Exhibit 10.13  
CERTAIN INFORMATION CONTAINED IN THIS EXHIBIT, MARKED BY [\*\*\*], HAS  
BEEN EXCLUDED FROM THIS EXHIBIT BECAUSE THE REGISTRANT HAS  
DETERMINED THAT IT IS BOTH NOT MATERIAL AND IS THE TYPE THAT THE  
REGISTRANT TREATS AS PRIVATE OR CONFIDENTIAL.  
LICENSE AGREEMENT  
THIS LICENSE AGREEMENT (this “Agreement”) dated as of October 14, 2021 (“Effective Date”), is entered into between UPSTREAM BIO, INC., a Delaware corporation (“Upstream”), having a place of business at care of: Xxxxxx Xxxxxxxx Innovations, 000 Xxxxxxxxxx Xxxxxx, Xxxxxxx, XX 00000, XXX, and MARUHO CO., LTD., a Japanese corporation (“Maruho”), having a place of business at 1-5-22, Nakatsu, Kita-ku, Osaka, 5310071, Japan.  
RECITALS  
WHEREAS, the parties recognize that Xxxxxx had identified the Astellas Assets through its long-term relationship with Astellas, had a formative role in securing the Astellas Asset Purchase Agreement, and is a co-founder of Upstream.  
WHEREAS, the parties recognize that Upstream, who has signed the Astellas Asset Purchase Agreement, will be responsible for and lead the global development of the Astellas Assets.  
WHEREAS, Maruho engages in a pharmaceutical activities such as research and development, manufacturing, marketing, promoting and distributing prescription drugs in Japan.  
WHEREAS, Upstream wishes to grant to Xxxxxx, and Xxxxxx wishes to accept from Upstream, exclusive, irrevocable, perpetual, royalty-free license under the Assets for Japan, as more fully set forth herein, in recognition of Xxxxxx’s role in securing the Astellas Asset Purchase Agreement and its contribution as a co-founder of Upstream.  
NOW, THEREFORE, in consideration of the mutual agreements and covenants set forth herein and other good and valuable consideration, the receipt and sufficiency of which the parties hereby acknowledge, the parties, intending to be legally bound hereby, agree to the foregoing and as follows:  
1. DEFINITIONS.  
For the purposes of this Agreement, the following terms shall have the respective meanings set forth below, and grammatical variations of such terms shall have corresponding meanings:  
1.1 “Affiliate” means, with respect to a party, any entity that controls or is controlled by such party, or is under common control with such party. For purposes of this definition, an entity shall be deemed to control another entity if it owns or controls, directly or indirectly, at least fifty percent (50%) of the voting equity of the other entity (or other comparable interest for an entity other than a corporation).  
1.2 “Astellas” means Astellas Pharma Inc.  
1.3 “Astellas Assets” means all assets and related intellectual property rights assigned, or to be assigned hereinafter, to Upstream by Astellas pursuant to the Astellas Asset Purchase Agreement.  
1.4 “Astellas Asset Purchase Agreement” means the Asset Purchase Agreement between Astellas and Upstream, dated as of October 14, 2021.  
1.5 “Bulk Licensed Compound” means the bulk form of the Licensed Compound.  
1.6 “Business Day” means any day other than a Saturday, a Sunday or a day on which commercial banks located in Dover, Delaware, or Osaka, Japan are authorized or required by law to remain closed.  
1.7 “Change of Control” means (i) a merger or consolidation of Upstream with an unaffiliated third party that results in the voting securities of Upstream outstanding immediately prior thereto, or any securities into which such voting securities have been converted or exchanged, ceasing to represent more than fifty percent (50%) of the combined voting power of the surviving entity or the parent of the surviving entity immediately after such merger or consolidation, or (ii) a transaction or series of related transactions in which an unaffiliated third party (or its Affiliates) becomes the beneficial owner of more than fifty percent (50%) of the combined voting power of the outstanding securities of Upstream, or (iii) the sale or other transfer to an unaffiliated third party of all or substantially all of Upstream’s business to which the subject matter of the Astellas Asset Purchase Agreement relates.  
1.8 “Confidential Information” means all information and data that (a) is provided by one party to the other party under this Agreement, and (b) if disclosed in writing or other tangible medium is marked or identified as confidential at the time of disclosure to the recipient, is acknowledged at the time of disclosure to be confidential, or otherwise should reasonably be deemed to be confidential. Notwithstanding the foregoing, Confidential Information of a party shall not include that portion of such information and data which, and only to the extent, the recipient can establish by written documentation: (i) is known to the recipient as evidenced by its written records before receipt thereof from the disclosing party, (ii) is disclosed to the recipient free of confidentiality obligations by a third person who has the right to make such disclosure, (iii) is or becomes part of the public domain through no fault of the recipient, or (iv) the recipient can reasonably establish is independently developed by persons on behalf of recipient without access to or use of the information disclosed by the disclosing party.  
1.9 “Japan-specific Studies” means preclinical or clinical studies that are executed specifically in Japan, without participation of any territory outside of Japan.  
1.10 “Joint Development Committee” or “JDC” means the joint steering committee, comprising representatives of Upstream and Maruho, described in Section 6.  
 2  
1.11 “Licensed Compound” means the compound that was designated by Astellas as ASP7266 (as further described in Exhibit A), together with all forms and components thereof.  
1.12 “Licensed IP Rights” means, collectively, the Licensed Know-How Rights, Licensed Patent Rights and Licensed Marks.  
1.13 “Licensed Know-How Rights” means, collectively, Upstream’s, its Affiliates’ rights in all trade secret and other know-how rights regarding the Licensed Compound, the Product or the manufacture or use thereof to the extent reasonably necessary to research, develop, obtain regulatory approval for or commercialize the Product in Japan, and to have made the Product in accordance with this Agreement for use or sale in Japan, including without limitation all such rights comprising the Astellas Assets (during the term of this Agreement). For clarity, all development data available, with the right to transfer to Maruho, to Upstream from its licensees shall be shared with Maruho under Licensed Know-How Rights.  
1.14 “Licensed Marks” means those certain trademarks, trade names, designs and markings owned or controlled by Upstream and upon Xxxxxx’s request licensed by Upstream for use by Maruho under this Agreement in the packaging, labeling, promotion, marketing and sale of the Product in Japan.  
1.15 “Licensed Patent Rights” means, collectively, Upstream’s, its Affiliate rights in (a) all patent applications heretofore or hereafter filed for or in Japan which claim, and only to the extent they claim, the Licensed Compound, the Product or the manufacture or use thereof to the extent reasonably necessary or useful to research, develop, obtain regulatory approval for or commercialize the Product in Japan, and to have made the Product in accordance with this Agreement for use or sale in Japan, including without limitation all such rights comprising the Astellas Assets (during the term of this Agreement) (For clarity, the initial Licensed Patent Rights as of the Effective Date shall be set forth in Exhibit B of this Agreement); (b) all patents that have issued or in the future issue from any of the foregoing patent applications, including without limitation utility models, design patents and certificates of invention; and (c) all divisionals, continuations, continuations-in-part, reissues, renewals, extensions or additions to any such patents and patent applications.  
1.16 “Lonza” means LONZA SALES AG, incorporated and registered in Switzerland whose registered office is at [\*\*\*].  
1.17 “Lonza Agreement” means the License Agreement between Lonza and Upstream to be executed soon before or after the date of this Agreement (as amended or restated from time to time. Upstream shall not amend any terms and provisions of Lonza Agreement, which have effect on Maruho’s rights and obligations under this Agreement without Maruho’s advance written consent, provided, however, that such consent shall not be unreasonably withheld or rejected.  
 3  
1.18 “Maruho Product Data” means all data, information and documents from or for the clinical development, regulatory approval or commercialization of the Product for or in Japan generated by or on behalf of Maruho, its Affiliates or sublicensees, including (as applicable and without limitation) safety data (including serious adverse event data), clinical data, regulatory roadmap and submissions, regulatory compliance information, pharmacovigilance, product quality vigilance, considerations for indication selection, and clinical trial design. Maruho Product Data excludes Upstream Product Data.  
1.19 “NDA” means a new drug application or similar application for marketing approval of a pharmaceutical product submitted to the PMDA.  
1.20 “Orphan Drug Designation” means a grant by the Food and Drug Administration of the United States of a request for designation as an orphan drug under Section 526 of the Federal Food, Drug and Cosmetics Act as amended by Section 2 of the Orphan Drug Act (sections 525-528 (21 U.S.C. §360aa-dd)), and its related regulations (including 21 C.F.R. §316 et seq.).  
1.21 “Phase II(a) Clinical Trial” means a human clinical trial that is intended to initially evaluate the dosing requirements of a product for a particular indication or indications in patients with the disease or indication under study or that would otherwise satisfy requirements of 21 C.F.R. §312.21(b).  
1.22 “Phase II(b) Clinical Trial” means a human clinical trial that is intended to determine the safe and effective dose range of a product for a particular indication or indications in patients with the disease or indication under study or that would otherwise satisfy requirements of 21 C.F.R. §312.21(b) following Phase II(a) Clinical Trial.  
1.23 “Phase II(b) Clinical Trial Activities” means Phase II(b) Clinical Trial, and any additional preclinical studies required therefor, in Japan that are required by the PMDA in order to obtain marketing approval for the Product in that indication in Japan.  
1.24 “Phase III Clinical Trial” means a pivotal human clinical trial the results of which may be used to establish safety and efficacy of a product as a basis for a NDA.  
1.25 “Phase III Clinical Trial Activities” means Phase III Clinical Trial and any additional preclinical or clinical studies in Japan required by the PMDA or any other regulatory authorities in Japan in order to obtain marketing approval for the Product in that indication in Japan.  
1.26 “PMDA” means the Pharmaceuticals and Medical Devices Agency in Japan.  
1.27 “Product” means any pharmaceutical, biologic or medical device product (or any combination thereof), which (a) was or is developed by or on behalf of Upstream or its Affiliates, and (b) incorporates or uses the Licensed Compound. For clarity, the Product shall include the Bulk Licensed Compounds and Licensed Compounds itself.  
1.28 “Regeneron” means Regeneron Pharmaceuticals, Inc., a New York corporation.  
 4  
1.29 “Regeneron Agreement” means the Letter Agreement between Regeneron and Upstream, to be executed soon before or after the date of this Agreement (as amended or restated from time to time). Upstream shall not amend any terms and provisions of Regeneron Agreement, which have effect on Maruho’s obligation under this Agreement without Xxxxxx’s advance written consent, provided, however, that such consent shall not be unreasonably withheld or rejected.  
1.30 “Supported IP Rights” means, collectively, the Supported Know-How Rights and Supported Patent Rights.  
1.31 “Supported Know-How Rights” means, collectively, Xxxxxx’s rights in all trade secret and other know-how rights regarding the Licensed Compound, the Product or the manufacture or use thereof to the extent reasonably necessary to develop, obtain regulatory approval for or commercialize the Product other than (during the term of this Agreement) solely in Japan.  
1.32 “Supported Patent Rights” means, collectively, Xxxxxx’s rights in (a) all patent applications heretofore or hereafter filed in Japan which claim, and only to the extent they claim, the Licensed Compound, the Product or the manufacture or use thereof to the extent reasonably necessary to develop, obtain regulatory approval for or commercialize the Product other than (during the term of this Agreement) solely in Japan; (b) all patents that have issued or in the future issue from any of the foregoing patent applications, including without limitation utility models, design patents and certificates of invention; and (c) all divisionals, continuations, continuations-in-part, reissues, renewals, extensions or additions to any such patents and patent applications.  
1.33 “Third Party Payments” means all royalties and other amounts owing under any Upstream In-License (other than the Astellas Asset Purchase Agreement) reasonably necessary for the development, regulatory approval or commercialization of the Product in Japan.  
1.34 “Upstream In-License” means a license, sublicense or other agreement under which Upstream has acquired, or hereafter acquires, rights to the Licensed IP Rights, including without limitation the Lonza Agreement and the Regeneron Agreement.  
1.35 “Upstream Product Data” means all data, information and documents from or for the preclinical development, clinical development or regulatory approval of the Product for or applicable to Japan generated by or on behalf of Upstream or its Affiliates , including (as applicable and without limitation) safety data (including serious adverse event data), clinical data, regulatory roadmap and submissions, regulatory compliance information, pharmacovigilance, product quality vigilance, considerations for indication selection, and clinical trial design. For clarity, all Product data available with the right to transfer to Maruho, to Upstream from its licensees shall be shared with Maruho as Upstream Product Data.  
 5  
2. REPRESENTATIONS AND WARRANTIES.  
2.1 By Each Party. Each party represents and warrants to the other party as follows:  
2.1.1 Organization. Such party is duly organized, validly existing and in good standing under the laws of the jurisdiction in which it is organized.  
2.1.2 Authorization and Enforcement of Obligations. Such party (a) has the requisite power and authority and the legal right to enter into this Agreement and to perform its obligations hereunder; and (b) has taken all requisite action on its part to authorize the execution and delivery of this Agreement and the performance of its obligations hereunder. This Agreement has been duly executed and delivered on behalf of such party, and constitutes a legal, valid, binding obligation, enforceable against such party in accordance with its terms.  
2.1.3 Consents. All necessary consents, approvals and authorizations of all governmental authorities and other persons or entities required to be obtained by such party in connection with this Agreement have been obtained.  
2.1.4 No Conflict. The execution and delivery of this Agreement and the performance of such party’s obligations hereunder (a) do not conflict with or violate any requirement of applicable laws, regulations or orders of governmental bodies; and (b) do not conflict with, or constitute a default under, any contractual obligation of such party.  
2.2 By Upstream. Upstream represents and warrants to Maruho that, as of the Effective Date, (a) the Licensed Patent Rights have not been held by a court of competent jurisdiction to be invalid or unenforceable, in whole or in part, (b) Upstream has not received written notice of any claim or litigation by any third party alleging that any of the Licensed IP Rights are invalid or unenforceable, and (c) Upstream has the right to grant the licenses under the Licensed IP Rights pursuant to this Agreement.  
2.3 DISCLAIMER OF WARRANTIES. EXCEPT AS OTHERWISE EXPRESSLY SET FORTH IN SECTION 2.2, UPSTREAM MAKES NO REPRESENTATIONS OR WARRANTIES, EXPRESS OR IMPLIED, REGARDING THE LICENSED IP RIGHTS, THE LICENSED COMPOUND OR ANY OTHER MATTER, INCLUDING WITHOUT LIMITATION, ANY REPRESENTATION OR WARRANTY REGARDING VALIDITY, ENFORCEABILITY, MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OR NONINFRINGEMENT.  
3. LICENSE.  
3.1 License Grant to Maruho.  
3.1.1 License to Maruho. Subject to the terms and conditions of this Agreement, Upstream hereby grants to Maruho an exclusive (even as to Upstream unless otherwise expressly provided herein), irrevocable, perpetual, royalty-free (except as set forth in Section 4.1) license (with the right to grant sublicenses) under the Licensed IP Rights to research, develop, have made in Japan or outside of Japan by a contract manufacturing organization (“CMO”) or contract research organization (“CRO”) in each case as set out in Section 5.3 below, use, offer for sale, sell and import the Product in Japan. Except as expressly set forth in this Agreement, Maruho shall not use the Licensed Compound or the Licensed IP Rights outside of Japan.  
 6  
3.1.2 Sublicenses. Maruho shall have the right to grant sublicenses to its Affiliates or third parties for the purpose of developing, having made, using, offering for sale, selling, importing or commercializing the Product in Japan subject to Upstream’s right of first negotiation set forth in Section 8 below. Maruho shall provide Upstream with a copy of each sublicense promptly after executing the same; provided, however, that Xxxxxx shall have the right to redact any confidential terms from the copy provided to Upstream. Any such sublicense shall be subject and subordinate to the terms and conditions of this Agreement, and Maruho shall remain responsible for all payments due to Upstream hereunder.  
3.1.3 Reservation of Rights. Notwithstanding anything to the contrary in this Agreement and without restricting the rights not expressly granted by Upstream to Maruho under this Agreement, Upstream retains all rights under the Licensed IP Rights to perform its obligations under this Agreement or under any supply agreement related to this Agreement.  
3.2 Grantback License to Upstream.  
3.2.1 Maruho hereby grants to Upstream an exclusive, irrevocable, perpetual, royalty-free, worldwide license (with the right to grant sublicenses) under the Supported IP Rights for the purpose of developing, making, having made or commercializing the Product, other than (during the term of this Agreement) to make, have made, use, offer for sale, sell and import the Product in Japan.  
3.2.2 Upstream shall use commercially reasonable efforts to obtain a similar grantback license from any third party that enters into an agreement with Upstream or its Affiliate for rights to develop and commercialize the Product outside Japan, and if Upstream is unable to obtain such a grantback license from any such third party, then Upstream shall not grant a sublicense to such third party under the license grant from Maruho under Section 3.2, and any such sublicense granted by Upstream to such third party shall be void.  
3.3 No Implied Licenses. Only licenses and rights expressly granted herein shall be of legal force and effect. No license or other right shall be created hereunder by implication, estoppel or otherwise.  
4. THIRD PARTY PAYMENT TERMS.  
4.1 Third-Party Payments.  
4.1.1 Maruho shall pay to Upstream such Third-Party Payments paid or owing by Upstream, on such terms and conditions as set forth in the applicable Upstream In-License and applicable to Upstream that is relating only to the sale of Products by Maruho, its Affiliates and its sublicensees in Japan. Maruho shall make all such payments to Upstream, no later than [\*\*\*] prior to the date that the applicable Third-Party Payment is due under the applicable Upstream In-License.  
 7  
4.1.2 If Upstream, in good faith, enters into an Upstream In-License Agreement after the Effective Date that would require Maruho to pay any such Third Party Payments, Upstream promptly shall provide Maruho with a copy of such Upstream In-License Agreement. If, within [\*\*\*] after receipt of such copy, Xxxxxx gives express written notice that it accepts the terms and conditions thereof, then the patent rights and other intellectual property rights granted to Upstream under such Upstream In-License Agreement shall be included in this Agreement. If Xxxxxx fails to timely give such express written notice, then the patent rights and other intellectual property rights granted to Upstream under such Upstream In-License Agreement shall be excluded from Agreement.  
4.2 Payment Reports. Maruho shall furnish to Upstream all reports regarding Third-Party Payments (the “Payment Reports”) in such form and content and on such terms and conditions as set forth in the applicable Upstream In-License and applicable to Upstream, no later than [\*\*\*] prior to the date that such Payment Report is due under the applicable Upstream In-License. With respect to sales of the Product invoiced in a currency other than United States dollars, all such amounts shall be expressed both in the currency in which the sale is invoiced and in the United States dollar equivalent. The United States dollar equivalent shall be calculated using the exchange rate specified in the applicable Upstream In-License.  
4.3 Records and Audits. Maruho shall keep complete and accurate records in sufficient detail to enable all Third-Party Payments to be determined. Upon the written request of Upstream and not more than once in each calendar year, Xxxxxx shall permit an independent certified public accounting firm of nationally recognized standing, selected by Upstream and reasonably acceptable to Xxxxxx, at Upstream’s expense, to have access during normal business hours to such records of Xxxxxx as may be reasonably necessary to verify the accuracy of the Payment Reports hereunder for any year ending not more than [\*\*\*] prior to the date of such request. The accounting firm shall disclose to Upstream only whether the reports are correct or not and the specific details concerning any discrepancies. No other information shall be shared. If such accounting firm concludes that additional amounts were owed during the audited period, Maruho shall pay such additional amounts within [\*\*\*] of the date Upstream delivers to Maruho such accounting firm’s written report so concluding. The fees charged by such accounting firm shall be paid by Upstream; provided, however, if the audit discloses that the aggregate amounts payable by Maruho for such period are more than [\*\*\*] of the amounts actually paid for such period, then Maruho shall pay the reasonable fees and expenses charged by such accounting firm. Upstream shall treat all financial information subject to review under this Section 4.3 as confidential, and shall cause its accounting firm to retain all such financial information in confidence.  
[\*\*\*]  
4.4 Payment Method. All payments by Xxxxxx to Upstream hereunder shall be in United States dollars in immediately available funds and shall be made by wire transfer to such bank account as designated by Upstream shown below to Maruho; provided, however, that Upstream shall have the right to change such bank account or instructions on written notice to Xxxxxx of such change. Any payment which falls due on a date which is not a Business Day may be made on the next succeeding Business Day.  
 8  
4.5 Taxes.  
4.5.1 The Party receiving payments under the Agreement will pay any taxes levied on account of such payment. If any taxes are required to be withheld by the paying Party, then to the extent a deduction is permitted by the applicable Upstream In-License, it will (a) deduct such taxes from the remitting payment, (b) timely pay the taxes to the proper taxing authority, and (c) send proof of payment to the other Party and certify its receipt by the taxing authority within [\*\*\*] following such payment. It is understood and agreed between the Parties that any amounts payable by a Party to the other Party hereunder are exclusive of any and all applicable sales, use, value-added tax, general sales tax, excise, property, and other taxes, levies, duties or fees in the Territory (collectively, “Taxes”)  
4.5.2 The Parties agree to cooperate and produce on a timely basis any tax forms or reports, including a valid residential certificate required for Japanese withholding tax exemption or reduction, reasonably requested by the other Party in connection with any payment made by Maruho to Upstream under this Agreement. If Maruho does not receive such application forms and other documents by a day before due date, Maruho may extend payment due [\*\*\*] after the receipt of such documents.  
5. DEVELOPMENT AND COMMERCIALIZATION.  
5.1 Development.  
5.1.1 Upstream Development Activities. On the terms and conditions of this Agreement, Upstream shall be responsible for and control the development of the Product on a global basis including Japan, and shall consider in good faith the interests of Maruho in so doing. Upstream shall perform a Phase II(a) Clinical Trial for Orphan Drug Designation as part of Upstream’s global development strategy and shall aim to obtain the regulatory approval of FDA for the Product in that Orphan Drug Designation within [\*\*\*] following the commencement of such global development; provided, however, that such obligation shall terminate immediately upon the effectiveness of a registration statement filed by Upstream pursuant to the Securities Act of 1933, as amended, for any equity securities of Upstream or Upstream becoming subject to the reporting requirements of the Securities Exchange Act of 1934. Upstream shall develop the Product for use in Japan as part of Upstream’s global development strategy and in accordance with industry practices for development of biological products for use in Japan as part of a global development, and as much as possible on a similar schedule it develops the Product for its initial territory/territories; provided that Upstream’s development of the Product for use in Japan shall be made in accordance with Section 6.1 below.  
5.1.2 Maruho Phase II(b) and/or III Clinical Development Right. Upstream shall, on a global basis, provide Maruho with (i) top-line data and CSR (clinical study report) from the Phase II(a) Clinical Trials conducted by Upstream and (ii) all data regarding development plan after the above said CSR as soon as practicable after Upstream’s receipt of such data. At Maruho’s request, Upstream shall conduct, at Xxxxxx’s sole cost and expense, specified Phase II(b) and/or III Clinical Trial Activities in Japan, in accordance with Section 5.1.7 below; provided that patient enrollment in Japan shall be expected to be sufficient to obtain regulatory approval in Japan but in any case, not exceed twenty percent (20%) of Upstream’s global Phase II(b) and/or III Clinical Trial patient enrollment. Notwithstanding the foregoing, in the course of the specified Phase II(b) and/or III Clinical Trial Activities in Japan, Upstream shall (a) take, in good faith, Xxxxxx’s opinions and list for site selection into consideration in the course of its decision making, (b) select Japan specific KOL in consultation  
 9  
with Maruho, (c) obtain, in advance, the approval of the JDC for such Japan-specific KOL selection, (d) JDC will decide which party, either Upstream or Maruho, will lead the interaction with such Japan specific KOLs, (e) allow Xxxxxx’s participation in consultation with such KOLs together with Upstream, (f) have Maruho review the draft protocol, IB (Investigator’s Brochure) and CSR necessary for Phase II(b) and/or III Clinical Trial Activities conducted by Upstream, (g) consult with Maruho on Japan-specific conditions, including without limitation market conditions of competing products for the Product, and compliance with regulations in Japan, and (h) subsequently conduct such Phase II(b) and/or Phase III Clinical Trial based on the result of the above said consultation with Xxxxxx. Notwithstanding the foregoing, Japan-Specific Studies are subject to Section 5.1.6 below. Upstream will exercise reasonable efforts to ensure a timely execution of the Phase II(b) and/or III Clinical Trial Activities. Without derogating from Upstream’s obligation set out immediately above, if Upstream fails to enable Maruho to submit CTN (clinical trial notification) for a Phase II(b) and/or III Clinical Trial in an indication in Japan within [\*\*\*] after the first dosing of a patient in the equivalent US or Europe II(b) and/or Phase III Clinical Trial (the first to be initiated) in that indication, Maruho will have the right to continue to develop the Product on its own in that indication in Japan, with clinically reasonable adherence to Upstream’s clinical design and protocols in the US and/or Europe with Upstream’s reasonable support. JDC shall discuss and decide reasonable timeline in advance of commencement of such development.  
5.1.3 Pre-Clinical Studies. Maruho may, at its sole discretion and at its sole expense, carry out non-GLP pre-clinical pharmacology and non-GLP pharmacokinetics/pharmacodynamics studies in Japan, either by itself or through CRO or research institutions, which studies will be coordinated in the JDC. If the JDC reasonably considers that such study may raise adverse regulatory implications on the global development level, the JDC may object to the intended study and will use best efforts to make risk reduction modifications.  
5.1.4 Maruho Participants. Maruho shall have the right to send representatives on its behalf in order to participate in scheduled meetings of the Upstream development team which meeting will handle clinical development in Japan.  
5.1.5 Additional Indications. Maruho may, at any time, suggest to JDC new indications to develop for Japan for discussion purpose. The JDC shall reasonably consider such additional indications in accordance with the principles set out in Section 6.1 below. [\*\*\*]. Once the new indication is approved by the JDC, this indication will become an integral part of Upstream’s development plan for execution using reasonable development efforts and JDC shall discuss and decide reasonable timeline in advance of commencement of such development. If Upstream fails to initiate clinical trials in the new indication within [\*\*\*] after the target date for initiation of such clinical trial agreed by the JDC, Upstream shall present to the JDC a detailed explanation for the delay and specify the actions it is taking to expedite development and further discuss with Xxxxxx whether to delegate the right to continue to develop the Product on its own in that indication in Japan. If Upstream fails to submit a CTN of clinical trials in the new indication within [\*\*\*] after the target date for submission of a CTN of such clinical trial agreed by the JDC, Xxxxxx will have the right to continue to develop the drug on its own in that indication in Japan, in consultation with and with reasonable support of Upstream.  
 10  
5.1.6 Japan-Specific Studies. Upstream will develop Japan-Specific Studies with reasonable effort, which shall be at least equal to those used by Upstream itself in developing the Product outside Japan, in close coordination with Maruho. Upstream will preferably ask Xxxxxx to assist in the design of Japan-Specific Studies, and for Xxxxxx to participate or lead the execution of Japan-Specific Studies. If Xxxxxx will participates or lead such Japan-Specific Studies, then Upstream shall support Maruho in a timely manner. Maruho may obtain pharmacokinetic data of Japanese through the Japan-specific Studies. Upstream shall conduct Japan-Specific Studies in accordance with requirements made on Maruho by governmental or regulatory authority, authoritative national academic or medical society, or a Japan-focused KOL, regarding a specific indication or label specification.  
5.1.7 Reimbursement of Certain Upstream Development Costs. Maruho shall reimburse Upstream for one hundred percent (100%) of Upstream’s fully-burdened costs reasonably necessary for any development activities for the Product that are specific to Japan except internal labor costs reasonably necessary for any development activities for the Product that are specific to Japan, where Xxxxxx shall reimburse for [\*\*\*] of such internal labor costs, provided that the estimation of such costs, including amendments of such estimation, was done in good faith and agreed by the JDC. Upstream shall invoice Maruho for such amounts on a [\*\*\*] basis, and Maruho shall pay to Upstream the invoiced amount within [\*\*\*] after the date of such invoice. For clarity, Upstream shall use commercially reasonable efforts to operate within such estimations.  
5.2 Regulatory.  
5.2.1 Maruho Regulatory Activities. Maruho shall be responsible for and control the preparation, filing, prosecution, obtaining and maintaining all regulatory approvals for the Product in Japan, and shall own all regulatory applications, filings, approvals and licenses thereof and shall be the Marketing Authorization Holder in Japan. Xxxxxx shall work in full coordination and adherence to Upstream’s global regulatory strategy, and in doing so both parties will comply with the PMDA’s timelines.  
5.2.2 Communication with PMDA. Maruho shall have the sole responsibility in close consultation with Upstream and consistent with Upstream’s global development strategy, to communicate with the PMDA regarding the Product in Japan. With respect to any filing, material communication or other submission with the PMDA regarding the Product in Japan, (a) Maruho shall provide Upstream with an advance copy of the reasonably complete draft thereof; (b) Upstream shall have a reasonable opportunity to review, comment and consult on each such draft, taking into consideration any PMDA response deadline; and (c) Maruho shall consider the reasonable comments of Upstream in good faith. Maruho shall provide Upstream with the final form of each such written communication within [\*\*\*] after submission to the PMDA. With respect to any meetings, telephone conferences, video conferences or other non-written communication with the PMDA regarding the Product in Japan, Maruho shall provide Upstream with reasonable advance written notice thereof and use commercially reasonable efforts to allow Upstream the opportunity to have representatives actively participate therein.  
 11  
5.2.3 Reimbursement of Upstream Regulatory Costs. Maruho shall reimburse Upstream for one hundred percent (100%) of Upstream’s fully-burdened reasonable costs of assisting Maruho in any regulatory activities for the Product that are specific to Japan, except internal labor costs reasonably necessary for assisting Maruho in any regulatory activities for the Product that are specific to Japan, where Xxxxxx shall reimburse for [\*\*\*] of such costs, provided that the estimation of such costs, including amendments of such estimation, was done in good faith and agreed by the JDC. Upstream shall invoice Maruho for such amounts on a quarterly basis, and Maruho shall pay to Upstream the invoiced amount within [\*\*\*] after the date of such invoice. For clarity, Upstream shall use commercially reasonable efforts to operate within such estimations.  
5.3 Manufacturing and Supply.  
5.3.1 Development Supply. Upstream shall be responsible, at the sole expense of Maruho, for the procurement or supply of the Bulk Licensed Compound, the Product and the related compounds including, without limitation, non-GLP pre-clinical and clinical development meeting applicable regulations and the specifications (as amended from time to time, the “Specifications”). Upstream will notify Maruho of any changes to the Specifications as soon as reasonably practicable. If regulatory authority, including, without limitation, PMDA requires the amendment of the Specifications for the development for Japan, Upstream shall agree Maruho in such amendment and supply the Bulk Licensed Compound, the Product and the foresaid related compounds subject to such amended Specification. Upstream shall invoice Maruho for one hundred percent (100%) of the fully burdened cost of such supply on delivery, and Maruho shall pay to Upstream the invoiced amount within [\*\*\*] after the date of such invoice.  
5.3.2 Commercial Supply. Maruho shall have made the Product for Maruho’s sale and use in Japan, by a CMO that is either a CMO used by Upstream or a CMO that went through the technology transfer process set out below. Upstream shall either (i) make available to Maruho the right to purchase Bulk Licensed Compound and/or Product from one or more CMOs with whom Upstream has contracted to manufacture and supply Product, or (ii) make available to Maruho the right to purchase Bulk Licensed Compound and/or Product directly from Upstream. In either case of the above, Upstream shall enter into a quality agreement setting forth such quality control obligation with Maruho together with, if applicable, CMOs. Maruho and any such CMO, or Upstream in case of manufacturing by itself, shall negotiate and enter one or more supply agreements for the manufacture and supply of the Product directly from such CMO or Upstream to Maruho for Maruho’s sale and use in Japan. Upstream shall make commercially reasonable efforts to enable Maruho to procure Bulk Licensed Compound and/or Product from such CMO at the same price level as Upstream procure Bulk Licensed Compound and/or Product. In the event that any such Bulk Licensed Compound or Product does not meet the Japanese industry standard and quality standards required by applicable law or regulation in Japan, Maruho may choose a new CMO in consultation with Upstream, subject any needed third party consents in accordance with the Lonza Agreement, if applicable. Maruho will be responsible for the technology transfer, at Maruho’s sole expense, to the new third party CMO with the assistance of Upstream, where Upstream shall transfer, at Maruho’s sole expense, to the new CMO, all necessary know-how, any data and technology relating to the manufacture of the Compound and the Product, including, but not limited to, Master Cell Bank, information on manufacture, analysis and quality assurance, and pharmaceutical preparations and drug substances necessary to confirm the consistency of manufacturing quality before and after technology transfer pursuant to this Section 5.3.2.  
 12  
5.3.3 The provisions of this section also apply in case Maruho gains the right to independently develop the Product in Japan as set out in Section 5.1.2 and Section 5.1.5.  
5.4 Commercialization.  
5.4.1 Maruho Commercialization Activities. On the terms and conditions of this Agreement, as between the parties, Maruho shall be solely responsible for and shall control, at its sole expense, the promotion, marketing, sale and other commercialization of the Product in Japan.  
5.4.2 Trademarks. Maruho, its sublicensees and their respective Affiliates may use the Licensed Marks without any additional consideration in the packaging, labeling, promotion, marketing and sale of the Product in Japan. Upstream shall notify Maruho of the filing of any trademark application for the Product as soon as reasonably practicable.  
5.5 Pharmacovigilance. Within [\*\*\*] of the Effective Date, but in any event prior to commencement by Maruho, its Affiliates and sublicensees of any clinical trials with the Licensed Compound or Product in Japan, the parties will in good faith negotiate and finalize a separate safety data exchange agreement (the “Pharmacovigilance Agreement”), the terms of which shall set forth the obligations, procedures and timelines for exchanging information (such as the occurrence of adverse events and serious adverse events) observed in connection with the Product in order to enable each party to comply with its safety reporting obligations to regulatory authorities. Prior to the execution of the Pharmacovigilance Agreement, each party shall promptly notify the other party of any information observed in connection with the Product necessary to enable such party to comply with its safety reporting obligations to regulatory authorities. Maruho shall maintain the safety database for the Licensed Compound and Product in Japan following regulatory approval in Japan, which shall include adverse events and other information relating to the safety of the Licensed Compound and Product. Upstream shall establish and maintain the global safety database for the Licensed Compound and Product at its costs and upon its responsibility, which shall include adverse events and other information relating to the safety of the Licensed Compound and Product.  
5.6 Access to Data.  
5.6.1 Astellas Data. [\*\*\*] following the Effective Date, Upstream shall deliver or provide access to Maruho (including rights of reference) all data comprising the Astellas Assets transferred to Upstream under the Astellas Asset Purchase Agreement that is reasonably necessary or useful for Maruho to exercise its rights and preform its obligations in Japan under this Agreement, and is not already in Maruho’s possession, for the sole purpose of exercising its rights and performing its obligations in Japan under this Agreement.  
5.6.2 Upstream Product Data. From time to time and pursuant to such process and schedule as shall be agreed to by the JDC, Upstream shall deliver or provide access to Maruho (including rights of reference) the Upstream Product Data, for the sole purpose of exercising its rights and performing its obligations in Japan under this Agreement. Without limiting the foregoing, Upstream shall make available to Maruho any other data reasonably requested by the Maruho JDC Representatives.  
 13  
5.6.3 Maruho Product Data. From time to time and pursuant to such process and schedule as shall be agreed to by the JDC, Maruho shall deliver or provide access to Upstream (including rights of reference) the Maruho Product Data for the sole purpose of developing or commercializing the Product other than (during the term of this Agreement) in Japan. Without limiting the foregoing, Maruho shall make available to Upstream any other data reasonably requested by the Upstream JDC Representatives.  
5.7 Cooperation. Each party and its respective Affiliates shall reasonably cooperate with the other party in the performance of its activities under this Section 5 that are specific or applicable to Japan, including in-person coordination of clinical development and regulatory filing activities at Upstream’s offices from time to time and pursuant to such process and schedule as the parties mutually agree.  
5.8 Compliance with Law. Each party and its respective Affiliates shall perform or cause to be performed its activities pursuant to this Agreement in compliance (and shall ensure compliance by any of its sublicensees and subcontractors) with all applicable laws /regulations or instruction of the regulatory authorities.  
6. JOINT DEVELOPMENT COMMITTEE.  
6.1 Responsibility and Authority. The purpose of the Joint Development Committee shall be to facilitate the exchange of information and to make decisions regarding each party’s activities under this Agreement applicable to Japan concerning development, regulatory activities and manufacture, and to coordinate the party’s respective activities applicable to Japan. The JDC shall not deal with marketing and sales in Japan which is to be exercised by Xxxxxx at Maruho’s sole discretion, provided, however, that JDC shall be held to facilitate the exchange of information regarding each party’s activities for commercialization. The JDC shall discuss and resolve issues based on, and taking into account, the following principals:  
6.1.1 The parties wish to collaborate, long-term with transparency and assist each other to maximize the exploitation of the Products world-wide and in Japan, which collaboration shall include regular updates by Upstream of progress in the global development of the Product, and in its development activities with regards to Japan.  
6.1.2 The JDC will exercise reasonable clinical development industry standards for its decision making and progress in Japan, which will not be unreasonably or untimely withheld unless Japanese development is reasonably expected to cause a material adverse impact to global development. For the avoidance of doubt, market size considerations (either in Japan or globally) will not be a reason for withholding development by Maruho in Japan.  
 14  
6.1.3 Upstream respects the fact that Maruho has decades of experience in development of pharmaceutical products in Japan which the JDC may rely on to maximize the value of the Products.  
6.2 Composition. Within [\*\*\*] after the Effective Date, each party shall appoint no more than [\*\*\*] named representatives of Upstream and no more than [\*\*\*] named representatives of Maruho to serve on the Joint Development Committee (the “JDC Representatives”). Each party may substitute its JDC Representative, in its sole discretion, effective upon written notice to the other party of such change. The chairperson of each meeting shall rotate between the JDC Representatives of the parties and shall be responsible to record the minutes and decisions, sign them and receive the signature of the other party’s representative. The unanimous approval of the JDC Representatives present at the relevant JDC meeting shall be required for the approval, determination or other action of the JDC. In addition to the above members, each Party may bring up to two non-voting experts to JDC meetings whenever deemed relevant for the purpose of adding competence in respect of matters at discussion, provided reasonable advance notice of such participation is given to the other Party.  
6.3 Meetings. The JDC Representatives shall, after appointment of its initial members, meet a least once every calendar quarter at times mutually agreed upon by the parties (“JDC Meeting”). Nonetheless, the parties may mutually agree not to hold a JDC Meeting if there is no topic, issue or matter to be included on an agenda for such meeting and to decrease the minimum frequency of the JDC meeting. The location of regularly scheduled in-person JDC Meetings shall alternate between the offices of the parties, unless otherwise agreed. Notwithstanding the foregoing, the JDC Meetings may be held via web conference. Each party shall use reasonable efforts to cause its JDC Representatives to attend the JDC Meeting on a regular basis and try to avoid frequent replacement of its representatives in order to achieve a good long-term collaboration. If a JDC Representative is unable to attend a JDC Meeting, the respective party may designate an alternate to attend such meeting in place of the absent JDC Representative. Each party shall bear all the expenses of its JDC Representatives on the JDC Meeting. The presence of one member from each party shall be deemed a quorum for the JDC Meeting.  
6.4 Minutes. The minutes of each JDC Meeting shall be distributed to the members within [\*\*\*] after the completion of the relevant meeting and shall provide a description in reasonable detail of the discussions held at the meeting and the decisions reached. Minutes of each JDC Meeting shall be approved or disapproved, and revised as necessary, within [\*\*\*] after the applicable JDC Meeting. Once finalized, minutes and decisions shall be signed by one representative of each Party and such decisions shall bind the Parties.  
6.5 Deadlocks. If the JDC Representatives, following an intense consultation period of [\*\*\*], cannot reach agreement on an issue that was raised by a party and was flagged as a material issue to be decided upon, (a “Deadlock”), the representatives of each party shall refer such issue to the chief executive officers of each party, or its direct report officer that is at least a senior vice president (the “Executives”), who promptly shall meet and resolve the issue by mutual agreement in such manner as they deem appropriate. For the purpose of the Executives meeting, JDC shall appoint an independent expert (having proven expertise on development and regulatory activities of pharmaceuticals worldwide (including in Japan) (“Expert”) and such Expert shall present the issues to be resolved and shall give its expert opinion on how to resolve the issue taking into account the basic principal set out in Section 6.1 above to the Executives. The Executive shall sincerely take such Expert’s opinion into consideration to resolve the issue. In the case the Executives fail to reach a mutual agreement, either party shall have the right to seek an arbitration resolution pursuant to Section 13.2.  
 15  
7. INVENTION AND PATENT RIGHTS.  
7.1 Notification of New Invention. Each party shall notify to the other party that effect in writing as promptly as practically possible, if a party makes a new patentable invention pertaining to the Asset, and shall discuss the ownership of intellectual property rights regarding such invention in good faith prior to the filing of any patent application for such intellectual property rights.  
7.2 Prosecution and Maintenance. Upstream shall have the sole right, at its sole expense, to prepare, file, prosecute, maintain and defend Licensed Patent Rights in Japan. Upstream shall consider in good faith the interests of Xxxxxx in so doing. With respect to each patent application and patent within the Licensed Patent Rights in Japan, Upstream shall (a) provide Maruho with any patent application filed by Upstream prior to filing; (b) provide Maruho with any patent application filed by Upstream after such filing; and (c) notify Maruho of any interference, opposition, reexamination request, nullity proceeding, appeal or other interparty action. Upstream may not abandon any Licensed Patent Rights in Japan without Xxxxxx’s prior written consent, which shall not be unreasonably withheld, delayed or conditioned. Maruho shall reimburse Upstream for one hundred percent (100%) of Upstream’s fully-burdened costs of conducting or having conducted such activities. Upstream shall invoice Maruho for such amounts on a [\*\*\*] basis, and Maruho shall pay to Upstream the invoiced amount within [\*\*\*] after the date of such invoice.  
7.3 Enforcement of Licensed Patent Rights.  
7.3.1 Notice. Each party will promptly notify the other party in writing of: (1) any actual or threatened infringement, misappropriation, or other violation, by a third party of any Licensed Patent Rights in Japan of which it becomes aware (each, an “Infringement”); and (2) any challenge to the validity, scope or enforceability of any Licensed Patent Rights in Japan by a third party, or any allegation by a third party that any intellectual property owned by it is infringed, misappropriated, or otherwise violated by the use of any Products of which it becomes aware.  
7.3.2 Xxxxxx’s Responsibility. Maruho shall have obligation, at its sole expense, to enforce the Licensed Patent Rights against an Infringement in Japan, except any procedures which require to be filed by the patentee under Japanese law or by the court, including, without limitation, injunctions and invalidation request. Notwithstanding the foregoing, Xxxxxx shall consider in good faith the interests of Upstream in so doing. Upstream shall assist Xxxxxx (upon Xxxxxx’s request and at Xxxxxx’s sole expense) to the extent commercially reasonable in connection therewith.  
 16  
7.3.3 Xxxxxx’s Prosecution. Maruho shall prosecute any actions to enforce the Licensed Patent Rights against an Infringement in Japan. Xxxxxx may take any lawful action that it determines is reasonably necessary to pursue such prosecution. Maruho may ask Upstream to join as a party to any such proceeding and Upstream, if so elects, shall cooperate in all respects with any such proceeding to the extent commercially reasonable. Maruho shall be solely responsible for all costs and expenses of any such proceeding and shall have the right to control the conduct thereof. Maruho shall retain all proceeds from any such proceeding after reimbursement of Upstream’s and Xxxxxx’s costs and expenses out of the proceeds thereof.  
7.3.4 Upstream’s Prosecution. In the event it is mutually agreed between the parties herein or the Japanese law or the court requires Upstream to file a proceeding to enforce the Licensed Patent Rights against an Infringement in Japan, Upstream shall take any lawful action that it determines is reasonably necessary to pursue such prosecution with Xxxxxx’s assistance. Upstream shall have the right to make Xxxxxx join as a party to any such proceeding and Maruho shall cooperate in all respects with any such proceeding. Maruho shall be solely responsible for all costs and expenses of any such proceeding and shall have the right to control the conduct thereof. Maruho shall retain all proceeds from any such proceeding after reimbursement of Upstream’s and Xxxxxx’s costs and expenses out of the proceeds thereof.  
7.4 Enforcement of Supported Patent Rights.  
7.4.1 Notice. Each party will promptly notify the other party in writing of: (1) any actual or threatened infringement, misappropriation, or other violation, by a third party of any Supported Patent Rights outside Japan of which it becomes aware (each, an “Infringement II”); and (2) any challenge to the validity, scope or enforceability of any Supported Patent Rights outside Japan by a third party, or any allegation by a third party that any intellectual property owned by it is infringed, misappropriated, or otherwise violated by the use of any Products of which it becomes aware.  
7.4.2 Upstream’s Responsibility. Upstream shall have the right, at its sole expense, to enforce the Supported Patent Rights against an Infringement II outside Japan, except any procedures which require to be filed by the patentee under applicable law or by the court. Notwithstanding the foregoing, Upstream shall consider in good faith the interests of Xxxxxx in so doing. Maruho shall assist Upstream (upon Upstream’s request and at Upstream’s sole expense) to the extent commercially reasonable in connection therewith.  
7.4.3 Upstream’s Prosecution. Upstream shall prosecute any actions to enforce the Licensed Patent Rights against an Infringement II outside Japan. Upstream may take any lawful action that it determines is reasonably necessary to pursue such prosecution. Upstream may ask Xxxxxx to join as a party to any such proceeding and Maruho, if so elects, shall cooperate in all respects with any such proceeding to the extent commercially reasonable. Upstream shall be solely responsible for all costs and expenses of any such proceeding and shall have the right to control the conduct thereof. Upstream shall retain all proceeds from any such proceeding after reimbursement of Upstream’s and Xxxxxx’s costs and expenses out of the proceeds thereof.  
 17  
7.4.4 Xxxxxx’s Prosecution. In the event it is mutually agreed between the parties herein or the applicable law or the court requires Maruho to file a proceeding to enforce the Licensed Patent Rights against an Infringement II outside Japan, Xxxxxx shall take any lawful action that it determines is reasonably necessary to pursue such prosecution with Upstream’s assistance. Maruho shall have the right to make Upstream join as a party to any such proceeding and Upstream shall cooperate in all respects with any such proceeding. Upstream shall be solely responsible for all costs and expenses of any such proceeding and shall have the right to control the conduct thereof. Upstream shall retain all proceeds from any such proceeding after reimbursement of Upstream’s and Xxxxxx’s costs and expenses out of the proceeds thereof.  
8. RIGHT OF FIRST NEGOTIATION.  
8.1 For a period commencing on the Effective Data and terminating upon the earlier of (a) the [\*\*\*] anniversary of an initial closing set forth in the Stock Purchase Agreement of the same date hereof between Maruho, Upstream and other investors on share purchase of Upstream; or (b) the occurrence of a merger and acquisition of Upstream by a third party, neither Upstream nor its Affiliates shall enter into any agreement with a third party (or engage in negotiations thereof), directly or indirectly (whether by contract, at law or otherwise), to sell, assign or otherwise transfer any or all of Upstream’s asset relating to the Product in the event of an actual liquidation of Upstream, except deemed liquidation events such as a merger and acquisition by third parties, without first giving to Maruho express written notice thereof, and Upstream hereby grants to Maruho the right to first negotiate to purchase all such asset of Upstream in such event. If, within [\*\*\*] after receipt of such written notice from Upstream, Xxxxxx gives written notice to Maruho of its exercise of such right of first negotiation, then the parties shall negotiate in good faith, for a period not to exceed [\*\*\*], and attempt to reach mutual agreement regarding terms and conditions of a mutually acceptable agreement to sell, assign or otherwise transfer such asset relating to the Product. If Maruho fails to timely give Upstream written notice of its exercise of such right of first negotiation, or if the parties fail to timely reach mutual agreement and enter into a written agreement to sell, assign or otherwise transfer such rights under this Agreement prior to the expiration of such [\*\*\*] period, thereafter Upstream shall have the right to reach mutual agreement and enter into an agreement with any third party to sell, assign or otherwise transfer such rights under this Agreement, provided that the terms and conditions of such agreement are not more favorable to such third party than the terms and conditions last offered by Xxxxxx to Upstream (taken as a whole). Any purported sale, assignment or other transfer in violation of this Section 8 shall be void.  
8.2 For a period commencing on the Effective Date and terminating upon the earlier of (a) the [\*\*\*] anniversary of the Effective Date; or (b) the occurrence of Change of Control, neither Maruho nor its Affiliates shall enter into any agreement with a third party (or engage in negotiations thereof), directly or indirectly (whether by contract, at law or otherwise), to sell, assign, sublicense or otherwise transfer any or all of Maruho’s rights under this Agreement without first giving to Upstream express written notice thereof, and Xxxxxx hereby grants to Upstream the first right to negotiate with Maruho to enter into an agreement to acquire such rights. If, within [\*\*\*] after receipt of such written notice from Xxxxxx, Upstream gives written notice to Maruho of its exercise of such right of first negotiation, then the parties shall negotiate in good faith, for a period not to exceed [\*\*\*], and attempt to reach mutual agreement regarding terms and conditions of a mutually acceptable agreement to sell, assign, sublicense or  
 18  
otherwise transfer such rights under this Agreement. If Upstream fails to timely give Xxxxxx written notice of its exercise of such right of first negotiation, or if the parties fail to timely reach mutual agreement and enter into a written agreement to sell, assign, sublicense or otherwise transfer such rights under this Agreement prior to the expiration of such [\*\*\*] period, thereafter Maruho shall have the right to reach mutual agreement and enter into an agreement with any third party to sell, assign, sublicense or otherwise transfer such rights under this Agreement, provided that the terms and conditions of such agreement are not more favorable to such third party than the terms and conditions last offered by Upstream to Maruho (taken as a whole). Any purported sale, assignment, sublicense or other transfer in violation of this Section 8 shall be void.  
9. CONFIDENTIALITY.  
9.1 Confidentiality. During the term of this Agreement and for a period of five (5) years following termination hereof, each party shall maintain in confidence the Confidential Information of the other party, shall not use or grant the use of the Confidential Information of the other party except as expressly permitted hereby, and shall not disclose the Confidential Information of the other party except on a need-to-know basis to such party’s directors, officers, employees, Affiliates, sublicensees, contractors and consultants, to the extent such disclosure is reasonably necessary in connection with such party’s activities as expressly authorized by this Agreement. To the extent that disclosure to any person is authorized by this Agreement, prior to disclosure, a party shall obtain written agreement of such person to hold in confidence and not disclose, use or grant the use of the Confidential Information of the other party except as expressly permitted under this Agreement. Each party shall notify the other party promptly upon discovery of any unauthorized use or disclosure of the other party’s Confidential Information.  
9.2 Terms of Agreement. Neither party shall disclose any terms or conditions of this Agreement to any third party without the prior consent of the other party.  
9.3 Permitted Disclosures. Notwithstanding the non-disclosure and non-use obligations of this Section 9, the party receiving Confidential Information shall have the right to disclose such Confidential Information or the terms of this Agreement (a) to the extent approved in writing in advance by the party disclosing such Confidential Information; (b) to investment bankers, actual and potential investors, potential sublicensees and financing sources, and actual and potential acquirers, collaboration partners and licensees, each of whom prior to disclosure must be bound by obligations of confidentiality and non-use not less restrictive than those set forth in this Agreement; or (c) to the extent that a party is required to disclose Confidential Information by applicable law, regulation or order of a governmental agency or a court of competent jurisdiction, including the rules of any securities exchange or automated quotation system applicable to such party (in each case as determined by such party’s legal counsel); provided, however, that such party shall provide advanced written notice thereof to the other party, consult with the other party with respect to such disclosure and provide the other party sufficient opportunity to object to any such disclosure or to request confidential treatment thereof (if applicable).  
 19  
10. INDEMNIFICATION AND INSURANCE.  
10.1 By Maruho. Maruho shall indemnify and hold harmless Upstream, and its directors, officers, employees and agents, from and against all losses, liabilities, damages and expenses, including reasonable attorneys’ fees and costs (collectively, “Liabilities”), from any claims, demands, actions or other proceedings by any third party to the extent resulting from (a) the breach of any representation, warranty or covenant by Maruho under this Agreement; (b) the use of the Licensed IP Rights by Maruho, its sublicensees or their respective Affiliates; (c) the development, manufacture, use, sale, handling or storage of Products in Japan by or on behalf of Maruho, its sublicensees or their respective Affiliates, customers or end-users; or (d) the use of the Confidential Information of Upstream by Maruho, its sublicensees or their respective Affiliates.  
10.2 By Upstream. Upstream shall indemnify and hold harmless Maruho, and its directors, officers, employees and agents, from and against all Liabilities from any claims, demands, actions or other proceedings by any third party to the extent resulting from (a) the breach of any representation, warranty or covenant by Upstream under this Agreement; (b) the development, manufacture, use, sale, handling or storage of Products outside Japan by or on behalf of Upstream, its other licensees or their respective Affiliates, customers or end-users; (c) the defective Bulk Licensed Compound and/or Product manufactured or supplied by or on behalf of Upstream; (d) the use of the Supported IP Rights by Upstream, its other licensees or their respective Affiliates; or (e) the use of the Confidential Information of Maruho by Upstream, its other licensees or their respective Affiliates.  
10.3 Procedure. If a party (the “Indemnitee”) intends to claim indemnification under this Section 10, it shall promptly notify the other party (the “Indemnitor”) in writing of any claim, demand, action or other proceeding for which the Indemnitee intends to claim such indemnification, and the Indemnitor shall have the right to participate in, and, to the extent the Indemnitor so desires, to assume the defense thereof with counsel mutually satisfactory to the parties; provided, however, that an Indemnitee shall have the right to retain its own counsel, with the fees and expenses to be paid by the Indemnitor, if representation of such Indemnitee by the counsel retained by the Indemnitor would be inappropriate due to actual or potential differing interests between the Indemnitee and any other party represented by such counsel in such proceeding. The obligations of this Section 10 shall not apply to amounts paid in settlement of any claim, demand, action or other proceeding if such settlement is effected without the consent of the Indemnitor, which consent shall not be unreasonably withheld or delayed. The failure to deliver written notice to the Indemnitor within a reasonable time after the commencement of any such action, if prejudicial to its ability to defend such action, shall relieve the Indemnitor of any obligation to the Indemnitee under this Section 10, but the omission so to deliver written notice to the Indemnitor shall not relieve it of any obligation that it may have to any party claiming indemnification otherwise than under this Section 10. The Indemnitee, its employees and agents, shall reasonably cooperate with the Indemnitor and its legal representatives in the investigation of any claim, demand, action or other proceeding covered by this Section 10.  
10.4 Insurance. Each party shall maintain insurance, including product liability insurance, with respect to its activities under this Agreement regarding the Licensed Compound and Products in such amount as such party customarily maintains with respect to similar activities for its other products, but not less than such amount as is reasonable and customary in the industry taking into account the activities to be conducted by such party under this Agreement. Each party shall maintain such insurance for so long as it continues its activities under this Agreement, and for [\*\*\*] thereafter.  
 20  
11. PUBLIC ANNOUNCEMENTS.  
Except as required by the Applicable Laws (including disclosure requirements of the SEC (US Securities and Exchange Commission) or any stock exchange or automated quotation system on which securities issued by a party are traded), neither Party shall make any other public announcement concerning this Agreement or the subject matter hereof without the prior written consent of the other, which shall not be unreasonably withheld or delayed. Furthermore, to the extent practicable under the circumstances, the Party making public announcement shall furnish to the other Party the draft text to be announced prior to [\*\*\*] of such announcement and the Parties shall subsequently contemplate to discuss and review the draft [\*\*\*] prior to such announcement, provided, however, that the Party making public announcement without the other Party’s name shall make such public announcement by reporting to the other Party that effect [\*\*\*] prior to such announcement. Once the parties have agreed upon the substance of information that can be used for any such public announcement, each party thereafter may disclose such information, as modified by mutual written agreement of the parties, without the consent of the other party.  
12. TERMINATION.  
12.1 Waiver of Termination Rights. The license granted by Upstream to Maruho under this Agreement is irrevocable and perpetual and therefore both parties waive their right of termination of this Agreement for any reason, except as set out below. An uncured material breach may be remedied by other available remedies including monetary remedies, injunction or other writs and legal remedies.  
12.2 Termination by Xxxxxx. Maruho may terminate this Agreement at any time upon sixty (60) days prior written notice to Upstream.  
12.3 Effects of Termination. Termination of this Agreement shall be without prejudice to any rights which shall have accrued to the benefit of a party prior to such termination. Without limiting the foregoing, Sections 2.3, 3.2, 5.6.3, 9, 10, 12.3 and 13 shall survive any termination of this Agreement. Except as otherwise expressly set forth in this Agreement, promptly upon the termination of this Agreement, each party shall return to the other party all tangible items regarding the Confidential Information of the other party and all copies thereof; provided, however, that each party shall have the right to retain one (1) copy for its legal files for the sole purpose of determining its obligations hereunder.  
13. MISCELLANEOUS.  
13.1 Governing Law. This Agreement shall be governed by, interpreted and construed in accordance with the laws of the State of Delaware, without regard to the conflicts of law principles thereof, and shall not be governed by the United Nations Convention on Contracts for the International Sale of Goods.  
 21  
13.2 Dispute Resolution. Any disputes that are not otherwise resolved by the Parties shall be submitted to binding arbitration with the International Centre for Dispute Resolution (“ICDR”) in the State of Delaware, USA in accordance with the then-prevailing commercial arbitration rules of the ICDR.  
13.2.1 The language of the arbitration shall be English. There shall be [\*\*\*] arbitrators, one selected by the initiating Party in the request for arbitration, the second selected by the other Party within [\*\*\*] of the request for arbitration, and the third (who shall act as chairperson of the arbitration tribunal) selected by the [\*\*\*] Party-appointed arbitrators within [\*\*\*] of the selection of the second arbitrator. In the event that the respondent fails to select an arbitrator, or if the [\*\*\*] Party-appointed arbitrators are unable or fail to agree upon the third arbitrator, the ICDR shall designate the remaining arbitrator(s) required to comprise the tribunal.  
13.2.2 Each arbitrator chosen shall speak, read, and write English fluently and shall be either (i) a practicing lawyer who has specialized in business litigation with at least [\*\*\*] of experience, or (ii) a retired judge of a court of general jurisdiction.  
13.2.3 The arbitrators shall issue an award within [\*\*\*] of the submission of the request for arbitration. This time limit may be extended by agreement of the Parties or by the tribunal if necessary. It is expressly understood and agreed by the Parties that the rulings and award of the tribunal shall be conclusive on the Parties, their successors and permitted assigns. Judgment on the award rendered by the tribunal may be entered in any court having jurisdiction thereof.  
13.2.4 The cost of the arbitration, including the fees and expenses of the arbitrator, will be shared equally by the Parties. The prevailing Party shall be entitled to recover from the losing Party the prevailing Party’s attorneys’ fees and costs. The arbitrator shall have the right to apportion liability between the Parties, but will not have the authority to award any damages or remedies not available under the express terms of this Agreement.  
13.3 Waiver. No waiver by a party hereto of any breach or default of any of the covenants or agreements herein set forth shall be deemed a waiver as to any subsequent and/or similar breach or default.  
13.4 Assignment. Neither this Agreement nor any right or obligation hereunder may be assigned or delegated, in whole or part, by either party without the prior express written consent of the other; provided, however, that either party may, without the written consent of the other, assign this Agreement and its rights and delegate its obligations hereunder in connection with the transfer or sale of all or substantially all of its business, or in the event of its merger, consolidation, change in control or similar transaction. Any permitted assignee shall assume all obligations of its assignor under this Agreement. Any purported assignment in violation of this Section 13.4 shall be void.  
13.5 Independent Contractors. The relationship of the parties hereto is that of independent contractors. The parties hereto are not deemed to be agents, partners or joint venturers of the others for any purpose as a result of this Agreement or the transactions contemplated thereby.  
 22  
13.6 Further Actions. Each party shall execute, acknowledge and deliver such further documents and instruments and to perform all such other acts as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement.  
13.7 Notices. All requests and notices required or permitted to be given to the parties hereto shall be given in writing, shall expressly reference the section(s) of this Agreement to which they pertain, and shall be delivered to the other party, effective on receipt, at the appropriate address as set forth below or to such other addresses as may be designated in writing by the parties from time to time during the term of this Agreement.  
 If to Upstream: Upstream Bio, Inc.  
 care of: Xxxxxx Xxxxxxxx Innovations, 000 Xxxxxxxxxx  
Xxxxxx, Xxxxxxx, XX 00000, XXX  
 Attn: Chief Executive Officer  
With a copy to: [\*\*\*]  
If to Maruho: Maruho Co., Ltd.  
 0-0-00, Xxxxxxx, Xxxx-xx, Xxxxx, 000-0000, Xxxxx  
 Attn: [\*\*\*]  
With a copy to: [\*\*\*]  
13.8 Force Majeure. Nonperformance of a party (other than for the payment of money) shall be excused to the extent that performance is rendered impossible by strike, fire, earthquake, flood, governmental acts or orders or restrictions, failure of suppliers, or any other reason where failure to perform is beyond the reasonable control and not caused by the negligence, intentional conduct or misconduct of the nonperforming party; provided, however, that the nonperforming party shall (a) notify the other party in writing of the reason for such nonperformance, and (b) use commercially reasonable efforts to resume performance as soon as reasonably practicable. If performance is unable to be resumed within [\*\*\*] after the initial date of nonperformance, the other party shall have the right to terminate this Agreement immediately upon written notice to the nonperforming party.  
13.9 No Consequential Damages. IN NO EVENT SHALL A PARTY BE LIABLE FOR SPECIAL, INCIDENTAL OR CONSEQUENTIAL DAMAGES ARISING OUT OF THIS AGREEMENT OR THE EXERCISE OF ITS RIGHTS HEREUNDER, INCLUDING WITHOUT LIMITATION LOST PROFITS ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT, REGARDLESS OF ANY NOTICE OF SUCH DAMAGES. NOTHING IN THIS SECTION 13.9 IS INTENDED TO LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF EITHER PARTY UNDER SECTION 10 OR THE LIABILITY OF EITHER PARTY FOR FRAUD, WILLFUL MISCONDUCT.  
 23  
13.10 Upstream In-Licenses. Notwithstanding anything to the contrary in this Agreement, the grant of rights by Upstream under this Agreement shall be subject to and limited in all respects by the terms of the applicable Upstream In-License(s) pursuant to which Upstream acquired Licensed IP Rights, and all rights or sublicenses granted under this Agreement shall be limited to the extent that Upstream may grant such rights and sublicenses under such Upstream In-Licenses. Upstream shall provide Maruho with a copy of each such Upstream In-License sufficient to enable Maruho to determine its obligations thereunder.  
13.11 Complete Agreement. This Agreement constitutes the entire agreement between the parties regarding the subject matter hereof, and all prior representations, understandings and agreements regarding the subject matter hereof, either written or oral, expressed or implied, including the term sheet exchanged by the parties relating to the subject of this Agreement, are superseded and shall be and of no effect.  
13.12 Counterparts. This Agreement may be executed in counterparts, each of which shall be deemed to be an original and together shall be deemed to be one and the same agreement. Execution of this Agreement may be accomplished via facsimile or via email exchange of signed PDF execution copies.  
13.13 Headings. The captions to the several sections hereof are not a part of this Agreement, but are included merely for convenience of reference only and shall not affect its meaning or interpretation.  
 24  
IN WITNESS WHEREOF, the parties hereto have each caused this Agreement to be executed by their duly-authorized representatives as of the Effective Date.  
 UPSTREAM BIO. INC.  
By:   
/s/ Xxxx Xxxxx  
Name: Xxxx Xxxxx  
Title: President  
MARUHO CO., LTD.  
By:   
/s/ Xxxxxxx Xxxxxx  
Name: Xxxxxxx Xxxxxx  
Title: President & CEO  
[Signature Page to License Agreement]  
EXHIBIT A  
LICENSED COMPOUND  
EXHIBIT B  
INITIAL LICENSED PATENT RIGHTS  
FIRST AMENDMENT TO LICENSE AGREEMENT  
THIS FIRST AMENDMENT TO LICENSE AGREEMENT (this “Amendment”), is effective as of the date signed by the last Party to sign below (the “Amendment Effective Date”), and is made by and between Upstream Bio, Inc., a Delaware corporation (the “Company”), and Maruho Co., Ltd., a Japanese corporation (“Maruho”). The Company and Xxxxxx may each be referred to herein as a “Party” or collectively as the “Parties”.  
WHEREAS, the Parties entered into that certain License Agreement dated as of October 14, 2021 (as amended and/or restated from time to time, the “License Agreement”); and  
WHEREAS, the Parties desire to amend the Agreement as hereinafter set forth.  
NOW, THEREFORE in consideration of the foregoing and the mutual agreements set forth below and other good and valuable consideration, the Parties agree as follows:  
14. Definitions. Capitalized terms used and not otherwise defined herein shall have the meanings given to such terms in the License Agreement.  
15. Amendment. Subsection 5.1.1 of the License Agreement shall be deleted and replaced in its entirety with the following:  
“5.1.1 Upstream Development Activities. On the terms and conditions of this Agreement, Upstream shall be responsible for and control the development of the Product on a global basis including Japan, and shall consider in good faith the interests of Maruho in so doing. Upstream shall make commercially reasonable efforts to perform clinical development as part of Upstream’s global development strategy and shall aim to obtain the regulatory approval for the Products from FDA as quickly as possible in accordance with such strategy. For reference, the current Upstream global development strategy and its estimated schedule are attached in Exhibit C. Upstream shall develop the Product for use in Japan as part of Upstream’s global development strategy and in accordance with industry practices for development of biological products for use in Japan as part of a global development, and as much as possible on a similar schedule it develops the Product for its initial territory/territories; provided that Upstream’s development of the Product for use in Japan shall be made in accordance with Section 6.1 below.”  
16. Effectiveness. Except to the extent waived or amended by this Amendment, the terms and provisions of the License Agreement shall remain in full force and effect.  
17. Governing Law. This Amendment shall be governed by, enforced, and shall be construed in accordance with the laws of the State of Delaware, without regard to the conflicts of law provisions thereof, and shall not be governed by the United Nations Convention on Contracts for the International Sale of Goods.  
18. Entire Agreement. This Amendment, together with the Agreement, contains the entire agreement of the parties and supersedes any prior or contemporaneous written or oral agreements between them concerning the subject matter of this Amendment.  
19. Counterparts. This Amendment 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. Signatures to this Amendment transmitted by email in “portable document format” (“.pdf”), or by any other electronic means intended to preserve the original graphic and pictorial appearance of this Amendment shall have the same effect as physical delivery of the paper document bearing original signature.  
[Signature Page Follows]  
IN WITNESS WHEREOF, the Parties have caused this Amendment to be executed by their respective duly authorized officers as of the Amendment Effective Date.  
 UPSTREAM BIO, INC.  
By:   
/s/ Xxxxxxxx Xxxxx  
Name: Xxxxxxxx Xxxxx  
Title: Chief Executive Officer  
MARUHO CO., LTD.  
By:   
/s/ Xxxxxxx Xxxxxx  
Name: Xxxxxxx Xxxxxx  
Title: President & Chief Executive Officer  
Date: May 30, 2023  
EXHIBIT C