EX-10.4 8 a2232291zex-10_4.htm EX-10.4

Exhibit 10.4

*****Text Omitted and Filed Separately**
Confidential Treatment Requested
Under 17 C.F.R. §§ 200.80(b)(4) and 230.406

YM477 LICENSE AGREEMENT

This Agreement is made as of August 15, 2005, by and between Astellas Pharma Inc., a company organized and existing under the laws of Japan and having its principal office at 3·11, Nihonbasbi-Honcho 2-chome, Chuo-ku, Tokyo 103-8411, Japan ("Licensor") and AkaRx Corp., a company organized and existing under the laws of Delaware and having its principal office at Mack Centre IV, 4th Floor, 61 S. Paramus Road, Paramus, NJ 07652 ("Licensee").

RECITALS

A. Licensor has invented and developed the Compound (as defined below).

B. Licensor owns the Licensor Patents and the Licensor Know-How (each as defined below).

C. Licensee desires to obtain the license to develop and commercialize the Compound and the Product in the Territory (as defined below) and Licensor is willing to grant such a license to Licensee under the terms and conditions as set forth below.

D. Robert Desjardins, Rudy Lucek, Steven Silbert, Donna Tempel and David Laveman, Licensor and Licensee entered into a certain Memorandum Of Understanding dated as of December 8, 2004, pertaining to the Compound, among other things (the **"MOU"**).

E. Licensor changed its name from Yarnanouchi Pharmaceutical Co., Ltd. to Astellas Pharma Inc.

NOW THEREFORE, in consideration of the premises and the mutual agreements hereinafter contained, the Parties hereto agree as follows:

1. DEFINITIONS

In this Agreement, the following terms when capitalized shall have the respective meanings set forth below and the singular shall include the plural and vice versa.

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

"Affiliate" shall mean any Person controlling, controlled by or under common control with the Person as to which such status is in question. For purposes of this definition, the term "control" means direct or indirect ownership of more than fifty percent (50%) of the voting stock or other voting interest of a Person or the possession of the power to direct the management and policies of a Person.

"Business Day" shall mean a day on which commercial banks in New York City, New York, United States of America are open for business.

"Calendar Quarter" shall mean, for each Calendar Year, each of the three month periods ending on March 31, June 30, September 30 and December 31; provided, however, that the first Calendar Quarter for the first Calendar Year shall extend from the Effective Date to the end of the next calendar quarter following the calendar quarter in which the Effective Date occurs.

"Calendar Year" shall mean, for the first Calendar Year, the period commencing on the Effective Date and ending on December 31 of the calendar year during which the Effective Date occurs, and each successive period beginning on January l and ending twelve (12) consecutive calendar months later on December 31.

"cGMP" shall mean the applicable then-current Good Manufacturing Practices guidelines and regulations, respectively, of the US Food and Drug Administration, or their equivalent outside the United States.

"cGMP Compound" shall have the meaning set forth in Section 10.01.

"Compound" shall mean [***] together with all other compounds covered by the Licensor Patents.

"Condition Precedent" shall have the meaning set forth in Section 2.01.

"Confidential Information" shall mean all information, data, technology and know-how disclosed by one Party to the other Party for the purposes of this Agreement whether orally, electronically, visually or in writing which (a) is marked "confidential" or with any similar marking or legend or is otherwise identified as confidential, (b) if orally, electronically or visually disclosed is further reduced to summary written form

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describing such information, data, technology and know-how and is delivered to the receiving Party within thirty (30) days after disclosure, referencing the place and date of such oral, visual, electronic or written disclosure and the names of the persons to whom such disclosure was made, or (c) is "Confidential Information" provided under the MOU.

"Control" or "Controlled" shall mean the legal authority or right of a Party to grant a license or sublicense of intellectual property rights to another Party.

"Date Of Launch" shall mean, with respect to a particular country in the Territory, the date on which Licensee or its Affiliate or sublicensee first sells or distributes the Product for its intended use to a Third Party following Regulatory Approval to engage in commercial sales in such country.

"EEA" shall mean the European Economic Area, currently comprising the 25 Member States of the European Union, as well as Norway, Iceland and Liechtenstein, as the same is constituted from time to time.

"Effective Date" shall mean the date on which the Condition Precedent is satisfied in accordance with Section 2.01.

"Knowledge of Licensor" shall mean the knowledge of the employees of Licensor holding managerial position in its intellectual property department, only to the extent that such knowledge is actually known to them.

"Licensor Information" shall mean Licensor Know-How and any and all information, data, technology, documents and other materials related to the Compound and/or the Product owned or Controlled by Licensor as of the Effective Date and which is needed by or useful to Licensee in order for Licensee to perform its obligations or to exploit its rights under this Agreement.

"Licensor Know-How" shall mean any and all scientific, medical, technical and/or regulatory information relating to the Compound and/or the Product which is in the possession of or available to Licensor or any of its Affiliate as of the Effective Date and which is needed by or useful to Licensee in order for Licensee to perform its obligations or to exploit its rights under this Agreement.

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"Licensor Patent(s)" shall mean the patent applications or patents identified in Appendix A attached hereto, as well as any patents granted thereon, continuations, continuations-in-part, continued prosecution applications, substitutes, divisions, reissues, revisions, re-

examinations, registrations, renewals, extensions, patents of addition, supplemental protection certificates, revivals and foreign counterparts of the foregoing.

"Licensor Material" shall mean reference standard for the Compound and reference material for Compound impurities.

"NDA" shall mean any application seeking Regulatory Approval.

"Net Sales" shall mean, for any period, the gross amounts invoiced for sales of the Product by Licensee, its Affiliates and sublicensees (or any of them), to Third Parties (but not including sales relating to transactions between Licensee, its Affiliates and their respective sublicensees), less the total of the following deductions which shall be directly related to such sale of the Product:

(a) direct or indirect credits and allowances or adjustments (consistent with United States generally accepted accounting principles, to the extent applicable) granted to such customers on account of price adjustments, government or other rebates (e.g. Medicare, Medicaid, pharmacy, insurance carrier, hospital or health maintenance organization rebates), whether or not in connection with promotion or formulary inclusion, rejections, rejections or returns in respect of the Product previously sold;

(b) any trade, volume and cash discounts (including any discounts for prompt payment), rebates, indigent patient programs and charge-backs granted to customers where there are direct shipments by Licensee, its Affiliates and/or its sublicensee to such customers, and management fees paid during the relevant time period to group purchasing organizations; and

(c) any sales or other like taxes imposed upon the sale of the Product to the extent included in the gross sales price (e.g. Value Added Tax);

(d) any freight, postage and transit insurance costs;

and

(e) any other specifically identifiable amounts included in Product gross invoice amount that should be credited for reasons substantially similar to those set forth above.

provided that the sum of (d) and (e) shall be no more than [***] percent ([***]%) of the

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gross amounts invoiced for sales of the Product.

"Non-cGMP Compound', shall have the meaning set forth in Section 10.01.

"Party" shall mean Licensor or Licensee; **"Parties"** shall mean Licensor and Licensee.

"Person" shall mean any natural person or persons, corporation, limited liability company, general partnership, limited partnership, joint venture, proprietorship or other business organization.

"Phase I Study" shall mean any study in healthy humans to obtain initial data regarding the safety and pharmacokinetics of a product

"Phase II Study" shall mean any study in humans of the safety, dose range and efficacy of a product which is conducted after Phase I Studies of such product have been complete and are usually intended to allow selection of doses for the conduct of a Phase III Study.

"Phase III Study" shall mean any controlled study in humans of the efficacy and safety of a product which is conducted after Phase II Study has been completed and which is prospectively designed to demonstrate statistically whether the product is safe and effective for use in a particular indication and is usually intended to be sufficient to support registration of the Product.

"Product" shall mean any product containing the Compound, in any dosage form, as a sole active ingredient or in any combination with other active ingredients, for all uses.

"Regulatory Approval" shall mean any and all approvals (including any applicable supplements, amendments, pre- and post-approvals, governmental price and reimbursement approvals and approvals of applications for regulatory exclusivity), licenses, registrations, or authorizations of any Regulatory Authority necessary for the manufacture, distribution, use, storage, import, export, transport, promotion, marketing and sale of the Compound or the Product in a country or jurisdiction.

"Regulatory Authority" shall mean any federal, national, multinational, state, provincial or local regulatory agency, department, bureau, commission, council, court, tribunal, arbitrator, official or other instrumentality of a governmental entity in any country in the

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Territory.

"Scientific Knowledge of Licensor" shall mean the knowledge of the employees of Licensor holding managerial position in its drug discovery research laboratory, only to the extent that such knowledge is actually known to them.

"Specifications" shall mean the specification of cGMP Compound decided by Licensor and delivered to Licensee in writing.

"Territory" shall mean the world.

"Third Party" shall mean any Person, other than a Party or any of its Affiliates.

2. CONDITION PRECEDENT

2.01 It is a condition precedent for this Agreement becoming effective that Licensee receives from an initial equity financing transaction or series of such transactions net proceeds equal to or exceeding five million U.S. dollars ($5,000,000) on or before September 30, 2005 (the "Condition Precedent"). In the event that the Condition Precedent is not fulfilled by such date, this Agreement will become null and void immediately without penalty to either party.

3. LICENSE

3.01 Licensor hereby grants to Licensee, and Licensee hereby accepts, an exclusive license, with the right to sublicense through multiple tiers, to make, have made, use, have used, develop, register, import, market, promote, distribute, offer to sell, sell, have sold and otherwise exploit in all regards the Compound and the Product in Territory under Licensor Patents and Licensor Information.

4. DEVELOPMENT

4.01 Licensee shall use commercially reasonable efforts to conduct, at its own cost, any pre-clinical and clinical development activities for the Product that are necessary to seek Regulatory Approval of the Product in those jurisdictions

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chosen by Licensee in the exercise of its reasonable business judgment, provided that such jurisdictions shall at least include the United States and EEA.

4.02 All results, data, information, know-how and technology obtained in the course of such development activities with respect to the Product conducted by Licensee or any of its Affiliates or sublicensees shall be solely owned by Licensee or such Affiliate or sublicensees.

4.03 To the extent necessary to meet applicable regulatory requirements, Licensor shall be responsible for preserving all types of raw data that are obtained in the course of all activities, studies and research in connection with the Compound and the Product. Licensor shall allow Licensee or any Regulatory Authority to audit on and have full access to, at any reasonable times and places, such raw data to the extent necessary or required for any Regulatory Approval in the Territory.

5. REGISTRATION

5.01 Licensee shall, as soon as practicable after the completion of the development activities set forth in Article 4, file an NDA in the name of Licensee or any of its Affiliates or sublicensees with Regulatory Authorities in those relevant jurisdictions chosen by Licensee in the exercise of its reasonable business judgment pursuant to Section 4.01 and shall use commercially reasonable efforts to obtain Regulatory Approvals in such jurisdictions.

5.02 Licensee shall be responsible for all regulatory matters (including communications with regulatory authorities) concerning the Compound and the Product. All regulatory filings pertaining to the clinical development and approval for sale of Product shall be in the name of, and owned by, Licensee.

6. RECALL

6.01 Licensee shall have the right to determine whether and upon what terms and conditions to recall the Product in any country in Territory. Licensee and its Affiliates shall be responsible for discussions with Regulatory Authorities regarding all aspects of a recall decision and the execution thereof. Any costs or expenses of any recall shall be borne by Licensee and Licensee shall reimburse

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Licensor for any costs or expenses reasonably incurred by Licensor in connection with the same, if any, provided however, if such recall is caused partially or solely by (i) any material breach of this Agreement by Licensor, (ii) any gross negligence, willful misconduct or violation of applicable law by Licensor or any of its Affiliates, or(iii) failure of the cGMP Compound supplied by Licensor or any of its Affiliates to meet the Specifications or applicable cGMPs or other applicable law, rule or regulation, then Licensor shall bear the costs and expenses of any recall under this Section to the extent such recall has resulted therefrom.

7. INFORMATION

7.01 Licensor shall provide, and shall cause its Affiliates to provide, Licensee with all Licensor Information. Licensee shall have the right to provide such Licensor Information to any of its Affiliates and sublicensees for the purpose of the development, registration and commercialization of the Product.

7.02 Licensee shall timely but at least semi-annually inform Licensor of its progress of any pre-clinical and clinical development activities for the Product.

8. PAYMENTS

8.01 In consideration for the rights granted under this Agreement by Licensor, Licensee shall make one-time non-refundable and non-creditable payments to Licensor in respect of the Product within thirty (30) days after the first occurrence of each of the corresponding events listed below, in the amount provided:

	Milestone Event	Milestone Payment Amount
(a)	The Condition Precedent is satisfied in accordance with Section 2.01.	Two hundred and fifty thousand U.S. Dollars ($250,000)
(b)	Initiation of Phase I Study in the United States	Two hundred and fifty thousand U.S. Dollars ($250,000)

(c)	Successful completion of Phase I Study in the United States	Five hundred thousand U.S. Dollars ($500,000)
(d)	Successful completion of Phase II Study in the United States	One million U.S. Dollars ($1,000,000)
(e)	[***]	[***]
(f)	[***]	[***]
(g)	[***]	[***]

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provided always that each milestone payment shall be made only onetime regardless of how many times such milestone event is achieved or the number of indications for which the Product is approved, and no milestone payment shall be owed for a milestone event that is not achieved. Success for purposes of subsections (c), and (d) above shall be deemed to have occurred when Licensee decides to proceed to the next step of clinical development, as reflected in the above chart.

8.02 In consideration for the rights with respect to each Product in the Territory granted under this Agreement by Licensor, Licensee shall pay to Licensor:

(i) [***] percent ([***]%) of Net Sales of the Product during a Calendar Quarter, within sixty (60) days after the end of such Calendar Quarter and,

(ii) the difference between (a) and (b) below within sixty (60) days after the end of a Calendar Year:

(a) the sum of (i) during a Calendar Year and,

(b) the total amount of;

(1) [***]percent ([***]%) of Net Sales up to and including [***] U.S. Dollars ($[***]) during a Calendar Year,

(2) [***] percent ([***]%) of Net Sales in excess of [***] U.S. Dollars ($[***]) up to and including [***] U.S. Dollars ($[***]) during a Calendar Year,

(3) [***] percent ([***]%) of Net Sales in excess of [***] U.S. Dollars ($[***]) during a Calendar Year,

provided that for any Net Sales in a country in which there are no issued claims of a Licensor Patent in force which would be infringed by Licensee but for the licenses granted under this Agreement ("Non Patent Net Sales"), Licensee shall pay Licensor half of the amount calculated as above, provided further that during the extension period of this Agreement as set forth in Section 19.01, Licensee shall pay Licensor [***] percent ([***]%) of Net Sales of the respective Product in the respective country if such Product embodies Licensor Information which

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has not entered the public domain through any action of AkaRx.

8.03 Licensee shall be responsible for obtaining and making payment for any licenses for rights or obtaining any ownership rights to any Third Party's intellectual property required to develop, commercialize, make, have made, use, sell, have sold, offer to sell or resell, import, export, distribute or otherwise transfer physic al possession of or otherwise transfer title in or to, the Compound and the Product Licensee shall be entitled to deduct [***] percent ([***]%) of such payments from amounts due to Licensor, whether license fees, milestone payments, royalties or as otherwise characterized until such deductible amount has been fully deducted; provided, however, no such deduction shall have the effect of reducing any payment made to Licensor by

more than [***] percent ([***]%). In the event the Compound or the Product is sold in a particular country in a finished dosage form containing a Compound in combination with one or more other active ingredients or a proprietary delivery system (a "Combination Product"), the Net Sales of the Product in such form in such country, for the purposes of determining royalty payments, shall be determined by multiplying the Net Sales of the Combination Product by the fraction, A/(A+B) where A is the weighted (by sales volume) average sale price in such country of the Product when sold separately in finished form and B is the weighted average sale price in such country of the other product(s) sold separately in finished form. In the event that such average sale price cannot be determined in such country for both the Product and the other product(s) in combination, then the prices in the United States will be used, and if the Product is not sold in the United States then Net Sales for purposes of determining royalty payments shall be agreed by the Parties based on the relative values contributed by each component, such agreement not to be unreasonably withheld or delayed. Furthermore, if in any jurisdiction, Licensee is required by a governmental authority to grant a compulsory sublicense to a Third Party with royalty rates or upon royalty rates more favorable to such Third Party than applicable to Licensee under this Agreement, then the royalty rates and terms of this Agreement shall immediately and without the need for further action be deemed to be reduced to such rates for purposes of calculating royalties due in respect of Net Sales in such jurisdiction.

8.04 All payments to be made by either Party under this Agreement shall be made in U.S. Dollars by bank wire transfer to a bank account designated in writing by the other Party.

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8.05 Net Sales or other revenues received or expenses or payments due in currencies other than U.S. Dollars shall first be calculated in the relevant foreign currency and then converted to U.S. Dollars against the currency in question on the rate of exchange applicable on the last Business Day of the Calendar Quarter in respect of which the funds are payable using the currency exchange rates (Telegram Transfer Selling) quoted by Citibank, N.A. in New York, New York during the period of such Net Sales, or in the event that exchange rate is not available then as reported in the eastern U.S. edition of The Wall Street Journal.

8.06 If Licensee fails to make a timely payment pursuant to this Article 8, interest shall accrue on the past due amount at a rate equal to the lesser of 110% of the prime rate of interest (or its equivalent) charged by Citibank, N.A. in New York, New York from time to time, or such lower maximum rate allowed by applicable law, from the first date on which the payment was delinquent, calculated on an actual/360 basis.

8.07 If laws or regulations require withholding by Licensee of any taxes imposed upon Licensor on account of any royalties and advance payments paid under this Agreement, such taxes shall be deducted by Licensee as required by law from such payment and shall be paid by Licensee to the proper taxing authorities. Official receipts of payment of any withholding tax shall be secured and sent to Licensor as evidence of such payment. The Parties will exercise their reasonable efforts to ensure that any withholding taxes imposed are reduced as far as possible under the provisions of any applicable tax treaty.

9. COMMERCIALIZATION

9.01 In no less than six (6) months after obtaining Regulatory Approval (including an approved price) from a Regulatory Authority, Licensee shall, or shall cause its Affiliates or sublicensees, to use commercially reasonable efforts to manufacture, promote, market, distribute and sell the Product in Territory in which such Regulatory Approval has been obtained at its own cost

9.02 Licensee shall be responsible for responding to all questions or inquiries relating to the Product sold in Territory and, upon the request of Licensee, Licensor shall reasonably assist and co-operate in the preparation of any such responses.

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10. SUPPLY OF MATERIAL

10.01 Licensor shall provide, or shall cause its Affiliates to provide (i) Licensor Material in possession of Licensor as of the Effective Date at the request of Licensee, to the extent that it is possible for Licensor to so provide and (ii) cGMP Compound and Non-cGMP Compound from among existing stocks as of the Effective Date. The Parties acknowledge that Licensor has in its possession approximately 7.9 kilograms of Compound manufactured in accordance with cGMP ("cGMP Compound") and approximately 35 kilograms of Compound manufactured not in accordance with cGMP (''Non-cGMP Compound"). Licensor agrees to sell to Licensee pursuant to a one-time purchase order delivered by Licensee to Licensor up to such amount of cGMP Compound as it may now have in its possession and to transfer to Licensee at no cost up to five (5) kilograms of Non-cGMP Product. Promptly following execution and delivery of this Agreement, Licensor shall take stock of its supply of cGMP Compound and inform Licensee of the quantity on hand.

10.02 Licensee shall submit one-time purchase order for cGMP Compound within ninety (90) days after the Effective Date to Licensor for fulfillment out of stock on hand at the time of the Effective Date of this Agreement. After consultation with Licensee, Licensor shall reasonably decide storage conditions, out-bound quality testing, ordering lead times, shipping methods, packaging, transit insurance and the like. cGMP Compound shall be delivered on the basis of Ex Works (Incoterms 2000), Licensor' manufacturing site in Japan. All cGMP Compound delivered pursuant to this Agreement shall conform to the Specifications and shall have been manufactured in compliance with all applicable laws and cGMPs. Licensor shall cooperate with Licensee by providing access to and copies of such manufacturing and quality records directly related to cGMP Compound supplied pursuant to Section 10.01 as Licensee may reasonably require in connection with the clinical development of the Product including providing Licensee an opportunity, to be exercised in Licensee's discretion, to audit Licensor's manufacturing records regarding the production of cGMP Compound during ordinary business hours of Licensor but such access and audit shall not be allowed more than once respectively, nor shall they be a11owed at all after the filing of the first NDA.

10.03 In the event that any facilities, operations and laboratories of Licensor or any of

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its Affiliates become the subject of an investigation or audit relating to the Compound or the Product by any Regulatory Authority, Licensor shall notify Licensee thereof promptly after receipt of a prior notice from such authorities. In the event Licensor or any of its Affiliates do not receive prior notice of said investigation or audit, Licensor shall notify Licensee as soon as practicable after becoming aware of said investigation or audit. Licensor shall provide Licensee with a reasonable description of each such investigation or audit, promptly after such investigation or audit, and with copies of any letters, reports, or other documents. Licensee, its Affiliate or designee shall have the right to be present at, or otherwise participate in, such investigation or audit.

10.04 Licensee shall pay to Licensor, i) in consideration for Licensor Material supplied pursuant to Section 10.01, 13,500 U.S. Dollars per kilogram, and ii) in consideration for cGMP Compound supplied pursuant to Section 10.02, 13,500 U.S. Dollars per kilogram. Such payment shall be made by Licensee within sixty (60) days after the end of the Calendar Quarter in which the delivery of Licensor Material or cGMP Compound occurs respectively.

11. ACCOUNT AND AUDIT

11.01 Licensee or its Affiliate shall deliver to Licensor within sixty (60) days after the end of each Calendar Quarter a written sales report for such Calendar Quarter, setting forth the gross invoiced price of the Product, itemized deductions therefrom and Net Sales on a country-by-country basis.

11.02 Licensee agrees that it shall keep, and cause its Affiliates and sublicensees to keep, accurate records in sufficient detail to enable the amounts due to Licensor hereunder to be determined and, upon Licensor's request, shall permit an independent certified public accountant, selected by Licensor, except to whom Licensee, its Affiliate or sublicensee has reasonable objection, to have access during ordinary business hours to such of Licensee's, its Affiliates' or sublicensees' records but such access shall not be allowed more than once per Calendar Year:

(a) to determine, in respect to any Calendar Year, the correctness of any report and/or payment made under this Agreement, and

(b) to obtain information as to the amount payable to Licensor for any such

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Calendar Year in the case of Licensee's or its Affiliate's failure to report and/or make payment pursuant to this Agreement.

Any review by Licensor shall beat Licensor's sole expense. This right of review shall terminate two (2) years after Licensor's receipt of each respective sales report. The records for any particular Calendar Year shall only be subject to one audit. Such independent certified public accountant shall not disclose to Licensor any information other than information relating to the accuracy of reports and payments made under this Agreement and in no event are the quantities and prices to individual customers or the names of those customers to be disclosed to Licensor.

11.03 In the event of a determination by such independent certified public accountant that there has been an inaccurate calculation or payment, an appropriate adjustment shall be made to the next payment.

12. OWNERSHIP

12.01 Licensor shall solely own all right, title and interest in and to the Licensor Patents, Licensor Know-How and Licensor Information, subject to the rights and licenses granted to Licensee under this Agreement.

12.02 All results, data, information, know-how and technology obtained in the course of, or related to, research and development activities of the Compound or Product conducted by Licensee or any of its Affiliates or sublicensee or the manufacturing process for the Compound or Product developed by Licensee or any of its Affiliates or sublicensee shall be solely owned by Licensee.

12.03 Other than as expressly set forth in this Agreement, neither Party shall have any right in and to any intellectual property owned or controlled by the other Party and, save as set out in this Agreement, neither Party shall have an obligation to license any rights in or to its intellectual property to the other Party.

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13. PROSECUTION AND MAINTENANCE OF INTELLECTUAL PROPERTY RIGHT

13.01 Licensee shall hereby assume from Licensor all responsibility and control for the preparation, filing, prosecution and maintenance as well as any cost to be incurred therefor of all relevant patent applications and patents included or to be included within the Licensor Patents and applications for patent extension or supplementary protection certificates or similar extensions in the name of Licensor, if required, for the benefit of Licensee. Licensee shall provide Licensor with copies of relevant documentation so that Licensor can be informed of continued prosecution and shall permit Licensor to comment on such documentation to the extent it relates to the Product or Compound. Licensee shall give due consideration to any reasonable comments by Licensor.

13.02 Notwithstanding Section 13.01, Licensee shall have the right, at any time and at its sole option, to elect not to proceed with and/or to abandon filing, prosecution, and/or maintenance of any Licensor Patents, provided that Licensee shall give Licensor notice of such intention at least thirty (30) days before a final due date which would result in the abandonment, cancellation or

lapse of an issued patent or pending patent application. In such case, Licensor, at its option, may assume the right to prepare, file, prosecute, maintain and/or defend any such Licensor Patents at Licensor's expense.

13.03 To the extent it relates to the Product or Compound, each Party agrees to co- operate with the other Party in the preparation, filing, prosecution, maintenance and defense of Licensor Patents and application for patent extension or supplementary protection certificates or the similar procedures, including the signing of any necessary legal papers, and *to* provide the other Party with data or other information in support thereof, and to use reasonable efforts to ensure the co-operation of any of their respective personnel as might reasonably be requested in any such matters.

13.04 The trademark for the Product shall be selected by Licensee or its Affiliate at their sole discretion and registered and owned by Licensee or its Affiliate.

14. ENFORCEMENT

14.01 If either Party learns of any infringement or threatened infringement by a Third Party of a Licensor Patent, such Party shall promptly notify the other Party in writing and shall provide such other Party with available evidence of such

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infringement,

14.02 Licensee, at its expense, shall have the exclusive right but not the obligation to initiate and prosecute any action or proceeding with respect to infringement of any Licensor Patent in the Territory ("Action") and Licensor shall be joined as a plaintiff to any such Action if Licensee so requests, at Licensee's expense.

14.03 Licensee shall, subject to prior consultation with Licensor, have the right to determine the strategy and to exclusively control the Action.

14.04 Any damages or other monetary awards recovered from an Action shall be allocated first to reimburse the costs and expenses of Party who brings the Action and, if the other Party joins as a party plaintiff, then the costs and expenses of the other Party. Any amounts remaining shall be paid to Licensor to the extent such damage represents a loss of royalties or loss of profit from the royalty and any remaining balance shall be paid to Licensee.

15. DEFENSE

15.01 Licensee, at its own expense and subject to prior consultation with Licensor, shall control and conduct the defense against any actual, alleged or threatened claim or action which names Licensor and/or Licensee and which claims the infringement of Third Party's patent rights or know-how through importing, using, manufacturing, and marketing, selling, leasing and/or distributing the Compound or the Product. Licensee shall not settle or compromise such proceedings that would affect Licensor's rights or interests, without the prior written consent of Licensor which shall be neither unreasonably withheld or delayed. When named, Licensor shall be entitled, at its own expense, to participate in and to have counsel selected by it participate in any action.

15.02 In the event Licensee fails within a reasonable time to initiate appropriate action in connection with the defense which in the reasonable judgment of Licensor adversely affects or might adversely affect Licensor's rights or interests, Licensor upon notice to Licensee shall have the right, but not the obligation, to initiate or pursue any such appropriate action in Licensor's name and at Licensee's expense, and Licensee shall cooperate fully in any such act ion, provided, however, that Licensee at all the time shall have the right to fully participate in

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[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

such action at its own expense. Any judgment, damages, settlement or award which results from any action shall be paid by Licensee.

16. REPRESENTATIONS AND WARRANTIES

16.01 Licensor represents and warrants to Licensee that:

(a) Licensor is a corporation duly incorporated, validly existing and in good standing under the law of the jurisdiction of its organization, and has the power to perform its obligations and to carry on its business under this Agreement.

(b) This Agreement has been duly executed and delivered by Licensor, is a legal and valid obligation binding upon Licensor and enforceable against Licensor in accordance with its terms, except as such enforceability may be limited by applicable bankruptcy, insolvency, fraudulent conveyance and other laws affecting creditors' rights generally or by the availability of equitable remedies.

(c) The execution, delivery and performance of this Agreement by Licensor is within the corporate power of Licensor, has been duly authorized by all necessary corporate action, does not conflict with any agreement, instrument or understanding, oral or written, to which it is a party or by which it is bound, nor violate any law or regulation of any court, governmental body or administrative or other agency having jurisdiction over it.

(d) As of the Effective Date, Licensor has not knowingly withheld any material information from Licensee in response to Licensee's reasonable inquiries in connection with Licensee's due diligence relating to the Compound or the Product and this Agreement.

(e) As of the Effective Date, to the Knowledge of Licensor, (i) there is no pending litigation which alleges or any written communication alleging that Licensor's activities with respect to the Compound or the Product have infringed or misappropriated any of the intellectual property rights of any Third Party, (ii) all fees required to be paid by Licensor in order to maintain the Licensor Patents have been paid to date, and (iii) it has not previously

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[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

assigned, transferred, conveyed or otherwise encumbered its right, title and interest in the Licensor Patents or the Licensor Information, and (iv) there is no pending proceeding which alleges or any written communication alleging that the issued claims contained within the Licensor Patents are not valid and that the pending claims within the Licensor Patents, if and when issued, will not be valid.

(f) Licensor has the right to grant the rights granted to Licensee under this Agreement.

(g) Licensor bas received no notices that Licensor's granting of the rights granted to Licensee under this Agreement, or Licensor's performing its obligations to Licensee under this Agreement, is in breach of its obligations under any agreement with a Third Party.

(h) As of the Effective Date, to the Scientific Knowledge of Licensor, the data of the study report (No. D200201688-01.00) included in Licensor Information which show that YM477 does not inhibit thrombopoietins from binding to the Mpl receptor up to a concentration of 100 μ. M are valid and scientifically sound.

16.02 Licensee represents and warrants to Licensor that:

(a) Licensee is a corporation duly organized, validly existing and in good standing under the law of the jurisdiction of its organization, and has the power to perform its obligations and to carry on its business under this Agreement

(b) Th.is Agreement has been duly executed and delivered by Licensee, is a legal and valid obligation binding upon Licensee and enforceable against Licensee.in accordance with its terms, except as such enforceability may be limited by applicable bankruptcy, insolvency, fraudulent conveyance and other laws affecting creditors' rights generally or by the availability of equitable remedies.

(c) The execution, delivery and performance of this Agreement by Licensee is within the corporate power of Licensee, has been duly authorized by at1

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

necessary corporate action, does not conflict with any agreement, instrument or understanding, oral or written, to which it is a party or by which it is bound, nor violate any law or regulation of any court, governmental body or administrative or other agency having jurisdiction over it.

16.03 THE EXPRESS REPRESENTATIONS AND WARRANTIES STATED IN THIS AGREEMENT ARE IN LIEU OF ALL OTHER REPRESENTATIONS AND WARRANTIES, EXPRESS OR IMPLIED. NOTWITHSTANDING ANYTHING IN THIS AGREEMENT OR OTHERWISE, NEITHER PARTY SHALL BE LIABLE TO THE OTHER WITH RESPECT TO ANY SUBJECT MATTER OF THIS AGREEMENT, WHETHER UNDER ANY CONTRACT, NEGLIGENCE, STRICT LIABILITY OR OTHER LEGAL OR EQUITABLE THEORY, FOR ANY INCIDENTAL, INDIRECT, SPECIAL, EXEMPLARY, PUNITIVE, MULTIPLE, OR CONSEQUENTIAL DAMAGES (INCLUDING, WITH-OUT LIMITATION, LOST PROFITS, LOSS OF USE, DAMAGE TO GOODWILL, OR LOSS OF BUSINESS) EXCEPT AS SPECIFICALLY PROVIDED IN THIS AGREEMENT AND EXCEPT FOR CLAIMS OF FRAUD AND FRAUDULENT INDUCEMENT.

16.04 All claims by either Party for breach or default by the other Party under this Agreement shall be brought within one (1) year after the cause of action accrued or shall be deemed waived.

17. INDEMNIFICATION

17.01 Licensee shall indemnify and hold Licensor and its Affiliates, its directors, officers, employees and agents (as well as those of its Affiliates) harmless from and against all suits, investigations, claims, damages, liabilities, losses, costs and expenses, including but not limited to payment of reasonable attorneys' fees and expenses and court costs (collectively "Loss") resulting from any and all Third Party claims for damage or injury to persons or property or for loss of life caused by (i) the use, sale and distribution of the Compound or the Product by Licensee, its Affiliates or its sublicensees hereunder, (ii) any negligence or willful misconduct of Licensee, its Affiliates or its sublicensees or (iii) infringement of Third Party intellectual property rights by the exercise of any rights by Licensee, its Affiliates or sublicensees pursuant to this agreement; provided however, that if such Loss is caused partially or solely by (i) any gross negligence or willful misconduct of Licensor or any of its Affiliates, (ii) failure of the CGMP

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

Compound supplied by Licensor or any of its Affiliates to meet the Specifications or applicable cGMPs or (iii) material breach of this Agreement by Licensor or its Affiliates, Licensee shall not be obligated under this Section to the extent such Loss has resulted therefrom and Licensor shall indemnify and hold Licensee and its Affiliates, directors, officers, employees and agents (as well as those of its Affiliates) harmless from and against all such Losses to the extent of Licensor's fault.

17.02 In the event that a Party receives notice of a claim, lawsuit, or liability by a Third Party for which the other Party is entitled to indemnification, the indemnified Party shall give prompt written notification to the indemnifying Party. The indemnifying Party shall keep the indemnified Party informed as to the progress of its defense of any such claim, lawsuit or liability and the

indemnifying Party shall have complete control over the conduct and disposition of the claim, lawsuit, or liability including the retention of legal counsel engaged to handle such matter, provided that the indemnifying Party shall not settle or compromise such claim, lawsuit, or liability that would affect the indemnified Party's rights or interests, without the prior written consent of the indemnified Party.

17.03 During term and for a period of five (5) years after expiration or termination of this Agreement, Licensee shall secure and maintain an insurance policy underwritten by a reputable insurance company and in a form and having limits standard and customary for entities in the biopharmaceutical industry for exposures related to products such as the Product

18. CONFIDENTIALITY

18.01 During the term of this Agreement and for a period of ten (10) years after termination or expiration of this Agreement, neither Party shall disclose to Third Parties or use, except as may be provided for under this Agreement, any Confidential Information without express prior written consent of the other Party; provided, however, that the foregoing restrictions on disclosure and use shall not apply to any Confidential Information which:

(a) at the time of disclosure can be demonstrated by competent evidence to be already known to the receiving Party;

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

(b) at the time of disclosure or subsequent thereto is in the public domain other than by an act or omission on the part of the receiving Party charged with the non-disclosure obligation;

(c) is acquired from or made available by a Third Party having the lawful right to disclose such information; or

(d) has been independently developed by employees or contractors of the receiving Party or any of its Affiliates without the aid, application or use of Confidential Information of the disclosing Party.

18.02 Notwithstanding Section 18.01, the Parties shall be permitted to disclose the Confidential Information (a) as required to be disclosed in seeking any Regulatory Approvals required in connection with the importation, exportation, offer for sale, sale, marketing, manufacturing, and/or use of the Product; (b) to consultants, clinicians, or others in connection with the performance of consulting services or laboratory or clinical studies necessary for the filing of applications for such approvals; (c) as reasonably necessary for purposes of marketing and promoting the Product; (d) to comply with applicable laws and regulations or (e) as required to be disclosed in a judicial or administrative proceeding, provided that the disclosure under (b) shall be further subject to appropriate confidentiality agreements and that each Party shall give a written notice to the other prior to the disclosure under (d) or (e). Information licensed exclusively by Licensor to Licensee pursuant to this Agreement shall continue to be the information of Licensor, but, Licensor shall not use or disclose such Information to Third Parties without express prior written consent of Licensee; provided, however, that (I) the foregoing restrictions on Licensor shall not apply to any Information which falls in ant of 18.01 (a), (b), (c) or (d) and that (II) Licensor may make publication presentation or other public announcement regarding research, studies and activates of Licensor and containing such Information if consented by Licensee in advance, which consent shall not be unreasonably withheld or delayed

18.03 Licensor shall have the right to disclose Confidential Information to any Affiliate of Licensor, and Licensee shall have the right to disclose Confidential Information to any of its Affiliates and sublicensees, provided that such disclosure shall be subject to obligations of confidentiality comparable to those contained herein and further that such disclosure does not violate any applicable

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

anti-trust laws within Territory.

18.04 Neither Party shall make any press release or other public announcement or other disclosure to a Third Party concerning any results, data, information, know-how and technology regarding research, studies and activities of the other Party in connection with this Agreement and the existence of or tern1S of this Agreement without the prior written consent of the other Party, which consent shall not be unreasonably withheld or delayed. The foregoing shall not be construed to preclude any disclosure required to be made by applicable law, rule or regulation.

19. TERM

19.01 This Agreement shall commence on the Effective Date and, unless sooner terminated in accordance with the terms hereof, continue in effect on a country-by-country basis and on a product-by-product basis for a period of the longer of (i) until the expiration of the last-to-expire claim of a Licensor Patent, (ii) any government-granted marketing exclusivity period for the Product or (iii) ten (10) years after the last Date Of Launch to have occurred in any country in Territory. Thereafter, this Agreement may be extended for successive terms of one year each if Licensee expresses its desire in writing to extend the term of this Agreement at least three (3) months prior to the expiry date of this Agreement.

20. TERMINATION

20.01 Licensee shall be entitled, upon thirty (30) days prior written notice to Licensor, to terminate this Agreement in whole, or on a country by country basis, in writing at any time without penalty.

20.02 This Agreement may be terminated whether in whole or as to one or more countries in Territory with written notice by either Party at any time during the term of this Agreement

(a) if it is proven by reasonable evidence that the other Party is in breach of its material obligations hereunder for reasons other than force majeure and has not cured such breach within sixty (60) days after submission of written notice requesting the correction of the breach; or

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[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

(b) upon the filing or institution of bankruptcy, reorganization, liquidation or receivership proceedings by the other Party or upon the failure by the other Party for more than sixty (60) days to take steps to oppose the initiation of such actions against it.

20.03 This Agreement may be terminated by Licensor with written notice for the countries in which both of the following events have occurred: i) Licensee has elected not to proceed with and/or abandoned filing, prosecution, and/or maintenance of Licensor Patents in accordance with Section 13.02, and ii) Licensee has failed to commercialize the Product in five (5) years after Licensee obtains the first Regulatory Approval from a Regulatory Authority.

20.04 Upon termination of this Agreement for whatever reasons, Licensee, its Affiliates and/or sublicensees shall pay in full all sums due to Licensor before the termination of this Agreement within thirty (30) days of the date of termination. Licensee shall not be obligated to pay any milestone payments if the relevant milestone event does not occur before the termination of this Agreement for whatever reason.

20.05 Upon termination of this Agreement by Licensee pursuant to Section 20.01 or by Licensor pursuant to Section 20.02 or Section 20.03, Licensee shall promptly take the following measures in each country in the Territory where this Agreement is terminated:

(a) cease to use the Licensor Patents and the Licensor Know-How in those jurisdictions where this Agreement has been terminated;

(b) return to Licensor or its designee, destroy or transfer to a country where this Agreement remains in full force and effect all the Licensor Information and Licensor Material supplied by Licensor hereunder;

(c) transfer all the registrations of the Product in terminated countries of the Territory including the NDA if applicable and legally possible, and any related information and know-how prepared by Licensee and its Affiliate to Licensor or its designee to enable Licensor or its designee to sell the Product as soon as practicable in such terminated countries of the

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

Territory;

(d) cease to use and sell the Product in the terminated countries of the Territory within one hundred eighty (180) days of termination;

(e) (i) at Licensor's request, destroy or return to Licensor all the Product on band in terminated countries of the Territory at Licensee's own expense after Licensee has had the opportunity to sell off the same during the one hundred eighty (180) day period following termination or (ii) Licensee shall promptly transfer all such Product to a country of the Territory where this Agreement remains in full force and effect; and

(f) grant to Licensor an exclusive license to use the trademark owned or controlled by Licensee for the Product, but only in terminated countries of the Territory, for the purpose of commercialization of the Product in such countries, provided that, Licensor shall pay Licensee a royalty equal to [***] percent ([***]%) of the net sales invoiced for sales of the Product by Licensor and its Affiliates to Third Parties.

20.06 Notwithstanding the provision of Section 18.01, Licensor and its designees shall be entitled to use free of charge the registrations including the NDA and related information and know-how prepared by Licensee and its Affiliate, and transferred to Licensor or its designee under the provision of Section 20.05(c).

21. GENERAL PROVISIONS

21.01 **FORCE MAJEURE**

The Parties shall not be liable for any failure of or de]ay in performing any obligation under this Agreement, if such failure or delay is due to acts of God, weather, earthquakes, fire, explosion; war, invasion, riot or other civil unrest; governmental laws, orders, restrictions, actions, embargoes or blockades; rational or regional emergency; injunctions, strikes, lockouts, labor trouble or other industrial disturbances; or any other cause beyond the control of the affected Party; provided, however, that the Party affected shall promptly notify the other Party of the force majeure and shall exert its best efforts to eliminate, cure or overcome any such causes and to resume performance of its obligations with all possible speed.

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

21.02 **SURVIVAL**

Termination or expiration of this Agreement will not affect Articles 17 (INDEMNIFICATION), 18 (CONFIDENTIALITY), 21.04 (GOVERNING LAW), 2l.05 (ARBITRATION) or any terms and conditions meant to survive such termination or expiration.

21.03 **ASSIGNMENT**

Neither of the Parties may assign, transfer or otherwise dispose of this Agreement to any Third Party without the prior written consent of the other party; provided, however, that each Party shall have the right to assign its rights and obligations under this Agreement to any Third Party successor to all or substantially all of (x) its entire business or (y) its pharmaceutical business. Notwithstanding the foregoing, either Party may assign this Agreement in whole or in part or extend the benefits thereof to any of its Affiliate(s) who shall be substituted directly in whole or in part for it hereunder, provided, however, that the assignor shall guarantee the performance of its Affiliate assignee hereunder.

21.04 **GOVERNING LAW**

This Agreement shall be deemed to have been made in the State of New York and its form, execution, validity, construction and effect shall be determined in accordance with the laws of the State of New York, U.S.A.

21.05 **ARBITRATION**

In the event of any controversy or claim arising out of or relating to this Agreement or breach thereof, the Parties shall try to settle those conflicts amicably between themselves. Should they fail to agree, the matter in dispute shall be finally settled under the Rules of Arbitration of the International Chamber of Commerce by three arbitrators appointed in accordance with said Rules. The language of any arbitration proceeding shall be English. The award rendered by the arbitrator(s) shall be final and binding upon the Parties hereto. The place of arbitration shall be in Tokyo, Japan.

21.06 **NOTICE**

Notice to Licensor shall be addressed to:

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

Astellas Pharma Inc.
3-11, Nihonbashi-Honcho 2-chome
Chuo-ku, Tokyo 103-8411
Japan
Attention:

with a copy to:

Notice to Licensee shall be addressed to:

AkaRx Corp.
Mack Centre IV, 4th Floor
61 S. Paramus Road
Paramus, NJ 07652
Attn.

with a copy to:

Heller Ehrman LLP
4350 La Jolla Village Drive, 7th Floor
San Diego, CA 92122
Attn: Richard A. Kaufman

Either Party may change its address by giving written notice to the other Party in advance.

Any notice or request required or permitted to be given in connection with this Agreement shall be in writing and shall be deemed to have been sufficiently given if sent by prepaid registered or certified air mail or personal courier at the address set forth in this Section 21.06 or to such other business address as may have been furnished in writing by the intended recipient to

the sender. The date of notice shall be deemed to be the date on which such notice has been given. Any required notice shall be given in the English language.

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

21.07 **WAIVER**

The failure of any Party to insist on the performance of any obligation hereunder shall not be deemed to be a waiver of such obligation. Waiver of any breach of any provision hereof shall not be deemed to be a waiver of any other breach of such provision or any other provisions on such occasion or any succeeding occasion. No waiver of any obligation under or provision of this Agreement shall be valid or effective unless in writing and signed by the Party waiving such obligation or provision.

21.08 **ENTIRE AGREEMENT AND AMENDMENTS**

This Agreement contains the entire agreement between the Parties in respect to the license of the Product and supersedes and cancels all previous agreements, negotiations, commitments and writings in respect to the subject matter hereof, including but not limited to, the relevant part of the MOU and may not be changed or modified in any manner, or released, discharged, abandoned, or otherwise terminated, orally or otherwise, unless in writing and signed by the duly authorized representatives of the Parties.

21.09 **SEVERANCE**

If any one or more of the provisions of this Agreement is held to be invalid or unenforceable, the provision shall be considered severed from this Agreement and shall not serve to invalidate any remaining provisions hereof. The Parties shall make a good faith effort to replace any invalid or unenforceable provision with a valid and enforceable one such that the objectives contemplated by the Parties when entering this Agreement may be realized.

21.10 **INTERPRETATION**

The titles of the Articles and Sections of this Agreement are for general information and reference only, and this Agreement shall not be construed by reference to such titles. All exhibits are incorporated into and made a part of this Agreement by reference. The term “including” (or any variation thereof such as “include”) shall be without limitation.

21.11 **THIRD PARTY BENEFICIARIES**

None of the provisions of this Agreement shall be for the benefit of or enforceable by any Third Party, including, without limitation, any creditor of either Party hereto. No such Third Party shall obtain any right under any provision of this Agreement or shall by reasons of any such provision make any

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claim in respect of any debt, liability or obligation (or otherwise) against either party hereto.

21.12 **LEGAL COMPLIANCE**

Each Party shall comply in all material respects with all laws, rules and regulations applicable to the conduct of its business in Territory pursuant to this Agreement.

21.13 **RELATIONSHIP OFTHE PARTIES**

Each Party is an independent contractor under this Agreement. Nothing contained herein is intended or is to be construed so as to constitute Licensee and Licensor as partners, agents or joint ventures. Neither Party shall have any express or implied right or authority to assume or create any obligations on behalf of or in the name of the other Party or to bind the other Party to any contract, agreement, or undertaking with any Third Party.

21.14 **COUNTERPARTS**

This Agreement may be executed in counterparts with the same effect as if both Parties had signed the same document. All such counterparts shall be deemed an original, shall be construed together and shall constitute one and the same instrument.

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

IN WITNESS WHEREOF, the Parties have executed this Agreement by the signature of their duly authorized representatives on the date written above.

ASTELLAS PHARMA INC.

	/s/ Toichi Takenaka
Name	Toichi Takenaka
Title	President and CEO

AKARX, INC.

	/s/ Robert E. Desjardins
Name	Robert E. Desjardins
Title	President & CEO

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

Appendix A

(Licensor Patent)

A) Basic Patent (reference number: Y0302)

[summary of the invention]	[***]
[priority application]	JP 2002-10413 filed on January 18, 2002 JP 2002-10447 filed on January 18, 2002
[PCT application]	PCT/JP03/00270 filed on January 15, 2003
[non-PCT application]	none
[International publication]	WO 03/062233 published on July 31, 2003
[pending country]	JP, US, EP, CA, CN, KR, IN
[details]	

country	filing date	application number	publication number	patent number	Status
Japan	15JAN03	2003-562111	—	—	pending
United States	15JAN03	unassigned	—	—	pending
Europe	15JAN03	03 700 571.7	EP 1 466 912	—	pending
Canada	15JAN03	SN 2,472,711	—	—	pending
China	15JAN03	03 804 457.9	—	—	pending
Korea	15JAN03	2004-7010846	KR 2004-0078122	—	pending
India	15JAN03	00942/KOLNP/2004	—	—	pending

B) Salt Patent (reference number: Y0355)

[summary of the invention]	[***]
[priority application]	JP 2002-284689 filed on September 30, 2002
[PCT application]	PCT/JP2003/012419 filed on September 29, 2003
[non-PCT application]	none
[International publication]	WO 2004/029049 published on April 8, 2004
[pending country]	JP
[details]	

country	filing date	application number	publication number	patent number	Status
Japan	29SEP03	2004-539569	—	—	pending

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

*****Text Omitted and Filed Separately**
Confidential Treatment Requested
Under 17 C.F.R. §§ 200.80(b)(4) and 230.406

AMENDMENT NO. 1

TO THE YM477 LICENSE AGREEMENT

This AMENDMENT NO. 1 TO THE YM477 LICENSE AGREEMENT (the "Amendment"), is entered into as of March 8, 2007 (the "Amendment Effective Date") by and among Astellas Pharma Inc., a company organized and existing under the laws of Japan and having its principal office at 3-11, Nihonbashi-Honcho 2-chome, Chuo-ku, Tokyo 103-8411, Japan ("Licensor"), and AkaRx Corp., a company organized and existing under the laws of Delaware and having its principal office at Mack Centre IV, 4th Floor, 61 S. Paramus Road, Paramus, NJ 07652 ("Licensee"). Licensor and Licensee are referred to collectively herein as the "Parties".

Whereas, the Parties entered into the YM477 License Agreement (the "Agreement") as of August 15, 2005 wherein Licensee obtained a license to the Licensor Patents which included the patents/patent applications identified in Appendix A attached thereto;

Whereas, the Parties wish to add to the Licensor Patents (i) the one (1) additional patent family identified on Schedule A hereto (the "Additional Patent Filings");

Whereas, the Parties wish to amend the Agreement to reflect the additions to the Licensor Patents identified in the Agreement; and

Now, therefore, in consideration of the mutual covenants and promises contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows:

1. DEFINITIONS

Capitalized terms used but not defined in this Amendment have the meaning given them in the Agreement.

2. AMENDMENT TO AGREEMENT

The Parties agree that, subject to Paragraphs 3, 4, 5 and 6 below, the Licensor Patents of the Agreement were amended to include the Additional Patent Filings of Schedule A, attached hereto, as of November 8, 2005.

3. DEFINITION OF "COMPOUND"

The definition of the Compound provided for in Article 1 of the Agreement shall be amended as follows:

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

""Compound" shall mean [***] together with all other compounds covered by the Licensor Patents designated in Appendix A attached to the Agreement, which Licensor Patents shall not include any of the Additional Patent Filings solely for purposes of the definition of "Compound.""

4. PROSECUTION AND MAINTENANCE OF LICENSOR PATENTS

Section 13.01 and 13.02 shall be amended as follows:

"13.01 Licensee shall hereby assume from Licensor all responsibility and control for the preparation, filing, prosecution and maintenance as well as any cost to be incurred therefor of all relevant patent applications and patents included or to be included within the Licensor Patents and applications for patent extension or supplementary protection certificates or similar extensions in the name of Licensor, if required, for the benefit of Licensee. Licensee shall provide Licensor with copies of relevant documentation so that Licensor can be informed of continued prosecution and shall permit Licensor to comment on such documentation. Licensee shall give due consideration to any reasonable comments by Licensor.

13.02 Notwithstanding Section 13.01, Licensee shall have the right, at any time and at its sole option, to elect not to proceed with and/or to abandon filing, prosecution, and/or maintenance of any Licensor Patents, provided that Licensee shall give Licensor notice of such intention at least thirty (30) days before a final due date which would result in the abandonment, cancellation or lapse of an issued patent or pending patent application. In such case, Licensor, at its option, may assume the right to prepare, file, prosecute, maintain and/or defend any such Licensor Patents at Licensor's expense. While the terms and conditions mentioned above in this Section 13.02 shall be applied, in principle, to filing, prosecution, and/or maintenance of a Licensor Patent as a whole (not any portion thereof), they shall also be applied to filing, prosecution, and/or maintenance of any portion of an Additional Patent Filing if such portion covers any compound or product other than the Compound or the Product."

5. ENFORCEMENT OF LISENSOR PATENT

Section 14.02 shall be amended as follows:

"Licensee, at its expense, shall have the exclusive right but not the obligation to initiate and prosecute any action or proceeding with respect to infringement of any Licensor Patent in the Territory ("Action") and Licensor shall be joined as a plaintiff to any such Action if Licensee so requests, at Licensee's expense; provided, however, that any action or proceeding with respect to infringement of any Additional Patent Filing shall be excluded from the Action if such infringement is not upon the portion(s) of the Additional Patent Filing covering the Compound or the Product, and Licensor shall have the sole and exclusive right but not the obligation to initiate, prosecute and otherwise control such action or proceeding (which is not the Action) and may retain all damages or other monetary award recovered from such action or proceeding to the exclusion of Licensee."

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

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6. REPRESENTATION AND WARRANTIES AS TO LICENSOR PATENT

Notwithstanding Paragraph 2 above, the provisions of Section 16.0l(e)(ii) shall not be applied to the Additional Patent Filings and Section 16.0l(e)(iv) with respect to the Additional Patent Filings will exclude patent office proceedings, patent office search reports and patent office examination reports from the representations and warranties.

7. FULL FORCE AND EFFECT

The Agreement, as amended by this Amendment and effective as of the Amendment Effective Date, remains in full force and effect.

IN WITNESS WHEREOF, the Parties' authorized representatives have executed this Amendment.

ASTELLAS PHARMA INC.

Name /s/ Masaki Doi

Masaki Doi, Ph.D.

Title Vice President, Business Development

AKARX, INC.

Name /s/ Robert E. Dejardins

Title CEO

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

SCHEDULE A

A) Additional Patent Filings

[title of the invention] [***]

[priority application] U.S Application No. 60/734,426 filed on November 8, 2005

[PCT application] PCT/IB2006/003142 filed on November 7, 2006

[non-PCT application] U.S. Application No. 11/593,758 filed November 7, 2006

[International publication]

[pending country] US, PCT

[details]

Country	Filing date	Application Number	Publication Number	Patent Number	Status
United States	07NOV06	11/593,758	—	—	pending
PCT	07NOV06	PCT/IB2006/003142	—	—	pending

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

*****Text Omitted and Filed Separately**
Confidential Treatment Requested
Under 17 C.F.R. §§ 200.80(b)(4) and 230.406

AMENDMENT N0.2 TO YM477 LICENSE AGREEMENT

This Amendment No.2 (this "Amendment") is made and entered as of October 10, 2007 ("Effective Date") by and between Astellas Pharma Inc., a company organized and existing under the laws of Japan and having its principal office at 3-11, Nihonbashi-Honcho 2-chome, Chuo-ku, Tokyo 103-8411, Japan ("Licensor") and AkaRx, Inc., a company organized and existing under the laws of Delaware and having its principal office at Mack Centre IV, 4th Floor, 61 S. Paramus Road, Paramus, NJ 07652 ("Licensee").

RECITALS

A. Licensor and Licensee entered into a certain YM477 License Agreement dated as of August 15, 2005 (the "License Agreement") and the AMENDMENT No.1 TO THE YM477 LICENSE AGEEMENT dated as of March 8, 2007.

B. Licensor and Licensee now desire to amend the License Agreement.

NOW THEREFORE, Licensor and Licensee agree to amend the License Agreement as follows:

1. The article 10 (SUPPLY OF MATERIAL) of the License Agreement is hereby amended to add a new Sections 10.05 and 10.06 which shall read as follows:

"10.05 Licensor agrees to sell to Licensee pursuant to a one-time purchase order delivered by Licensee to Licensor twenty-nine point nine (29.9) kilograms of Non-cGMP Compound. Licensee shall submit such one-time purchase order to Licensor within one hundred and eighty (180) days after the Effective Date. After consultation with Licensee, Licensor shall reasonably decide ordering lead times, shipping methods, packaging, transit insurance and the like with respect to such sale. Such Non-cGMP Compound shall be delivered on the basis of Ex Works (Incoterms 2000), Licensor' manufacturing site in Japan. Licensee shall pay to Licensor, in consideration for Non-cGMP Compound supplied pursuant to this Section 10.05, 8,500 U.S. Dollars per kilogram. Such payment shall be made by Licensee within sixty (60) days after the delivery of Non-cGMP Compound occurs.

10.06 ALL THE NON-CGMP COMPOUNDS ARE PROVIDED TO LICENSEE "AS IS" WITHOUT WARRANTY OF ANY KIND. TO THE MAXIMUM EXTENT ALLOWABLE BYLAW, LICENSOR EXPRESSLY DISCLAIMS ALL WARRANTIES, WHETHER EXPRESS, IMPLIED OR STATUTORY, AS TO ANY ASPECT OF NON-CGMP COMPOUND OR ITS USE AND DELIVERY, INCLUDING WITHOUT LIMITATION, WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE."

2. Except as amended and supplemented hereby, the License Agreement shall remain in full force and effect.

3. This Amendment shall come into effect on the Effective Date of this Agreement and continue until the expiration or termination of the License Agreement.

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

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4. This Amendment may be executed in counterparts, each such counterpart constituting an original and all such counterparts constituting on and the same agreement.

IN WITNESS WHEREOF, the parties have caused this Amendment to be duly executed and delivered by their proper and duly authorized officers as of the date and year first written above.

LICENSEE:

AKARX, INC.

By: /s/ Robert Desjardins
Name: Robert Desjardins, MD
Title: President and Chief Executive Officer

LICENSOR:

ASTELLAS PHARMA INC.

By: /s/ Hirofumi Onosaka
Name: Hirofumi Onosaka
Title: Senior Corporate Officer
CFO & Chief Strategy Officer

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

*****Text Omitted and Filed Separately**
Confidential Treatment Requested
Under 17 C.F.R. §§ 200.80(b)(4) and 230.406

AMENDMENT N0.3

TO THE YM477 LICENSE AGREEMENT

This AMENDMENT N0.3 TO THE YM477 LICENSE AGREEMENT (the "Amendment"), is entered into as of this 12th day of March, 2012 (the "Amendment Effective Date") by and between Astellas Pharma Inc., a company organized and existing under the laws of Japan and having its principal office at 3-11, Nihonbashi-Honcho 2-chome, Chuo-ku, Tokyo 103-8411, Japan ("Licensor"), and AkaRx, Inc., organized and existing under the laws of Delaware and having its principal office at 100 Tice Blvd., Woodcliff Lake, NJ, a wholly-owned subsidiary of Eisai Inc., ("Licensee"). Licensor and Licensee are referred to collectively herein as the "Parties".

Whereas, the Parties entered into YM477 License Agreement as of August15, 2005, the Amendment No. 1 on March 8, 2007 and Amendment No. 2 as of October 10, 2007 (collectively the "License Agreement"), under which AkaRx Inc. received exclusive license rights to the Licensor Patents (as defined in the License Agreement);

Whereas, the Parties now wish to add one (1) additional patent family identified on Schedule A hereto (the "Polymorph Additional Patent Filings") to the Licensor Patents; and

Whereas, the Parties wish to amend the License Agreement to reflect such additions to the definition of Licensor Patents in the License Agreement;

Now, therefore, in consideration of the mutual covenants and promises contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows:

1. DEFINITIONS

Capitalized terms used but not defined in this Amendment have the meaning given them in the Agreement.

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

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2. AMENDMENT TO AGREEMENT

The Parties agree that, effective as of August 3, 2011, the Polymorph Additional Patent Filings described on Schedule A, attached hereto, shall be included as Licensor Patents under the License Agreement.

3. DEFINITION OF "COMPOUND"

The definition of the Compound provided for in Article I of the License Agreement shall be amended as follows:

""Compound" shall mean [***] including for the avoidance of doubt, any polymorph forms thereof, and all other compounds, covered by the Licensor Patents."

4. FULL FORCE AND EFFECT

The Agreement, as amended by this Amendment and effective as of the Amendment Effective Date, remains in full force and effect until expiration or termination of the License Agreement.

IN WITNESS WHEREOF, the Parties' authorized representatives have executed this Amendment.

Astellas Pharma Inc.	AkaRx, Inc.
/s/ C Yokota	/s/ Vincent P. Andrews
Chihiro Yokota	Vincent P. Andress
Vice President	Assistant Secretary
License & Alliances	AkaRx, Inc.
Astellas Pharma Inc.	

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

SCHEDULE A

A) Polymorph Additional Patent Filings

[title of the invention] [***]

[priority application] Japanese Patent Application 2011-169730, filed Aug. 3, 2011

[PCT application] To be filed

[pending country] Japan

[details]

Country	Filing date	Application Number	Publication Number	Patent Number	Status
Japan	3 AUG 2011	Japanese Patent Application 2011-169730	—	—	Pending

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

*****Text Omitted and Filed Separately**
Confidential Treatment Requested
Under 17 C.F.R. §§ 200.80(b)(4) and 230.406

AMENDMENT NO.4

TO THE YM477 LICENSE AGREEMENT

This AMENDMENT NO.4 TO THE YM477 LICENSE AGREEMENT (the "Amendment"), is entered into as of this 21st day of October, 2013 (the "Amendment Effective Date") by and between Astellas Pharma Inc., a company organized and existing under the laws of Japan and having its principal office at 5-1, Nihonbashi-Honcho 2-chome, Chuo-ku, Tokyo 103-8411, Japan ("Licensor"), and AkaRx, Inc., organized and existing under the laws of Delaware and having its principal office at I 00 Tice Blvd., Woodcliff Lake, NJ, a wholly-owned subsidiary of Eisai Inc. ("Licensee"). Licensor and Licensee are referred to collectively herein as the "Parties".

Whereas, the Parties entered into YM477 License Agreement as of Augustl5, 2005, the Amendment No. 1 on March 8, 2007, Amendment No. 2 as of October 10, 2007 and Amendment No.3 as of March 12, 2012 (collectively the "License Agreement"), under which Licensee has been conducting pre-clinical and clinical development activities for the Product that are necessary to seek Regulatory Approval of the Product in those jurisdictions chosen by Licensee;

Whereas, Licensee wishes to receive certain consulting and advisory services as Licensee may need within the scope of Licensor Information furnished to Licensee pursuant to the provisions of Section 7.01 of the License Agreement and Licensor is willing to provide such consulting and advisory services to the extent that Licensor deems it necessary for Licensee to meet applicable regulatory requirements or facilitate the obtainment of Regulatory Approval;

Whereas, the Parties wish to amend the License Agreement to reflect the above;

Now, therefore, in consideration of the mutual covenants and promises contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows:

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

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1. DEFINITIONS

Capitalized terms used but not defined in this Amendment have the meaning given them in the License Agreement.

2. AMENDMENT TO AGREEMENT

The following paragraph shall be newly added as Section 4.04 of the License Agreement:

"4.04 At the request of Licensee from time to time prior to the completion of the development activities set forth in Article 4, Licensor shall provide certain consulting and advisory services as Licensee may need within the scope of Licensor Information furnished to Licensee pursuant to the provisions of Section 7.01 (the "Services") provided that such Services shall only be made available to Licensee if and when Licensor deems it necessary for Licensee to meet applicable regulatory requirements or facilitate the obtainment of Regulatory Approval and Licensor and Licensee shall then have mutually agreed upon any other related conditions for such Services including the scope thereof, and provided further that, in any event Licensee shall pay Licensor [***] Japanese Yen (JPY[***]) per FTE/hour for any Services by Licensor under this Section, where such payment from Licensee to Licensor shall be made within thirty (30) days after the receipt of a relevant invoice issued by Licensor in Japanese Yen by bank wire transfer to a bank account designated in writing by Licensor."

3. SERVICES PROVIDED PRIOR TO THE EXECUTION OF THIS AMEMDMENT

In consideration of the consulting and advisory services which Licensor provided to Licensee prior to the execution of this Amendment, the details of which is described in Schedule A attached hereto, Licensee shall pay Licensor [***] Japanese Yen (JPY[***]), where such payment shall be made within thirty (30) days after the receipt of a relevant invoice issued by Licensor immediately after the Amendment Effective Date in Japanese Yen by bank wire transfer to a bank account designated in writing by Licensor. For the purpose of clarification, notwithstanding the amended Section 4.04 above, [***] Japanese Yen (JPY[***]) per FTE/hour is employed to calculate the aforementioned

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[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

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payment for the consulting and advisory services provided from Licensor to Licensee prior to the execution of this Amendment.

4. FULL FORCE AND EFFECT

The License Agreement, as amended by this Amendment and effective as of the Amendment Effective Date, remains in full force and effect until expiration or termination of the License Agreement.

IN WITNESS WHEREOF, the Parties' authorized representatives have executed this Amendment.

Astellas Pharma, Inc.	AkaRx, Inc.
/s/ Chihiro Yokota	/s/ Vincent P. Andrews
Chihiro Yokota	Vincent P. Andrews
Corporate Executive	Assistant Secretary
Vice President	AkaRx, Inc.
Licensing & Alliances	
Astellas Pharma Inc	

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.

Services Provided	Number of Scientists	Hours						Sub-Total
		Jan	Feb	Mar	Apr	May	Jun	
Advance preparation for preclinical data review								
(1) Advance preparation for an on-site review of preclinical data on additional study about action site of YM447, and checking and confirming quality control of the study	3	22	18	0	0	0	0	40
(2) Advance preparation for the on-site review of preclinical data, and checking and confirming quality control of the studies reviewed at the 1st	14	91.25	45.5	11.25	98	64	58.5	368.5

review (Feb. 7&8), 2nd review (May 17), and 3rd review (planned but not done on July 9)								
Quality control and response to Eisai's request on additional study								
(3) Quality control of draft report prepared by Eisai on additional study about action site ofYM477	2	0	0	0	6	2	0	8
(4) Preparation of revised Figure 2 in additional study report YM477-2 about action site ofYM477 (this was part of the service (3) above, but was performed at different month.)	2	0	2	0	0	0	0	2
Services on the day of on-site review of preclinical l data								
(5) Answering to Eisai's questions about study materials (as binding hours)	5	0	9	0	0	7	0	16
(6) Consultation about overall study materials considering future NOA filing in Japan (as binding hours)	4	0	3	0	0	2	0	5
Post-on-site review services								
(7) Review and confirm draft amendments prepared by Eisai for the study reports (SK-971417,971435, 971454, 971615), which were subject of the 1st data review	1	0	0	0	9	8	0	17
(8) Connecting the construction record of gene recombinant cells and the actual gene recombinant cells used in the preclinical study, and quality control of the construction of the gene	2	8	12	0	14	8	6	48
							Total Hours	504.5

[***] = Portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment requested under 17 C.F.R. Sections 200.80(b)(4) and 230.406.