UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or Section 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): April 10, 2019

BioDelivery Sciences International, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-31361**	**35-2089858**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

4131 ParkLake Ave., Suite #225 **Raleigh, NC** **(Address of principal executive offices)**	**27612** **(Zip Code)**

Registrant's telephone number, including area code: 919-582-9050

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation to the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 1.01 Entry into a Material Definitive Agreement

License Agreement with Shionogi Inc.

On April 4, 2019 (the "Effective Date"), BioDelivery Sciences International, Inc. (the "Company") and Shionogi Inc., a Delaware corporation ("Shionogi"), entered into an exclusive license agreement (the "License Agreement") for the commercialization of Symproic® (naldemedine tosylate) (the "Product") in the United States including Puerto Rico (the "Territory") for opioid-induced constipation in adult patients with chronic non-cancer pain (the "Field").

Pursuant to the terms of the License Agreement, and subject to the conditions set forth therein, the Company will pay Shionogi a $30 million up-front payment, payable in two installments (i.e., $20 million on the Effective Date and $10 million on the six-month anniversary of the Effective Date (or earlier if the License Agreement is assigned or transferred), and quarterly, tiered royalty payments on potential sales of the Product in the Territory that range from 8.5% to 17.5% (plus an additional 1% of net sales on a pass-through basis to a third party licensor of Shionogi) of net sales based on volume of net sales and whether the Product is being sold as an authorized generic.

The Company and Shionogi have made customary representations and warranties and have agreed to certain other customary covenants, including confidentiality, limitation of liability and indemnity provisions.

Either party may terminate the License Agreement for cause if the other party materially breaches or defaults in the performance of its obligations, and, if curable, such material breach remains uncured for 120 days (30 days for non-payment). Unless earlier terminated, the License Agreement will continue in effect until the expiration of the Company's royalty obligations which expire on the latest of: (a) the expiration of all regulatory exclusivity for the Product in the Field in the Territory, (b) expiration of the last to expire orange book patent in the Territory, (c) the date of a final court decision holding all the unexpired claims of the orange book patents to be invalid or unenforceable, or (d) the tenth (10th) anniversary of the Effective Date for Product (or, for Symproic commercialized by the Company as an authorized generic in accordance with the License Agreement (the "AG Product"), the seventh (7th) anniversary of the first commercial sale of AG Product in the Territory). Upon expiration of the License Agreement, all licenses granted to Company for the Product in the Field and in the Territory survive and become fully-paid, royalty-free, perpetual and irrevocable.

The Company and Shionogi have also entered into a customary supply agreement under which Shionogi will supply the Product to the Company at cost plus an agreed upon markup for an initial term of up to two years. In the event the Company elects to source the Product from a third party supplier, Shionogi would continue to supply the Company with naldemedine tosylate for use in such Product at cost plus such agreed upon markup for the duration of the License Agreement. The Company and Shionogi also entered into a customary transition services and distribution agreement under which Shionogi will continue to perform certain sales, distribution and related activities and commercialization and administrative services on the Company's behalf until June 30, 2019, or such later date as may be agreed by the parties pursuant to the transition services and distribution agreement (the "Transition Date") (during which time, in lieu of paying royalties and cost-plus supply, distribution and transitional services during this period, Shionogi will retain 35% of the net sales of Product in the Territory and remit the remaining 65% of net sales to the Company) and certain other customary transitional services (if so requested by the Company), initially at no cost and thereafter, at a specified hourly rate for a term not to exceed three months from the Transition Date or the term of the Agreement.

The foregoing description of the License Agreement does not purport to be complete and is qualified in its entirety by reference to the text of the License Agreement, a copy of which is filed as Exhibit 10.1 hereto.

CRG Term Loan Amendment

On April 4, 2019, the Company entered into a third amendment (the "Third Amendment") to the term loan agreement, dated as of February 21, 2017 and as amended on December 15, 2017 and on May 16, 2018 (the "Loan Agreement"), among the Company, the subsidiary guarantors, CRG Servicing LLC, as administrative agent and collateral agent (in such capacity, the "Administrative Agent"), and the lenders listed therein (the "Lenders"). The general terms, conditions and covenants of the Loan Agreement and the security granted by the Company and its subsidiaries thereunder are described in the Company's Current Report on Form 8-K, filed with the SEC on February 27, 2017, as subsequently amended, which description is incorporated herein by reference.

Pursuant to the Third Amendment, the Administrative Agent and the Lenders consent to the Borrower's entry into the License Agreement. The foregoing description of the Third Amendment does not purport to be complete and is qualified in its entirety by reference to the text of the Amendment, a copy of which is filed as Exhibit 10.2 hereto.

Item 7.01 Regulation FD Disclosure.

On April 10, 2019, the Company and Shionogi issued a press release announcing the execution of the License Agreement. A copy of the press release is attached as Exhibit 99.1 hereto.

The information set forth under Item 7.01 and in Exhibit 99.1 is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 8.01 Other Information.

With respect to the Company's ongoing litigation related to BUNAVAIL®, as disclosed in its Annual Report on Form 10-K for the fiscal year ended December 31, 2018, on February 7, 2019, the Patent Trial and Appeal Board of the U.S. Patent and Trademark Office ("USPTO") issued its decision on the remanded claims, denying three of the Company's *inter partes* review claims. On March 11, 2019, the Company filed a notice of appeal with the USPTO. Aquestive Therapeutics, Inc. (formerly known as MonoSol Rx LLC) has filed a motion to dismiss the appeal, which is pending.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

10.1*	License Agreement, by and between the Company and Shionogi, dated as of April 4, 2019.
10.2	Third Amendment to the Loan Agreement, among the Company, the subsidiary guarantors, the Administrative Agent and the Lenders, dated as of April 4, 2019.
99.1	Press release, dated April 10, 2019, announcing the License Agreement between the Company and Shionogi.

* Confidential portions of this exhibit have been omitted.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

April 10, 2019

BIODELIVERY SCIENCES INTERNATIONAL, INC.

By: /s/ Mary Theresa Coelho
Name: Mary Theresa Coelho
Title: Chief Financial Officer and Treasurer

Exhibit 10.1

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [***], HAS BEEN OMITTED BECAUSE IT IS NOT MATERIAL AND WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

EXCLUSIVE LICENSE AGREEMENT

This Exclusive License Agreement (the "**Agreement**") is entered into as of April 4, 2019 (the "**Effective Date**") by and between Shionogi Inc., a Delaware corporation having its principal place of business at 300 Campus Drive, Florham Park, New Jersey ("**Shionogi**"), and BioDelivery Sciences International, Inc., a Delaware corporation having its principal place of business at 4131 ParkLake Avenue, Suite 225, Raleigh, NC 27612 ("**BDSI**"). Shionogi on the one hand and BDSI on the other hand are sometimes referred to herein individually as a "**Party**" and collectively as the "**Parties**".

Background

BDSI is a specialty biopharmaceutical company specializing in the development and commercialization of branded products focused on treating patients with chronic pain;

Shionogi has exclusive rights to Symproic (as defined below) in the Territory (as defined below); and

BDSI desires to obtain an exclusive license and certain assets from Shionogi, and Shionogi desires to grant BDSI certain licenses, under Shionogi's intellectual property rights related to Symproic, and assign to BDSI certain assets, to enable BDSI to Commercialize (as defined below) Symproic in the Territory.

Now, therefore, in consideration of the foregoing premises and the mutual promises, covenants and conditions contained in this Agreement, the Parties agree as follows:

Article 1

Definitions

As used in this Agreement, the following initially capitalized terms, whether used in the singular or plural form, shall have the meanings set forth in this Article 1. In addition, the terms "includes," "including," "include" and derivative forms of them shall be deemed followed by the phrase "without limitation" (regardless of whether it is actually written there (and drawing no implication from the actual inclusion of such phrase in some instances after such terms but not others)).

1.1 "Accounting Standards" means the current accounting standards applicable to Shionogi or BDSI, as applicable, for the relevant time period. As of the Effective Date, the Accounting Standards are U.S. GAAP for Shionogi and BDSI, but in the event Shionogi or BDSI, as applicable, adopts a different accounting standard, such as the International Financial Reporting Standards, then such accounting standard shall become the Accounting Standards applicable to such Party as of the effective date of its adoption, as applicable.

1.2 "**Acquired Entity**" means, in the event a Party or any Affiliate of a Party acquires all or substantially all of the stock, assets, or business of a Third Party or otherwise obtains control of a Third Party (with "control", for purposes of this definition, having the meaning set forth below in the definition of "Affiliate"), such Third Party or any Affiliate thereof.

1.3 "**Acquiring Entity**" means any Third Party that acquires all or substantially all of the stock, assets, or business of a Party or any Affiliate of a Party (or all or substantially all of the assets or business thereof related, in either case, to this Agreement) or otherwise obtains control of a Party or any Affiliate thereof (with "control", for purposes of this definition, having the meaning set forth below in the definition of "Affiliate"), or any Affiliate of such Third Party.

1.4 "**Affiliate**" means, with respect to a particular party, a person, corporation, partnership, or other entity that controls, is controlled by or is under common control with such party, whether now or in the future. For the purposes of this definition, the word "control" (including, with correlative meaning, the terms "controlled by" or "under the common control with") means the actual power, either directly or indirectly through one or more intermediaries, to direct or cause the direction of the management and policies of such entity, whether by the ownership of more than fifty percent (50%) of the voting stock or equity securities of such entity, or by contract or otherwise.

1.5 "**AG Product**" means Symproic Commercialized by BDSI, an Affiliate thereof, or a BDSI Licensee under the Assigned NDA as a generic product (i.e., without use of any Symproic Marks or BDSI Marks).

1.6 "**AG Royalty Term**" means for AG Product, the period beginning upon First Commercial Sale of an AG Product and ending upon the last to occur of: (a) the expiration of all regulatory exclusivity for Symproic in the Field in the Territory; (b) expiration of the last to expire Orange Book Patent in the Territory; (c) the date of a Final Court Decision holding all the unexpired claims of the Orange Book Patents to be invalid or unenforceable, or (d) the seventh (7th) anniversary of the First Commercial Sale of an AG Product in the Territory.

1.7 "**Agreement**" has the meaning set forth in the Preamble.

1.8 "**Alliance Manager**" has the meaning set forth in Section 9.4.

1.9 "**ANDA**" means Abbreviated New Drug Application as defined in the FD&C Act and all applicable regulations promulgated thereunder.

1.10 "**API**" means active pharmaceutical ingredient (or in the case of any product that is not a pharmaceutical or biologic, active ingredient).

1.11 "**API Supply Agreement**" shall have the meaning set forth in the Supply Agreement.

1.12 "**Assigned NDA**" means NDA #208854.

1.13 "**Assigned NDA Letters**" means the letters from each Party to the FDA, duly executed by each Party, the forms of which are attached hereto as EXHIBIT A.

1.14 "**Bankrupt Party**" has the meaning set forth in Section 14.5.

1.15 "**BDSI**" has the meaning set forth in the Preamble.

1.16 "**BDSI Claims**" has the meaning set forth in Section 12.1.

1.17 "**BDSI Damages**" has the meaning set forth in Section 12.1.

1.18 "**BDSI Indemnitees**" has the meaning set forth in Section 12.1.

1.19 "**BDSI Know-How**" means all Information that (a) is (1) generated during the Term (in the course of any activities with respect to Symproic or Naldemedine) by or on behalf of, or if any of the foregoing Information generated in the course of any activities with respect to Symproic or Naldemedine otherwise becomes Controlled during the Term by, BDSI, any of its Affiliate(s), and/or any BDSI Licensee, and (2) reasonably necessary or useful for the research, development, manufacture, use, importation, sale, development or commercialization of Symproic or manufacture or use of Naldemedine (or any analog or derivative thereof), (b) is Controlled by BDSI, an Affiliate thereof, and/or any BDSI Licensee and incorporated into Symproic by or on behalf of BDSI, its Affiliate(s), and/or BDSI Licensees (and is not already included in clause (a) above), (c) is pharmacovigilance data or documentation generated during the Term in the course of any activities with respect to specific to Symproic or Naldemedine by or on behalf of BDSI, any of its Affiliate(s), and/or any BDSI Licensee (and is not already included in clause (a) or (b) above), or (d) is otherwise used by BDSI, its Affiliate(s), and/or BDSI Licensees to Develop, Manufacture, or Commercialize Symproic in the Field in the Territory during the Term (and is not already included in clause (a), (b), or (c) above). Notwithstanding anything to the contrary, however, BDSI Know-How shall not include any Information (1) to the extent directly concerning any API other than Naldemedine (or any analog or derivative thereof) or (2) that is owned, licensed, or otherwise controlled by any Acquiring Entity with respect to BDSI (a "**BDSI Acquiring Entity**") or Acquired Entity with respect to BDSI (a "**BDSI Acquired Entity**") at the time such Acquiring Entity or Acquired Entity first became an Acquiring Entity or Acquired Entity of, in either case, BDSI, except to the extent such Information (i) is incorporated into Symproic, or utilized in the Development, Manufacture, or Commercialization of Symproic (or manufacture of Naldemedine for use in the Manufacture of Symproic), by or on behalf of BDSI, any Affiliate thereof, or any BDSI Licensee, (ii) was generated following the Effective Date by or on behalf of such Acquiring Entity or Acquired Entity in the course of their activities under this Agreement with respect to Symproic or Naldemedine, or (iii) was already included within the BDSI Know-How immediately prior to the date of the transaction by which such Acquiring Entity or Acquired Entity first became a BDSI Acquiring Entity or BDSI Acquired Entity. For additional clarity, BDSI Know-How shall exclude rights under any BDSI Patents.

1.20 "**BDSI Licensee**" means any Third Party to whom BDSI or any Affiliate thereof grants any rights under the Shionogi Technology to Commercialize Symproic in the Field in the Territory, including (a) any such Third Party granted such rights under a Sublicense Agreement or (b) any further sublicensee of any such rights granted pursuant to a sublicense thereto granted by another BDSI Licensee.

1.21 "**BDSI Marks**" has the meaning set forth in Section 10.7.

1.22 "**BDSI Patents**" means all Patents that, during the Term, (a) become owned, licensed, or otherwise Controlled (in the course of any activities with respect to Symproic or Naldemedine) by BDSI, its Affiliate(s), and/or BDSI Licensees and cover BDSI Know-How or (b) are Controlled by BDSI, its Affiliates, and/or BDSI Licensees and used by or on behalf of BDSI, its Affiliates, and/or BDSI Licensees to manufacture, develop, or commercialize Symproic or manufacture or use Naldemedine (or any analog or derivative thereof). Notwithstanding anything to the contrary, however, BDSI Patents shall not include any Patents (1) to the extent claiming any API other than Naldemedine (or any analog or derivative thereof) or (2) owned, licensed, or otherwise controlled by any BDSI Acquiring Entity or BDSI Acquired Entity at the time such Acquiring Entity or Acquired Entity first became a BDSI Acquiring Entity or BDSI Acquired Entity, except to the extent such Patents (i) cover technology incorporated into Symproic, or utilized in the Development, Manufacture, or Commercialization of Symproic (or manufacture of Naldemedine for use in the Manufacture of Symproic), by or on behalf of BDSI, any Affiliate thereof, or any BDSI Licensee, (ii) cover technology that was generated following the Effective Date by or on behalf of such Acquiring Entity or Acquired Entity in the course of their activities under this Agreement with respect to Symproic or Naldemedine, or (iii) were already included within the BDSI Patents immediately prior to the date of the transaction by which such Acquiring Entity or Acquired Entity first became a BDSI Acquiring Entity or BDSI Acquired Entity.

1.23 "**BDSI Technology**" means the BDSI Patents and BDSI Know-How.

1.24 "**Branded Net Sales**" shall have the meaning set forth in Section 3.2(a).

1.25 "**Branded Product**" means Symproic Commercialized by BDSI, an Affiliate thereof or a BDSI Licensee that is not an AG Product.

1.26 "**Branded Royalty Term**" means, for Branded Product, the period beginning on the Effective Date and continuing until the last to occur of: (a) the expiration of all regulatory exclusivity for Symproic in the Field in the Territory; (b) expiration of the last to expire Orange Book Patent in the Territory; (c) the date of a Final Court Decision holding all the unexpired claims of the Orange Book Patents to be invalid or unenforceable, or (d) the tenth (10th) anniversary of the Effective Date.

1.27 "**Calendar Quarter**" means each of those three (3) complete calendar month periods of each Calendar Year ending March 31, June 30, September 30 and December 31.

1.28 "**Calendar Year**" means each twelve complete consecutive calendar month period beginning January 1 and ending December 31, provided that the initial Calendar Year hereunder shall begin on the Effective Date and end December 31, 2019.

1.29 "**Certification**" has the meaning set forth in Section 10.3(c).

1.30 "**Change of Control**" means, with respect to a Party, any of the following: (a) any Third Party (or group of Third Parties acting in concert) acquires, directly or indirectly, a majority of voting stock or other securities then outstanding of such Party; (b) the sale of substantially all assets of such Party in a transaction or a series of transactions to a Third Party buyer; or (c) a merger or consolidation of such Party with or into any Third Party, as a result of which the holders of voting stock or other securities of such Party immediately prior to such event hold less than a majority of the outstanding voting stock or other securities of the surviving entity or parent of the surviving entity.

1.31 "**Claim**" has the meaning set forth in Section 12.3.

1.32 "**Clinical Trial**" means any human clinical trial of Symproic.

1.33 "**Commercialization**" means the Promotion and Distribution of Symproic, but excluding the conduct of any Phase 4 Trials other than Phase 4 Trials that are required by a Regulatory Authority as a condition of maintaining Regulatory Approval (including, without limitation, the Current Phase 4 Studies). "Commercialize" has a correlative meaning.

1.34 "**Commercialization Report**" has the meaning set forth in Section 6.4.

1.35 Confidential Information" means, with respect to a Party, all Information (subject to the exceptions set forth in Section 13.1) of such Party that is disclosed to the other Party or its Affiliate under this Agreement, which may include, without limitation, specifications, know-how, trade secrets, technical information, models, business information, inventions, discoveries, methods, procedures, formulae, protocols, techniques, data, and unpublished patent applications, whether disclosed in oral, written, graphic, or electronic form. All Information disclosed by a Party pursuant to the Existing Confidentiality Agreement shall be deemed to be such Party's Confidential Information hereunder (with the mutual understanding and agreement that any use or disclosure thereof that is authorized under Article 13 shall not be restricted by, or be deemed a violation of, such Existing Confidentiality Agreement).

1.36 "**Control**" means, with respect to any material, Information, or intellectual property right, that a Party (a) owns such material, Information, or intellectual property right or (b) has a license or right to use to such material, Information, or intellectual property right, in the case of (a) and (b) with the ability to grant to the other Party access, a right to use, or a license or sublicense (as applicable) to such material, Information, or intellectual property right on the terms and conditions set forth herein, without violating the terms of any agreement or other arrangement with any Third Party. For Information or Patents of which a Party obtains "Control" after the Effective Date, such Control shall only be deemed to exist if the grant of a license or sublicense thereunder in accordance with this Agreement does not result in the granting Party owing payment to a Third Party, unless the Party receiving the grant of rights agrees in writing to pay the resulting amounts due to the Third Party as a condition of receiving such grant of rights.

1.37 "**Current Phase 4 Studies**" means those Phase 4 Trials required by the FDA as a condition to obtaining and/or maintaining the Assigned NDA, as further described on EXHIBIT B.

1.38 "**DEA**" means the U.S. Drug Enforcement Administration or its successor entity.

1.39 "**Debarment Laws**" has the meaning set forth in Section 11.1(d).

1.40 "Definitive Agreements" means, individually or collectively, this Agreement, the Transition Services and Distribution Agreement, the Supply Agreement, the API Supply Agreement, the Quality Agreement, and the PVG Agreement.

1.41 "**Designated Executives**" means the Chief Executive Officer of Shionogi (or, if there is no Chief Executive Officer, the highest-ranking officer of Shionogi) and the Chief Executive Officer of BDSI (or, if there is no Chief Executive Officer, the highest-ranking officer of BDSI).

1.42 "**Detailing**" means any in-person sales presentation of Symproic made by or on behalf of BDSI, any Affiliate thereof, or any BDSI Licensee to physicians and other health care practitioners licensed to prescribe pharmaceutical products, describing it in a fair and balanced manner consistent with the requirements of this Agreement, the product label and all applicable laws, rules, and regulations, and in a manner that is customary in the industry for the purpose of promoting a prescription pharmaceutical product. When used as a verb, "Detail" shall mean to engage in a Detail.

1.43 "**Development**" means, except as provided below, all development activities that relate to expanding Regulatory Approval of Symproic with respect to new or improved indications, presentations, formulations, dosage forms, dosage strengths, and/or line extensions including, without limitation: (a) research, nonclinical studies, toxicology, and Clinical Trials; and (b) preparation, submission, review, and development of data or information for the purpose of submission to a Regulatory Authority to obtain, maintain and/or expand Regulatory Approval of Symproic with respect to such new or improved indications, presentations, formulations, dosage forms, dosage strengths, and/or line extensions; provided, however, that Development shall exclude Commercialization of Symproic. For clarity, Development shall not include Phase 4 Trial commitments that are required by a Regulatory Authority as a condition of Regulatory Approval of Symproic in the Field in the Territory. "Develop" has a correlative meaning.

1.44 "**Diligent Efforts**" means, with respect to a Party's obligations under this Agreement or any other Definitive Agreement, the carrying out of such obligations or tasks with a level of efforts and resources consistent with the [***] or [***] of a [***] as [***] at a [***], taking into account [***] (including [***] and any [***]), [***], and all other relevant factors, all based on conditions then prevailing.

1.45 "**Distribution**" means the commercial sale and distribution of Symproic. "Distribute" has a correlative meaning.

1.46 "**Effective Date**" has the meaning set forth in the preamble.

1.47 **"Existing Confidentiality Agreement**" means that certain Mutual Confidentiality Agreement, dated [***], between Shionogi and BDSI.

1.48 "**FDA**" means the U.S. Food and Drug Administration or its successor.

1.49 "**FD&C Act**" means the U.S. Federal Food, Drug and Cosmetic Act, as amended.

1.50 "**Field**" means the treatment of opioid-induced constipation in humans.

1.51 "**Final Court Decision**" means a decision of a court or of the United States Patent and Trademark Office from which no appeal has been or can be taken, excluding any petition for a writ of certiorari or other proceedings before the United States Supreme Court.

1.52 "First Commercial Sale" means the first sale of Symproic by or on behalf of BDSI, its Affiliates, or a BDSI Licensee, for end use or consumption, in the Territory. A First Commercial Sale excludes any sale or distribution for use in any clinical trial or other Development activity, promotional use (including samples) or for compassionate use or on a named patient basis.

1.53 "**Generic Competition**" means, on a Calendar Quarterly basis, a fraction (expressed as a percentage), the numerator of which shall be the aggregate number of units of Generic Equivalents sold by Third Parties in the Territory during such Calendar Quarter, and the denominator of which shall be the aggregate number of units of all such Generic Equivalents plus the aggregate number of units of Symproic (including AG Products) sold by BDSI, its Affiliates, and BDSI Licensees under this Agreement in the Territory during such Calendar Quarter, based on independent market data published by IQVIA, or if such data is not available from such source, such other reliable data source as is reasonably agreed to by the Parties.

1.54 "**Generic Equivalent**" means, with respect to Symproic in the Territory, a product, other than an AG Product, that (a) contains Naldemedine as its sole API in the same dosage(s) as Symproic, (b) is bioequivalent to Symproic, (c) may be legally substituted by pharmacies in the Territory for Symproic when filling a prescription written therefor without, as a legal requirement, having to seek authorization to do so from the physician or other health care provider writing such prescription, (d) is not marketed or sold under the approval of the Assigned NDA (but instead is sold under the authorization of a Third Party's ANDA or NDA submitted by a Third Party under §505(b)(2) of the FD&C Act with reference to, in either case, the Assigned NDA), and (e) is sold in the Territory by any Third Party.

1.55 "**Governmental Authority**" means any multi-national, federal, state, local, municipal or other government authority of any nature (including any governmental division, subdivision, department, agency, bureau, branch, office, commission, council, court or other tribunal).

1.56 "**Hatch-Waxman Act**" has the meaning set forth in Section 10.3(c).

1.57 "[***] Service Agreement" means the Services Agreement, effective as of September 1, 2017, by and between Shionogi and [***], as amended by the Amendment and Change Order No. 1, effective as of [***], a copy of which has been provided to BDSI.

1.58 "H-W Suit Notice" has the meaning set forth in Section 10.3(c).

1.59 "**IND**" means an Investigational New Drug Application as defined in the FD&C Act and applicable regulations promulgated thereunder by the FDA.

1.60 "**Information**" means any data, results, and information of any type whatsoever, in any tangible or intangible form, including know-how, trade secrets, practices, techniques, methods, processes, inventions, developments, specifications, formulations, formulae, materials or compositions of matter of any type or kind (patentable or otherwise), software, algorithms, marketing reports, expertise, stability, technology, test data including pharmacological, biological, chemical, biochemical, toxicological, and clinical test data, analytical and quality control data, stability data, studies and procedures.

1.61 "**MAC**" means the Medical Affairs Committee formed by the Parties as described in Section 9.2(a).

1.62 "**Manufacturing**" or "**Manufacture**" means, with respect to Symproic, all activities related to the manufacture of Symproic (but excluding in all cases the manufacture of Naldemedine) including, but not limited to, manufacturing supplies of Symproic (but not Naldemedine) for Development or Commercialization, packaging, in-process and finished product testing, release of Symproic, quality assurance and quality control activities related to manufacturing and release of Symproic, ongoing stability tests, storage, shipment, and regulatory activities related to any of the foregoing.

1.63 "**Medical Affairs Activities**" means (a) publications relating to Symproic or Naldemedine in scientific or medical journals and similar forums and (b) attendance at scientific or medical conferences concerning Symproic or Naldemedine. For clarity, Medical Affairs Activities shall not include [***].

1.64 "**Naldemedine**" means the compound known as naldemedine tosylate having the structure set forth on EXHIBIT C.

1.65 "**NDA**" means a New Drug Application, as defined in the FD&C Act and applicable regulations promulgated thereunder by the FDA.

1.66 "**Net Sales**" means, with respect to Symproic, the gross amount invoiced or, if not invoiced, received, by BDSI, its Affiliate, or a BDSI Licensee, as applicable, for sales of Symproic to a Third Party less deductions for:

[***]

[***]

[***]

[***]

Sales between BDSI, its Affiliates, and/or BDSI Licensees, as applicable, for purposes of resale shall be disregarded for purposes of calculating Net Sales so long as such resale is subject to royalties under Section 3.2.

With respect to any sale of Symproic for any substantive consideration other than monetary consideration on arm's length terms (which has the effect of reducing the invoiced amount below what it would have been in the absence of such non-monetary consideration), for purposes of calculating the Net Sales under this Agreement, such Symproic shall be deemed to be sold exclusively for cash at the average Net Sales price charged to Third Parties for cash sales during the applicable reporting period (or if there were only de minimus cash sales, at the fair market value as determined by comparable markets). Notwithstanding the foregoing, Net Sales shall not include amounts (whether actually existing or deemed to exist for purposes of calculation) for Symproic distributed for Promotional Activities or for distribution as samples.

Net Sales shall be determined in accordance with those generally accepted Accounting Standards regularly and consistently employed by BDSI, its Affiliate(s), and/or BDSI Licensees, as applicable, with respect to the transactions in questions.

1.67 "**Orange Book**" means the FDA publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations" or any replacement thereof established or approved by the FDA.

1.68 "**Orange Book Patent**" means, with respect to Symproic, any patent listed in the Orange Book pursuant to 21 U.S.C. § 355(b)(1) for the Assigned NDA.

1.69 "**Party**" or "**Parties**" has the meaning set forth in the Preamble.

1.70 "**Patent**" means any granted patents and pending patent applications, together with all additions, divisionals, continuations, continuations-in-part, substitutions, reissues, re-examinations, extensions, registrations, patent term extensions, revalidations, supplementary protection certificates, and renewals of any of the foregoing and all foreign applications and patents corresponding to or claiming priority from any of the foregoing.

1.71 "**Phase 4 Trial**" means a Clinical Trial commenced after receipt of Regulatory Approval and which is intended to support the Commercialization of Symproic. Phase 4 Trials may include, without limitation, epidemiological studies, modeling and pharmacoeconomic studies, investigator-sponsored clinical trials of Symproic and post-marketing surveillance studies.

1.72 "**Promotion**" and "**Promotional Activities**" means those activities normally undertaken by a pharmaceutical company to implement marketing plans and strategies aimed at encouraging the Regulatory Authority-approved use of a prescription pharmaceutical product, including Detailing, marketing, advertising and related activities. When used as a verb, "Promote" or "Promoting" means engagement in such activities.

1.73 "**Promotional Materials**" means the written, printed, graphic, electronic, audio or video matter, including sales visual aids, reprints, direct mail, and direct-to-consumer advertising, in each case, intended for use or used by in connection with the advertising, marketing or promotion of Symproic in the Field set forth on EXHIBIT D.

1.74 "**PVG Agreement**" means that certain Pharmacovigilance Agreement to be executed by the Parties as contemplated by Section 5.3.

1.75 "**Quality Agreement**" means that certain Quality Agreement to be executed by the Parties as described in the Supply Agreement.

1.76 "**Regulatory Approval**" means any and all approvals by Regulatory Authorities necessary or useful for the manufacture, use, marketing, importation, sale, Development or Commercialization of Symproic in the Field in the Territory.

1.77 "**Regulatory Authority**" means any applicable Governmental Authority involved in granting Regulatory Approval in an applicable regulatory jurisdiction, including without limitation the FDA and the DEA and any successor agency(ies) thereto.

1.78 "**Regulatory Materials**" means regulatory applications, submissions, notifications, registrations, Regulatory Approvals and/or other filings or correspondence to or from, or other approvals granted by, a Regulatory Authority that are necessary or reasonably useful in order to develop, manufacture, market, sell or otherwise commercialize Symproic in a particular jurisdiction. Regulatory Materials include INDs, NDAs, and any other application to a relevant Regulatory Authority for approval of Symproic for commercial sale in a particular jurisdiction. For the avoidance of doubt, Regulatory Materials shall not include agreements or related filings or correspondence with Regulatory Authorities covering the purchase of Symproic, or payment of any rebates or chargebacks in respect of Symproic, by any Regulatory Authority.

1.79 "**SEC**" means the U.S. Securities and Exchange Commission.

1.80 "**Senior Managers**" has the meaning set forth in Section 4.1(d).

1.81 "**Shionogi**" has the meaning set forth in the Preamble.

1.82 "**Shionogi Claims**" has the meaning set forth in Section 12.2.

1.83 "**Shionogi Corporate Marks**" means those logos, trade names, and trademarks, other than the Symproic Marks, appearing on the Promotional Materials.

1.84 "**Shionogi Damages**" has the meaning set forth in Section 12.2.

1.85 "**Shionogi Indemnitees**" has the meaning set forth in Section 12.2.

1.86 "**Shionogi Know-How**" means all Information (excluding any Shionogi Corporate Marks or Symproic Marks) Controlled as of the Effective Date by, or thereafter coming under the Control of, Shionogi and reasonably necessary for the Commercialization of Symproic in the Field in the Territory, including any such Information made or generated by or on behalf of Shionogi in the course of performing Shionogi's obligations or exercising Shionogi's rights under this Agreement or the other Definitive Agreements. Notwithstanding anything to the contrary, however, Shionogi Know-How shall not include any Information that is owned, licensed, or otherwise controlled at any time by any Acquiring Entity with respect to Shionogi (a "**Shionogi Acquiring Entity**") or Acquired Entity with respect to Shionogi (a "**Shionogi Acquired Entity**"), except to the extent such Information was already included within the Shionogi Know-How immediately prior to the date of the transaction by which such Acquiring Entity or Acquired Entity first became a Shionogi Acquiring Entity or Shionogi Acquired Entity. For additional clarity, Shionogi Know-How shall exclude rights under any Shionogi Patents.

1.87 "**Shionogi Licensee**" means any Third Party to whom Shionogi, any Affiliate thereof, or any prior Shionogi Licensee grants any of the rights granted under Section 2.5.

1.88 "**Shionogi Patents**" means (a) all Orange Book Patents, (b) Patents in the Territory set forth on EXHIBIT E and, with respect to the patent applications set forth on EXHIBIT E, all Patents in the Territory issuing therefrom, and (c) all other Patents in the Territory Controlled by Shionogi during the Term that are reasonably necessary for BDSI to exercise its rights under Section 2.1. Notwithstanding anything to the contrary, however, Shionogi Patents shall not include any Patents that are owned, licensed, or otherwise controlled at any time by any Shionogi

Acquiring Entity or Shionogi Acquired Entity, except to the extent such Patents were already included within the Shionogi Patents immediately prior to the date of the transaction by which such Shionogi Acquiring Entity or Shionogi Acquired Entity first became a Shionogi Acquiring Entity or Shionogi Acquired Entity.

1.89 "**Shionogi Products**" has the meaning set forth in Section 2.5(b).

1.90 "**Shionogi Technology**" means the Shionogi Patents and the Shionogi Know-How.

1.91 "**Sublicense Agreement**" has the meaning set forth in Section 2.3(a).

1.92 "**Supply Agreement**" means that certain Supply Agreement to be executed by the Parties and effective as of the Effective Date.

1.93 "**Symproic**" means Symproic® tablets containing 0.2mg Naldemedine as approved pursuant to the Assigned NDA, and all amendments and supplements thereto, and all new or improved forms, presentations, strengths, doses, and formulations (including any method of delivery or administration), improvements, and line extensions thereto Developed under any Development Plan approved by the JDC pursuant to Article 4, whether Commercialized under the brand name Symproic®, any other Symproic Mark, or any BDSI Mark or as an AG Product.

1.94 "**Symproic Domain Names**" means those domain names set forth on EXHIBIT F.

1.95 "**Symproic Infringement**" has the meaning set forth in Section 10.3(a).

1.96 "**Symproic Marks**" means those logos, trade names, trade dress, trademarks, and associated registrations or applications therefor with respect to the Territory set forth on EXHIBIT G. Symproic Marks shall not include the Symproic Domain Names.

1.97 "**Term**" has the meaning set forth in Section 14.1.

1.98 "**Territory**" means the U.S.

1.99 "**Third Party**" means any entity other than Shionogi, BDSI, or an Affiliate of any of the foregoing.

1.100 "**[***]**" means [***]

1.101 "**[***]**" means [***].

1.102 "**[***]**" has the meaning set forth in Section 3.2(d).

1.103 "**Transferred Sample Inventory**" means the inventory of Symproic described on EXHIBIT H hereto.

1.104 "**Transition Services and Distribution Agreement**" means that certain Transition Services and Distribution Agreement to be executed by the Parties and effective as of the Effective Date.

1.105 "**U.S.**" means the United States of America and its territories, districts and possessions, including the Commonwealth of Puerto Rico.

1.106 "**Upfront Payment**" has the meaning set forth in Section 3.1.

Article 2

Licenses; Trademarks

2.1 Licenses to BDSI under Shionogi Technology. Subject to the terms and conditions of this Agreement, Shionogi hereby grants BDSI a royalty-bearing, sublicensable (solely as permitted in accordance with Section 2.3), transferable with this Agreement pursuant to Section 16.5, exclusive (even as to Shionogi) license under the Shionogi Technology to:

(a) Commercialize Symproic in the Field in the Territory;

(b) As and to the extent the Development thereof by BDSI is contemplated by any Development Plan approved by the JDC pursuant to Article 4, Develop Symproic in the Field in the Territory; and

(c) Following the termination or expiration of the Supply Agreement or as otherwise expressly permitted by the Supply Agreement, Manufacture and have Manufactured Symproic anywhere in the Territory, solely for (i) Development of Symproic in the Field in the Territory as and to the extent contemplated by any Development Plan approved by the JDC pursuant to Article 4; and (ii) Commercialization of Symproic in the Field in the Territory.

Subject to the terms and conditions of this Agreement, Shionogi hereby grants BDSI and its Affiliates a "Right of Reference" as that term is defined in 21 C.F.R. § 314.3(b) (or any successor rule) to [***] and all other Regulatory Materials related to such IND to the extent necessary to exercise the rights granted under Section 2.1, and such right shall be sublicensable in conjunction with the sublicense of any of the rights granted under Section 2.1. In addition, Shionogi shall take all actions and execute all documents (e.g. Certificates of Pharmaceutical Products (CPPs)) reasonably requested by BDSI in its exercise of the foregoing rights. Without limiting the foregoing, Shionogi shall submit a letter of authorization permitting the FDA to reference such IND on behalf of BDSI and its Affiliates in connection with the activities under this Agreement. For clarity, the rights granted by Shionogi under this Agreement shall not include any rights (i) other than as specifically outlined in Article 4, to Develop Symproic, Naldemedine, or any product, (ii) to Commercialize any product incorporating Naldemedine (or any analog or derivative thereof) other than Symproic, or (iii) except for any new indication the development of which is expressly authorized by the JDC pursuant to Article 4, with respect to any indications other than the Field.

Shionogi shall use Diligent Efforts to make available to BDSI all material Shionogi Know-How of which Shionogi has actual knowledge (after reasonable inquiry) existing as of the Effective Date and, after the Effective Date, (i) Shionogi shall use Diligent Efforts to make available to BDSI all Shionogi Know-How arising after the Effective Date of which Shionogi has actual knowledge (after reasonable inquiry) as such Information is generated (to the extent reasonably possible and

practicable) and (ii) BDSI shall use Diligent Efforts to make available to Shionogi all BDSI Know-How arising after the Effective Date of which BDSI has actual knowledge (after reasonable inquiry) as such Information is generated (to the extent reasonably possible and practicable).

2.2 Trademark Rights.

(a) Subject to the terms and conditions of this Agreement, Shionogi hereby grants BDSI a sublicensable (solely as permitted in accordance with Section 2.3), transferable (with this Agreement pursuant to Section 16.5), exclusive (even as to Shionogi) license to use and display the Symproic Marks in the exercise of the rights granted BDSI under Section 2.1.

(b) Subject to the terms and conditions of this Agreement, Shionogi hereby grants BDSI a limited, non-exclusive license to use and display the Shionogi Corporate Marks solely to the extent such rights are necessary for the use of the Promotional Materials in the Commercialization of Symproic in the Field in the Territory for a period of [***] after the Effective Date. The license granted under this Section 2.2(b) shall terminate upon the end of the [***] following the Effective Date.

(c) BDSI shall comply with all applicable laws, rules, and regulations pertaining to the proper use and designation of the Symproic Marks and Shionogi Corporate Marks. Additionally, BDSI shall not:

(i) use any Symproic Mark or Shionogi Corporate Mark other than for such specific purposes set forth above; nor

(ii) conduct, without the written consent of Shionogi, the whole or any part of its business under a business name or trading style which incorporates any of the Shionogi Corporate Marks.

(d) BDSI shall not take any action inconsistent with Shionogi's ownership of the Symproic Marks or Shionogi Corporate Marks. Any benefits (including goodwill) accruing from BDSI's use of the Symproic Marks and Shionogi Corporate Marks shall automatically vest in Shionogi. Upon Shionogi's reasonable request, BDSI shall provide to Shionogi samples of BDSI's and its Affiliates' packaging, labeling, marketing, promotional and other materials for the purpose of inspecting the use of the Symproic Marks and Shionogi Corporate Marks pursuant to this Agreement.

(e) Shionogi shall be entitled to terminate the rights to any Symproic Mark(s) or Shionogi Corporate Mark(s) granted above on written notice to BDSI if BDSI fails to correct any noncompliance with the terms of any license granted in Section 2.2(a) or 2.2(b) or uses any Symproic Mark(s) or Shionogi Corporate Mark(s) in any manner not authorized by any such license, within [***] of BDSI's receipt of written notice from Shionogi describing such non-compliance.

2.3 Sublicensing by BDSI.

(a) Scope of Permissible Sublicensing. The licenses granted by Shionogi to BDSI in Sections 2.1 and 2.2 may be sublicensed (through multiple tiers) by BDSI to a Third Party or any

Affiliate of BDSI without any requirement of consent, subject to the requirements of this Section 2.3(a) and Section 2.3(b). At least [***] prior to entering into any sublicense of its rights under Sections 2.1 or 2.2, BDSI shall provide to Shionogi, on a confidential basis, written notice of its intent to enter into such sublicense, including [***]. BDSI shall consider diligently, reasonably and in good faith all input received in writing from Shionogi within such [***] period, which for the avoidance of doubt, shall not begin until Shionogi has received all information BDSI is required pursuant to the immediately preceding sentence to provide to Shionogi, with respect to such proposed sublicense. For the avoidance of doubt, subject to the preceding and Section 2.3(b), BDSI shall have final say on, and Shionogi shall not attempt to interfere with, any sublicense and the terms thereunder.

(b) Sublicense Agreements. Each agreement under which BDSI grants a sublicense under the licenses set forth in Sections 2.1 and 2.2 (each, a "**Sublicense Agreement**") shall be subject to the applicable terms and conditions of this Agreement. BDSI shall be responsible for each of its Affiliates' and each BDSI Licensee's compliance with the terms of this Agreement, including the provision of Diligent Efforts by such sublicensee for the full term of their responsibilities under this Agreement during the AG Royalty Term and Branded Royalty Term and adherence to 2.7(a) and 2.7(c) BDSI shall, in each Sublicense Agreement, require such Affiliate or BDSI Licensee to provide the following to BDSI if such Sublicense Agreement terminates: (i) [***]) and (ii) [***]. BDSI will, as soon as reasonably practicable following the execution of any Sublicense Agreement, provide Shionogi with a copy of any executed Sublicense Agreement (which copy may be redacted to remove financial provisions and other provisions which are not necessary to monitor compliance with this Section 2.3(b)).

2.4 Shionogi Reserved Rights in the Territory. Notwithstanding anything to the contrary, all rights granted to BDSI under this Article 2 shall not be construed to in any event limit Shionogi's, its Affiliates', or its or their licensees', sublicensees' or any of its or their Third Party contractors' or agents' rights to (a) perform Shionogi's obligations or exercise Shionogi's rights under this Agreement or any other Definitive Agreement or (b) without limiting Section 2.7(b), research, develop, manufacture, have manufactured, sell, offer for sale, import, export, or use Symproic or Naldemedine for any purposes related to the development or commercialization of Symproic, Naldemedine, or any product incorporating Naldemedine either outside the Territory or outside the Field.

2.5 Licenses to Shionogi.

(a) Subject to the terms and conditions of this Agreement, BDSI hereby grants Shionogi and its Affiliates a worldwide, nonexclusive, sublicensable (through multiple tiers of sublicenses), royalty-free, fully-paid license, transferable with this Agreement pursuant to Section 16.5, under the BDSI Technology during the Term to perform Shionogi's obligations under this Agreement and any other Definitive Agreement, such license to be for a term commencing on the Effective Date and terminating on the day of termination or expiration of the last Definitive Agreement.

(b) Subject to the terms and conditions of this Agreement, BDSI hereby grants Shionogi and its Affiliates a worldwide, perpetual and irrevocable, sublicensable (through multiple tiers of sublicenses in accordance with this Section 2.5(b)), royalty-free, fully-paid,

nonexclusive license, transferable with this Agreement pursuant to Section 16.5, under the BDSI Technology to (i) research, develop, manufacture, have manufactured, sell, offer for sale, import, export, and use Symproic for any purposes related to the development, manufacture, or commercialization thereof outside the Territory or outside the Field and (ii) research, develop, manufacture, have manufactured, sell, offer for sale, import, export, and use Shionogi Products. Without limiting the foregoing, BDSI hereby grants Shionogi and its Affiliates a right of reference to all Regulatory Approvals (including the Assigned NDA), applications therefor, or other Regulatory Materials owned or controlled by BDSI, any Affiliate thereof, or any BDSI Licensee to exercise the rights granted in this Section 2.5(b), including without limitation in connection with seeking, obtaining and maintaining INDs and NDAs (and any other analogous regulatory approvals in foreign jurisdictions) in relation to Shionogi Products both inside and outside the Territory. In addition, BDSI shall take all actions and execute all documents (e.g. Certificates of Pharmaceutical Products (CPPs)) reasonably requested by Shionogi in its exercise of the foregoing rights. For clarity, the foregoing rights (A) shall be subject to the negative covenants in Section 2.7 below and (B) shall not create any right in favor of Shionogi to amend or supplement the Assigned NDA after the Effective Date. Shionogi and its Affiliates may grant sublicenses to Third Parties, with the rights for such sublicensees to grant further sublicenses, of the rights granted to Shionogi and its Affiliates under this Section 2.5(b) solely in connection with the grant of a license or other rights to any Information (other than BDSI Know-How), Patents (other than BDSI Patents), other intellectual property rights (e.g., trademarks), or regulatory assets that are owned, licensed, or otherwise controlled by Shionogi or any Affiliate thereof and relate to any of the Shionogi Product(s) that are the subject of such sublicense. Notwithstanding anything to the contrary contained herein, Shionogi shall ensure that any written agreement pursuant to which Shionogi or its Affiliate or any of their sublicensees grant a sublicense pursuant to this Section 2.5(b) contains terms and conditions reasonably sufficient to ensure Shionogi's ability to comply with the applicable terms of this Agreement. For purposes of this Agreement "**Shionogi Products**" means any of the following: Naldemedine, any analog or derivative thereof, or any product (other than Symproic) incorporating Naldemedine or any analog or derivative thereof (alone or with any other API).

2.6 Domain Names. On the Effective Date, Shionogi shall transfer, and hereby assigns, to BDSI all of Shionogi's right, title and interest in and to the Symproic Domain Names. Such transfer shall be accomplished via the delivery by each Party to the other of a duly executed Domain Name Assignment substantially in the form attached hereto as EXHIBIT I. BDSI shall, at its cost and expense, use Diligent Efforts to maintain the Symproic Domain Names in good standing throughout the Term.

2.7 Negative Covenants.

(a) During the Term, BDSI shall not develop, commercialize, nor enable any Third Party to develop or commercialize (by license or otherwise), and BDSI shall ensure that none of its Affiliates nor any BDSI Licensees develop, commercialize, nor enable any Third Party to develop or commercialize (by license or otherwise), any product (other than Symproic Developed or Commercialized in accordance with this Agreement) in the Territory that, alone or in combination with another product, (i) is indicated (or intended to be indicated) or the subject of regulatory approval for the treatment of opioid-induced constipation in humans or (ii) is a peripherally-acting mu-opioid receptor antagonist for any indication.

(b) During the Term, Shionogi shall not (i) develop any pharmaceutical product with the intention of seeking regulatory approval in the Territory for the treatment of opioid-induced constipation in humans or (ii) commercialize or promote in the Territory any pharmaceutical product that (x) is indicated (or intended to be indicated) for the treatment of opioid-induced constipation in humans or (y) [***], provided that for the avoidance of doubt and notwithstanding anything to the contrary, Shionogi shall be free to commercialize Naldemedine or any other product incorporating Naldemedine or any analog or derivative thereof in the Territory outside the Field.

(c) Each Party covenants that it will not knowingly use or practice any of the other Party's intellectual property rights licensed to it under this Article 2 except for the purposes expressly permitted in the applicable license grant.

2.8 No Implied Licenses. Except as explicitly set forth in this Agreement, neither Party grants to the other Party any license, express or implied, under its intellectual property rights.

Article 3

Payments

3.1 Upfront Payment. In consideration of the licenses granted by Shionogi herein and the other assets transferred by Shionogi, BDSI will pay Shionogi the amount of thirty million U.S. dollars (US$30,000,000) (the "**Upfront Payment**"). The Upfront Payment shall be payable by BDSI as follows: (a) twenty million U.S. dollars (US$20,000,000) shall be paid by BDSI on the Effective Date, and (b) ten million U.S. dollars (US$10,000,000) shall be paid by BDSI on or before the earlier to occur of (i) the six-month anniversary of the Effective Date or (ii) any assignment or other transfer of this Agreement by BDSI. Such payments shall be nonrefundable and non-creditable and shall be made by wire transfer of immediately available funds into an account designated by Shionogi.

3.2 Royalties.

(a) Branded Product Royalties. BDSI shall pay Shionogi the applicable percentage set forth below of Net Sales of Branded Products during the Branded Royalty Term ("**Branded Net Sales**"):

Portion of Branded Net Sales in a Calendar Year	Applicable Royalty Rate
That portion of Branded Net Sales in a given Calendar Year that is less than or equal to [***]	8.5%
That portion of Branded Net Sales in a given Calendar Year that exceeds [***] and is less than or equal to [***]	[***]
That portion of Branded Net Sales in a given Calendar Year that exceeds [***] and is less than or equal to [***]	[***]
All Branded Net Sales in a given Calendar Year in excess of [***])	17.5%

(b) Branded Product Royalty Adjustments. During the Branded Royalty Term,

(i) Upon the date that Generic Competition is greater than [***] but less than [***], all royalty rates set forth in Section 3.2(a) shall be reduced by [***] with respect to all Branded Net Sales occurring on or after such date;

(ii) Upon the date that Generic Competition equals or exceeds [***], but less than [***], all royalty rates set forth in Section 3.2(a) shall be reduced by [***] with respect to all Branded Net Sales occurring on or after such date; and

(iii) Upon the date that Generic Competition equals or exceeds [***], all royalty rates set forth in Section 3.2(a) shall be reduced by [***] with respect to all Branded Net Sales occurring on or after such date.

Notwithstanding the foregoing, if and when all Orange Book Patents have expired or have been held invalid or unenforceable by a Final Court Decision and the Branded Royalty Term otherwise remains in effect, then the greater of the following reductions shall apply to the royalties payable on Branded Net Sales occurring following the occurrence of such circumstances: (a) the reductions contemplated in (i) through (iii) above or (b) an amount equal to [***] of the applicable royalty rates set forth in Section 3.2(a) above.

(c) AG Product Royalties. BDSI shall pay Shionogi [***] of all Net Sales of AG Product during the AG Royalty Term; provided, however that the royalties payable by BDSI with respect to Net Sales of such AG Product shall be [***] for the then-remaining AG Royalty Term on all Net Sales of AG Product occurring after the date on which all Orange Book Patents have expired or have been held invalid or unenforceable by a Final Court Decision.

(d) Third Party Royalties. The Parties acknowledge that pursuant to the [***], Shionogi's parent company, Shionogi & Co., Ltd., is obligated to pay [***] a royalty of [***] of net sales of Symproic (where such net sales are determined in accordance with the terms of the [***]). In addition to the payments required by Section 3.2(a) through (c), BDSI shall pay to Shionogi, [***] of Net Sales of Symproic under this Agreement (as determined in accordance with the terms of this Agreement) during the applicable AG Royalty Term and Branded Royalty Term for so long as such obligation of Shionogi & Co., Ltd. continues under the [***] (the "[***] **Royalty**").

3.3 Anti-Stacking. If BDSI is required by (a) a future court order or (b) settlement, license, or other agreement between BDSI and any Third Party that, in the case of clause (b), has been consented to in writing and in advance by Shionogi (such consent not to be unreasonably withheld, conditioned or delayed), to make any payments to a Third Party for the practice of any Patents owned by such Third Party with respect to the Commercialization or Development (pursuant to a Development Plan approved by the JDC pursuant to Article 4) of Symproic in the Field in the

Territory, then BDSI will be entitled to deduct from all royalties due under Section 3.2 an amount equal to [***] of the royalties actually paid to such Third Party in any Calendar Quarter, up to a maximum amount of [***] of the royalties due to Shionogi in such Calendar Quarter.

3.4 Royalty Payments and Reports. All amounts payable to Shionogi pursuant to this Section 3.2 shall be paid by BDSI in U.S. dollars within forty-five (45) days after the end of each Calendar Quarter with respect to royalties earned in such Calendar Quarter. Each payment of royalties due hereunder shall be accompanied by a statement of the amount of gross sales of Symproic during the applicable Calendar Quarter, a calculation of Net Sales detailing the deductions from gross sales provided for in the definitions of Net Sales during such Calendar Quarter, and a calculation of the amount of royalty payment due on such sales for such Calendar Quarter.

3.5 Taxes. All payments under this Agreement shall be made without any deduction or withholding for or on account of any tax unless such deduction or withholding is required by applicable laws or by a governmental entity. If a Party is entitled under an applicable tax treaty to a refund, reduction of rate, or the elimination of, any applicable withholding tax, it must deliver to the other Party or the appropriate governmental entity with the assistance of the other Party, to the extent that this is reasonably required, the prescribed forms and information necessary to obtain such refund or to reduce the applicable rate of withholding or to relieve the other Party of its obligation to withhold tax, and the other Party shall apply the reduced rate of withholding, or dispense with withholding, as the case may be, provided that the other Party has received evidence, in a form reasonably satisfactory to the other Party, of the delivery of all applicable forms and information (and, if necessary, the receipt of appropriate governmental authorization) at least ten (10) days prior to the time that the payment is due. The Parties shall cooperate in accordance with applicable law to minimize withholding taxes. If, in accordance with the foregoing, a Party withholds any amount, it shall pay to the other Party the balance when due and make a proper and timely payment of the withheld tax to the proper taxing authority, and send the other Party proof of such payment within thirty (30) days following that payment. Notwithstanding a Party's acceptance to reduce or dispense with any withholding, in the event it is determined by a Governmental Authority that there is a liability to such Party for failure to deduct, withhold or collect and remit any amount exceeding the amount withheld, if any, then, subject to the provisions of Section 12.3, the other Party shall defend, indemnify and hold said first Party harmless from and against any and all any liability for any amount that it should have deducted, withheld, collected or remitted (as well as any interest and penalties relating thereto). In furtherance of the above, each Party shall use commercially reasonable efforts to collaborate with the other Parties to defend such Claim and to mitigate any and all damages, losses, costs and expenses related to such Claim.

3.6 Late Payments. If Shionogi does not receive payment of any sum due to it on or before the due date therefor (other than amounts that are the subject of a good faith dispute), interest shall thereafter accrue on the sum due to Shionogi from the due date until the date of payment on a [***] basis at a rate equal to LIBOR (as published in The Wall Street Journal, New York edition) plus [***] or the maximum rate allowable by applicable law, whichever is less.

3.7 Financial Records; Audits. BDSI shall maintain complete and accurate records in sufficient detail to permit Shionogi to confirm the accuracy of any amounts that are payable under this Agreement. Upon reasonable prior notice, such records shall be open during regular business

hours for a period of three (3) years from the creation of individual records, in each case, for examination at Shionogi's expense, and not more often than once each Calendar Year, by an independent certified public accountant selected by the examining Party and reasonably acceptable to BDSI, for the sole purpose of verifying the accuracy of the financial information and reports furnished by BDSI pursuant to this Agreement or of any payments made, or required to be made, to Shionogi pursuant to this Agreement. Any amounts shown to be owed but unpaid, or overpaid and in need of reimbursement, shall be paid or refunded (as the case may be) within thirty (30) days after the accountant's report, plus interest (to the extent set forth in Section 3.6) from the original due date. Shionogi shall bear the full cost of such audit unless such audit reveals an underpayment by BDSI of more than [***] of the amount set forth in the applicable report, in which case BDSI shall bear the reasonable, out-of-pocket costs of such audit.

3.8 Manner and Place of Payment. All payments owed under this Agreement shall be made by wire transfer in immediately available funds to a bank and account designated in writing by the Party to receive such payment, unless otherwise specified in writing by such Party.

Article 4

Development

4.1 Joint Development Committee

(a) Formation; Role. Within [***] of the Effective Date, the Parties shall establish a joint development committee (or "**JDC**") as described in this Article 4, which shall exist during the Term of this Agreement. The JDC shall review (x) all development activities being conducted or proposed to be conducted by or on behalf of Shionogi, its Affiliates and/or Shionogi Licensees for products incorporating Naldemedine outside the Field or outside the Territory and (y) all proposals submitted by BDSI to Develop Symproic in the Field in the Territory (e.g., to seek additional indications, presentations, formulations, dosage forms, dosage strengths, and/or line extensions) ("**Development Proposals**") and discuss implementation of such Development Proposals in good faith. If a Development Proposal is approved by the JDC, then the terms and conditions governing such Development Proposal, including any performance and financial obligations of the Parties, shall be memorialized in a "**Development Plan**" mutually agreeable to the Parties (which shall not be effective until such mutual agreement). As applicable, the JDC shall (i) review and approve the Development Plan, (ii) monitor and oversee the Parties' progress under any Development Plan, (iii) review, comment, and approve any changes or amendments to the Development Plan proposed by any Party, provided that any such changes and amendments shall only be effective upon approval thereof by the JDC, and (iv) have such other responsibilities and powers as may be specified in this Agreement. Each Party shall keep the JDC reasonably informed of its progress and activities under any Development Plan.

(b) Membership. The JDC will be comprised of two (2) members in total and one (1) representative from each Party, and, each Party will designate its initial, respective members and representative prior to the date scheduled for the first meeting of the JDC. Each Party may replace its representative on the JDC at any time upon written notice to the other Party and may involve other representatives from such Party at their discretion. Any member of the JDC may designate a substitute to attend and perform the functions of that member at any meeting of the JDC. Each Party may, in its sole discretion, choose to have its Alliance Manager attend any meeting of the JDC.

(c) Meetings. The JDC shall meet as reasonably necessary or appropriate, on such dates and times as the Parties may agree, and by means of telecommunications and video conferences, or by such other means as the Parties may agree.

(d) Decision-Making**.** The JDC shall make its decisions by consensus, with each Party's representatives collectively having one vote. In the event the JDC is unable to reach consensus on any issue for which the JDC is responsible, the issue shall be presented to the Alliance Managers (as defined in Section 9.4) jointly with the Parties' respective senior managers who are responsible for the matters in dispute ("**Senior Managers**"). If the Alliance Managers and Senior Managers are unable to resolve such dispute within [***], then the dispute shall be referred to the Parties' Designated Executives. Once such an issue has been presented to the Designated Executives, they shall have [***] to make a final determination regarding the issue in dispute. In the event that the Designated Executives are unable to reach a final determination within such [***] period with respect to any issue properly before the JDC (including any issues related to Development of Symproic), then Shionogi shall have final decision-making authority with respect thereto.

(e) Termination of JDC. The JDC shall be disbanded, and no longer meet or have any obligations or responsibilities under this Agreement, upon termination or expiration of this Agreement.

Article 5

Regulatory Matters

5.1 Regulatory Filings, Approvals, and Related Know-How.

(a) Rights and Obligations. Upon the Effective Date, Shionogi shall assign, and hereby assigns, to BDSI all right, title, and interest to the Assigned NDA, and the Parties shall file the Assigned NDA Letters as soon as reasonably possible, but in any event no later than, [***] following the Effective Date. For clarity, the transfer of the Assigned NDA contemplated by the foregoing sentence shall not include the transfer of ownership of any of the Information contained therein as of the Effective Date. BDSI shall use Diligent Efforts to maintain the Assigned NDA in good standing and full effect and otherwise preserve and maintain the right to Commercialize Symproic in the Field in the Territory, including through the payment of all PDUFA fees or other fees payable to Governmental Authorities in the Territory with respect thereto. Without limiting the foregoing, BDSI shall (i) use Diligent Efforts to complete, at its sole cost and expense, the Current Phase 4 Studies in a timely fashion in accordance with the requirements thereof established by the FDA and the [***] Service Agreement, and (ii) shall update Shionogi periodically, upon Shionogi's reasonable request, on the status and progress toward completion of the Current Phase 4 Studies. Prior to making any material modification to the Current Phase 4 Studies or the [***] Service Agreement, BDSI shall consult with Shionogi and shall consider diligently, reasonably and in good faith all input received from Shionogi with respect to such proposed modification, and BDSI and Shionogi shall use reasonable efforts to reach consensus on

all input provided by Shionogi prior to BDSI proceeding with any such modification. For the avoidance of doubt, subject to the immediately preceding sentence, BDSI shall have final say on, and Shionogi shall not attempt to interfere with, the Current Phase 4 Studies, the [***] Service Agreement and any amendments to the foregoing. Upon the Effective Date, (A) Shionogi will assign, and hereby assigns, to BDSI the [***] Service Agreement and Shionogi's rights and obligations thereunder and (B) BDSI shall assume, and hereby assumes, the [***] Service Agreement and all rights and obligations of Shionogi thereunder and agrees to pay, perform and discharge when due all liabilities under or in respect of the [***] Service Agreement arising after the Effective Date, except to the extent arising from a breach thereof by Shionogi that occurred prior to the Effective Date.

(b) Dealings and Filings**.** BDSI shall be responsible for all dealings with Regulatory Authorities with respect to Symproic in the Field in the Territory, including filing all supplements and other documents with such Regulatory Authorities with respect to the Assigned NDA and responding to all requests, inquiries or other communications from such Regulatory Authorities, including those relating to the Promotion of Symproic in the Field in the Territory. BDSI shall take all actions reasonably requested by Shionogi to update, modify or supplement the applicable Regulatory Approvals for Symproic in the Field in the Territory in connection with the manufacture of Symproic by or on behalf of Shionogi, including relative to the purchase of raw materials, the manufacture of Naldemedine therefor, the filling, labeling, packaging, serialization and finishing of Symproic, the release, holding and storage of Symproic, validation, quality control and assurance, validation, quality control and assurance and any tests and analysis of Symproic, in each case, to the extent such manufacturing activities are conducted for BDSI under the Supply Agreement or API Supply Agreement.

(c) Right of Reference; Reporting and Review.

(i) Subject to the terms and conditions of this Agreement, BDSI hereby grants Shionogi and its Affiliates a "Right of Reference" as that term is defined in 21 C.F.R. § 314.3(b) (or any successor rule or analogous law recognized outside of the United States) to the Assigned NDA to the extent necessary to exercise the rights granted under Section 2.5, and such right shall be sublicensable in conjunction with the sublicense of any of the rights granted under Section 2.5.

(ii) BDSI shall promptly notify Shionogi of, and shall promptly, and in any event within [***] from the submission date, provide Shionogi with a copy (which shall be in electronic form to the extent reasonably possible) of all Regulatory Materials with respect to the Field in the Territory, including but not limited to those that are (A) amendments or supplements to the Assigned NDA, (B) related to the safety or efficacy of Symproic in the Field in the Territory, (C) related to any clinical Development pursuant to Article 4 (but excluding, for clarity, the Current Phase 4 Studies), or (D) reasonably necessary to enable the right of reference in the foregoing Section 5.1(c)(i).

5.2 Symproic Withdrawals and Recalls. If any Regulatory Authority (a) threatens, initiates or advises any action to remove Symproic from the market in the Field in the Territory or (b) requires or advises Shionogi, BDSI, or their Affiliates to distribute a "Dear Doctor" letter or its equivalent regarding use of Symproic in the Field in the Territory, then Shionogi or BDSI, as

applicable, shall notify the other Party of such event within [***] (or sooner if necessary to enable a Party to comply with law) after such Party becomes aware of the action, threat, advice or requirement (as applicable) and BDSI shall have the right to decide whether to recall, withdraw or issue a field alert in the Field in the Territory in connection with Symproic, and as between the Parties, BDSI shall be responsible for conducting any recalls or withdrawals, issuing any field alerts, or taking such other necessary remedial action in the Field in the Territory, provided that, notwithstanding anything to the contrary, with respect to Symproic sold in the Field in the Territory bearing any Shionogi name, any Shionogi Corporate Mark, or any Shionogi national drug code, Shionogi shall be entitled to effect (or to require BDSI to effect) any recall, withdrawal, or field alert in the Territory, if Shionogi reasonably determines in good faith that such action is necessary or appropriate after providing BDSI a reasonable opportunity to do so and BDSI shall take all actions reasonably requested by Shionogi in connection therewith. All costs and expenses relating to withdrawals or recalls of Symproic sold prior to the Effective Date shall be borne by Shionogi and all costs and expenses relating to withdrawals or recalls of Symproic sold in the Field in the Territory after the Effective Date shall be borne by BDSI, except as otherwise set forth in the Transition Services and Distribution Agreement, Supply Agreement, Quality Agreement or API Supply Agreement. The preceding shall not be in lieu of or limit any obligation of indemnity of any Party hereto pursuant to this Agreement or other Definitive Agreements.

5.3 Pharmacovigilance and Safety Reporting Obligations. The Parties' obligations with respect to exchanging and reporting adverse events and other safety information relating to Symproic in the Field will be set forth in a reasonable and customary form of pharmacovigilance agreement to be entered into between the Parties effective as of the Effective Date. Pursuant to the terms of the PVG Agreement, BDSI shall be primarily responsible for collecting information related to adverse events in the Territory with respect to Symproic in the Field and providing such information to Shionogi in a reasonably timely fashion, all as set forth therein. Each Party shall comply with its obligations under the PVG Agreement.

Article 6

Commercialization

6.1 Commercialization of Symproic. BDSI shall control, have sole decision-making authority, and be solely responsible for, the Commercialization (including marketing, strategy and implementation thereof, pricing, promotion, physician targeting, reimbursement, branding and sale) of Symproic in the Field in the Territory, including the costs associated therewith, the whole subject to the rights and obligations that are specifically provided herein or in the other Definitive Agreements. BDSI shall use Diligent Efforts to Commercialize Symproic in the Field in the Territory during the AG Royalty Term and Branded Royalty Term. For greater clarity, from the Effective Date of this Agreement, except as contemplated by the Transition Services and Distribution Agreement, Shionogi shall not engage in any Commercialization of Symproic in the Field in the Territory, and accordingly shall not be responsible for any Promotional Activity with respect to Symproic in the Field in the Territory. BDSI shall provide to Shionogi at least [***] prior written notice before the launch of any AG Product in the Territory by BSDI, any Affiliate of BDSI, any BDSI Licensee or any Third Party; provided that if BDSI has less than [***] notice of an anticipated launch of a Generic Equivalent, then BDSI shall provide Shionogi with such notice as is reasonably practicable.

6.2 Managed Care.

(a) BDSI shall be responsible for market access, managed care and reimbursement matters, including for the operational aspects of managing and carrying out efforts related to obtaining reimbursement for Symproic in the Territory and negotiation of market access and managed care arrangements with respect thereto.

(b) BDSI shall use commercially reasonable efforts to negotiate and enter into an agreement with [***] for [***] of Symproic in the form substantially similar to BDSI's existing agreement with [***] for [***] of Symproic as soon as possible following the Effective Date. In any event, BDSI shall reimburse Shionogi within [***] of BDSI's receipt of an invoice (with reasonable supporting documentation) therefor all amounts paid by Shionogi in respect of sales of Symproic made by BDSI (whether bearing BDSI's, a BDSI Affiliate's or a BDSI Sublicensee's NDC number) for which rebates and other amounts are due under Shionogi's existing agreement with [***] for [***] of Symproic.

6.3 Commercialization Standards. BDSI shall comply with all applicable laws and regulations in Commercializing Symproic under this Agreement, including the FD&C Act, the Prescription Drug Marketing Act of 1987, as amended, and the rules, regulations and guidelines promulgated thereunder, the FDA Guidance for Industry-Supported Scientific and Educational Activities, the Pharmaceutical Research and Manufacturers of America Code on Interactions with Healthcare Professionals, the Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers, the Accreditation Council for Continuing Medical Education Standards for Commercial Support of Continuing Medical Education, the Pharmaceutical Marketing Research Group Guidelines on market research activities, and all payor "fraud and abuse" and consumer protection and false claims statutes and regulations, including the Medicare and Medicaid Anti-Kickback Statute and the "Safe Harbor Regulations" found at 42 C.F.R. §1001.952 et seq.

6.4 Commercialization Reports. From and after the Effective Date, within [***] after the end of each Calendar Year during the Term, BDSI shall provide Shionogi with a reasonably detailed written report (each, a "**Commercialization Report**") regarding the progress and results of Commercialization activities for Symproic in the Territory and Field in the previous Calendar Year and plans for the then current Calendar Year. Each Commercialization Report shall include an annual review of results versus plans for Symproic in the Field and Territory, [***] and all other material activities concerning such Commercialization of Symproic occurring during the prior Calendar Year. Each Commercialization Report shall also address plans for each of the items described in the foregoing sentence with respect to the then current Calendar Year and shall indicate whether BDSI intends to launch an AG Product during such period (and if so, shall provide BDSI's rationale for doing so). BDSI shall respond promptly and in good faith to any reasonable questions Shionogi may have with respect to any Commercialization Report provided by BDSI pursuant to this Section 6.4, including by participating in one or more meetings (by teleconference) to review and discuss the same.

Article 7

Commercial Transition

7.1 Transition Services and Distribution Agreement. Shionogi shall perform certain sales, distribution and related activities and certain transitional services with respect to Symproic during the term of the Transition Services and Distribution Agreement, all on the terms and conditions set forth therein.

Article 8

Manufacture and Supply

8.1 Transferred Sample Inventory. Shionogi shall sell and deliver to BDSI the Transferred Sample Inventory as soon as reasonably practicable following the Effective Date. In respect of the Transferred Sample Inventory, on the Effective Date, BDSI shall pay Shionogi the amount set forth in EXHIBIT H by wire transfer of immediately available funds into an account designated by Shionogi.

8.2 Supply Obligations. Shionogi shall supply Symproic to BDSI as set forth in the Supply Agreement, provided that any failure to supply Symproic under the Supply Agreement on the part of Shionogi shall not be considered a breach of this Agreement. [***].

Article 9

Medical Affairs Activities; Alliance Manager

9.1 Global Medical Affairs. The Parties shall use Diligent Efforts to update the MAC on a reasonably periodic basis (in accordance with the meeting scheduled outlined in Section 9.2(d)) with respect to their respective Medical Affairs Activities. The Parties hereby confirm that (a) Shionogi will retain the right to complete, submit and publish scientific or medical publications as outlined in its current publication plan (a copy of which has been provided to BDSI) with respect to Symproic and (b) BDSI will have the right to complete, submit and publish scientific or medical publications relating to the Current Phase 4 Studies.

9.2 Medical Affairs Committee.

(a) Formation; Composition. BDSI and Shionogi hereby establish a committee to facilitate communications between BDSI and Shionogi with respect to the conduct of Medical Affairs Activities by or on behalf of either Party or any of their Affiliates or Sublicensees occurring anywhere in the world (the "**MAC**"). BDSI's and Shionogi's initial representative to the MAC are [***] (for Shionogi) and [***] (for BDSI).

(b) No Authority. The MAC shall not have any decision-making authority, power to amend, modify or waive compliance with this Agreement, nor power or right to govern the conduct of Medical Affairs Activities by or on behalf of either Party or any of their Affiliates or Sublicensees.

(c) Representatives. Each Party shall initially appoint one (1) representative to the MAC, with each representative having relevant knowledge and expertise and having sufficient authority within the applicable Party to make decisions arising within the scope of the MAC's responsibilities. The MAC may change its size from time to time by mutual written consent of the Parties, provided that the MAC shall consist at all times of an equal number of representatives of each Party. Each Party may replace its MAC representatives at any time upon written notice to the other Party and may involve other representatives from such Party at their discretion. Any member of the MAC may designate a substitute to attend and perform the functions of that member at any meeting of the MAC. Each Party may, in its sole discretion, choose to have its Alliance Manager attend any meeting of the MAC.

(d) Meetings. The MAC shall meet once per Quarter during the 2019 Calendar Year and semi-annually each Calendar Year thereafter during the Term, unless the Parties mutually agree to a different frequency. The MAC may meet by videoconference or by teleconference, or in-person at the mutual agreement of the Parties.

9.3 Discontinuation of the MAC. The MAC shall continue to exist until the first to occur of (a) the Parties mutually agreeing in writing to disband the MAC or (b) the expiration or termination of this Agreement. Once the MAC has disbanded in accordance with the foregoing, the MAC shall have no further rights or obligations under this Agreement.

9.4 Alliance Manager. Each of Shionogi and BDSI shall appoint one (1) representative who possesses a general understanding of this Agreement and Symproic to act as its respective alliance manager for this relationship (each, an "**Alliance Manager**"). The initial Alliance Managers are [***] (for Shionogi) and [***] (for BDSI). Each of Shionogi and BDSI may replace its respective Alliance Manager at any time upon written notice to the other. Any Alliance Manager may designate a substitute to temporarily perform the functions of that Alliance Manager. Each Alliance Manager shall be charged with creating and maintaining a collaborative work environment concerning the subject matter of this Agreement within and among the Parties.

Article 10

Intellectual Property

10.1 Ownership of Inventions. Subject to the licenses and other rights granted herein, ownership of Information first made, conceived, developed or reduced to practice during the course of the performance of activities pursuant to this Agreement, and all intellectual property related thereto, shall follow inventorship, as determined in accordance with applicable United States law, including without limitation United States patent law.

10.2 Prosecution of Patents.

(a) Shionogi Patents. Except as otherwise provided in this Section 10.2(a), Shionogi and its Affiliates shall have the first right and authority to prepare, file, prosecute (including any interferences, reissue applications, post-grant proceedings and reexaminations) and maintain the Shionogi Patents in the Territory, at its sole expense. Upon BDSI's reasonable request, Shionogi shall provide BDSI copies of, and update BDSI on the status of, any issued or published, pending

Shionogi Patents. If Shionogi determines in its sole discretion to abandon, cease prosecution, or not maintain any Shionogi Patent in the Territory, then Shionogi shall provide BDSI with written notice of such determination at least [***] before any deadline for taking action to avoid abandonment (or other loss of rights) and use Diligent Efforts to provide BDSI with a reasonable opportunity, prior to such deadline, to discuss such proposed abandonment. Under such circumstances, BDSI will have the right (but not the obligation), at BDSI's sole discretion and sole responsibility for all applicable patent costs, to assume the prosecution and maintenance in the Territory of such Shionogi Patents in BDSI's own name (which right will include the right to file additional Patents claiming priority to such Shionogi Patents). Upon such election, Shionogi shall assign all right, title and interest in and to such Shionogi Patent to BDSI. Shionogi will sign, or will use commercially reasonable efforts to have signed, all legal documents as are reasonably necessary to assign such Shionogi Patents to BDSI and for BDSI to assume the prosecution and maintenance of such assumed Shionogi Patents in the Territory.

(b) BDSI Patents. Except as otherwise provided in this Section 10.2(b), BDSI and its Affiliates shall have the sole right and authority to prepare, file, prosecute (including any interferences, reissue applications, post-grant proceedings and reexaminations) and maintain the BDSI Patents in any jurisdiction, at its sole expense. Upon Shionogi's reasonable request, BDSI shall provide Shionogi copies of, and update Shionogi on the status of, any issued or published, pending BDSI Patents. If BDSI determines in its sole discretion to abandon, cease prosecution, or not maintain any BDSI Patent anywhere, then BDSI shall provide Shionogi with (i) written notice of such determination at least [***] before any deadline for taking action to avoid abandonment (or other loss of rights) and (ii) a reasonable opportunity, prior to such deadline, to discuss such proposed abandonment. Under such circumstances, Shionogi will have the right (but not the obligation), at Shionogi's sole discretion and sole responsibility for all applicable patent costs, to assume the prosecution and maintenance of such BDSI Patents in Shionogi's own name (which right will include the right to file additional Patents claiming priority to such BDSI Patents). Upon such election, BDSI shall assign all right, title and interest in and to such BDSI Patent to Shionogi. BDSI will sign, or will use commercially reasonable efforts to have signed, all legal documents as are reasonably necessary to assign such BDSI Patents to Shionogi and for Shionogi to assume the prosecution and maintenance of such assumed BDSI Patents.

(c) Cooperation in Prosecution. Each Party shall provide each other all reasonable assistance and cooperation in the Patent prosecution efforts provided above in this Section 10.2, including providing any necessary powers of attorney and executing any other required documents or instruments for such prosecution, at no charge to the other Party.

10.3 Infringement by Third Parties.

(a) Notification. If there is any infringement, threatened infringement, or alleged infringement in the Field and the Territory of the Shionogi Patents or BDSI Patents, or any other intellectual property rights Controlled by a Party and directly related to Symproic by a Third Party (in each case, a "**Symproic Infringement**"), then each Party shall promptly notify the other Party in writing of any such Symproic Infringement of which it becomes aware, and shall provide evidence in such Party's possession demonstrating such Symproic Infringement.

(b) Enforcement Rights in the Territory.

(i) Shionogi Patents. Subject to the remainder of this Section 10.3(b)(i) and Section 10.3(c), Shionogi shall have the exclusive first right, but not the obligation, to bring a suit or other action against any person or entity allegedly engaged in Symproic Infringement of any Shionogi Patents or Symproic Marks in the Territory. Shionogi shall have a period of [***] after its receipt or delivery of notice and evidence pursuant to Section 10.3(a), to elect to so enforce any such Shionogi Patent or Symproic Mark in the Territory (or to settle or otherwise secure the abatement of such Symproic Infringement). In the event Shionogi does not so elect to bring a suit or other action against any person or entity allegedly engaged in Symproic Infringement in the Field in the Territory (or settle or otherwise secure the abatement of such Symproic Infringement), it shall promptly so notify BDSI in writing, and BDSI shall have the right, at BDSI's expense, and if and as elected by BDSI in writing to Shionogi within [***] of receipt of Shionogi's notice that it will not make an election above, to commence a suit or take action to enforce the applicable Shionogi Patents or Symproic Marks with respect to such Symproic Infringement in the Field in the Territory, and Shionogi shall have the right to join such action at its own expense. Each Party shall provide to the Party enforcing any such rights under this Section 10.3(b)(i) reasonable assistance in such enforcement, at such enforcing Party's request and at the enforcing Party's expense (except as otherwise provided above), including joining such action as a party plaintiff if required by applicable law to pursue such action, making its personnel available, providing any necessary Information, and executing documents. The enforcing Party shall keep the other Party regularly informed of the status and progress of such enforcement and settlement efforts and related filings, and shall reasonably consider the other Parties' comments on any such efforts and related filings.

(ii) BDSI Patents. Subject to the remainder of this Section 10.3(b)(ii) and Section 10.3(c), BDSI shall have the exclusive first right, but not the obligation, to bring a suit or other action against any person or entity allegedly engaged in Symproic Infringement of any BDSI Patents or BDSI Marks in the Territory. BDSI shall have a period of [***] after its receipt or delivery of notice and evidence pursuant to Section 10.3(a), to elect to so enforce any such BDSI Patent or BDSI Mark in the Territory (or to settle or otherwise secure the abatement of such Symproic Infringement). Upon electing to bring, or to forego bringing, any such suit or other action (or settle or otherwise secure the abatement of such Symproic Infringement), BDSI shall promptly notify Shionogi in writing of its decision. In the event BDSI does not so elect to bring a suit or other action against any person or entity allegedly engaged in Symproic Infringement in the Field in the Territory (or settle or otherwise secure the abatement of such Symproic Infringement), Shionogi shall have the right, at Shionogi's expense, subject to BDSI's prior written approval, such approval not to be unreasonably withheld, if and as elected by Shionogi in writing to BDSI within [***] of the later of (A) BDSI's notice that it will not make an election above or (B) the end of the above-referenced [***] period, to commence a suit or take action to enforce the applicable BDSI Patents or BDSI Marks with respect to such Symproic Infringement in the Field in the Territory, and BDSI shall have the right to join such action at its own expense. Each Party shall provide to the Party enforcing any such rights under this Section 10.3(b)(ii) reasonable assistance in such enforcement, at such enforcing Party's request and at no cost to the enforcing Party (except as otherwise

provided above), including joining such action as a party plaintiff if required by applicable law to pursue such action, making its personnel available, providing any necessary Information, and executing documents. The enforcing Party shall keep the other Party regularly informed of the status and progress of such enforcement efforts and related filings, and shall reasonably consider the other Parties' comments on any such efforts and related filings.

(c) Hatch-Waxman Act Litigation. Notwithstanding anything herein to the contrary, should a Party receive a certification pursuant to the Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98-417), as amended (the "**Hatch-Waxman Act**"), including any notice under 21 U.S.C. §355(b)(2)(A)(iv) or 355(j)(2)(A)(vii)(IV) or a similar notice (the "**Certification**") relating to any Orange Book Patent in the Field in the Territory, then such Party shall immediately (and in any event no later than within [***] after such receipt) provide the other Party with a copy of such Certification. Shionogi shall have [***] from the date on which it receives a Certification to provide written notice to BDSI ("**H-W Suit Notice**") stating whether it will bring suit within a [***] period from the date of such Certification, including any patent infringement suit (or other applicable time limit for bringing such suit) and, if Shionogi or any Affiliate thereof does bring such suit within such period, BDSI shall have the right to join such action using its own counsel and at its own expense. Should such [***] expire without Shionogi providing such H-W Suit Notice, then BDSI shall be free to bring suit at BDSI's expense. Each Party shall reasonably assist the other Party in such enforcement, including joining such action as a party plaintiff if required by applicable law to pursue such action, making its personnel available, providing any necessary Information, and executing documents.

(d) Enforcement Rights Outside the Territory. Subject to the remainder of this Section 10.3(d), Shionogi shall have the sole and exclusive right, but not the obligation, with respect to the Shionogi Patents and Symproic Marks to bring a suit or other action against any person or entity allegedly engaged in infringement of the Shionogi Patents or Symproic Marks outside the Territory, outside the Field, or with respect to any product other than Symproic. Subject to Section 10.3(a) and the remainder of this Section 10.3(d), BDSI shall have the sole and exclusive right, but not the obligation, with respect to the BDSI Patents and BDSI Marks to bring a suit or other action against any person or entity allegedly engaged in infringement of the BDSI Patents outside the Territory or outside the Field. Each Party shall provide to the Party enforcing any such rights under this Section 10.3(d) reasonable assistance in such enforcement, at such enforcing Party's request and at no cost to the enforcing Party, including joining such action as a party plaintiff if required by applicable law to pursue such action, making its personnel available, providing any necessary Information, and executing documents. The enforcing Party shall keep the other Party regularly informed of the status and progress of such enforcement efforts, and shall reasonably consider the other Party's comments on any such efforts.

(e) Settlement. Subject to the remainder of this Section 10.3(e), the Party enforcing any claim, suit or action that it brought under this Section 10.3 with respect to any BDSI Patents, Shionogi Patents, or Symproic Marks in the Field in the Territory shall be entitled to settle, voluntarily dispose of or otherwise resolve any such matter without the prior written consent of the other Party, notwithstanding that the other Party may have joined the action with its own counsel at its own expense. Notwithstanding the foregoing, (i) no Party shall take any action in the course of exercising its rights under this Section 10.3 (including entering into any settlement, voluntary

disposition or other resolution of any claim, suit or action) that admits fault or wrongdoing, or incurs liability, on the part of any other Party without the prior written consent of such other Party, which such other Party may withhold in its sole discretion; and (ii) BDSI shall not take any action in the course of exercising its rights under this Section 10.3 (including entering into any settlement, voluntary disposition or other resolution of any claim, suit or action) that (A) materially limits the scope, validity, or enforceability of any Shionogi Patents or (B) could reasonably be expected to materially adversely affect the ability of BDSI, Shionogi, any Affiliate of any of the foregoing, or any licensee or sublicensee of any of the foregoing to develop, manufacture, or commercialize Symproic, Naldemedine (or any analog or derivative thereof), or any product (other than Symproic) to the extent incorporating Naldemedine (or any analog or derivative thereof) without, in either case, Shionogi's prior written consent.

(f) Expenses and Recoveries. Except as otherwise explicitly set forth in Sections 10.3(b), 10.3(c) and 10.3(d), the Party bringing a claim, suit or action under Section 10.3(b), 10.3(c) or 10.3(d) shall be solely responsible for any expenses incurred by such Party as a result of such claim, suit or action. If such enforcing Party recovers monetary damages from such Third Party in such suit or action or in settlement of any Symproic Infringement pursuant to Section 10.3(e), (i) such recovery shall be allocated first to the reimbursement of all expenses incurred by the other Party in such litigation (including, for this purpose, reasonable, documented expenses of counsel and, in the case of BDSI, any amounts reimbursed to Shionogi pursuant to Section 10.3(b)(i) or 10.3(c)), second to the reimbursement of all expenses incurred by such enforcing Party in such litigation (including, for this purpose, reasonable, documented expenses of counsel), (ii) any remaining amount with respect to any Symproic Infringement in the Field in the Territory shall be allocated [***] to BDSI (which amounts should be treated as Net Sales under this Agreement), and (iii) any remaining amount with respect to any other alleged or actual infringement of any Shionogi Patents, Symproic Marks, or Shionogi Corporate Marks outside the Field or outside the Territory shall be allocated [***] to Shionogi.

10.4 Defense of Infringement Actions. During the term of this Agreement, each Party shall notify the other Parties of all information regarding potential infringement of Third Party intellectual property rights in connection with the development, manufacture, production, use, importation, offer for sale, sale or other Development or Commercialization of Symproic in the Field in the Territory. The Parties shall, in good faith, diligently discuss such information and decide how to handle such matter. Except as set forth below and subject to Article 12, Shionogi shall have the first right to defend, and to control the settlement or voluntary disposition of, any action, suit, or other proceeding brought against any Party alleging that the development, manufacture, production, use, importation, offer for sale, sale or other Development or Commercialization of Symproic in the Field in the Territory infringes any Third Party intellectual property rights. In the event Shionogi does not so elect within [***] of it becoming aware of such action, suit or proceeding, it shall so notify BDSI in writing, and BDSI shall have the right to defend such suit, action or proceeding at BDSI's expense, provided that (a) BDSI shall reasonably consult with Shionogi with respect to the conduct of such defense and (b) BDSI shall not (and shall ensure that its Affiliates and BDSI Licensees do not), in the course of conducting such defense or settling any litigation or dispute related thereto, take any actions, make any statements, or enter into any settlement or voluntary disposition of such matter that would (A) would reasonably be anticipated to adversely affect any Shionogi Patent (or the validity or enforceability thereof), either Party's ability to develop, manufacture, or commercialize Symproic, or Shionogi's, its Affiliates',

or any of its or their licensees' ability to develop, manufacture, or commercialize Naldemedine (or any analog or derivative thereof) or any other product to the extent incorporating Naldemedine (or any analog or derivative thereof), (B) admit any liability, fault, or wrongdoing by Shionogi or any Affiliate thereof or (C) impose any liability or obligation to pay money damages on Shionogi or any Affiliate thereof.

10.5 Patent Marking. BDSI shall, and shall require its Affiliates and BDSI Licensees, to mark Symproic sold by it, its Affiliates, and BDSI Licensees hereunder (in a reasonable manner consistent with industry custom and practice) with appropriate patent numbers or indicia to the extent permitted or required by applicable law and regulations, in those jurisdictions in which such markings or such notices impact recoveries of damages or equitable remedies available with respect to infringements of patents.

10.6 Personnel Obligations. Prior to beginning work relating to Symproic, each employee, agent or independent contractor of BDSI, its Affiliates, and BDSI Licensees shall be bound by nondisclosure and invention assignment obligations which are consistent with the obligations of BDSI in this Article 10, including: (a) promptly reporting any invention, discovery, process or other intellectual property right; (b) assigning to BDSI or its Affiliate, as appropriate, all of his or her right, title and interest in and to any invention, discovery, process or other intellectual property right; (c) cooperating in the preparation, filing, prosecution, maintenance, enforcement and defense of any patent and patent application; (d) performing all acts and signing, executing, acknowledging and delivering any and all documents required for effecting the obligations and purposes of this Agreement; and (e) abiding by the obligations of confidentiality and non-use set forth in Article 13. It is understood and agreed that such nondisclosure and invention assignment agreement need not reference or be specific to this Agreement.

10.7 Trademarks. Subject to Sections 2.2 and 14.3 of this Agreement, BDSI shall be responsible for the selection, registration, maintenance and defense of any trademarks, logos, or trade dress used in connection with the Commercialization of Symproic in the Field in the Territory hereunder, other than the Symproic Marks or Shionogi Corporate Marks (the "**BDSI Marks**"), as well as all expenses associated therewith. All uses by BDSI, any Affiliate thereof, or any BDSI Licensee of the BDSI Marks, Symproic Marks, and Shionogi Corporate Marks shall comply with all applicable laws and regulations. BDSI shall not, without Shionogi's prior written consent, use any trademarks or house marks of Shionogi (including Shionogi's corporate name), or marks confusingly similar thereto, in connection with its Commercialization of Symproic under this Agreement, except as set forth in Section 2.2 of this Agreement or may be expressly authorized by Shionogi in writing, and except to the extent required to comply with applicable laws and regulations. Shionogi and its Affiliates, as applicable, shall retain sole ownership of the Symproic Marks, and registrations or applications therefor, and all Shionogi Corporate Marks.

Article 11

Representations, Warranties, and Covenants

11.1 Mutual Representations and Warranties. Each Party hereby represents, warrants, and covenants (as applicable) to the other Party as follows:

(a) Corporate Existence and Power. As of the Effective Date, it is a company or corporation duly organized, validly existing, and in good standing under the laws of the jurisdiction in which it is incorporated or organized, as applicable, and has full corporate power and authority and the legal right to own and operate its property and assets and to carry on its business as it is now being conducted and as contemplated in this Agreement, including the right to grant the licenses granted by it and perform its obligations hereunder.

(b) Authority and Binding Agreement. As of the Effective Date, (i) it has the corporate power and authority and the legal right to enter into this Agreement and the other Definitive Agreements and perform its obligations hereunder and thereunder; (ii) it has taken all necessary corporate action on its part required to authorize the execution and delivery of this Agreement and the other Definitive Agreements and the performance of its obligations hereunder and thereunder; and (iii) this Agreement and the other Definitive Agreements have been duly executed and delivered on behalf of such Party, and each constitutes a legal, valid, and binding obligation of such Party that is enforceable against it in accordance with its terms.

(c) No Conflict. As of the Effective Date, it is not a party to, and it will not enter into during the Term, any agreement that would prevent it from granting the rights granted to the other Party under this Agreement or the other Definitive Agreements or performing its obligations under this Agreement or the other Definitive Agreements. The execution, delivery and performance of this Agreement and the other Definitive Agreements by such Party: (i) is not prohibited or limited by, and will not result in the breach of or a default under, any provision of the charter documents or bylaws of such Party, (ii) does not conflict with, result in a breach of, constitute (with or without due notice or lapse of time or both) a default under, result in the acceleration of obligations under, create in any party the right to terminate, modify or cancel, or require any notice, consent or waiver not otherwise obtained prior to the Effective Date under any material agreement or instrument binding on such Party, and (iii) does not necessitate any consent or other approval from any Third Party.

(d) No Debarment. None of such Party's employees, consultants or contractors:

(i) is debarred under Section 306(a) or 306(b) of the FD&C Act or by the analogous applicable laws, rules, and regulations of any Governmental Authority;

(ii) has, to such Party's knowledge, been charged with, or convicted of, any felony or misdemeanor within the ambit of 42 U.S.C. §§ 1320a-7(a), 1320a-7(b)(l)-(3), or pursuant to any analogous applicable laws, rules, and regulations, or is proposed for exclusion, or is the subject of exclusion or debarment proceedings by a Governmental Authority; or

(iii) is excluded, suspended or debarred from participation, or is otherwise ineligible to participate, in any U.S. or non-U.S. healthcare programs, or is excluded, suspended or debarred by any Governmental Authority from participation, or is otherwise ineligible to participate, in any procurement or non-procurement programs, (the foregoing (i) through (iii), collectively, the "**Debarment Laws**").

11.2 Representations and Warranties by Shionogi. Shionogi hereby represents and warrants to BDSI as of the Effective Date as follows:

(a) Title; Encumbrances. As of the Effective Date, it has sufficient legal and/or beneficial title, ownership or license, free and clear from any mortgages, pledges, liens, security interests, encumbrances, options or third party rights, to (i) the Shionogi Technology, Symproic Marks, and Shionogi Corporate Marks to grant the licenses to BDSI as set forth in and pursuant to this Agreement and (ii) the Symproic Domain Names and the Assigned NDA to comply with its assignment obligations with respect thereto under this Agreement and the other Definitive Agreements.

(b) Validity; Enforceability. As of the Effective Date, none of the issued Shionogi Patents existing as of the Effective Date has been adjudged, in a final and non-appealable decision, invalid, unenforceable or unpatentable in whole or part by any Governmental Authority of competent jurisdiction, and to the actual knowledge of Shionogi, all such issued Shionogi Patents existing as of the Effective Date are valid and enforceable.

(c) Adequacy. The Shionogi Technology constitutes all of the Patents and Information Controlled by Shionogi or any of its Affiliates as of the Effective Date that are necessary for the sale of Symproic (as Symproic exists and is sold as of the Effective Date). The Shionogi Know-How constitutes all Information Controlled by Shionogi or any of its Affiliates as of the Effective Date that is incorporated in the Promotional Materials (as such Promotional Materials are used by Shionogi in the Promotion of Symproic in the Field in the Territory as of the Effective Date).

(d) No Notice of Infringement or Misappropriation. As of the Effective Date, Shionogi has not received any written notice from any Third Party asserting or alleging that any manufacture, sale, offering for sale, import or other Commercialization of Symproic by Shionogi in the Territory prior to or as of the Effective Date infringed or misappropriated the intellectual property rights of such Third Party.

(e) Non-infringement of Third Party Rights. As of the Effective Date, to Shionogi's actual knowledge, the Development, use, Manufacture, or Commercialization of Symproic (as such Symproic exists as of the Effective Date) in the Territory does not infringe any patents or other intellectual property rights owned or controlled by a Third Party or any Affiliate of Shionogi.

(f) No Proceedings. As of the Effective Date, there are no pending, and to Shionogi's actual knowledge, no threatened, actions, suits or proceedings against Shionogi involving the ownership or use of the Shionogi Technology or any product liability or other cause of action relating to Symproic.

(g) Third-Party Activities. As of the Effective Date, to Shionogi's actual knowledge, there are no activities by Third Parties that would constitute infringement or misappropriation of the Shionogi Technology in the Field in the Territory.

11.3 Governmental Approvals. No consents or approvals of or filings or registrations with any Governmental Authority are necessary for the execution and delivery by the Parties or their applicable Affiliates of this Agreement and each of the other Definitive Agreements to which it is

a party, the performance by the Parties and their applicable their applicable Affiliates of their obligations hereunder and thereunder, including under the Hart Scott Rodino Antitrust Improvements Act of 1976 and all rules and regulations promulgated thereunder from time to time, in each case as amended.

11.4 Disclaimer. EXCEPT AS EXPRESSLY STATED IN THIS Article 11, NO REPRESENTATIONS OR WARRANTIES WHATSOEVER, WHETHER EXPRESS OR IMPLIED, INCLUDING WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, NON-INFRINGEMENT, OR NON-MISAPPROPRIATION OF THIRD PARTY INTELLECTUAL PROPERTY RIGHTS, IS MADE OR GIVEN BY OR ON BEHALF OF A PARTY. EXCEPT AS EXPRESSLY STATED IN THIS AGREEMENT, ALL REPRESENTATIONS AND WARRANTIES, WHETHER ARISING BY OPERATION OF LAW OR OTHERWISE, ARE HEREBY EXPRESSLY EXCLUDED.

11.5 Compliance with Laws. Each Party shall comply, and shall ensure that its Affiliates and, with respect to BDSI, all BDSI Licensees, comply with all applicable laws, rules, and regulations in the exercise of their rights and performance of their obligations under this Agreement and the other Definitive Agreements. Without limiting the foregoing, neither Party will use in connection with the Development or Commercialization of Symproic, during the Term, any employee, consultant or contractor who has been or is subject to debarment, exclusion, or suspension under any Debarment Laws.

Article 12

Indemnification; Insurance; Limit of Liability

12.1 Indemnification by Shionogi. Shionogi shall defend, indemnify, and hold BDSI, its Affiliates, and its and their respective officers, directors, employees, and agents (the "**BDSI Indemnitees**") harmless from and against any and all damages, losses, costs and expenses or other amounts payable to a Third Party claimant, as well as any reasonable attorneys' fees and costs of litigation of such BDSI Indemnitees (collectively, "**BDSI Damages**"), all to the extent resulting from claims, suits, proceedings or causes of action brought by such Third Party ("**BDSI Claims**") against such BDSI Indemnitees that arise from or are based on: (a) a breach of any of Shionogi's representations, warranties, covenants or obligations under this Agreement or the other Definitive Agreements, (b) willful misconduct or grossly negligent acts or omissions on the part of Shionogi, its Affiliates, or the officers, directors, employees, or agents of Shionogi or its Affiliates, or (c) any breach by Shionogi of the [***] Service Agreement occurring prior to the Effective Date or liability of Shionogi arising under or in respect of the [***] Service Agreement prior to the Effective Date. The foregoing indemnity obligation shall not apply to the extent Shionogi's ability to perform the preceding obligations is prejudiced by any BDSI Indemnitees' material failure to comply with the indemnification procedures set forth in Section 12.3, or as and to the extent that any BDSI Claim is based on or alleges: (i) a breach of any of BDSI's representations, warranties, covenants or obligations under this Agreement or any Definitive Agreement; or (ii) the willful misconduct, grossly negligent acts or omissions, or failure to comply with applicable laws, rules or regulations on the part of BDSI, its Affiliates, any BDSI Licensees, or their respective officers, directors, employees, or agents; or (iii) infringement or misappropriation of any Third Party's intellectual property rights in the exercise by or on behalf of BDSI, any Affiliate thereof, or any

BDSI Licensee of the rights granted to BDSI under this Agreement (except to the extent such BDSI Claim directly results from a breach by Shionogi of Section 11.2(e)); or (iv) in the case of clause (c) above, any breach by BDSI of the [***] Service Agreement following the Effective Date.

12.2 Indemnification by BDSI. BDSI shall defend, indemnify, and hold Shionogi, its Affiliates, and its and their respective officers, directors, employees, and agents (the "**Shionogi Indemnitees**") harmless from and against any and all damages, losses, costs and expenses or other amounts payable to a Third Party claimant, as well as any reasonable attorneys' fees and costs of litigation incurred by such Shionogi Indemnitees (collectively, "**Shionogi Damages**"), all to the extent resulting from claims, suits, proceedings or causes of action brought by such Third Party (collectively, "**Shionogi Claims**") against such Shionogi Indemnitee that arise from or are based on: (a) the Development, Manufacture, storage, handling, use, sale, offer for sale, importation, or Commercialization of Symproic by or on behalf of BDSI, its Affiliates, BDSI Licensees, or its or their distributors after the Effective Date; (b) infringement or misappropriation of any Third Party's intellectual property rights in the exercise of the rights granted under this Agreement, or Development, Manufacture, use, or Commercialization of Symproic, by or on behalf of BDSI, its Affiliates, or BDSI Licensees after the Effective Date; (c) a breach of any of BDSI's representations, warranties, covenants or obligations under this Agreement or the other Definitive Agreements; (d) any breach of the [***] Service Agreement occurring following the Effective Date or liability arising under or in respect of the [***] Service Agreement after the Effective Date; or (e) willful misconduct or grossly negligent acts or omissions on the part of BDSI, its Affiliates, BDSI Licensees (other than Shionogi and its Affiliates), or the officers, directors, employees, or agents of any of the foregoing. The foregoing indemnity obligation shall not apply to the extent BDSI's ability to perform the preceding obligations is prejudiced by any Shionogi Indemnitees' material failure to comply with the indemnification procedures set forth in Section 12.3, or as and to the extent that any Shionogi Claim is based on or alleges: (i) a breach of Shionogi's representations, warranties, and obligations under this Agreement or any Definitive Agreement, (ii) the willful misconduct, grossly negligent acts or omissions, or failure to comply with applicable laws, rules or regulations on the part of Shionogi, its Affiliates, or its or their officers, directors, employees, or agents, or (iii) in the case of clause (d) above, any breach by Shionogi of the [***] Service Agreement prior to the Effective Date.

12.3 Indemnification Procedures. Each Party's agreement to indemnify, defend, and hold harmless under this Article 12, as applicable, is conditioned upon the indemnified Party (a) providing written notice to the indemnifying Party of any Shionogi Claim or BDSI Claim (each, a "**Claim**") or Shionogi Damages or BDSI Damages, as applicable, arising out of the indemnified matter as soon as reasonably possible, and in any event no later than [***] after the indemnified Party has actual knowledge of such Claim or Shionogi Damages or BDSI Damages, as applicable; *provided* that the failure to give such notice will not relieve the indemnifying Party of its indemnity obligation hereunder except to the extent that such failure materially prejudices the indemnifying Party, and (b) permitting the indemnifying Party to participate (at its expense) in the investigation of, preparation and defense against, and settlement or voluntary disposition of any Claim; it being understood and agreed that the indemnifying Party shall have the right to assume control over (at its expense) the investigation of, preparation and defense against, and settlement or voluntary disposition of any Claim, if the Claim is solely a monetary Claim and the indemnifying Party agrees to cover all Shionogi Damages or BDSI Damages, as applicable, and

provides the indemnified Party with reasonable guaranty with respect to same. No Party shall compromise, settle, or enter into any voluntary disposition of any such Claim without the other Party's prior written consent, which consent shall not be unreasonably withheld, except if such compromise or settlement solely involves payment obligations and such payment obligations are fulfilled in full upon the entering into of the compromise or settlement; provided, however, that, if the Party entitled to indemnification fails to promptly notify the indemnifying Party pursuant to the foregoing clause (a), the indemnifying Party will only be relieved of its indemnification obligation under this Article 12 to the extent materially prejudiced by such failure. In no event may BDSI settle, compromise, or agree to any voluntary disposition of any matter subject to indemnification hereunder in any manner which would reasonably be anticipated to have a material likelihood of adversely affecting (i) any portion of the Shionogi Technology, Symproic Marks, or Shionogi Corporate Marks or (ii) Shionogi's, BDSI's, any of their respective Affiliates', or any of their respective licensees' or sublicensees' ability to manufacture, develop, or commercialize Symproic or, in the case of Shionogi, its Affiliates, and its and their licensees or sublicensees, Naldemedine or any product (other than Symproic) to the extent incorporating Naldemedine (or any analog or derivative thereof) without, in the case of (i) or (ii), Shionogi's prior written consent. In no event may Shionogi settle, compromise, or agree to any voluntary disposition of any matter subject to indemnification hereunder in any manner which would reasonably be anticipated to have a material likelihood of adversely affecting (A) any portion of the BDSI Technology or BDSI Marks or (B) BDSI's, any of its Affiliates', or any of their respective licensees' or sublicensees' ability to manufacture, develop, or commercialize Symproic in Field and in the Territory in accordance with this Agreement without, in the case of (A) or (B), BDSI's prior written consent.

12.4 Insurance.

(a) Shionogi and BDSI shall each procure and maintain insurance, including product liability insurance, with respect to its activities hereunder and under the other Definitive Agreements and which are consistent with normal business practices of prudent companies similarly situated at all times during which Symproic is being commercially distributed or sold. It is understood that such insurance shall not be construed to create a limit of a Party's liability with respect to its indemnification obligations under this Article 12 or otherwise under this Agreement or the other Definitive Agreements. Shionogi and BDSI shall each provide the other with written evidence of such insurance upon request. Shionogi and BDSI shall each provide the other with written notice at least [***] prior to the cancellation or non-renewal in such insurance or self-insurance which materially adversely affects the rights of the other hereunder.

(b) In addition to, and without limitation of the foregoing, and except as otherwise set forth below, BDSI shall maintain insurance, including commercial general liability, product liability and workers compensation and employer's liability, with respect to its activities under this Agreement regarding Symproic in such amount as it customarily maintains with respect to similar activities for its other products, but not less than the greater of (i) [***] each occurrence and aggregate for commercial general liability, (ii) [***] each occurrence and aggregate for product liability, and (iii) [***] each occurrence and aggregate for workers compensation and employer's liability. Such coverage shall be maintained for not less than [***] following expiration or termination of this Agreement or if such coverage is of the "claims made" type, for [***] following expiration or termination of this Agreement. Upon written request, BDSI shall provide Shionogi with written evidence of the required coverage. Coverage may be in the form of primary insurance or a combination of primary and excess insurance.

12.5 Limitation of Liability. NO PARTY SHALL BE LIABLE TO THE OTHER PARTY FOR ANY SPECIAL, INCIDENTAL, PUNITIVE, OR INDIRECT DAMAGES ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT OR ANY TORT CLAIMS ARISING HEREUNDER, REGARDLESS OF ANY NOTICE OF THE POSSIBILITY OF SUCH DAMAGES. NOTWITHSTANDING THE FOREGOING, NOTHING IN THIS SECTION 12.5 IS INTENDED TO OR SHALL LIMIT OR RESTRICT (A) THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF ANY PARTY UNDER THIS ARTICLE 12, (B) DAMAGES AVAILABLE AS A RESULT OF THE FRAUD OR GROSS NEGLIGENCE OF A PARTY, (C) DAMAGES AVAILABLE FOR A PARTY'S BREACH OF ARTICLE 13, OR (D) DAMAGES AVAILABLE FOR A PARTY'S BREACH OF SECTION 2.7.

12.6 Direct Damages. This Article 12 shall in no way limit the Parties ability to seek remedies for direct damages suffered not resulting from claims, suits, proceedings or causes of action brought by a Third Party.

12.7 Set-Off. Notwithstanding anything to the contrary, and without limiting either Party's obligations under Section 12.1 and 12.2, should a Party be in material breach of any of its obligations under this Agreement or any other Definitive Agreement, including in default of paying, when due, any amount payable to any other Party under this Agreement or any other Definitive Agreement, such other Party shall have the right to withhold payments to be made to the breaching Party hereunder or thereunder until such breach is remedied.

Article 13

Confidentiality

13.1 Confidentiality. Except to the extent expressly authorized by this Agreement or otherwise agreed in writing by the Parties, each Party agrees that, for the Term and for [***] thereafter, it shall keep confidential and shall not publish or otherwise disclose and shall not use for any purpose other than as provided for in this Agreement and the other Definitive Agreements (which includes the exercise of any rights or the performance of any obligations hereunder and thereunder) any Confidential Information furnished to it by any other Party pursuant to this Agreement except for that portion of such information or materials that the receiving Party can demonstrate by competent written proof:

(a) was already known to the receiving Party or its Affiliate, other than under an obligation of confidentiality, at the time of disclosure by such other Party;

(b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the receiving Party;

(c) became generally available to the public or otherwise part of the public domain after its disclosure and other than through any act or omission of the receiving Party in breach of this Agreement;

(d) is subsequently disclosed to the receiving Party or its Affiliate by a Third Party without obligations of confidentiality with respect thereto; or

(e) is subsequently independently discovered or developed by the receiving Party or its Affiliate without the aid, application, or use of the disclosing Party's Confidential Information.

Notwithstanding the definition of "Confidential Information" in Section 1.34, all Information generated under this Agreement, whether generated by one or both of the Parties, shall be deemed the Confidential Information of all Parties. In addition, the exceptions set forth in subsections (a) and (e) shall not apply to Information generated during or resulting from activities under this Agreement or the other Definitive Agreements, which Information shall be deemed Confidential Information regardless of whether such Information satisfies the criteria set forth in one or both subsections. For clarity, any Information generated by a Party under this Agreement may be used by such Party for any purpose that does not violate applicable law, but the disclosure of such Information shall be governed by this Section 13.1.

13.2 Authorized Disclosure. Each Party may disclose Confidential Information belonging to another Party to the extent such disclosure is reasonably necessary in the following situations:

(a) filing or prosecuting patent applications in accordance with Section 10.2;

(b) regulatory filings and other filings with Governmental Authorities (including Regulatory Authorities), including filings with the SEC or FDA, with respect to Symproic;

(c) prosecuting or defending litigation, provided that, to the extent reasonably possible, a suitable protective order is in place, documents are filed under seal, or other reasonable measures are taken to maintain the confidentiality of such Confidential Information;

(d) complying with applicable laws and regulations, including regulations promulgated by securities exchanges;

(e) disclosure to its Affiliates, its and their employees, agents, and independent contractors, BDSI Licensees (in the case of BDSI), and Shionogi Licensees (in the case of Shionogi) on a need-to-know basis and solely in connection with the performance of this Agreement or the other Definitive Agreements or exercise of rights under this Agreement or the other Definitive Agreements, provided that each disclosee must be bound by obligations of confidentiality and non-use materially as protective as those set forth in this Section 13.2 prior to any such disclosure; and

(f) disclosure on a need-to-know basis to any bona fide potential or actual investor, investment banker, acquirer, acquisition target, merger partner, licensee, licensor, or other potential or actual financial or strategic partner; provided that in connection with such disclosure, the disclosing Party shall use reasonable efforts to inform each disclosee of the confidential nature of such Confidential Information and cause each disclosee to treat such Confidential Information as confidential.

Notwithstanding the foregoing, in the event a Party is required to make a disclosure of the other Party's Confidential Information pursuant to Section 13.2(a), 13.2(b), 13.2(c) or 13.2(d), it will use reasonable efforts to secure confidential treatment of such information. In any event, the Parties agree to take all reasonable action to avoid disclosure of the other Party's Confidential Information hereunder.

13.3 Publicity; Terms of Agreement.

(a) The Parties agree that the material terms of this Agreement are the Confidential Information of all Parties, subject to the authorized disclosure provisions set forth in Section 13.2 and this Section 13.3. The Parties (and/or their Affiliates, as applicable) have agreed to each make a public announcement of the execution of this Agreement substantially in the forms of the press release attached as EXHIBIT J-1 and EXHIBIT J-2 within [***] of the Effective Date, but in no event later than as may be required by applicable law, rule or regulation.

(b) After release of such press release, if any Party desires to make a public announcement concerning the material terms of this Agreement, such Party shall give reasonable prior advance notice of the proposed text of such announcement to the other Parties for their prior review and approval (except as otherwise provided herein), such approval not to be unreasonably withheld, except that in the case of a press release or governmental filing required by law or the rules of any securities exchange to which a Party is subject, the disclosing Party shall provide the other Parties with such advance notice as it reasonably can and shall not be required to obtain approval therefor but shall reasonably consider and incorporate the other Parties' comments to the extent reasonably practicable. A Party commenting on such a proposed press release shall provide its comments, if any, within [***] after receiving the press release for review. No Party shall be required to seek the permission of any other Party to repeat any information regarding the terms of this Agreement that have already been publicly disclosed by such Party, or by any other Party, in accordance with this Section 13.3.

(c) If a Party or one of its Affiliates, as applicable, is obligated to file a copy of this Agreement with any Governmental Authority(ies) (e.g., the SEC), such Party or its Affiliate, as applicable, shall be entitled to make such a required filing, provided that it requests confidential treatment of at least the commercial terms and sensitive technical terms of this Agreement to the extent such confidential treatment is reasonably available to such Party or its Affiliate. In the event of any such filing, each Party will provide the other Party with a copy of the Agreement marked to show provisions for which such Party or its Affiliate intends to seek confidential treatment and shall reasonably consider and incorporate the other Party's reasonable, good faith comments thereon to the extent consistent with the legal requirements governing redaction of information from material agreements that must be publicly filed.

Article 14

Term and Termination

14.1 Term. This Agreement shall become effective on the Effective Date and, unless earlier terminated pursuant to this Article 14, shall remain in effect until the later of (a) the expiration of the Branded Royalty Term and (b) the expiration of the AG Royalty Term (the period from the Effective Date until the later of clause (a) or (b), the "**Term**"). Upon expiration of the Term, all licenses granted under Article 2 shall survive such expiration and become fully-paid, royalty-free, perpetual, and irrevocable.

14.2 Termination for Breach. Each Party shall have the right to terminate this Agreement upon written notice to the other Party if such other Party (or any of its Affiliates) materially breaches its obligations under this Agreement and, after receiving written notice from the non-breaching Party identifying such material breach in reasonable detail, fails to cure such material breach within [***] from the date of such notice (or within [***] from the date of such notice in the event such material breach is solely based upon failure to pay any amounts due (and not subject to a bona fide dispute memorialized in writing) hereunder).

14.3 Effects of Termination of the Agreement by Shionogi. Upon termination of this Agreement by Shionogi pursuant to Section 14.2, the following shall apply (in addition to any other rights and obligations under this Agreement with respect to such termination):

(a) Licenses. The licenses granted to BDSI in Article 2 (and any sublicenses granted thereunder to Affiliates or Third Parties) shall terminate.

(b) Remaining Inventories. Shionogi shall have the right, but not the obligation, to purchase from BDSI any or all of the inventory of Symproic held by BDSI or any Affiliate thereof as of the date of termination (that are not committed to be supplied to any Third Party or BDSI Licensee, in the ordinary course of business, as of the date of termination) at a price [***] of such cost, provided, however, in the case of Symproic acquired by BDSI from Shionogi under the Supply Agreement, Shionogi's price to acquire such Symproic hereunder shall be the purchase price paid therefor by BDSI thereunder (with no markup of [***]). All reasonable, documented, direct costs incurred in transporting and transferring such inventory shall be at Shionogi's sole expense. BDSI shall provide Shionogi with a detailed report describing all such inventory within [***] of termination, and Shionogi shall notify BDSI within [***] after receipt of such notice to what extent, and with respect to which inventory, Shionogi elects to exercise such right.

(c) BDSI Technology. BDSI hereby grants to Shionogi, effective only upon such termination, an exclusive, worldwide, fully-paid, perpetual, irrevocable, royalty-free license, with the right to grant multiple tiers of sublicenses and transferable with this Agreement pursuant to Section 16.5, under the BDSI Technology to research, develop, make, have made, use, import, export, offer for sale, sell, and commercialize Symproic and Naldemedine in the Field and in the Territory.

(d) BDSI Marks. BDSI shall, if and as requested by Shionogi within [***] of termination, transfer and assign, and hereby assigns, to Shionogi all right, title and interest in and to the BDSI Marks (excluding any such BDSI Marks that include, in whole or part, any corporate name or logo of BDSI or its Affiliate or BDSI Licensee).

(e) Symproic Domain Names. BDSI shall, if and as requested by Shionogi within [***] of termination, transfer and assign, and hereby assigns, free and clear of all liens, claims, and encumbrances, to Shionogi all right, title and interest in and to the Symproic Domain Names.

(f) Regulatory Materials and Assigned Symproic Data. BDSI shall, if and as requested by Shionogi within [***] of termination, promptly (but in no event later than [***] following such

request) transfer and assign, and hereby assigns, free and clear of all liens, claims, and encumbrances, to Shionogi all right, title, and interest in Regulatory Materials and Regulatory Approvals for Symproic in the Territory that are owned or controlled by BDSI, its Affiliates or BDSI Licensees, including but not limited to the Assigned NDA and Regulatory Materials with respect thereto.

(g) Transition Assistance. BDSI shall, if and as requested by Shionogi within [***] of termination, at no cost to Shionogi, provide reasonable consultation and assistance for the purpose of promptly transferring or transitioning to Shionogi all BDSI Know-How not already in Shionogi's possession and, at Shionogi's request, all then-existing commercial arrangements relating specifically to Symproic in the Field in the Territory that BDSI is able, using reasonable commercial efforts, to assign, transfer or transition to Shionogi or Affiliate thereof designated by Shionogi to the extent reasonably necessary or useful for Shionogi or any Affiliate thereof to continue any Development in progress at such time of termination, manufacture, or Commercialize Symproic in the Territory. The foregoing shall include, but not be limited to, BDSI using Diligent Efforts to assign or transfer, upon request of Shionogi, any agreements with Third Party suppliers, contractors, or vendors that relate to such development, manufacture, or Commercialization of Symproic in the Territory. If any such contract between BDSI or an Affiliate thereof and a Third Party is not assignable or transferable to Shionogi or an Affiliate of Shionogi (whether by such contract's terms or because such contract does not relate specifically or solely to Symproic) but is otherwise reasonably necessary or useful for Shionogi or any Affiliate thereof to continue any Development in progress at such time of termination, manufacture, or Commercialize Symproic in the Territory, then BDSI shall reasonably cooperate with Shionogi to negotiate for the continuation of such services and/or supply from the applicable entity.

14.4 Other Remedies. Termination or expiration of this Agreement for any reason shall not release either Party from any liability or obligation that already has accrued prior to such expiration or termination, nor affect the survival of any provision hereof to the extent it is expressly stated to survive such termination. Termination or expiration of this Agreement for any reason shall not constitute a waiver or release of, or otherwise be deemed to prejudice or adversely affect, any rights, remedies or claims, whether for damages or otherwise, that a Party may have hereunder or that may arise out of or in connection with such termination or expiration.

14.5 Rights in Bankruptcy. All rights and licenses granted under or pursuant to this Agreement by Shionogi and BDSI are, and shall otherwise be deemed to be, for purposes of Section 365(n) of the U.S. Bankruptcy Code, licenses of right to "intellectual property" as defined under Section 101 of the U.S. Bankruptcy Code. The Parties agree that each Party, as licensee of certain rights under this Agreement, shall retain and may fully exercise all of its rights and elections under the U.S. Bankruptcy Code. The Parties further agree that, in the event of the commencement a bankruptcy proceeding by or against a Party (such Party, the "**Bankrupt Party**") under the U.S. Bankruptcy Code, the other Party shall be entitled to a complete duplicate of (or complete access to, as appropriate) any intellectual property licensed to such other Party and all embodiments of such intellectual property, which, if not already in such other Party's possession, shall be promptly delivered to it (a) upon any such commencement of a bankruptcy proceeding upon such other Party's written request therefor, unless the Bankrupt Party elects to continue to perform all of its obligations under this Agreement or (b) if not delivered under clause (a), following the rejection of this Agreement by the Bankrupt Party upon written request therefor by the other Party.

14.6 Survival. Termination or expiration of this Agreement shall not affect rights or obligations of the Parties under this Agreement that have accrued prior to the date of termination or expiration of this Agreement or that are explicitly indicated by their terms to survive termination or expiration. Notwithstanding anything to the contrary, the following provisions shall survive and apply after expiration or termination of this Agreement: Section 1, Section 2.5(b), Section 2.8, Section 3.4, Section 3.5, Section 3.6, Section 3.7, Section 3.8, Section 5.1(c), Section 5.2, Section 5.3, Section 6.2(b) (with respect to the second sentence thereof), Section 10.1, Section 11.4, Article 12, Article 13, Section 14.3, Section 14.4, Section 14.5, this Section 14.6, Article 15 and Article 16, and the following provisions shall survive expiration, but not termination, of this Agreement: Sections 2.1, 2.2, 2.3, 2.4, 2.6, 5.1(b), 6.1, 6.2(a), 6.3, 10.3 (with respect to infringements occurring prior to expiration), 10.4, 10.5 and 10.7. All provisions not surviving in accordance with the foregoing shall terminate upon expiration or termination of this Agreement and be of no further force and effect.

Article 15

Governing Law and Venue

15.1 Governing Law. Resolution of all disputes arising out of or related to this Agreement or the validity, construction, interpretation, enforcement, breach, performance, application or termination of this Agreement and any remedies relating thereto, shall be governed by and construed under the substantive laws of the State of New York, excluding any conflicts or choice of law rule or principle that might otherwise refer construction or interpretation of this Agreement to the substantive law of another jurisdiction.

15.2 Venue. Each Party (a) irrevocably submits to the exclusive jurisdiction of the state and federal courts sitting in New York County, New York, with respect to actions or proceedings arising in whole or in part out of, related to, based upon or in connection with this Agreement or the subject matter hereof; (b) agrees that all claims in respect of such actions or proceedings may be heard and determined only in any such court; and (c) agrees not to bring any action or proceeding arising out of or relating to this Agreement in any other court. Each Party waives any defense of inconvenient forum to the maintenance of any action or proceeding so brought and waives any bond, surety or other security that might be required of the other Party with respect thereto.

Article 16

Miscellaneous

16.1 Entire Agreement; Amendment. This Agreement and the other Definitive Agreements, along with all exhibits, appendices, or schedules to any of the foregoing and all other agreements between the Parties and/or their Affiliates executed in conjunction therewith as referenced therein, set forth the complete, final and exclusive agreement and all the covenants, promises, agreements, warranties, representations, conditions and understandings between the Parties hereto with respect to the subject matter hereof and supersedes, as of the Effective Date, all prior agreements and

understandings between the Parties with respect to the subject matter hereof. There are no covenants, promises, agreements, warranties, representations, conditions or understandings, either oral or written, between the Parties other than as are set forth herein and therein. No subsequent alteration, amendment, change or addition to this Agreement shall be binding upon the Parties unless reduced to writing and signed by an authorized officer of each Party.

16.2 Force Majeure. Each Party shall be excused from the performance of their obligations under this Agreement to the extent that such performance is prevented or delayed by force majeure (as defined below) and the nonperforming Party promptly provides notice thereof to the other Party. Such excuse shall be continued so long as the condition constituting force majeure continues and the nonperforming Party takes reasonable efforts to remove the condition. For purposes of this Agreement, force majeure shall mean any event or condition beyond the reasonable control of a Party, including, but not limited to, an act of God, war, civil commotion, terrorist act, labor strike or lock-out, epidemic, failure or default of public utilities or common carriers, destruction of production facilities or materials by fire, earthquake, storm or like catastrophe, and failure of plant or machinery (provided that such failure could not have been prevented by the exercise of skill, diligence, and prudence that would be reasonably and ordinarily expected from a skilled and experienced person engaged in the same type of undertaking under the same or similar circumstances). For clarity, force majeure shall not include a failure to commit sufficient resources, financial or otherwise, to the performance of obligations under this Agreement or general market or economic conditions not accompanied by circumstances described in the immediately preceding sentence. Notwithstanding the foregoing, a Party shall not be excused from making payments owed hereunder because of a force majeure affecting such Party.

16.3 Notices. Any notice required or permitted to be given under this Agreement shall be in writing, shall specifically refer to this Agreement, and shall be addressed to the appropriate Party at the address specified below or such other address as may be specified by such Party in writing in accordance with this Section 16.3, and shall be deemed to have been given for all purposes (a) when received, if hand-delivered or sent by a reputable international expedited delivery service, or (b) [***] after mailing, if mailed by first class certified or registered mail, postage prepaid, return receipt requested.

If to Shionogi:

Shionogi Inc.
300 Campus Drive
Florham Park, NJ 07932
Attn: General Counsel

With a copy (which shall not serve as notice) to:

Wyrick Robbins Yates & Ponton LLP
4101 Lake Boone Trail, Suite 300
Raleigh, NC 27607
Attn: Donald R. Reynolds

If to BDSI:

BioDelivery Sciences International, Inc.
4131 ParkLake Avenue, Suite 225
Raleigh, NC 27612
Attn: Jim Vollins

With a copy (which shall not serve as notice) to:

Goodwin Procter LLP
100 Northern Avenue
Boston, MA 02210
Attn: Robert Crawford
Email: rcrawford@goodwinlaw.com

16.4 No Strict Construction; Headings. This Agreement has been prepared jointly and shall not be strictly construed against either Party. Ambiguities, if any, in this Agreement shall not be construed against any Party, irrespective of which Party may be deemed to have authored the ambiguous provision. The headings of each Article and Section in this Agreement have been inserted for convenience of reference only and are not intended to limit or expand on the meaning of the language contained in the particular Article or Section.

16.5 Assignment. Neither Party may assign its rights or delegate its obligations under this Agreement, in whole or in part, without the prior written consent of the other Party (which consent shall not be unreasonably withheld, conditioned or delayed). Notwithstanding the foregoing, each Party shall be permitted to assign, without the consent of the other Party, all (but not a portion) of its rights and obligations under this Agreement to a successor of all or substantially all of the assets or business of such Party to which this Agreement relates (i.e., Symproic), whether by way of merger, sale of stock, sale of assets or other transaction (or series of transactions); provided, however, that except in the case of a Change of Control of a Party, at least [***] prior to the effective date of any such assignment, the Party proposing such assignment shall provide to the other Party, on a confidential basis, with written notice of its intent to make such assignment, including (i) the identity of the proposed assignee, (ii) if BDSI is the proposed assignor, a description of the proposed assignee's commercial capabilities sufficient to establish such proposed assignee's ability to comply with the obligation to use Diligent Efforts to Commercialize Symproic in the Field in the Territory during the AG Royalty Term and the Branded Royalty Term, and (iii) the rationale for the proposed assignment. The Party proposing such assignment shall consider diligently, reasonably and in good faith all input received from the other Party within such [***] period (which for the avoidance of doubt, shall not begin until the Party proposing assignment has provided to the other Party all information required by the immediately preceding sentence) with respect to such proposed assignment. For the avoidance of doubt, subject to the preceding and foregoing, BDSI shall have final say on, and Shionogi shall not attempt to interfere with, any assignment of its rights and obligations and the terms thereunder. Any permitted successor or assignee of rights or obligations hereunder shall, in writing to the other Party, expressly assume performance of such rights or obligations, including but not limited to, with respect to an assignment by BDSI, those relating to Diligent Efforts and Sections 2.7(a) and 2.7(c). Notwithstanding the foregoing, in the event of an assignment hereof to an Affiliate of a

Party, such Party shall remain responsible for any failure to perform on the part of such Affiliate. Any assignment or attempted assignment by a Party in violation of the terms of this Section 16.5 shall be null, void and of no legal effect.

16.6 Performance by Affiliates. Subject to the limitations of Section 2.3, each Party may discharge any obligations and/or exercise any right hereunder through any of its Affiliates and in such case, each Party hereby guarantees the performance by its Affiliates of such Party's corresponding obligations under this Agreement, and shall cause its Affiliates to comply with the provisions of this Agreement in connection with such performance. Any breach by a Party's Affiliate of any such obligations under this Agreement shall be deemed a breach by such Party, and the other Party may proceed directly against such Party without any obligation to first proceed against such Party's Affiliate.

16.7 Further Actions. Each Party agrees to execute, acknowledge and deliver such further instruments, and to do all such other reasonable acts, as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement.

16.8 Severability. If any one or more of the provisions of this Agreement is held to be invalid or unenforceable by an arbitrator or by any court of competent jurisdiction from which no appeal can be or is taken, 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.

16.9 No Waiver. Any delay in enforcing a Party's rights under this Agreement or any waiver as to a particular default or other matter shall not constitute a waiver of such Party's rights to the future enforcement of its rights under this Agreement, except with respect to an express written and signed waiver relating to a particular matter for a particular period of time.

16.10 Independent Contractors. Each Party shall act solely as an independent contractor, and nothing in this Agreement shall be construed to give either Party the power or authority to act for, bind, or commit any other Party in any way. Nothing herein shall be construed to create the relationship of partners, principal and agent, or joint-venture partners between the Parties.

16.11 Counterparts. This Agreement may be executed in one or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Scanned, pdf and facsimile signatures will be as binding as original signatures.

[Signature Page Follows]

IN WITNESS WHEREOF, the Parties have executed this Exclusive License Agreement in duplicate originals by their duly authorized officers as of the Effective Date.

SHIONOGI INC.		**BIODELIVERY SCIENCES INTERNATIONAL, INC.**	
BY:	_____	BY:	_____
NAME:	_____	NAME:	_____
TITLE:	_____	TITLE:	_____

[Signature Page to Exclusive License Agreement]

EXHIBIT A

FORMS OF ASSIGNED NDA LETTERS

[***]

Exhibit A

EXHIBIT B

CURRENT PHASE 4 STUDIES

The post-approval, observational study required by FDA as a condition to approval of the Assigned NDA comparing major adverse cardiovascular events (MACE) between patients with chronic non-cancer pain taking Symproic and those receiving other treatments for indications in the Field.

EXHIBIT C

NALDEMEDINE STRUCTURE

[***]

Exhibit C

EXHIBIT D

[***]

Exhibit D

EXHIBIT E

SHIONOGI PATENTS

US RE46,365

US RE46,375

US 9,108,975

[***]

EXHIBIT F

SYMPROIC DOMAIN NAMES

[***]

EXHIBIT G

SYMPROIC MARKS

Trademark	Country	Status	Serial No.	Registration No.
SYMPROIC	United States	Registered	79168243	4887392
	United States	Registered	87003968	5169678

TABLET AND TRADE DRESS

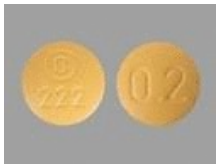

EXHIBIT H

TRANSFERRED SAMPLE INVENTORY

[***]

Exhibit H

EXHIBIT I

FORM OF DOMAIN NAME ASSIGNMENT

[***]

Exhibit I

EXHIBIT J-1

BDSI PRESS RELEASE

[*To be inserted once agreed upon*.]

EXHIBIT J-2

SHIONOGI PRESS RELEASE

[*To be inserted once agreed upon*.]

Exhibit 10.2

AMENDMENT 3 TO TERM LOAN AGREEMENT

THIS AMENDMENT 3 TO TERM LOAN AGREEMENT, dated as of April 4, 2019 (this "***Amendment***") is made among BioDelivery Sciences International, Inc. ("***Borrower***"), the Subsidiary Guarantors, CRG Servicing LLC, as administrative agent and collateral agent (in such capacity, "***Administrative Agent***") and the lenders listed on the signature pages hereof under the heading "LENDERS" (each, a "***Lender***" and, collectively, the "***Lenders***"), with respect to the Loan Agreement referred to below.

RECITALS

WHEREAS, Borrower, the Subsidiary Guarantors, Administrative Agent and the Lenders are parties to the Term Loan Agreement, dated as of February 21, 2017, with the Subsidiary Guarantors from time to time party thereto, as amended by (x) Amendment 1 to Term Loan Agreement, dated as of December 15, 2017 and (y) Amendment 2 to the Term Loan Agreement, dated as of May 16, 2018 (as the same has been amended, restated, supplemented or otherwise modified from time to time, collectively, the "***Loan Agreement***");

WHEREAS, substantially concurrently with the execution of this Amendment, Borrower has entered into that certain Shionogi Exclusive License Agreement (as defined below), which is attached as Exhibit A hereto; and

WHEREAS, the parties hereto desire to amend the Loan Agreement on the terms and subject to the conditions set forth herein.

NOW, THEREFORE, in consideration of the mutual agreements, provisions and covenants contained herein, the parties agree as follows:

SECTION 1. Definitions; Interpretation.

(a) **Terms Defined in Loan Agreement.** All capitalized terms used in this Amendment (including in the recitals hereof) and not otherwise defined herein shall have the meanings assigned to them in the Loan Agreement.

(b) **Interpretation.** The rules of interpretation set forth in **Section 1.03** of the Loan Agreement shall be applicable to this Amendment and are incorporated herein by this reference.

SECTION 2. Amendments to Loan Agreement. Subject to **Section 4** of this Amendment, the Loan Agreement is hereby amended as follows:

2.1 **Section 1.01** of the Loan Agreement is hereby amended by adding thereto in proper alphabetical order the following defined terms:

"***acceleration***" and "***Acceleration***" have the meanings set forth in

Section 11.02.

"***Acceleration Premium***" has the meaning set forth in **Section 11.02(c)**.

"***Amendment No. 3 Date***" means April 4, 2019.

"***Amendment No. 3 to Term Loan Agreement***" means that certain Amendment No. 3 to Term Loan Agreement dated as of the Amendment No. 3 Date by and among Borrower, the Subsidiary Guarantors, Administrative Agent and the Lenders party thereto.

"***Back-End Facility Fee***" has the meaning set forth in the Fee Letter.

"***Shionogi Exclusive License Agreement***" means that certain Exclusive License Agreement, entered into as of April 4, 2019, by and among Borrower, Shionogi Inc., a Delaware corporation and the other parties thereto, in the form attached as Exhibit A to Amendment No. 3 to Term Loan Agreement, which Shionogi Exclusive License Agreement may be amended, restated, supplemented, modified, renewed or replaced from time to time in compliance with **Section 9.12**. For the avoidance of doubt, the Shionogi Exclusive License Agreement shall be a Material Agreement for purposes of the Loan Documents.

"***Shionogi Transactions***" means the entry into the Shionogi Exclusive License Agreement and the Acquisition of certain rights and assets relating to Symproic pursuant to the Shionogi Exclusive License Agreement.

2.2 The following **Section 1.05** is hereby added to the Loan Agreement immediately following **Section 1.04** of the Loan Agreement:

1.05 Divisions. For all purposes under the Loan Documents, in connection with any division or plan of division under Delaware law (or any comparable event under a different jurisdiction's laws): (a) if any asset, right, obligation or liability of any Person becomes the asset, right, obligation or liability of a different Person, then it shall be deemed to have been transferred from the original Person to the subsequent Person, and (b) if any new Person comes into existence, such new Person shall be deemed to have been organized on the first date of its existence by the holders of its Equity Interests at such time.

2.3 The following **Section 3.02(e)** is hereby added to the Loan Agreement immediately following **Section 3.02(d)** of the Loan Agreement:

(e) Redemption Price. For the avoidance of doubt, in the event any Loans shall become due and payable for any reason, interest pursuant to **Sections 3.02(a)** and **(b)** shall accrue on the Redemption Price for such Loans from and after the date such Redemption Price is due and payable until paid in full.

2.4 **Section 7.05(b)(ii)(J)** of the Loan Agreement is hereby amended and restated in its entirety as follows:

(J) there are no pending or, to the Knowledge of any of the Obligors, threatening in writing Claims against the Obligors asserted by any other Person relating to the Material Agreements (other than the Shionogi Exclusive License Agreement), including any Claims of breach or default under such Material Agreements;

2.5 The second sentence of **Section 7.14** of the Loan Agreement is hereby amended and restated in its entirety as follows:

No Obligor is in default under any such Material Agreement (other than the Shionogi Exclusive License Agreement) or agreement creating or evidencing any Material Indebtedness.

2.6 **Section 9.01(c)** of the Loan Agreement is hereby amended and restated in its entirety as follows:

(c) Indebtedness consisting of the upfront payments and royalties payable pursuant to Sections 3.1 and 3.2 of the Shionogi Exclusive License Agreement;

2.7 **Section 9.01(m)** of the Loan Agreement is hereby amended by replacing the number "$1,000,000" with the number $2,000,000" therein.

2.8 **Section 9.02(d)** of the Loan Agreement is hereby amended and restated in its entirety as follows:

(d) (i) Liens securing Indebtedness permitted under **Section 9.01(h)**; *provided* that such Liens are restricted solely to the collateral described in **Section 9.01(h)** and (ii) Liens securing Indebtedness permitted under **Section 9.01(m)**; *provided* that such Liens are restricted solely to the collateral described in **Section 9.01(m)**;

2.9 **Section 9.03** of the Loan Agreement is hereby amended as follows:

(a) **Section 9.03(e)** is amended by deleting "and" at the end of such clause;

(b) **Section 9.03(f)** is amended by replacing "." at the end thereof with "; and"; and

(c) the following new **Section 9.03(g)** is added immediately following **Section 9.03(f)**:

(g) the Shionogi Transactions.

2.10 **Section 9.07** of the Loan Agreement is hereby amended and restated in its entirety as follows:

9.07 Payments of Indebtedness. Such Obligor will not, and will not permit any of its Subsidiaries to, make any payments in respect of any Indebtedness other than (i) payments of Obligations, (ii) scheduled payments of other Indebtedness permitted under the terms of any subordination to the Obligations, (iii) repayment of intercompany Indebtedness permitted in reliance upon **Section 9.02(f)** and (iv) payments of Indebtedness permitted in reliance upon **Section 9.01(c)**.

2.11 **Section 11.01(g)(i)** of the Loan Agreement is hereby amended and restated in its entirety as follows:

(i) any material breach of, or "event of default" or similar event by any Obligor under, any Material Agreement (other than the Shionogi Exclusive License Agreement) shall occur and continue unredeemed, uncured or unwaived for more than 30 days after the expiration of any contractual cure period provided thereunder,

2.12 **Section 11.02** of the Loan Agreement is hereby amended and restated in its entirety as follows:

11.02 Remedies.

(a) Upon the occurrence of any Event of Default, then, and in every such event (other than an Event of Default described in **Section 11.01(h)**, **(i)** or **(j)**), and at any time thereafter during the continuance of such event, the Majority Lenders may, by notice to Borrower, take either or both of the following actions, at the same or different times: (i) terminate the Commitments, and thereupon the Commitments shall terminate immediately, and (ii) declare the Loans then outstanding to be due and payable in whole (or in part, in which case any principal not so declared to be due and payable may thereafter be declared to be due and payable) (an "***acceleration***"), and thereupon the principal of the Loans so declared to be due and payable, together with accrued interest thereon and all fees and other Obligations shall become due and payable immediately and the Obligors shall immediately pay all Obligations, including the Back-End Facility Fee and an Acceleration Premium as calculated below, all without presentment, demand, protest or other notice of any kind, all of which are hereby waived by each Obligor.

(b) Upon the occurrence of any Event of Default described in **Section 11.01(h)**, **(i)** or **(j)**, the Commitments shall automatically terminate and the principal of the Loans then outstanding, together with accrued interest thereon and all fees and other Obligations, shall automatically become due and payable immediately (an "***acceleration***" and, together with any acceleration defined in **Section 11.02(a)**, each, an "***Acceleration***") and the Obligors shall immediately pay all Obligations, including the Back-End Facility Fee and an Acceleration Premium as calculated below, all without presentment, demand, protest or other notice of any kind, all of which are hereby waived by each Obligor.

(c) Acceleration Premium Calculation. The applicable "***Acceleration Premium***" shall be an amount calculated as follows:

(i) If the date of Acceleration occurs:

(A) on or prior to the fourth (4th) Payment Date, the Acceleration Premium shall be an amount equal to 8.00% of the aggregate outstanding principal amount of the Loans subject to Acceleration;

(B) after the fourth (4th) Payment Date and on or prior to the eighth (8th) Payment Date, the Acceleration Premium shall be an amount equal to 6.00% of the aggregate outstanding principal amount of the Loans subject to Acceleration;

(C) after the eighth (8th) Payment Date and on or prior to the twelfth (12th) Payment Date, the Acceleration Premium shall be an amount equal to 4.00% of the aggregate outstanding principal amount of the Loans subject to Acceleration;

(D) after the twelfth (12th) Payment Date and on or prior to the sixteenth (16th) Payment Date, the Acceleration Premium shall be an amount equal to 2.00% of the aggregate outstanding principal amount of the Loans subject to Acceleration;

(E) after the sixteenth (16th) Payment Date and on or prior to the twentieth (20th) Payment Date, the Acceleration Premium shall be an amount equal to 1.00% of the aggregate outstanding principal amount of the Loans subject to Acceleration; and

(F) after the twentieth (20th) Payment Date, the Acceleration Premium shall be an amount equal to 0.00% of the aggregate outstanding principal amount of the Loans subject to Acceleration.

(ii) To determine the aggregate outstanding principal amount of the Loans subject to the Acceleration, and how many Payment Dates have occurred, as of any date of Acceleration, for purposes of this **Section 11.02(c)**:

(A) if, as of such date of Acceleration, Borrower shall have made only one Borrowing, the number of Payment Dates shall be deemed to be the number of Payment Dates that shall have occurred following the first Borrowing Date; and

(B) if, as of such date of Acceleration, Borrower shall have made more than one Borrowing, then the Acceleration Premium shall equal the sum of multiple Acceleration Premiums calculated with respect to the Loans of each Borrowing, each of which Acceleration Premiums shall be calculated based on solely the aggregate outstanding principal amount of the Loans borrowed in such Borrowing (and PIK Loans subsequently borrowed in respect of interest payments thereon), as though the applicable number of Payment Dates equals the number of Payment Dates that shall have occurred following the applicable Borrowing Date. In the case that the Loans subject to Acceleration does not equal the full principal amount of Loans outstanding, the amount of such payment shall be allocated to Loans made in the various Borrowings (and PIK Loans in respect thereof) in the order in which such Borrowings were made.

(d) (i) For the avoidance of doubt, the Acceleration Premium and the Back-End Facility Fee that are payable upon Acceleration of the Loans shall be due and payable at any time the Loans become due and payable prior to the Stated Maturity Date due to Acceleration pursuant to the terms of this Agreement (in which case it shall be due immediately, upon the giving of notice to Borrower in accordance with **Section 11.02(a)**, or automatically, in accordance with **Section 11.02(b)**), whether by operation of law or otherwise (including where bankruptcy filings or the exercise of any bankruptcy right or power, whether in any plan of reorganization or otherwise, results or would result in a payment, discharge, modification or other treatment of the Loans or Loan Documents that would otherwise evade, avoid, or otherwise disappoint the expectations of Lenders in receiving the full benefit of their bargained-for Acceleration Premium and their bargained-for Back-End Facility Fee as provided herein and in the Fee Letter). The Obligors and Lenders acknowledge and agree that any Acceleration Premium and the Back-End Facility Fee due and payable in accordance with the Loan Documents shall not constitute unmatured interest, whether under section 502(b)(2) of the Bankruptcy Code or otherwise, but instead is reasonably calculated to ensure that the Lenders receive the benefit of their bargain under the terms of this Agreement, whether in a bankruptcy case or otherwise.

(ii) Each Obligor acknowledges and agrees that, prior to executing this Agreement, it has had the opportunity to review, evaluate and negotiate the Acceleration Premium calculation and the Back-End Facility Fee with its advisors and acknowledges that the Acceleration Premium is a reasonable approximation of Lenders' liquidated damages upon Acceleration and, accordingly, each Obligor will not contest or object to the reasonableness thereof. Each Obligor understands and acknowledges that Lenders have entered into this Agreement in reliance upon the Acceleration Premium and the Back-End Facility Fee. Each Obligor acknowledges and agrees that the Lenders shall be entitled to recover the full amount of the Obligations, including the Acceleration Premium and the Back-End Facility Fee in each and every circumstance in which such amount is due pursuant to or in connection with this Agreement and the Fee Letter, including in the case of any Obligor's bankruptcy filing, so that the Lenders shall receive the benefit of their bargain hereunder and otherwise receive full recovery of the agreed-upon return under every possible circumstance, and Borrower hereby waives any defense to payment, whether such defense may be based in public policy, ambiguity, or otherwise. Each Obligor further acknowledges and agrees, and waives any argument to the contrary, that payment of such amounts does not constitute a penalty or an otherwise unenforceable or invalid obligation. Any damages that the Lenders may suffer or incur resulting from or arising in connection with any breach by Borrower shall constitute secured obligations owing to the Lenders.

(iii) For the avoidance of doubt, in the event of any Acceleration, interest pursuant to **Sections 3.02(a)** and **(b)** shall accrue on all Obligations, including the Back-End Facility Fee and any Acceleration Premium, from and after the date such Obligations are due and payable until paid in full.

2.13 The following **Section 13.22** is hereby added to the Loan Agreement immediately following **Section 13.21** of the Loan Agreement:

13.22 Redemption Price.

(a) For the avoidance of doubt, the Prepayment Premium (as a component of the Redemption Price) and Back-End Facility Fee shall be due and payable whenever so stated in this Agreement (and the Fee Letter, as applicable), or by any applicable operation of law, regardless of the circumstances causing any related payment prior to the Stated Maturity Date (other than an Acceleration, in which case the Acceleration Premium instead shall be payable).

(b) The Obligors and the Lenders acknowledge and agree that any Prepayment Premium due and payable in accordance with the Loan Documents shall not constitute unmatured interest, whether under section 502(b)(2) of the Bankruptcy Code or otherwise, but instead is reasonably calculated to ensure that the Lenders receive the benefit of their bargain under the terms of this Agreement.

(c) Each Obligor acknowledges and agrees that, prior to executing this Agreement, it has had the opportunity to review, evaluate and negotiate the Prepayment Premium calculation with its advisors and acknowledges that the

Prepayment Premium is a reasonable approximation of the Lenders' liquidated damages upon repayment on any Redemption Date or other day on which payment is due or prior to the Stated Maturity Date and, accordingly, each Obligor will not contest or object to the reasonableness thereof. Each Obligor understands and acknowledges that the Lenders have entered into this Agreement in reliance upon the Prepayment Premium. Each Obligor acknowledges and agrees that the Lenders shall be entitled to recover the full amount of the Obligations, including the Prepayment Premium in each and every circumstance in which such amount is due pursuant to or in connection with this Agreement, so that the Lenders shall receive the benefit of their bargain hereunder and otherwise receive full recovery of the agreed-upon return under every possible circumstance, and Borrower hereby waives any defense to payment, whether such defense may be based in public policy, ambiguity, or otherwise. Each Obligor further acknowledges and agrees, and waives any argument to the contrary, that payment of such amounts does not constitute a penalty or an otherwise unenforceable or invalid obligation. Any damages that the Lenders may suffer or incur resulting from or arising in connection with any breach by Borrower shall constitute secured obligations owing to the Lenders.

SECTION 3. Consent. Administrative Agent and the Lenders hereby consent to (x) Borrower's execution of and entry into the Shionogi Exclusive License Agreement and (y) the Shionogi Transactions.

SECTION 4. Conditions of Effectiveness. The effectiveness of **Sections 2** and **3** of this Amendment shall be subject to the following conditions precedent:

(a) Borrower, the Subsidiary Guarantors, Administrative Agent and all of the Lenders shall have duly executed and delivered this Amendment pursuant to **Section 13.04** of the Loan Agreement; *provided*, *however*, that this Amendment shall have no binding force or effect unless all conditions set forth in this **Section 4** have been satisfied;

(b) No Default or Event of Default under the Loan Agreement shall have occurred and be continuing;

(c) Borrower shall have paid or reimbursed Lenders for Lenders' reasonable out of pocket costs and expenses incurred in connection with this Amendment, including Lenders' reasonable and documented out of pocket legal fees and costs, pursuant to **Section 13.03(a)(i)(z)** of the Loan Agreement; and

(d) Administrative Agent has confirmed to Borrower in writing of its receipt of the executed Amendment required in **Section 3(a)** and receipt of costs and expenses required by **Section 3(c)**.

SECTION 5. **Representations and Warranties; Reaffirmation.**

(a) Each Obligor hereby represents and warrants to each Lender as follows:

(i) Borrower has full power, authority and legal right to make and perform this Amendment. This Amendment is within Borrower's corporate powers and has been duly authorized by all necessary corporate board of directors and, if required, by all necessary shareholder action. This Amendment has been duly executed and delivered by Borrower and constitutes a legal, valid and binding obligation of Borrower, enforceable against Borrower in accordance with its terms, except as such enforceability may be limited by (a) bankruptcy, insolvency, reorganization, moratorium or similar laws of general applicability affecting the enforcement of creditors' rights and (b) the application of general principles of equity (regardless of whether such enforceability is considered in a proceeding in equity or at law). This Amendment (w) does not require any consent or approval of, registration or filing with, or any other action by, any Governmental Authority or any third party, except for such as have been obtained or made and are in full force and effect, (x) will not violate any applicable law or regulation or the charter, bylaws or other organizational documents of Borrower and its Subsidiaries, (y) will not violate any order of any Governmental Authority and (z) will not violate or result in a default under any indenture, agreement or other instrument binding upon Borrower and its Subsidiaries or assets, or give rise to a right thereunder to require any payment to be made by any such Person.

(ii) No Default has occurred or is continuing or will result after giving effect to this Amendment.

(iii) There has been no Material Adverse Effect since the date of this Loan Agreement.

(iv) The representations and warranties made by or with respect to Borrower in **Section 7** of the Loan Agreement are (A) in the case of representations qualified by "materiality," "Material Adverse Effect" or similar language, true and correct in all respects and (B) in the case of all other representations and warranties, true and correct in all material respects (except that the representation regarding representations and warranties that refer to a specific earlier date are true and correct on the basis set forth above as of such earlier date), in each case taking into account any changes made to schedules updated in accordance with **Section 7.21** of the Loan Agreement or attached hereto.

(v) Each Obligor hereby ratifies, confirms, reaffirms, and acknowledges its obligations under the Loan Documents to which it is a party and agrees that the Loan Documents remain in full force and effect, undiminished by this Amendment, except as expressly provided herein. By executing this Amendment, Borrower acknowledges that it has read, consulted with its attorneys regarding, and understands, this Amendment.

SECTION 6. GOVERNING LAW; SUBMISSION TO JURISDICTION; WAIVER OF JURY TRIAL.

(a) **Governing Law.** This Amendment and the rights and obligations of the parties hereunder shall be governed by, and construed in accordance with, the law of the State of New York, without regard to principles of conflicts of laws that would result in the

application of the laws of any other jurisdiction; provided that Section 5-1401 of the New York General Obligations Law shall apply.

(b) **Submission to Jurisdiction.** Borrower agrees that any suit, action or proceeding with respect to this Amendment or any other Loan Document to which it is a party or any judgment entered by any court in respect thereof may be brought initially in the federal or state courts in Houston, Texas or in the courts of its own corporate domicile and irrevocably submits to the non-exclusive jurisdiction of each such court for the purpose of any such suit, action, proceeding or judgment. This **Section 6** is for the benefit of Administrative Agent and the Lenders only and, as a result, none of Administrative Agent or any Lender shall be prevented from taking proceedings in any other courts with jurisdiction. To the extent allowed by applicable Laws, Administrative Agent and the Lenders may take concurrent proceedings in any number of jurisdictions.

(c) **Waiver of Jury Trial.** BORROWER AND EACH LENDER HEREBY

IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY SUIT, ACTION OR PROCEEDING ARISING OUT OF OR RELATING TO THIS AMENDMENT, THE OTHER LOAN DOCUMENTS OR THE TRANSACTIONS CONTEMPLATED HEREBY OR THEREBY.

SECTION 7. Miscellaneous.

(a) **No Waiver**. Nothing contained herein shall be deemed to constitute a waiver of compliance with any term or condition contained in the Loan Agreement or any of the other Loan Documents or constitute a course of conduct or dealing among the parties. Except as expressly stated herein, the Lenders reserve all rights, privileges and remedies under the Loan Documents. Except as amended hereby, the Loan Agreement and other Loan Documents remain unmodified and in full force and effect. All references in the Loan Documents to the Loan Agreement shall be deemed to be references to the Loan Agreement as amended hereby.

(b) **Severability.** In case any provision of or obligation under this Amendment shall be invalid, illegal or unenforceable in any jurisdiction, the validity, legality and enforceability of the remaining provisions or obligations, or of such provision or obligation in any other jurisdiction, shall not in any way be affected or impaired thereby.

(c) **Headings.** Headings and captions used in this Amendment (including the Exhibits, Schedules and Annexes hereto, if any) are included for convenience of reference only and shall not be given any substantive effect.

(d) **Integration.** This Amendment constitutes a Loan Document and, together with the other Loan Documents, incorporates all negotiations of the parties hereto with respect to the subject matter hereof and is the final expression and agreement of the parties hereto with respect to the subject matter hereof.

(e) **Counterparts.** This Amendment may be executed in any number of counterparts, all of which taken together shall constitute one and the same instrument and any of the parties hereto may execute this Amendment by signing any such counterpart. Signatures to this Amendment transmitted by facsimile transmission, by electronic mail in "portable document format" (.pdf) form, or by any other electronic means intended to preserve the original graphic and pictorial appearance of a document, will have the same effect as physical delivery of the paper document bearing the original signature.

(f) **Controlling Provisions.** In the event of any inconsistencies between the provisions of this Amendment and the provisions of any other Loan Document, the provisions of this Amendment shall govern and prevail. Except as expressly modified by this Amendment, the Loan Documents shall not be modified and shall remain in full force and effect.

[Remainder of page intentionally left blank]

IN WITNESS WHEREOF, the parties hereto have duly executed this Amendment, as of the date first above written.

BORROWER:

BIODELIVERY SCIENCES INTERNATIONAL INC.

By: /s/ Herm Cukier
Name: Herm Cukier
Title: Chief Executive Officer

SUBSIDIARY GUARANTORS:

ARIUS PHARMACEUTICALS, INC.

By: /s/ Herm Cukier
Name: Herm Cukier
Title: Chief Executive Officer

ARIUS TWO, INC.

By: /s/ Herm Cukier
Name: Herm Cukier
Title: Chief Executive Officer

ADMINISTRATIVE AGENT:

CRG SERVICING LLC

By: /s/ Nathan Hukill
Nathan Hukill
Authorized Signatory

LENDERS:

CRG ISSUER 2017-1
By: CRG SERVICING LLC, acting by power of attorney

By: /s/ Nathan Hukill
Nathan Hukill
Authorized Signatory

CRG PARTNERS III –PARALLEL FUND "A" L.P.
By CRG PARTNERS III –PARALLEL FUND "A" GP L.P., its General Partner
By CRG PARTNERS III –PARALLEL FUND "A" GP LLC, its General Partner

By: /s/ Nathan Hukill
Nathan Hukill
Authorized Signatory

CRG PARTNERS III (CAYMAN) UNLEV AIV I L.P.
By CRG PARTNERS III (CAYMAN) GP L.P., its General Partner
By CRG PARTNERS III (CAYMAN) GP LLC, its General Partner

By: /s/ Nathan Hukill
Nathan Hukill
Authorized Signatory

Witness: /s/ Nicole Nesson

Name Nicole Nesson

EXHIBIT A TO AMENDMENT NO. 3 TO TERM LOAN AGREEMENT

Form of Shionogi Exclusive License Agreement

Exhibit 99.1

BioDelivery Sciences Acquires U.S. Commercial Rights to Symproic®

Long-term revenue potential of over $75 million for NME with IP protection through 2031

Leverages existing commercial capabilities to provide a novel treatment option for OIC

Total 2019 Company Net Sales expected to be $92-$100 million with Symproic Net Sales of $7-$9 million

Long-term potential of BELBUCA® and Symproic® combined Net Sales expected to be $325-$400 million

Raleigh, North Carolina – April 10, 2019 — BioDelivery Sciences International, Inc. (NASDAQ: BDSI), a rapidly growing commercial-stage specialty pharmaceutical company dedicated to patients living with chronic pain, today announced that it has entered into an exclusive licensing agreement with Shionogi, Inc., to commercialize Symproic® (naldemedine) tablets 0.2 mg in the United States and Puerto Rico effective immediately. Symproic is indicated for the treatment of opioid-induced constipation (OIC) in adults with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation. Symproic is a comprehensively studied OIC product with seven global Phase III clinical trials and received the highest category of endorsement from the American Gastroenterological Association in patients with laxative-refractory OIC.

It is estimated that approximately 40% - 60% of adults with chronic non-cancer pain on non-buprenorphine based opioid therapy will experience OIC, making it one of the most commonly reported side effects in this patient population and can significantly interfere with the appropriate management of chronic pain. Symproic has the potential to become a leading therapy option for OIC given its proven clinical profile and differentiation.

“We are very excited to add Symproic to our commercial portfolio of highly differentiated products for patients suffering from chronic pain and its associated conditions,” stated Herm Cukier, CEO of BDSI. “The product fits very synergistically both strategically and operationally with BELBUCA® (buprenorphine buccal film) CIII, enabling us to leverage our existing commercial organization and capabilities. We are confident Symproic has the potential to become a leading treatment option for OIC and expect to see an accretive contribution to cash flow in the first half of 2020.”

Under the terms of the agreement, BDSI will pay Shionogi, Inc., an initial payment of $20 million and an additional $10 million in six months. In addition, Shionogi is eligible to receive tiered royalty payments based on Net Sales of Symproic.

With the addition of Symproic, the company expects the long-term net sales potential of its product portfolio to be in the range of $325 - $400 million. Additionally, the company has reaffirmed its expectation to become operating cash flow positive by the end of 2019.

ABOUT SYMPROIC

Symproic® (naldemedine) tablets 0.2 mg is indicated for the treatment of OIC in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation. Symproic® was made available to patients in the U.S. in October 2017.

IMPORTANT SAFETY INFORMATION ABOUT SYMPROIC®

CONTRAINDICATIONS

Patients with known or suspected gastrointestinal (GI) obstruction and patients at increased risk of recurrent obstruction, due to the potential for GI perforation.

Patients with a history of a hypersensitivity reaction to Symproic. Reactions have included bronchospasm and rash.

WARNINGS AND PRECAUTIONS

Cases of GI perforation have been reported with use of another peripherally acting opioid antagonist in patients with conditions that may be associated with localized or diffuse reduction of structural integrity in the wall of the GI tract. Monitor for the development of severe, persistent, or worsening abdominal pain; discontinue if this symptom develops.

Symptoms consistent with opioid withdrawal, including hyperhidrosis, chills, increased lacrimation, hot flush/flushing, pyrexia, sneezing, feeling cold, abdominal pain, diarrhea, nausea, and vomiting have occurred in patients treated with Symproic.

Patients having disruptions to the blood-brain barrier may be at increased risk for opioid withdrawal or reduced analgesia. Take into account the overall risk-benefit profile when using Symproic in such patients. Monitor for symptoms of opioid withdrawal in such patients.

DRUG INTERACTIONS

Avoid use with strong CYP3A inducers (e.g., rifampin) because they may reduce the efficacy of Symproic.

Use with moderate (e.g., fluconazole) and strong (e.g., itraconazole) CYP3A inhibitors and P-glycoprotein inhibitors (e.g., cyclosporine) may increase Symproic concentrations. Monitor for potential adverse reactions.

Avoid use of Symproic with another opioid antagonist due to potential for additive effect and increased risk of opioid withdrawal.

USE IN SPECIFIC POPULATIONS

Symproic crosses the placenta and may precipitate opioid withdrawal in a fetus due to the immature fetal blood-brain barrier. Symproic should be used during pregnancy only if the potential benefit justifies the potential risk. Because of the potential for serious adverse reactions, including opioid withdrawal in breastfed infants, a decision should be made to discontinue breastfeeding or discontinue the drug, taking into account the importance of the drug to the mother.

Avoid use in patients with severe hepatic impairment. No dose adjustment of Symproic is required in patients with mild or moderate hepatic impairment.

ADVERSE REACTIONS

The most common adverse reactions with Symproic as compared to placebo in clinical trials were: abdominal pain (8% vs 2%), diarrhea (7% vs 2%), nausea (4% vs 2%), and gastroenteritis (2% vs 1%).

In pooled Studies 1 and 2, the incidence of adverse reactions of opioid withdrawal was 1% (8/542) for Symproic and 1% (3/546) for placebo. In Study 3 (52-week data), the incidence was 3% (20/621) for Symproic and 1% (9/619) for placebo.

To report suspected Adverse Reactions, contact Shionogi at 1-800-849-9707 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see accompanying Full Prescribing Information including Medication Guide for Symproic or visit www.symproic.com/pi.

References:

1. Sehgal N, Colson J, Smith HS. Chronic pain treatment with opioid analgesics: benefits versus harms of long-term therapy. Expert Rev Neurother. 2013;13:1201-1220.
2. Camilleri M, Drossman DA, Becker G, Webster LR, Davies AN, Mawe GM. Emerging treatments in neurogastroenterology: a multidisciplinary working group consensus statement on opioid-induced constipation. Neurogastroenterol Motil. 2014;26: 1386-1395.
3. Kalso E, Edwards JE, Moore RA, McQuay HJ. Opioids in chronic noncancer pain: systematic review of efficacy and safety. Pain. 2004;112:372–80.
4. Cook SF, Lanza L, Zhou X, et al. Gastrointestinal side effects in chronic opioid users: results from a population based survey.Aliment Pharmacol Ther. 2008;27(12):1224-1232.
5. Brown RT, Zuelsdorff M, Fleming M. Adverse effects and cognitive function among primary care patients taking opioids for chronic nonmalignant pain. J Opioid Manag. 2006;2(3):137–146.
6. Tuteja AK, Biskupiak J, Stoddard GJ, Lipman AG. Opioid induced bowel disorders and narcotic bowel syndrome in patients with chronic non-cancer pain. Neurogastroenterol Motil. 2010;22(4):424-430.

IMPORTANT SAFETY INFORMATION ABOUT BELBUCA®

BELBUCA® (buprenorphine buccal film), CIII is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations of Use

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with long-acting opioid formulations, reserve BELBUCA® for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.

BELBUCA® is not indicated as an as-needed (prn) analgesic.

WARNING: ADDICTION, ABUSE, AND MISUSE; RISK EVALUATION AND MITIGATION STRATEGY (REMS); LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL EXPOSURE; NEONATAL OPIOID WITHDRAWAL SYNDROME; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES AND OTHER CNS DEPRESSANTS

Addiction, Abuse, and Misuse

BELBUCA® exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess patient's risk prior to prescribing BELBUCA®, and monitor patients regularly for these behaviors and conditions.

Risk Evaluation and Mitigation Strategy (REMS)

To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the FDA has required a REMS for these products. Under the requirements of the REMS, drug companies with approved opioid analgesic products must make REMS-compliant education programs available to healthcare providers. Healthcare providers are strongly encouraged to

- **complete a REMS-compliant education program,**
- **counsel patients and/or their caregivers, with every prescription, on safe use, serious risks, storage, and disposal of these products,**
- **emphasize to patients and their caregivers the importance of reading the Medication Guide every time it is provided by their pharmacist, and**
- **consider other tools to improve patient, household, and community safety.**

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of BELBUCA®. Monitor for respiratory depression, especially during initiation of BELBUCA® or following a dose increase.

Accidental Exposure

Accidental exposure to even one dose of BELBUCA®, especially by children, can result in a fatal overdose of buprenorphine.

Neonatal Opioid Withdrawal Syndrome

Prolonged use of BELBUCA® during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Risks from Concomitant Use with Benzodiazepines or Other CNS Depressants

Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate; limit dosages and durations to the minimum required; and follow patients for signs and symptoms of respiratory depression and sedation.

BELBUCA® is contraindicated in patients with significant respiratory depression; acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment; known or suspected gastrointestinal obstruction, including paralytic ileus; and hypersensitivity (e.g., anaphylaxis) to buprenorphine.

BELBUCA® contains buprenorphine, a Schedule III controlled substance. As an opioid, BELBUCA® exposes users to the risks of addiction, abuse, and misuse. Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed BELBUCA® and in those who obtain the drug illicitly. Addiction can occur at recommended doses and if the drug is misused or abused.

Potential serious adverse events caused by opioids include addiction, abuse, and misuse; life-threatening respiratory depression; neonatal opioid withdrawal syndrome; risks due to interactions with benzodiazepines or other central nervous system depressants; risk of life-threatening respiratory depression in patients with chronic pulmonary disease or in elderly, cachectic, or debilitated patients; adrenal insufficiency; QTc prolongation; severe hypotension; risks of use in patients with increased intracranial pressure, brain tumors, head injury, or impaired consciousness; hepatotoxicity; risk of overdose in patients with moderate or severe hepatic impairment; anaphylactic/allergic reactions; risk of use in patients with gastrointestinal conditions; increased risk of seizures in patients with seizure disorders; risks of use in cancer patients with oral mucositis; risks of driving and operating machinery.

The most common adverse reactions (≥5%) reported by patients treated with BELBUCA® in the clinical trials were nausea, constipation, headache, vomiting, fatigue, dizziness, somnolence, diarrhea, dry mouth, and upper respiratory tract infection.

For full Prescribing Information, including Boxed Warning, visit www.belbuca.com**.**

To report SUSPECTED ADVERSE REACTIONS, contact BioDelivery Sciences International, Inc. at 1-800-469-0261 or FDA at 1-800-FDA-1088 or www.fda.gov/safety/medwatch.

ABOUT BIODELIVERY SCIENCES INTERNATIONAL, INC.

BioDelivery Sciences International, Inc. (NASDAQ: BDSI) is a rapidly growing commercial-stage specialty pharmaceutical company dedicated to patients living with chronic pain. BDSI is utilizing its novel and proprietary BioErodible MucoAdhesive (BEMA®) technology and other drug delivery technologies to develop and commercialize, either on its own or in partnership with third parties, new applications of proven therapies aimed at addressing important unmet medical needs. BDSI's marketed products and those in development address serious and debilitating conditions such as chronic pain, breakthrough cancer pain, and opioid dependence. For more information, please visit us at www.bdsi.com or follow us on Facebook.com/BioDeliverySI or Twitter BDSI@BioDeliverySI.

ABOUT SHIONOGI

Shionogi & Co., Ltd. is a Japanese major research-driven pharmaceutical company dedicated to bringing benefits to patients based on its corporate philosophy of supplying the best possible medicine to protect the health and wellbeing of the patients it serves. Shionogi Inc., the US- based subsidiary of Shionogi & Co., Ltd., continues this focus on the development and commercialization of high quality medicines that protect the health and well-being of the patients it serves. The company currently markets products in several therapeutic areas including anti-infectives, pain, cardiovascular diseases and gastroenterology. Its pipeline is focused on infectious disease, pain, CNS and oncology. For more information on Shionogi Inc., visit www.shionogi.com (https://www.shionogi.com/). For more information on Shionogi & Co., Ltd., visit www.shionogi.co.jp.en (http://shionogi.co.jp.en/).

CAUTIONARY NOTE ON FORWARD-LOOKING STATEMENTS

This press release, the presentation described herein, and any statements of employees, representatives, and partners of BioDelivery Sciences International, Inc. ("BDSI") related thereto contain, or may contain, among other things, certain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements involve significant risks and uncertainties. Such statements may include, without limitation, statements with respect to the BDSI's plans, objectives, projections, expectations and intentions and other statements identified by words such as "projects," "may," "will," "could," "would," "should," "believes," "expects," "anticipates," "estimates," "intends," "plans," "potential" or similar expressions. These statements are based upon the current beliefs and expectations of the BDSI's management and are subject to significant risks and uncertainties, including those detailed in the BDSI's filings with the Securities and Exchange Commission.

Actual results (including, without limitation, the anticipated benefits to the Company related to the preferred access to additional commercial lives as described herein) may differ significantly from those set forth or implied in the forward-looking statements. These forward-looking statements involve certain risks and uncertainties that are subject to change based on various factors (many of which are beyond the BDSI's control). BDSI undertakes no obligation to publicly update any forward-looking statements, whether as a result of new information, future presentations or otherwise, except as required by applicable law.

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