, that if the Improvement is patentable new invention or discovery, such Improvement shall be subject to Article 15.

3.04 SENJU shall supply, free of charge, ISTA with a reasonable quantity of the Compound necessary for the Development Activities and obtaining Governmental Approval by ISTA. The quantity to be supplied by SENJU to ISTA under this Paragraph 3.04 shall be discussed and decided by SENJU and ISTA.

3.05 SENJU agrees and acknowledges that TANABE or TANABE's contract manufacturer of the Compound shall have USFDA make reference to the "Drug Master File" filed by TANABE or the contract manufacturer for the sole purpose of obtaining Governmental Approval by ISTA in ISTA Territory, provided, however that ISTA shall not receive a copy of said Drug Master File, except as provided in Paragraph 3.01. SENJU shall have TANABE not withdraw "Drug Master File" without prior written approval of SENJU.

3.06 Notwithstanding any other provision of this License Agreement, including but not limited to Articles 3, 4, 10, 12 and 15, ISTA shall disclose, provide and/or grant rights in any Improvement, Technical Information & Know How, Information, invention, intellectual property right, confidential information, or other right or information to SENJU for its benefit or the benefit of TANABE or their respective Licensees or Subsidiaries as obligated under this License Agreement, only to the extent ISTA has the absolute right to do so without liability or cost to ISTA. ISTA shall use commercially reasonable efforts to secure such rights from each ISTA Developer, ISTA Manufacturer and ISTA Marketing Agent but ISTA makes no guarantee that it will be able to secure such rights. Any inability of ISTA to secure such rights shall not be deemed a breach by ISTA of this License Agreement or a basis for termination by SENJU of this License Agreement.

Article 4. - Development Activities and Governmental Approvals

4.01 Soon after the Effective Date, ISTA shall provide SENJU with a development plan and schedule of the Preparation in ISTA Territory ("Development Plan and Schedule") for SENJU's review and comment. SENJU shall provide TANABE with the Development Plan and Schedule. SENJU shall provide ISTA with SENJU's comments and advice. ISTA shall take SENJU's comments and advice into consideration, for the Development Activities. In the event that ISTA renews or updates the Development Plan and Schedule, above procedure shall be applied.

4.02 ISTA shall conduct promptly, at its own expenses and responsibility, the Development Activities in accordance with Development Plan and Schedule, and shall secure and maintain Governmental Approval as may be necessary with respect to the sale of the Preparation. Governmental Approval shall be in ISTA's name and owned by ISTA, under its own expenses and responsibility. Provided, however, that nothing herein shall constitute a guarantee or warranty of ISTA that it will obtain any Governmental Approval or that it will have any degree of success in the development or commercialization of the Preparation in ISTA Territory.

4.03 Notwithstanding anything else to the contrary stated herein, in the event that Development Activities are delayed from the Development Schedule due to ISTA's complete omission and gross negligence, SENJU shall have a right to notify ISTA thereof and if ISTA fails to remedy the situation in all material respects within thirty (30) days after receiving SENJU's notice then SENJU shall have a right, upon notice to ISTA, to terminate this License Agreement without any remaining obligations between SENJU and ISTA. Notwithstanding anything herein to the contrary except for the case of Paragraph 17.03 (i), SENJU's right to terminate this License Agreement as provided above shall be its sole and exclusive remedy, whether in contract, by statute or otherwise, for any delay or lack of

efforts in the Development Schedule or any failure of ISTA with respect to any of the Development Activities.

4.04 From time to time during the term of this License Agreement and upon the request of SENJU, ISTA shall provide SENJU with the written report concerning the progress of Development Activities and procedure of obtaining the Governmental Approval. Further ISTA shall promptly notify SENJU upon obtaining the Governmental Approval. SENJU shall provide **TANABE** with these reports provided by ISTA under this Paragraph 4.04.

4.05 Upon the request of SENJU, ISTA shall provide SENJU with any and all copies of New Drug Application Dossier submitted to U. S. Food and Drug Administration for obtaining the Governmental Approval and copy of certificate of Governmental Approval. ISTA agrees and acknowledges that SENJU, SENJU Licensee, SENJU Subsidiary, **TANABE, TANABE Subsidiary and Tanabe Licensee** shall have the right to use such copies of New Drug Application Dossier and copy of certificate of Governmental Approval for the sole purpose of development, manufacture, obtaining the governmental approval and sale of the Preparation outside ISTA Territory, without any compensation to ISTA.

Article 5. - Marketing

5.01 Within **six (6) months** from when the Governmental Approval has been obtained, ISTA shall use commercially reasonable efforts to launch the Preparation in ISTA Territory as soon as possible and thereafter, use its commercially reasonable efforts to promote and sell the Preparation in ISTA Territory.

5.02 ISTA shall furnish SENJU with a copy of the package inserts of the Preparation prepared for use in ISTA Territory, and thereafter, any revised version thereof.

5.03 ISTA shall prepare, at its own costs and expenses, appropriate marketing, advertising and promotional material for the Preparation in ISTA Territory. ISTA shall furnish SENJU with those materials for SENJU's review.

5.04 Alliance indication to the bottle, outer package, brochure, insert leaflet, advertising and/or promotional materials shall be discussed and decided between SENJU and ISTA; provided that, ISTA may use any alliance indication required by law.

5.05 Starting at least **two (2) months before** the occurrence of First Commercialization, ISTA shall submit to SENJU a sales forecast of the Preparation made around the time of the First Commercialization covering the next **five (5) Financial Years** after the **Financial Year** of the First Commercialization, addressing each subsequent Financial Year separately, including a forecast of a sales peak of the Preparation and its timing, for SENJU review and approval. Any sales forecast submitted by ISTA shall be deemed approved by SENJU **fifteen (15) days** after its submission, unless ISTA receives from SENJU written objections to such forecast within such **fifteen (15) day** period. If SENJU disagrees with ISTA's sales forecast within the aforementioned **fifteen (15) day** period, SENJU and ISTA shall have an independent market research agent, which is acceptable to SENJU and ISTA, calculate the sales forecast for such **five (5) Financial Years** after the **Financial Year** of the First Commercialization. ISTA and SENJU shall bear equally the cost of such market research agent. SENJU and ISTA agree and acknowledge that the sales forecast submitted by ISTA or, if SENJU objects to ISTA's sales forecast, the sales forecast calculated by such independent

market research agent, will be subject to minimum annual sales forecast for calculation of minimum royalties under Paragraph 8.03.

5.06 Should ISTA's actual sales amount of the Preparation be far below the then existing sales forecast adopted by the Parties due to the occurrence of an unexpected event, a material change in the market or the Preparation's prospects, SENJU and ISTA will meet to discuss the modification of such sales forecast. In the event that ISTA and SENJU fail to reach an agreement for the modification of such sales forecast within **thirty (30) days** from the commencement of the discussion between SENJU and ISTA, ISTA and SENJU will refer the matter to an independent market research agent, which is acceptable to SENJU and ISTA, to recalculate the sales forecast, on a timely basis, taking into consideration, among other things, the unexpected event, material change in the market, the Preparation's prospects and other relevant factors. ISTA and SENJU shall bear equally the cost of such market research agent. SENJU and ISTA agree and acknowledge that the revised sales forecast agreed to by ISTA and SENJU or, if the Parties fail to agree, the revised sales forecast calculated by such independent market research agent, will supercede any prior sale forecast and will be the basis for calculation of minimum royalties under Paragraph 8.03 (until another sales forecast is adopted by the Parties pursuant to this Paragraph 5.06). Pending the Parties agreement to a revised sales forecast or, if the Parties fail to agree, the submission by the independent market research agent of its revised sales forecast, ISTA will continue to pay minimum royalties under Paragraph 8.03 calculated based on the last sales forecast adopted by the Parties.

Article 6. - Trademark

6.01 If and when SENJU and ISTA discuss the trademark to be used in connection with the marketing of the Preparation by ISTA, SENJU shall submit to ISTA, a list of **TANABE** Trademarks for ISTA's selection. ISTA shall have the right, at its option but not obligation, to use the **TANABE** Trademark subject to the royalty obligation in accordance with Paragraph 8.01(ii) (b). If ISTA decides to use **TANABE** Trademark, SENJU shall have **TANABE**, at **TANABE**'s cost and risk, file to obtain the registration of the **TANABE** Trademark in ISTA Territory, and thereafter shall have **TANABE** maintain the **TANABE** Trademark in ISTA Territory. ISTA agrees that in using **TANABE**'s Trademark upon the Preparation, it will not represent in any way that it has any right or title to the ownership of **TANABE** Trademark or the registration thereof, and the registration will remain in the ownership of **TANABE**.

6.02 Notwithstanding Paragraph 6.01, ISTA shall have the right, to select the ISTA Trademark to be used in connection with the marketing of the Preparation by ISTA in ISTA Territory subject to obtaining prior written approval of SENJU, such approval not to be unreasonably withheld. In this case, ISTA shall, at its sole cost and risk, and at its option (after discussion with SENJU), file to obtain the registration of the ISTA Trademark in ISTA Territory, and thereafter maintain the ISTA Trademark in ISTA Territory. Any ISTA Trademark submitted by ISTA to SENJU for use in ISTA Territory shall be deemed approved by SENJU **fifteen (15) business days** after its submission, unless ISTA receives from SENJU written objection to such ISTA Trademark within such **fifteen (15) day** period.

6.03 In the event that SENJU, SENJU Licensee, SENJU Subsidiary, **TANABE, TANABE Licensee and/or TANABE Subsidiary** desire to use ISTA Trademark in certain countries or areas outside ISTA Territory, ISTA shall discuss with SENJU and/or **TANABE** for their use of the language corresponding to ISTA Trademark in such countries or areas and the form of compensation to ISTA and other license terms for such use.

Article 7. - Compensation

7.01 In consideration of SENJU's grant of the exclusive license in ISTA Territory in accordance with Article 2 hereof, ISTA shall, during the term of this License Agreement, pay SENJU the following milestone payments:

<i>Milestone:</i>	<i>Amount of Payment due:</i>
(i) The Effective Date of this Agreement	U.S. \$1,000,000.00
(ii) ISTA's commencement of a Phase III clinical trials for the Preparation, commencement being first patient dosing	U.S. \$1,000,000.00
(iii) The acceptance for filing by the FDA of ISTA's New Drug Application ("NDA") for the Preparation	U.S. \$1,000,000.00

7.02 Unless otherwise provided herein, no milestone payments to SENJU under this License Agreement shall be refundable in whole or in part. Each of the foregoing milestone payments shall be payable one time only, even if the milestone is met on more than one occasion. Each milestone payment shall be due and payable by ISTA within **fifteen (15) days** of completion of the applicable milestone.

Article 8. - Royalties

8.01 In consideration of the rights granted under this License Agreement, and subject to the terms hereof, ISTA shall pay SENJU as running royalties during the term of the License Agreement the royalties set forth in Paragraphs 8.01(i) and (ii) below; provided that, the price of the Compound purchase by ISTA under Article 11 shall be credited against such royalties:

(i) For ten (10) years from First Commercialization or until the date of the last valid claim to expire under U.S. Patent No. 5,830,913, whichever is longer (hereinafter "Initial Period of Term"), ISTA shall pay SENJU running royalties of **twenty percent (20%)** of the Net Sales of the Preparation in ISTA Territory. Notwithstanding the foregoing, if the Net Sales in any Financial Year **decreases** more than **twenty percent (20%)** compared to the preceding Financial Year due to the commercialization of a generic product of the Preparation in ISTA Territory (hereinafter called "**Decreasing Year of Net Sales**"), then the running royalty rate during the Initial Period of Term shall be immediately **reduced to ten percent (10%)**, provided, however, that if Net Sales in any year during Initial Period of Term **recovers** from **Decreasing Year of Net Sales** by **twenty percent (20%)**, running royalty rate during remaining term for Initial Period of Term shall be re-applied to **twenty percent (20%)**, subject to additional adjustments from time to time as provided above.

(ii) In addition, beginning the day following Initial Period of Term (i.e., the day after ten (10) years after First Commercialization or the date of the last valid claim to expire under U.S. Patent No. 5,830,913, whichever is longer), ISTA shall pay SENJU running royalties of:

(a) Six percent (6%) of Net Sales of the Preparation in ISTA Territory for five (5) years and, thereafter for an additional five (5) years, three percent (3%) of Net Sales of the Preparation in ISTA Territory, provided that ISTA uses a ISTA Trademark for the marketing of the Preparation in ISTA Territory,

or;

(b) Six percent (6%) of Net Sales of the Preparation in ISTA Territory for five (5) years and, thereafter, three percent (3%) of Net Sales of the Preparation in ISTA Territory for so long as ISTA uses the TANABE Trademarks for the marketing of the Preparation in ISTA Territory.

8.02 No multiple running royalty will be payable even if the Preparation, its manufacture, use or sale, are or will be covered by more than one claim or patent.

8.03 For five (5) years, starting in the Financial Year following the Financial Year of First Commercialization in ISTA Territory, during the term of this Agreement and subject to timely and adequate supply of Compound, ISTA shall pay minimum annual royalties based on royalties due on forty (40%) of each sales forecast under Paragraph 5.05. Minimum annual royalties shall be paid with the first Semi-Annual Period royalty for each applicable Financial Year should running royalties for a Financial Year not exceed the applicable minimum royalty obligation.

8.04 All of the running royalties shall be paid to SENJU within thirty (30) days following the end of each Semi-Annual Period according to Financial Year. Namely, ISTA shall pay to SENJU the royalty arising from the period of April 1 through September 30 by October 30 of the same year and shall pay the royalty arising from the period of October 1 through March 31 of the next year by April 30 of the next year.

8.05 Unless otherwise expressly provided herein, no running royalty payment to SENJU under this License Agreement shall be refundable in whole or in part except for the case of overpayment.

Article 9. - Payments and Records

9.01 Within thirty (30) days after each Semi-Annual Period, ISTA shall furnish SENJU with an accurate report stating the total quantity of the Preparation in units sold by ISTA and ISTA Marketing Agent during the preceding Semi-Annual Period, the gross invoiced sales price and the Net Sales thereof and amount of the royalties accrued. SENJU shall provide TANABE with such report.

9.02 ISTA shall make and keep true and accurate records of the production and sales of the Preparation by ISTA, ISTA Manufacturer and ISTA Marketing Agent.

9.03 SENJU shall have the right to inspect the records prepared and kept in accordance with Paragraph 9.02 above. This inspection shall be carried out by a certified public accountant designated by SENJU, and reasonably acceptable to ISTA, on a confidential basis, for the sole purpose of verifying the accuracy of ISTA running royalty payments for all or any portion of a period not exceeding three (3) years prior to the date of the last running royalty payment. This inspection shall be carried out during usual business hours at ISTA's appropriate facility. The fees and expenses of the accountants performing such inspection shall be borne by SENJU, as the case may

be, unless any amount actually due exceed **five percent (5%)** or more of amounts reported, in which case ISTA shall bear the costs and expenses of such inspection.

9.04 ISTA shall not have any obligation to keep the records kept pursuant to Paragraph 9.02 for more than **three (3) years** from the date of a given running royalty payment.

9.05 Any payment from ISTA to SENJU under this License Agreement shall be remitted to the bank account designated by SENJU.

Article 10. Exchange of Information/Reports

10.01 From time to time during the term of this License Agreement, Parties shall exchange clinical and commercial information concerning the Preparation which is deemed useful for the sale and marketing of the Preparation. Furthermore, each Party shall notify the other of any important regulatory advices or instructions which come to either Party's attention during the term of this License Agreement concerning quality, safety, efficacy of Compound and/or Preparation. SENJU shall provide **TANABE** with such information and regulatory advices or instructions.

10.02 As long as ISTA develops and commercializes the Preparation in ISTA Territory, SENJU and ISTA shall exchange the information concerning any findings associated with the use of the Preparation that may suggest significant hazards, contraindications, side effect or precautions pertinent to the safety of the Preparation. The detailed procedure to exchange such information shall be set forth in a memorandum otherwise executed between SENJU and ISTA.

Article 11. -Availability of the Compound

11.01 During the term of this License Agreement after completing the Development Activities and obtaining Governmental Approval of the Preparation, SENJU will supply and ISTA will purchase the Compound from SENJU for commercial manufacture of the Preparation, as set forth in a separately executed supply agreement between SENJU and ISTA (hereinafter called "Supply Agreement").

11.02 The price of the Compound supplied by SENJU to ISTA under the Supply Agreement for manufacture of commercial Preparation will be below **one thousand United States Dollars (US\$1,000)** per kilogram.

11.03 The price of the Compound supplied by SENJU to ISTA under the Supply Agreement for manufacture of Promotional Sample of the Preparation will be **fifty percent (50%)** of the price for manufacture of commercial Preparation set forth in Paragraph 11.02, with the maximum annual volume of **five hundred kilo grams (500kg)** provided for such Promotional Samples of the Preparation. The price of the Compound for manufacture of Promotional Sample of the Preparation exceeding **five hundred kilo grams (500kg)** on an annual basis shall apply to the price of the Compound for manufacture of commercial Preparation set forth in the Supply Agreement subject to Paragraph 11.02. "Promotional Sample of the Preparation" shall mean the Preparation that ISTA or ISTA Marketing Agent provides the ophthalmologist, optometrist, pharmacist, managed care or wholesalers for promotional purpose of the Preparation, free of charge.

11.04 The prices of the Compound set forth in the Supply Agreement subject to Paragraph 11.02 and 11.03 may be changed, from time to time during the Supply Agreement, to reflect changes in

costs of manufacture of the Compound; provided that, the Compound's price shall not increase by more than fifteen (15%) in comparison with the previous Financial Year.

11.05 ISTA and SENJU shall monitor market prices from Third Parties of the Compound. If at any time during the term of this License Agreement, the price per kilogram of the Compound supplied by SENJU is twenty percent (20%) or more greater than the price per kilogram of the Compound available to ISTA from a Third Party, then SENJU shall use its reasonable efforts to reduce its Compound price to the Third Party price,.

11.06 ISTA shall be entitled to a credit on royalties due under Paragraphs 8.01(i) of the cost of the Compound purchased from SENJU by ISTA under the Supply Agreement for manufacture of commercial Preparation during each Semi-Annual Period that ISTA pays a royalty of twenty percent (20%) and no credit for the Compound shall be given for payment of less than twenty percent (20%) hereunder. For confirmation purpose, ISTA shall not be entitled to a credit on royalties due under Paragraph 8.01 (i) of the cost of the Compound purchased from SENJU by ISTA under the Supply Agreement subject to Paragraph 11.03 for manufacture of Promotional Sample of the Preparation.

Article 12. –Confidentiality

12.01 Parties hereto undertake to keep confidential all of the information and reports, materials, data and results of the investigation and so on regarding the Compound and/or the Preparation which is/are received from or provided by the other Party under this License Agreement and/or the Secrecy Agreement, and is/are marked or otherwise indicated that the same is/are confidential nature (hereinafter collectively called "Information" in this Article 12), provided, however, that such Information as itemized below shall be excluded from this confidentiality obligation:

- (i) Information which was at the time of disclosure in the public domain,
- (ii) Information which after the time of disclosure became a part of the public domain, through no fault or act of omission by the recipient Party,
- (iii) Information which was at the time of disclosure lawfully in the recipient's possession on a non-disclosure basis,
- (iv) Information received from any Third Party who has no obligation to keep the Information confidential against any of Parties hereto,
- (v) Information which both Parties hereto agree in writing to disclose to a Third Party or to make the same public, or
- (vi) Information which is independently developed by recipient Party without actual knowledge and use of the Information.

Provided, further, that the recipient Party shall have competent proof for proving the fact that the Information in question falls into the category of either one of the items herein above.

12.02 Notwithstanding the provision of Paragraph 12.01, ISTA may disclose the Information disclosed by SENJU to ISTA Developer, ISTA Manufacturer and ISTA Marketing Agent including ISTA's or their respective officers, employees, consultants or contract workers, engaging in any activity for the commercialization of the Preparation including clinical studies and other activities for

obtaining the Government Approval in ISTA Territory, so far as the disclosure is necessary for their performance of such activity, provided, however, that ISTA shall take any adequate measure to cause them to keep the information disclosed confidential under the same conditions provided in any provision of this License Agreement.

12.03 Notwithstanding the provision of Paragraph 12.01, SENJU may, in addition to the stipulations of Paragraph 4.04 and Paragraph 10.02, and subject to Article 15, disclose the Information disclosed by ISTA including the Information from ISTA Developer, ISTA Manufacturer and ISTA Marketing Agent, to SENJU Licensee, **TANABE, TANABE Licensee and TANABE Subsidiary** including their officers, employees, consultants or contract workers engaging in any activity for the commercialization of the Preparation including clinical studies and other activities for obtaining the governmental approval outside ISTA Territory or for obtaining patent rights including any patent application and prosecution of the patent application, so far as the disclosure is necessary for their performance of such activity, provided, however, that SENJU shall take any adequate measure to cause them to keep the Information disclosed confidential under the same conditions provided in this Article 12 of this License Agreement, and, provided further however, that SENJU shall, at ISTA's request and SENJU's agreement thereon, enter into a confidentiality agreement directly with ISTA Developer, ISTA Manufacturer, ISTA Marketing Agent with respect to such party's Information and if requested by such party, SENJU shall not disclose or use such party's Information except as permitted by such party.

12.04 Notwithstanding anything else to the contrary stated herein, ISTA agrees and acknowledges that SENJU shall have a right to disclose any and all part of this License Agreement to **TANABE**, subject to the confidentiality obligations contained in this Article 12.

12.05 Notwithstanding this Article 12, a Party (a "disclosing Party") may disclose the Information of the other Party (the "nondisclosing Party") in response to a valid order of a court or any governmental agency or regulatory body or as otherwise required by law or regulation or the requirements of the exchange or listing body on which a disclosing Party's securities are listed; provided that, the disclosing Party notifies the non-disclosing Party of such requirement so that the non-disclosing Party may seek a protective order or other appropriate remedy; and provided further that, in the event that no such protective order or other remedy is obtained, then the disclosing Party will furnish only that portion of the nondisclosing Party's Information which it is advised by counsel it is legally required to furnish and will exercise all reasonable efforts to obtain assurance that confidential treatment will be accorded the Information so furnished.

Article 13. – Publication

13.01 ISTA shall not, nor shall it permit ISTA Developer, ISTA Manufacturer and ISTA Marketing Agent to, submit for written or oral publication any manuscript, abstract or the like which includes data or other information relating to the Preparation or the Compound without first obtaining the prior written approval of SENJU, which shall not be unreasonably withheld. SENJU shall not, nor shall it permit SENJU Licensee or SENJU Subsidiary to, submit for written or oral publication any manuscript or the like which includes ISTA Technical Information & Know-How without first obtaining the prior written approval of ISTA, which shall not be unreasonably withheld.

Article 14. - Indemnification

14.01 ISTA shall defend, indemnify and hold SENJU and **TANABE**, their directors, officers, shareholders, employees, consultants, contract workers and assigns harmless from and against any lawsuit, claims, loss, damages or expenses (including attorney's fees) arising from the Development Activities or the manufacture, use or sale of the Preparation by ISTA, ISTA Developers, ISTA Manufacture or ISTA Marketing Agent in ISTA Territory.

14.02 SENJU shall defend, indemnify and hold ISTA and its directors, officers, shareholders, employees, consultants, contract workers and assigns harmless from and against any lawsuit, claims, loss, damages or expenses (including attorney's fees) arising from any breach by SENJU of this License Agreement or failure by SENJU to perform its obligations hereunder.

Article 15. - New Invention or Discovery

15.01 In the event that SENJU (including SENJU Licensee and SENJU Subsidiary) and ISTA (including ISTA Developer, ISTA Manufacturer and ISTA Marketing Agent) will jointly make, conceive, reduce into practice or generate any invention, discovery or know-how related to the Preparation in the course or as a result of their activities undertaken pursuant to this License Agreement (hereinafter called "SENJU-ISTA Joint Invention"), SENJU and ISTA agree and acknowledge the following:

(i) SENJU and ISTA shall discuss, and as decided, shall file a patent application claiming SENJU-ISTA Joint Invention and maintain the granted patent jointly under SENJU's and ISTA's name throughout the world, and the costs and expenses for the preparation, filing, prosecution of patent application and maintenance of granted patent shall be shared equally by SENJU and ISTA with SENJU responsible for clerical procedures of preparation, filing, prosecution of patent application and maintenance of granted patent outside ISTA Territory and ISTA responsible for clerical procedures of preparation, filing, prosecution of patent application and maintenance of granted patent in ISTA Territory, unless otherwise agreed between SENJU and ISTA;

(ii) ISTA shall have an exclusive right to use and otherwise practice SENJU-ISTA Joint Invention in ISTA Territory, SENJU shall be compensated for ISTA's use of SENJU-ISTA Joint Invention in ISTA Territory as long as ISTA pays the running royalty to SENJU under Paragraph 8.01;

(iii) SENJU shall have an exclusive right, with the right to sub-license, to use and otherwise practice SENJU-ISTA Joint Invention outside ISTA Territory, ISTA shall be compensated for SENJU's use of SENJU-ISTA Joint Invention during the term of this Agreement;

(iv) **TANABE** shall have perpetual, irrevocable, fully paid up exclusive right, with the right to sub-license, to use and otherwise practice SENJU-ISTA Joint Invention for any purpose in **TANABE** Territory;

(v) Each Party shall not transfer, license, dispose or withdraw its share of the patent application and granted patent claiming SENJU-ISTA Joint Invention under Paragraph 15.01, without prior written approval of the other Party.

15.02 In the event that SENJU (including SENJU Licensee and SENJU Subsidiary), ISTA (including ISTA Developer, ISTA Manufacturer and ISTA Marketing Agent) and TANABE (including TANABE Subsidiary) will jointly make, conceive, reduce into practice or generate any invention, discovery or know-how related to the Preparation in the course or as a result of their activities pursuant to this License Agreement or SENJU-TANABE License Agreement, respectively (hereinafter called "SENJU-ISTA-TANABE Joint Invention"), SENJU and ISTA agree and acknowledge following:

(i) SENJU, ISTA and TANABE shall discuss, and as decided, shall file a patent application claiming SENJU-ISTA-TANABE Joint Invention and maintain the granted patent jointly under SENJU's, ISTA's and TANABE's name throughout the world. The costs and expenses for preparation, filing, prosecution of patent application claiming SENJU-ISTA-TANABE Joint Invention and maintenance of granted patent shall be shared by SENJU, ISTA and TANABE, equally;

(ii) Clerical Procedures for preparation, filing, prosecution of patent application claiming SENJU-ISTA-TANABE Joint Invention and maintenance of granted patent shall be discussed and decided among SENJU, ISTA and TANABE;

(iii) ISTA shall have an exclusive right to use and otherwise practice SENJU-ISTA-TANABE Joint Invention in ISTA Territory, SENJU and TANABE shall be compensated for ISTA's use of SENJU-ISTA-TANABE Joint Invention in ISTA Territory as long as ISTA pays the running royalty to SENJU under Paragraph 8.01;

(iv) SENJU shall have an exclusive right, with the right to sub-license, to use and otherwise practice SENJU-ISTA-TANABE Joint Invention outside ISTA Territory, ISTA shall be compensated for SENJU's use of SENJU-ISTA-TANABE Joint Invention during the term of this Agreement;

(v) TANABE shall have perpetual, irrevocable, fully paid up exclusive right, with the right to sub-license, to use and otherwise practice SENJU-ISTA-TANABE Joint Invention for any purpose in TANABE Territory;

(vi) Each Party shall not, and SENJU shall have TANABE not, transfer, license, dispose or withdraw its share of the patent application and granted patent claiming SENJU-ISTA-TANABE Joint Invention under Paragraph 15.02 without prior written approval of the other Party.

15.03 In the event that SENJU (including SENJU Licensee and Senju Subsidiary) and TANABE (including TANABE Subsidiary) will jointly make, conceive, reduce into practice or generate any invention, discovery or know-how related to the Preparation in the course or as a result of their activities undertaken pursuant to SENJU-TANABE License Agreement (hereinafter called "SENJU-TANABE Joint Invention"), SENJU and ISTA agree and acknowledge the following:

(i) At SENJU's and TANABE's discretion, SENJU and/or TANABE shall file a patent application claiming SENJU-TANABE Joint Invention and maintain the granted patent;

(ii) ISTA shall have an exclusive right to use and otherwise practice SENJU-TANABE Joint Invention in ISTA Territory, SENJU and TANABE shall be compensated for ISTA's use of

SENJU-TANABE Joint Invention in ISTA Territory as long as ISTA pays the running royalty to SENJU under Paragraph 8.01;

(iii) SENJU shall not and shall have TANABE not transfer, license, dispose or withdraw its share of the patent application and granted patent claiming SENJU-TANABE Joint Invention under Paragraph 15.03 without prior written approval of ISTA in ISTA Territory.

15.04 In the event that SENJU (including SENJU Licensee and SENJU Subsidiary) will solely make, conceive, reduce into practice or generate any invention, discovery or know-how related to the Preparation in the course or as a result of their activities undertaken pursuant to this License Agreement and SENJU-TANABE License Agreement (hereinafter called "SENJU Sole Invention"), SENJU and ISTA agree and acknowledge the following:

(i) At SENJU's and ISTA's discretion, SENJU shall file a patent application claiming SENJU Sole Invention and maintain the granted patent under SENJU sole name in ISTA Territory, and the costs and expenses for the preparation, filing, prosecution and maintenance of granted patent shall be paid by SENJU;

(ii) ISTA shall have an exclusive right to use and otherwise practice SENJU Sole Invention in ISTA Territory, SENJU shall be compensated for ISTA's use of SENJU Sole Invention in ISTA Territory as long as ISTA pays the running royalty to SENJU under Paragraph 8.01;

(iii) SENJU shall not transfer, license, dispose or withdraw the patent application and granted patent claiming SENJU Sole Invention under Paragraph 15.04 without prior written approval of ISTA in ISTA Territory.

15.05 In the event that ISTA (including ISTA Developer, ISTA Manufacturer and ISTA Marketing Agent) will solely make, conceive, reduce into practice or generate any invention, discovery or know-how related to the Preparation in the course or as a result of their activities undertaken pursuant to this License Agreement (hereinafter called "ISTA Sole Invention"), SENJU and ISTA agree as following:

(i) SENJU and ISTA shall discuss, and as decided, shall file a patent application claiming ISTA Sole Invention and maintain the granted patent under SENJU and ISTA joint name throughout the world, and the costs and expenses for the preparation, filing, prosecution and maintenance of granted patent shall be paid by SENJU and ISTA equally, with SENJU responsible for clerical procedures of preparation, filing, prosecution of patent application and maintenance of granted patent outside ISTA Territory and ISTA responsible for clerical procedures of preparation, filing, prosecution of patent application and maintenance of granted patent in ISTA Territory;

(ii) ISTA shall have exclusive right to use and otherwise practice ISTA Sole Invention in ISTA Territory, SENJU shall be compensated for ISTA's use of ISTA Sole Invention in ISTA Territory as long as ISTA pays the running royalty to SENJU under Paragraph 8.01;

(iii) SENJU shall have an exclusive right, with the right to sub-license, to use and otherwise practice ISTA Sole Invention outside ISTA Territory, ISTA shall be compensated for SENJU's use of ISTA Sole Invention during the term of this Agreement;

(iv) **TANABE** shall have perpetual, irrevocable, fully paid up exclusive right, with the right to sub-license, to use and otherwise practice ISTA Sole Invention for any purpose in **TANABE** Territory;

(v) Each Party shall not transfer, license, dispose or withdraw the patent application and granted patent claiming ISTA Sole Invention under Paragraph 15.05 without prior written approval of the other Party in SENJU Territory and **TANABE** Territory.

15.06 In the event that **TANABE** (including **TANABE** Subsidiary) will solely or **TANABE** and **TANABE** Subsidiary will jointly, make, conceive, reduce into practice or generate any invention, discovery or know-how related to the Preparation in the course or as a result of their activities (hereinafter called "**TANABE** Sole Invention"), SENJU and ISTA agree and acknowledge the following:

(i) Clerical procedures for preparation, filing, prosecution of patent application claiming **TANABE** Sole Invention and maintenance of granted patent shall be discussed and decided, by **TANABE** solely or between **TANABE** and **TANABE** Subsidiary jointly, as the case may be;

(ii) ISTA shall have an exclusive right to use and otherwise practice **TANABE** Sole Invention in ISTA Territory, SENJU and **TANABE** shall be compensated for ISTA's use of **TANABE** Sole Invention in ISTA Territory as long as ISTA pays the running royalty to SENJU under Paragraph 8.01;

(iii) Each SENJU and **TANABE** shall have an exclusive right, with the right to sub-license, to use and otherwise practice **TANABE** Sole Invention in each Territory outside of ISTA Territory in accordance with SENJU-**TANABE** License Agreement.

15.07 In the event that **TANABE** Licensee will solely or **TANABE** and **TANABE** Licensee will jointly, make, conceive, reduce into practice or generate any invention, discovery or know-how related to the Preparation in the course or as a result of their activities (hereinafter called "**TANABE** Licensee Invention"), SENJU and ISTA agree and acknowledge the following:

(i) Clerical procedures for preparation, filing, prosecution of patent application claiming **TANABE** Licensee Invention and maintenance of granted patent shall be discussed and decided between **TANABE** and **TANABE** Licensee;

(ii) ISTA shall have an exclusive right to use and otherwise practice **TANABE** Licensee Invention in ISTA Territory, under the conditions otherwise agreed among SENJU, ISTA and **TANABE**, provided, however, that if **TANABE** Licensee Invention fails to grant the patent right in ISTA Territory, ISTA shall have no obligation to pay any compensation for ISTA's using and otherwise practicing **TANABE** Licensee Invention;

(iii) SENJU shall have an exclusive right, with the right to sub-license, to use and otherwise practice **TANABE** Licensee Invention outside ISTA Territory, under the conditions otherwise agreed in accordance with SENJU-**TANABE** License Agreement;

(iv) SENJU shall have **TANABE** not to transfer, license, dispose or withdraw the patent application and granted patent claiming **TANABE** Licensee Invention under Paragraph 15.07 without prior written approval of ISTA in ISTA Territory.

15.08 The wording of “Joint Invention” referred in this Article 15 shall mean the invention or discovery generated from direct cooperation or communication among the Parties or the result of such cooperation and communication.

15.09 Notwithstanding Paragraphs 15.01(i), 15.02(i) and 15.05(i), ISTA may elect, on a country by country basis, not to pay its share of any costs and expenses for the preparation, filing, prosecution and maintenance of any patent applied for or issued in a country or countries claiming a SENJU-ISTA Joint Invention, SENJU-ISTA-TANABE Joint Invention or ISTA Sole Invention. In such event, ISTA shall not be a joint holder of any such patent for which ISTA elects not to pay its share of the costs. For the avoidance of doubt, if such patent for which ISTA elects not to pay its share of the costs is applied for or issued in the ISTA Territory, then ISTA shall have exclusive right to use and otherwise practice the Invention claimed by such patent in ISTA Territory and SENJU and/or TANABE (as the case may be) shall be compensated for ISTA’s use of such Invention in ISTA Territory as long as ISTA pays the running royalty to SENJU under Paragraph 8.01. If ISTA desires to continue to use such Invention after this License Agreement terminates in accordance with Paragraph 17.01, then ISTA and SENJU and/or TANABE (as the case may be) shall discuss and decide the terms and conditions for such use. Provided, however, that with respect to such Invention, if the patent application claiming such Invention fails to grant the patent in the ISTA Territory, then ISTA shall have the right to use and otherwise practice the Invention in the ISTA Territory, free of charge.

Article 16. - Representations and Warranties

16.01 SENJU represents and warrants the following with respect to the Patent Rights and SENJU Technical Information & Know-How to the extent that the Patent Rights and SENJU Technical Information & Know-How relates to develop and commercialize the Preparation as of the Effective Date and during the term hereof (except as expressly provided below):

(i) SENJU solely owns the entire right, title and interest or right to license in and to the Patent Rights and SENJU Technical Information & Know-How in ISTA Territory, subject only to the SENJU-TANABE License Agreement;

(ii) The license grant to ISTA under Article 2 effectively licenses to ISTA the necessary rights owned or controlled by SENJU and TANABE for ISTA to develop and commercialize the Preparation in ISTA Territory and to otherwise practice the license granted hereunder, including but not limited to any and all rights granted to SENJU by TANABE under the SENJU-TANABE License Agreement in and to the Patent Rights and SENJU Technical Information & Know-How in ISTA Territory;

(iii) SENJU-TANABE License Agreement is in full force and effect as of the Effective Date, will continue to be in full force and effect during the term hereof, and will not be terminated, amended or waived in any way that would adversely effect the exclusive rights granted to ISTA hereunder or ISTA’s full exercise of such rights, without prior written approval of ISTA;

(iv) SENJU has not granted any license or sublicense or entered into any contract with any Third Party concerning the Patent Rights and SENJU Technical Information & Know-How within ISTA Territory;

(v) SENJU has not taken or failed to take any action that might result in the invalidity or unenforceability of any patent included with the Patent Rights against any Third Party;

(vi) SENJU has no information, at the Effective Date, that the Patent Rights and SENJU Technical Information & Know-How may be subject to challenge or interference or be invalid or unenforceable;

(vii) SENJU has the full legal power, authority and right to enter into this License Agreement, and to grant the exclusive license under the Patent Rights and the SENJU Technical Information & Know-How and to perform its obligations under this License Agreement. Upon execution and delivery by SENJU, this License Agreement will constitute a valid and binding agreement of SENJU enforceable in accordance with its terms. The execution, delivery and consummation of this License Agreement will not result in the breach of or give rise to cause for termination of any agreement to which SENJU may be a party which relates to the Patent Rights and SENJU Technical Information & Know-How (including but not limited to the SENJU-TANABE License Agreement); and

(viii) Each patent and patent application included in the Patent Rights as of the Effective Date is listed on Schedule A to this Agreement.

16.02 SENJU represents and warrants to ISTA that:

(i) Other than US Patent Number 5,830,913, there are no patents or patent applications owned or controlled by SENJU, or owned or controlled by SENJU and TANABE jointly, or licensed to SENJU under SENJU-TANABE License Agreement, relating to the Preparation or the Compound or covering SENJU Technical Information & Know-How;

(ii) There are no divisions, continuations or continuations-in-part to, or any other patent application claiming priority from, U.S. Patent Application No. 747,647;

(iii) SENJU's license of US Patent Number 5,830,913 to ISTA are the only patent rights necessary for ISTA to develop, make, have made, use, offer to sell, sell and otherwise commercialize the Preparation in the Territory as contemplated under the License Agreement.

16.03 Except as expressly provided in Paragraph 16.01, nothing in this License Agreement or any license pursuant to it shall be construed or implied as a representation or warranty by SENJU that the Patent Rights, SENJU Technical Information & Know-How, Improvement made by SENJU or TANABE, SENJU Sole Invention, TANABE Sole Invention or other invention, discovery, know-how, proprietary information or right licensed by SENJU hereunder are valid or that the commercialization of the Preparation or any other activities of ISTA under this License Agreement shall not be an infringement of the rights of any Third Party including, but not limited to, patent, know-how, trade-secret, trademark or other intellectual property rights of Third Party. In addition, ISTA makes no representation or warranty that the use by SENJU, SENJU Licensee, SENJU Subsidiary, TANABE, TANABE Subsidiary or TANABE Licensee of any ISTA Technical Information & Know-How, Improvement and ISTA Sole Invention or other invention, discovery, know-how, proprietary information or right licensed by ISTA hereunder will not be an infringement of the rights of any Third Party including, but not limited to, patent, know-how, trade-secret, trademark or other intellectual property rights of Third Party.

16.04 In the event that SENJU or ISTA become aware of any actual or threatened infringement by any Third Party upon SENJU proprietary right relating to the Preparation, such Party shall immediately notify the other Party in writing. SENJU shall notify **TANABE** of such actual or threatened infringement by any Third Party. SENJU and ISTA joining **TANABE** shall discuss and decide the resolution of the matter.

16.05 Notwithstanding Paragraph 16.02, in the event of a claim or suit made by Third Party against SENJU and/or ISTA for patent infringement involving the manufacture, use, sale, distribution or marketing of the Preparation using the formulation including the future formulation which SENJU uses in Japan, in ISTA Territory, the Party sued shall promptly notify the other Party in writing thereof.

In this case, the following shall apply:

(i) ISTA shall have sole responsibility to defend such claim or suit made by Third Party. SENJU may, at its option, decide whether or not SENJU is involved in the defense, provided, however, that regardless of whether SENJU decides to participate in the defense, it shall pay those litigation costs specified in 16.04 (ii) below. SENJU shall cooperate in the defense to the extent that SENJU shall provide any and all documents requested by ISTA to substantiate the patent;

(ii) ISTA and SENJU shall share equally the damages awarded to, all litigation cost and attorney fees as a result of the suit or settlement thereof. However, SENJU's total liability shall not exceed the half of milestone payments received from ISTA by the time of resolution of the suit or settlement under Paragraph 7.01; and

(iii) Notwithstanding Paragraph 16.05 (ii), if ISTA is obligated to pay a running royalty to the Third Party as a result of such claim or suit made by said Third Party, SENJU and ISTA shall equally share the burden of the running royalty. And the percentage of running royalty paid by ISTA to SENJU under Paragraph 8.01 herein shall be **decreased** by the share equivalent to **fifty percent (50%)** of the running royalty to be paid to said Third Party, during the remaining term of Initial Period of Term. However, the running royalty to be paid by ISTA to SENJU for the Initial Period of Term shall not be less than **ten percent (10%)** of the Net Sales of the Preparation by ISTA for the Initial Period of Term and shall not be decreased the royalty percentage set forth in paragraph 8.01 (ii) following Initial Period of Term, even if the running royalty to be paid by ISTA to SENJU decreases due to the payment of running royalty to said Third Party.

16.06 In the event of a claim or suit made by Third Party against SENJU and/or ISTA for patent infringement involving the manufacture, use, sale, distribution or marketing of the Preparation using the formulation which ISTA develops by itself, the Party sued shall promptly notify the other Party in writing thereof. In this case, ISTA shall settle or defend the claim or suit under the sole cost and responsibility of ISTA with its total monetary obligation, and shall indemnify and hold harmless SENJU and **TANABE** from such claim or suit.

16.07 SENJU shall, or shall cause **TANABE** to, diligently prosecute and/or maintain, at the expense of SENJU or **TANABE** (as the case may be), the patents and patent application included in the Patent Rights. In the event that SENJU or **TANABE** is unable or unwilling to fully comply with the obligations set forth above, then ISTA may elect, by providing notice SENJU, to file and/or prosecute the patent applications and/or maintain the patents included in the Patent Rights in ISTA's

own name and on ISTA's own behalf. In such event, SENJU shall reimburse ISTA for all costs and expenses incurred.

16.08 SENJU SHALL MAKE NO WARRANTIES WHATSOEVER, EXPRESS OR IMPLIED, WITH RESPECT TO THE PREPARATION MANUFACTURED AND/OR SOLD HEREUNDER INCLUDING WITHOUT LIMITATION ANY WARRANTY OF THE MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE OF THE PREPARATION SOLD BY ISTA.

16.09 NOTWITHSTANDING ANYTHING HEREIN TO THE CONTRARY, IN NO EVENT SHALL EITHER PARTY BE LIABLE TO THE OTHER PARTY FOR LOSS OF PROFITS OR INDIRECT, INCIDENTAL, SPECIAL, CONSEQUENTIAL OR PUNITIVE DAMAGES RESULTING FROM THIS LICENSE AGREEMENT.

Article 17. - Term and Termination

17.01 This License Agreement shall become effective as of the Effective Date and shall be in full force and effect for ten (10) years after Initial Period of Term.

17.02 In the event that this License Agreement terminates in accordance with Paragraph 17.01:

(i) ISTA shall have the perpetual, irrevocable, fully paid up license for SENJU Technical Information & Know-How related to the Preparation in ISTA Territory and shall have the right to make, have made, use, offer to sell and sell the Preparation continuously without any compensation to SENJU or **TANABE**;

(ii) ISTA shall have the license to use **TANABE** Trademark continuously under the Trademark License Agreement otherwise agreed among SENJU, **TANABE** and ISTA subject to the payment of royalty set forth Paragraph 8.01 (ii)(b), if ISTA uses **TANABE** Trademark for the Preparation;

(iii) SENJU, ISTA and/or **TANABE** shall discuss and decide the terms and conditions for their use of following each Invention under Article 15 if:

(a) ISTA desires to use, continuously and exclusively, SENJU's and/or **TANABE**'s share in each SENJU-ISTA Joint Invention, SENJU-**TANABE** Joint Invention, SENJU-ISTA-**TANABE** Joint Invention, SENJU Sole Invention, ISTA Sole Invention and/or **TANABE** Sole Invention in ISTA Territory;

(b) SENJU (including SENJU Licensee and SENJU Subsidiary) desires to use, continuously and exclusively, ISTA's share in each SENJU-ISTA Joint Invention, SENJU-ISTA-**TANABE** Joint Invention and/or ISTA Sole Invention outside ISTA Territory;

(c) Provided, however, that with respect to each Invention, if the patent application claiming such Invention fails to grant the patent in country or area where such Party desires to use and otherwise practice, such party shall have the right to use and otherwise practice the Invention in such country or area, free of charge.

17.03 Notwithstanding the stipulation of Paragraph 17.01 above, either a Party may terminate this License Agreement at any time by giving notice to the other Party in the event;

(i) that the other Party materially defaults or is in breach of the performance of any material obligation imposed on it in this License Agreement and such default is not remedied in all material respects within **thirty (30) days** of receipt of written demand from the notifying Party to cure the default; or

(ii) that the other Party shall have become insolvent or bankrupt, or shall have made a general assignment for the benefit of its creditors, or any case or proceeding shall have been commenced by or against the other Party in bankruptcy or seeking reorganization, liquidation, dissolution, or any other relief under any bankruptcy, insolvency, reorganization or other similar act or law, and any such event shall have continued for **sixty (60) days** undismissed or undischarged.

17.04 If ISTA decides, in its sole discretion, to give up the Development Activities due to the lack of effectiveness of the Preparation or, occurrence of serious and unexpected adverse event of the Preparation in the course of Development Activities, change in market, ISTA's business or the Preparation's prospects, or other good and valid reason, ISTA shall inform SENJU of ISTA's decision and the reasons for such decision by written notice and, **twelve (12) months** after such notice, this License Agreement shall be terminated.

17.05 If ISTA decides, in its sole discretion, and bona fide business judgment due to the lack of effectiveness of the Preparation or, occurrence of serious and unexpected adverse event of the Preparation, change in market, ISTA's business or the Preparation's prospects, or other good and valid reason, to give up pursuit or maintain the Governmental Approval or the manufacture, sale or commercialization of the Preparation in the ISTA Territory, ISTA shall inform SENJU of its decision and the reasons for such decision by written notice and, **twelve (12)** after such notice, this License Agreement shall be terminated.

17.06 If this License Agreement is terminated by ISTA in accordance with Paragraph 17.03 through 17.05, ISTA shall promptly cease its Development Activity, manufacture and/or commercial activities, as the case may be, concerning the Preparation, and, at its option, destroy the Preparation then stocked by ISTA including the cost of the inventory, or sell the remaining inventory of the Preparation and settle its obligation, if any, to pay any royalties or other payment due under this License Agreement within **one hundred and twenty (120) days** after the termination thereof. Upon SENJU's request, ISTA shall return to SENJU all the SENJU Technical Information & Know-How and remaining Compound provided by SENJU under this License Agreement and shall assign to SENJU, without any compensation all of the rights, titles and interests pertaining to the Preparation including without limitation, all rights to Governmental Approval in ISTA Territory.

17.07 In the event that (i) SENJU materially defaults or is in breach of the performance of any material obligation imposed on it in SENJU-TANABE License Agreement and such default is not remedied in all material respects within **thirty (30) days** of receipt of written demand from **TANABE** to cure the default; and **TANABE** seeks to terminate SENJU-TANABE License Agreement due to SENJU's breach or (ii) SENJU assigns or makes any composition or sequestration of its assets for the benefit of its creditors, or assigns its rights hereunder partially or in their entirety to any Third Party, then prior to any termination of the SENJU-TANABE License Agreement, SENJU shall have **TANABE** enter into a direct license with ISTA for the Patent Rights and Technical Information & Know-How in ISTA Territory to allow ISTA to make, have made, use, offer to sell, sell and otherwise develop and commercialize the Preparation in ISTA Territory. The terms of such direct license shall be agreed to between ISTA and **TANABE** through a good faith discussion based on those terms as set forth in this License Agreement (as amended from time to time), said direct license

cannot, however, modify Article 7 (Compensation), Article 8 (Royalties), Article 11 (Availability of Compound), Article 15 (New Invention and Discovery), Paragraph 17.01 and 17.02 of Article 17 (Term and Termination) of this License Agreement. It is understood that some of SENJU's obligations under this License Agreement may not be TANABE's obligations under the SENJU-TANABE License Agreement, and vice versa. Provided, however, that notwithstanding anything else contrary hereof, ISTA acknowledges and agrees that TANABE will be released from and not have the obligation to provide ISTA with the assistance in the field of ophthalmology even if TANABE would be a party of this License Agreement on behalf of SENJU under this Paragraph 17.07.

17.08 Expiration or termination of this License Agreement shall not affect the rights and obligations of the Parties which are expressly intended to survive expiration or termination of the License Agreement, including, without limitation, those rights and obligations set forth in Articles 12 and 14 and in Paragraphs 9.03, 15.01(iv), 15.02(v), 15.05(iv), 15.06(ii), 16.08, 16.09, 17.02, 17.06, 17.07, 18.01, 18.02, 19.01 and 22.01.

Article 18. - Governing Laws and Arbitration

18.01 This License Agreement shall be governed by and interpreted in accordance with the Laws of Japan.

18.02 All disputes, controversies or differences which may arise between the Parties hereto or for the breach thereof shall be referred to and settled by arbitration in accordance with the Arbitration Rules of the International Chambers of Commerce as currently in force by one or more arbitrators appointed under the Rules. Such arbitration hereunder shall be proceeded in English language and shall be held in Japan if the arbitration is requested by ISTA and in Los Angeles, California, U.S.A. if the arbitration is requested by SENJU. The determination of the arbitration shall be final, binding and conclusive upon the Parties hereto. Notwithstanding anything herein to the contrary, the relevant cure periods for breach under this License Agreement shall toll while either Party pursues resolution to a dispute through arbitration.

Article 19. - Notice

19.01 Any notice to be given to a Party under or in connection with this License Agreement shall be in writing and shall be (i) personally delivered, (ii) delivered by a nationally recognized overnight courier, (iii) delivered by certified mail, postage prepaid, return receipt requested to the Party or (iv) delivered by facsimile transmission to the Party, at the address or facsimile number set forth below for such Party or such other address or facsimile number as a Party may from time to time designate by written notice to the other:

to SENJU:

Executive Vice President
SENJU Pharmaceutical Co., Ltd.
5-8, Hiranomachi 2-chome
Chuo-ku, Osaka, 541-0046
Japan
Facsimile: +81-6-6226-0406

to ISTA:

Chief Executive Officer
ISTA Pharmaceuticals, Inc.
15279 Alton Parkway, Suite 100
Irvine, CA 92618
U.S.A.
Facsimile: (949) 789-7744

Any such notice shall be deemed to have been received by the addressee **five (5) business days** following the date of dispatch of the notice or other document by post or, where the notice or other document is sent by overnight courier, by hand or is given by facsimile, simultaneously with the transmission or delivery. To prove the giving of a notice or other document it shall be sufficient to show that it was dispatched.

Article 20. - Force Majeure

20.01 Neither Party hereto shall be liable for any failure to perform as required through this License Agreement by reason of Force Majeure, to the extent such failure to perform is due to circumstances reasonably beyond the control of such Party, such as requisition or interference by any government, state or local authorities, war, strikes, lockout or other labor disputes, accident or breakdown in whole or in part of transportation or loading facility, other accidents, failure to secure required Governmental Approval, civil disorders or commotions, act of aggression, acts of God, energy or other conservation shortages, disease, or occurrences of a similar nature.

20.02 If and when any Party is hindered in its performance of its obligations under this License Agreement by reason of Force Majeure, the performance of those obligations shall be suspended for the duration of, but not longer than, the continuance of such circumstances.

20.03 Either Party hereto whose performance of obligation has been hindered by reason of Force Majeure shall inform the other Party immediately, and shall use its reasonable best effort to overcome the effect of the Force Majeure.

Article 21. - Non-Assignability

21.01 This License Agreement is personal to the Parties hereto and shall not be assignable, transferable or saleable (including asset sale of solely that Party's rights in the License Agreement) to any Third Party by either Party, without the prior express written consent of the other Party, such consent not to be unreasonably withheld; provided, however, that no such consent shall be required from SENJU if ISTA or ISTA's business is merged or acquired by a Third Party by way of merger, consolidation or sale of all or substantially all of its assets and SENJU is given written notice thereof at least **two (2) weeks** in advance of the closing thereof.

Article 22. - Authentic Text

22.01 This Text of this License Agreement in the English language shall be the authentic text, and any text in another language, even if such text is made by translation of this Text of this License Agreement or prepared by any of the Parties hereto for any purpose, shall have no meaning for any purpose between the Parties hereto.

Article 23. - Entire Agreement

23.01 Secrecy Agreement shall be replaced by this License Agreement as of the Effective Date so that Secrecy Agreement shall terminate simultaneously.

23.02 This License Agreement shall constitute the entire agreement between the Parties hereto concerning the subject matter hereof and shall supersede any other agreements, whether oral or written, express or implied, and may not be changed or modified or revised except as specifically

agreed upon by the Parties hereto in a written document bearing the respective signatures of the authorized officers.

Article 24. - Separability

24.01 Even in the event that any portion of this License Agreement shall be held illegal, void, ineffective or unenforceable, the remaining portion shall remain in full force and effect.

24.02 If any of the terms or provisions of this License Agreement are in conflict with any applicable statute or rule of law, such terms and provisions shall be deemed inoperative to the extent that may conflict therewith and shall be deemed to be modified to conform with such statute or rule of law.

24.03 In the event that the terms and conditions of this License Agreement are materially altered as a result of the provision in Paragraph 24.02, the Parties will re-negotiate the terms and conditions of this License Agreement to resolve any inequities.

Article 25. Parties in Interest.

25.01 Nothing in this License Agreement, whether express or implied, is intended to confer any rights or remedies under or by reason of this License Agreement on any persons other than the Parties to it and their respective successors and assigns, nor is anything in this License Agreement intended to relieve or discharge the obligation or liability of any third persons to any Party to this License Agreement, nor shall any provision give any third persons any right of subrogation or action over or against any party to this License Agreement.

Article 26. Independent Contractor Status, No Agency.

26.01 SENJU's and ISTA's activities hereunder shall be conducted as independent contractors and no agency relationship shall exist between the parties.

IN WITNESS WHEREOF, SENJU and ISTA have caused this License Agreement to be executed in duplicate counterparts by their duly authorized officers, each fully executed copy hereof to be deemed as original, as of the date and year first above written.

SENJU:

ISTA:

SENJU Pharmaceutical Co. Ltd.

ISTA Pharmaceuticals, Inc.

signature: _____

signature: _____

name: Shoji Yoshida

name: Vicente Anido Jr., Ph.D.

title: President

title: Chief Executive Officer

SCHEDULE A
PATENT RIGHT

Title of Invention: Method for Preventing or Treating Dry Eye or Disease caused Therefrom

Application Number: 747,647

Date of Application: November 13, 1996

Patent Number: US 5,830,913

Date of Patent: November 3, 1998

Proprietor: Tanabe Seiyaku Co., Ltd.
Senju Pharmaceutical Co., Ltd.