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

FORM 8-K

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

Date of Report (Date of earliest event reported): **November 27, 2019**

RELMADA THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Nevada	**001-39082**	**45-5401931**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

880 Third Avenue, 12th Floor New York, NY	**10022**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code **(212) 547-9591**

(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 of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ 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))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of exchange on which registered
Common stock, $0.001 par value per share	**RLMD**	**The Nasdaq Capital Market**

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.

On November 27, 2019, Relmada Therapeutics, Inc. (the "Company" or "Relmada") amended and restated its Unit Purchase Agreement with certain accredited investors who purchased shares of the Company's common stock and five-year warrants to purchase shares of common stock in the Company's private placement offering on February 12, 2019. The only changes made in the amended and restated Unit Purchase Agreement are in Section 5.4 thereof, which provides that until February 12, 2020, such investors have the right to participate in the Company's offerings of equity securities, subject to certain conditions, including that such investor's beneficial ownership of common stock of the Company will not exceed 4.99% of the issued and outstanding common stock giving effect to closing of such offerings, and that such right shall not apply to any issuance of equity securities being issued (i) as compensation to officers, directors or consultants to the Company, or (ii) in connection with mergers, acquisitions, strategic alliances or similar transactions, the principal purpose of which is not capital raising. A copy of the amended and restated Unit Purchase Agreement is filed herewith as Exhibit 10.1 hereto.

On December 2, 2019, the Company entered into an amendment of the License Agreement, dated January 16, 2018 (the "License Agreement"), with Dr. Charles E. Inturrisi and Dr. Paolo Manfredi (collectively, the "Licensor"). Pursuant to an Intellectual Property Assignment Agreement, dated January 16, 2018, Relmada assigned its existing rights, including patents and patent applications, to d-methadone in the context of psychiatric use to Licensor, and pursuant to the License Agreement, Licensor then granted Relmada an exclusive, perpetual, worldwide license under the assigned intellectual property rights as well as patents and know-how covering certain new inventions developed by Licensor and relating to d-methadone in neurological and other uses, to develop and commercialize d-methadone in all fields of use. The License Agreement includes certain provisions permitting Licensor to terminate the License Agreement during the period commencing on the effective date and the later of five years following such date, or December 31, 2022 (the "Key Man Term"), if the employment of our Chief Executive Officer, Mr Sergio Traversa, is terminated other than for "cause", or in certain circumstances if we modify the scope of his responsibilities in connection with the development and commercialization of d-methadone, or materially reduce his compensation. The purpose of the amendment was to amend the License Agreement to, among other things (i) modify and expand the definition of "cause" permitting termination of Mr. Sergio Traversa, our Chief Executive Officer, without enabling termination of the License Agreement, including Mr Traversa's death or disability resulting in his termination, and (ii) to enable the appointment of a suitable replacement for Mr. Traversa for the remainder of the Key Man Term in the event of such death or disability. The description set forth below in Item 8.01 under "Business—Intellectual Property Portfolio and Market Exclusivity—D-Methadone License Agreement" of the d-methadone Agreements as amended is incorporated herein by reference. A copy of the amendment to the d-methadone Agreements is filed herewith as Exhibit 10.2 hereto.

Item 8.01 Other Events.

The Company is filing an updated description of certain aspects of the Company's business, its directors and executive officers and certain relationships and related transactions, as well as updated risk factors describing risks and uncertainties that may affect the Company and the market price of its common stock with this report for the purpose of updating the disclosures contained in the Company's prior filings with the SEC, including the Company's Annual Report on Form 10-K for the year ended June 30, 2019 and Quarterly Report on Form 10-Q for the quarter ended September 30, 2019. The updated description of the Company's business and the updated risk factors are filed herewith as Exhibit 99.1 and Exhibit 99.2, respectively, and are incorporated herein by reference.

The Company additionally updated its corporate presentation, a copy of which is attached as Exhibit 99.3 hereto and is incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
10.1	Amended and Restated Unit Purchase Agreement dated November 27, 2019, between Relmada Therapeutics, Inc., and certain accredited investors
10.2	Amendment No.1 To License Agreement dated December 2, 2019, to the License Agreement dated January 16, 2018 between Relmada Therapeutics, Inc., and Dr. Charles E. Inturrisi and Dr. Paolo Manfredi
99.1	Updated Business, Directors and Executive Officers and Certain Relationships and Related Transactions Disclosures
99.2	Updated Risk Factors
99.3	Corporate Presentation, dated December 2019

SIGNATURES

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

Dated: December 3, 2019

RELMADA THERAPEUTICS, INC.

By: */s/ Sergio Traversa*
Name: Sergio Traversa
Title: Chief Executive Officer

Exhibit 10.1

AMENDED AND RESTATED

UNIT PURCHASE AGREEMENT

BY AND AMONG

RELMADA THERAPEUTICS, INC.

AND

EACH PURCHASER IDENTIFIED ON APPENDIX A HERETO

DISCLOSURE SCHEDULES AND EXHIBITS TO
UNIT PURCHASE AGREEMENT

Schedule 3.1(d)(iii)	Conflicts
Schedule 3.1(g)	Capitalization
Schedule 3.1(j)	Litigation
Schedule 3.1(m)	Title to Assets
Schedule 3.1(n)	Intellectual Property
Schedule 3.1(r)	Certain Fees
Schedule 3.1(y)	Indebtedness
Exhibit A	Form of Warrant
Exhibit B	Form of Subscription Agreement
Exhibit C	Form of Registration Rights Agreement
Exhibit D	Form of Legal Opinion of Company Counsel

AMENDED AND RESTATED UNIT PURCHASE AGREEMENT

This AMENDED AND RESTATED UNIT PURCHASE AGREEMENT (this "Agreement") entered into as of November 27, 2019, and effective as of February 12, 2019, by and among Relmada Therapeutics, Inc., a Nevada corporation (the "Company"), and each purchaser identified on Appendix A hereto (each, including its successors and assigns, a "Purchaser" and collectively, the "Purchasers") amends and restates in its entirety the Unit Purchase Agreement among the parties hereto dated as of February 12, 2019.

WHEREAS, the Company is offering (the "***Offering***") up to 11,111,111 units (the "***Units***"), each Unit consisting of (i) one (1) share of the Company's common stock, par value $0.001 per share (the "***Common Stock***") and (ii) a warrant to purchase 0.65 share of Common Stock (collectively, the "***Warrants***," and together with the Units, the Common Stock and the shares of Common Stock issuable upon exercise of the Warrants (the "***Warrant Shares***"), the "***Securities***"), at a price per Unit of $0.90 (the "***Price Per Unit***");

WHEREAS, the Units are being offered on a "*best efforts*" basis with respect to a maximum of $10,000,000 (the "***Maximum Offering Amount***") to a limited number of "accredited investors" (as that term is defined by Rule 501(a) of Regulation D ("***Regulation D***") promulgated by the Securities and Exchange Commission under the Securities Act of 1933, as amended (the "***Securities Act***");

WHEREAS, the Company and each Purchaser is executing and delivering this agreement in reliance upon the exemption from securities registration afforded by Section 4(a)(2) of the Securities Act and Rule 506 of Regulation D promulgated by the SEC under the Securities Act;

WHEREAS, the Company has retained Alexander Capital LP to act as its placement agent in connection with the sale of the Units pursuant to this Agreement (the "***Placement Agent***");

WHEREAS, the minimum investment amount that may be purchased by a Purchaser is 11,111 Units for an aggregate minimum purchase price of $10,000, unless the Company and the Placement Agent waive such requirement in their sole discretion; and

WHEREAS, the Company desires to issue and sell the Units to each Purchaser in one or more Closings (as defined below) as set forth herein.

WHEREAS the subscription for the Securities will be made in accordance with and subject to the terms and conditions of the Subscription Agreement and the Company's Confidential Private Placement Memorandum dated September 21, 2018, together with all amendments thereof and supplements and exhibits thereto and as such may be amended from time to time (the "***Memorandum***").

NOW, THEREFORE, IN CONSIDERATION of the mutual covenants contained in this Agreement, and for other good and valuable consideration, the receipt and adequacy of which are hereby acknowledged, the Company and each Purchaser agree as follows:

ARTICLE I.
DEFINITIONS

1.1 Definitions. In addition to the terms defined elsewhere in this Agreement, the following terms have the meanings set forth in this Section 1.1:

"Action" shall have the meaning ascribed to such term in Section 3.1(j).

"Affiliate" means any Person that, directly or indirectly through one or more intermediaries, controls or is controlled by or is under common control with a Person, as such terms are used in and construed under Rule 405 under the Securities Act.

"Board of Directors" means the board of directors of the Company.

"Business Day" means any day except any Saturday, any Sunday, any day which is a federal legal holiday in the United States or any day on which banking institutions in the State of New York are authorized or required by law or other governmental action to close.

"Cap" shall have the meaning ascribed to such term in Section 5.2.

"Closing" means a closing of the purchase and sale of the Units pursuant to Section 2.1.

"Closing Date" means a Trading Day on which all of the Transaction Documents have been executed and delivered by the Company and each of the Purchasers purchasing Units at the relevant Closing, and all conditions precedent to (i) the Purchasers' obligations to pay the Subscription Amount and
(ii) the Company's obligations to deliver the Units, in each case, have been satisfied or waived, but in no event later than the third Trading Day following the relevant Closing.

"Commission" means the United States Securities and Exchange Commission.

"Common Stock" means the common stock of the Company, par value $0.001 per share, and any other class of securities into which such securities may hereafter be reclassified or changed.

"Common Stock Equivalents" means any securities of the Company or the Subsidiaries which would entitle the holder thereof to acquire at any time Common Stock, including, without limitation, any debt, preferred stock, right, option, warrant or other instrument that is at any time convertible into or exercisable or exchangeable for, or otherwise entitles the holder thereof to receive, Common Stock.

"Company Counsel" means The Matt Law Firm, PLLC, with offices located at 1701 Genesee Street, Utica, NY 13501, Fax: 315-624-7359.

"Disclosure Schedules" means the Disclosure Schedules of the Company delivered concurrently herewith.

"Effective Date" means the earliest of the date that (a) the initial Registration Statement has been declared effective by the Commission, (b) all of the Offering Shares have been sold pursuant to Rule 144 or may be sold pursuant to Rule 144 without the requirement for the Company to be in compliance with the current public information requirements under Rule 144 and without volume or manner-of-sale restrictions or (c) following the one year anniversary of the final Closing Date hereunder, provided that a holder of Offering Shares is not an Affiliate of the Company, all of the Offering Shares may be sold pursuant to an exemption from registration under Section 4(a)(1) of the Securities Act without volume or manner-of-sale restrictions or the need for the Company to provide current public information and Company counsel has delivered to such holders a written opinion that resales may then be made by such holders of the Offering Shares pursuant to such exemption which opinion shall be in form and substance reasonably acceptable to such holders.

"Exchange Act" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

"FCPA" means the Foreign Corrupt Practices Act of 1977, as amended.

"GAAP" shall have the meaning ascribed to such term in Section 3.1(h).

"Indebtedness" shall have the meaning ascribed to such term in Section 3.1(y).

"Initial Closing" shall have the meaning ascribed to such term in Section 2.1(b).

"Initial Closing Date" shall have the meaning ascribed to such term in Section 2.1(b).

"Intellectual Property Rights" shall have the meaning ascribed to such term in Section 3.1(n).

"Investor Warrants" means the Warrants which are included in the Units delivered to the Purchasers at each Closing in accordance with Section 2.2(a) hereof, which Warrants shall be substantially in the form of Exhibit A attached hereto.

"Investor Warrant Shares" means the shares of Common Stock issuable upon exercise of the Investor Warrants.

"Liens" means a lien, charge, pledge, security interest, encumbrance, right of first refusal, preemptive right or other restriction.

"Material Adverse Effect" shall have the meaning assigned to such term in Section 3.1(b).

"Material Permits" shall have the meaning ascribed to such term in Section 3.1(l).

"Memorandum" means the Company's Confidential Private Placement Memorandum, dated as of September 21, 2018, with respect to the Offering.

"Offering Shares" means the shares of Common Stock included in the Units issued pursuant to this Agreement and Investor Warrant Shares.

"Person" means an individual or corporation, partnership, trust, incorporated or unincorporated association, joint venture, limited liability company, joint stock company, government (or an agency or subdivision thereof) or other entity of any kind.

"Price Per Unit" means $0.90.

"Proceeding" means an action, claim, suit, investigation or proceeding (including, without limitation, an informal investigation or partial proceeding, such as a deposition), whether commenced or threatened.

"Purchaser Party" shall have the meaning ascribed to such term in Section 4.9.

"Registration Rights Agreement" means the Registration Rights Agreement, dated February 12, 2019, among the Company and the Purchasers, in the form of Exhibit C attached hereto.

"Registration Statement" means a registration statement meeting the requirements set forth in the Registration Rights Agreement and covering the resale of the Offering Shares by each Purchaser as provided for in the Registration Rights Agreement.

"Required Approvals" shall have the meaning ascribed to such term in Section 3.1(e).

"Required Minimum" shall have the meaning ascribed to such term in Section 4.10.

"Rule 144" means Rule 144 promulgated by the Commission pursuant to the Securities Act, as such Rule may be amended or interpreted from time to time, or any similar rule or regulation hereafter adopted by the Commission having substantially the same purpose and effect as such Rule.

"SEC Reports" shall have the meaning ascribed to such term in Section 3.1(h).

"Securities" means the Units, the Offering Shares and the Investor Warrants.

"Securities Act" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

"Short Sales" means all "short sales" as defined in Rule 200 of Regulation SHO under the Exchange Act (but shall not be deemed to include the location and/or reservation of borrowable shares of Common Stock).

"Subscription Agreement" means the Subscription Agreement, dated February 12, 2019, among the Company and the Purchasers, in the form ofExhibit B attached hereto.

"Subscription Amount" means, as to each Purchaser, the aggregate amount to be paid for the Units purchased hereunder as specified next to such Purchaser's name on Appendix A of this Agreement under the heading "Subscription Amount".

"Subsequent Closing Date" shall have the meaning ascribed to such term in Section 2.1(b).

"Subsidiary" means any direct or indirect subsidiary of the Company formed or acquired after February 12, 2019.

"Termination Date" shall have the meaning ascribed to such term in Section 2.1(a).

"Trading Day" means a day on which the principal Trading Market is open for trading; provided, that in the event that the Common Stock is not listed or quoted for trading on a Trading Market on the date in question, then Trading Day shall mean a Business Day.

"Trading Market" means any of the following markets or exchanges on which the Common Stock is listed or quoted for trading on the date in question: the NYSE MKT, the Nasdaq Capital Market, the Nasdaq Global Market, the Nasdaq Global Select Market, the New York Stock Exchange, the OTC Bulletin Board, the OTC QB Marketplace or the OTC QX Marketplace (or any successors to any of the foregoing).

"Transaction Documents" means this Agreement, the Memorandum, the Subscription Agreement, the Investor Warrants, the Registration Rights Agreement, all exhibits and schedules thereto and hereto and any other documents or agreements executed in connection with the transactions contemplated hereunder.

"Transfer Agent" means a transfer agent for the Company's Common Stock and the Offering Shares, if any, and any successor transfer agent of the Company.

"Units" means the Units issued pursuant to this Agreement, which shall consist of (a) one (1) share of Common Stock and (b) an Investor Warrant to purchase 0.50 share of Common Stock, exercisable at a price of $1.50 per share of Common Stock for a period of five (5) years from the date of the final Closing (the "Warrant").

ARTICLE II.
PURCHASE AND SALE

2.1 Closing.

(a) The Securities will be offered for sale until the earlier of (i) the date upon which subscriptions for the Maximum Offering offered hereunder have been accepted, (ii) September 30, 2018 (subject to the right of the Company and the Placement Agent to extend the offering until December 31, 2018 without further notice to investors), (iii) the date upon which the Company and the Placement Agent elect to terminate the Offering or (iv) the date upon which the Company elects to terminate the Offering (the "Termination Date"). The Offering is being conducted on a "*reasonable efforts*" basis with respect to the Maximum Offering.

(b) On the initial Closing Date (the "Initial Closing Date"), upon the terms and subject to the conditions set forth herein, substantially concurrent with the execution and delivery of this Agreement by the parties hereto, the Company agrees to sell at the initial Closing (the "Initial Closing"), and the Purchasers, severally and not jointly, agree to purchase at the Initial Closing, up to an aggregate of $10,000,000 of Units, calculated based upon the Price Per Unit, for each Purchaser equal to such Purchaser's Subscription Amount as set forth on Appendix A hereto, and Investor Warrants as determined pursuant to Section 2.2(a). Thereafter, on any subsequent Closing Date (each a "Subsequent Closing Date"), upon the terms and subject to the conditions set forth herein, substantially concurrent with the execution and delivery of this Agreement by the Purchasers purchasing Units on such Subsequent Closing Date, the Company agrees to sell, and each Purchaser purchasing Units at such subsequent Closing, severally and not jointly, agrees to purchase an aggregate of up to $10,000,000 of Units, calculated as set forth above, less the amount of Units issued and sold at all previous Closings. Each Purchaser purchasing Units on a Closing Date shall deliver to the Company such Purchaser's Subscription Amount by wire transfer of immediately available funds in accordance with the Company's written wire instructions, and the Company shall deliver to each Purchaser its respective Units, as determined pursuant to Section 2.2(a), and the Company and each Purchaser shall deliver the other items set forth in Section 2.2 deliverable at the Closing. Upon satisfaction of the covenants and conditions set forth in Sections 2.2 and 2.3, a Closing shall occur at the offices of Company Counsel or such other location as the parties shall mutually agree..

(c) The last Closing of the Offering, occurring on or prior to the Termination Date, shall be referred to as the "Final Closing". Any subscription documents or funds received after the Final Closing will be returned, without interest or deduction. If a Closing is not held on or before the Termination Date, the Company shall cause all subscription documents and funds to be returned, without interest or deduction, to each prospective Purchaser. The Company shall also cause any subscription documents or funds received following the final Closing to be returned, without interest or deduction, to each applicable prospective Purchaser. Notwithstanding the foregoing, the Company in its sole discretion may elect not to sell to any Person any or all of the Units requested to be purchased hereunder, provided that the Company causes all corresponding subscription documents and funds received from such Person to be promptly returned.

(d) The Subscriber may revoke its subscription and obtain a return of the subscription amount paid to the Escrow Account at any time before the date of the Initial Closing by providing written notice to the Placement Agent, the Company and the Escrow Agent as provided herein. Upon receipt of a revocation notice from the Subscriber prior to the date of the Initial Closing, all amounts paid by the Subscriber shall be returned to the Subscriber, without interest or deduction. The Subscriber may not revoke this subscription or obtain a return of the subscription amount paid to the Escrow Agent on or after the date of the Initial Closing. Any subscription received after the Initial Closing but prior to the Termination Date shall be irrevocable.

2.2 Deliveries.

(a) On or prior to each Closing Date, the Company shall deliver or cause to be delivered to each Purchaser purchasing Units on such Closing Date each of the following:

(i) this Agreement duly executed by the Company;

(ii) the Subscription Agreement duly executed by the Company;

(iii) a legal opinion of Company Counsel, substantially in the form of Exhibit D attached hereto;

(iv) the Registration Rights Agreement duly executed by the Company;

(v) (1) irrevocable instructions to the Transfer Agent authorizing the issuance of the shares of Common Stock included in the Units purchased by such Purchaser at such Closing and (2) a Warrant registered in such Purchaser's name to purchase such number of Investor Warrant Shares included in the Units purchased by such Purchaser at such Closing (such Warrant certificate may be delivered within three (3) Trading Days of such Closing Date). Within five (5) days following any Closing, the Company will deliver, unless otherwise requested by any Purchaser, one (1) certificate registered in such Purchaser's name representing the shares of Common Stock included in the Units purchased by such Purchaser at such Closing; and

(vi) a good standing certificate of the Company, dated within four Trading Days of the Closing Date, from the State of Nevada.

(b) On or prior to each Closing Date, each Purchaser purchasing Units on such Closing Date shall deliver or cause to be delivered to the Company the following:

(i) the Subscription Agreement duly executed by such Purchaser; and

(ii) such Purchaser's Subscription Amount by wire transfer to the account specified in writing by the Company, which such Subscription Amount is a for a purchase of a minimum of 11,111 Units at an aggregate minimum purchase price of $10,000, unless the Company and the Placement Agent waive such requirement in their sole discretion.

2.3 Closing Conditions.

(a) The obligations of the Company hereunder in connection with each Closing are subject to the following conditions being met:

(i) the accuracy in all material respects on such Closing Date of the representations and warranties of the Purchasers contained herein (unless as of a specific date therein in which case they shall be accurate in all material respects as of such date);

(ii) all obligations, covenants and agreements of each Purchaser required to be performed at or prior to such Closing Date shall have been performed; and

(iii) the delivery by each Purchaser of the items set forth in Section 2.2(b) of this Agreement.

(b) The respective obligations of the Purchasers hereunder in connection with each Closing are subject to the following conditions being met:

(i) the accuracy in all material respects when made and on such Closing Date of the representations and warranties of the Company contained herein (unless as of a specific date therein in which case they shall be accurate in all material respects as of such date);

(ii) all obligations, covenants and agreements of the Company required to be performed at or prior to such Closing Date shall have been performed;

(iii) the delivery by the Company of the items set forth in Section 2.2(a) of this Agreement;

(iv) there shall have been no Material Adverse Effect with respect to the Company since February 12, 2019; and

(v) from February 12, 2019 to such Closing Date, trading in the Common Stock shall not have been suspended by the Commission or the Company's principal Trading Market (except for any suspension of trading of limited duration agreed to by the Company, which suspension shall be terminated prior to the Closing), and, at any time prior to the Closing Date, trading in securities generally as reported by Bloomberg L.P. shall not have been suspended or limited, or minimum prices shall not have been established on securities whose trades are reported by such service, or on any Trading Market, nor shall a banking moratorium have been declared either by the United States or New York State authorities nor shall there have occurred any material outbreak or escalation of hostilities or other national or international calamity of such magnitude in its effect on, or any material adverse change in, any financial market which, in each case, in the reasonable good faith judgment of such Purchaser, makes it impracticable or inadvisable to purchase the Units at such Closing.

ARTICLE III.
REPRESENTATIONS AND WARRANTIES

3.1 Representations and Warranties of the Company. Except as set forth in the Disclosure Schedules, which Disclosure Schedules shall be deemed a part hereof and shall qualify any representation made herein only to the extent of the disclosure contained in the corresponding section of the Disclosure Schedules, the Company hereby makes the following representations and warranties to each Purchaser:

(a) Subsidiaries. The Company has one subsidiary, Relmada Therapeutics, Inc., a Delaware corporation.

(b) Organization and Qualification. Each of the Company and its Subsidiaries is an entity duly incorporated or otherwise organized, validly existing and in good standing under the laws of the jurisdiction of its incorporation or organization, with the requisite power and authority to own and use its properties and assets and to carry on its business as currently conducted. Neither the Company nor any Subsidiary is in violation or default of any of the provisions of its respective certificate or articles of incorporation, bylaws or other organizational or charter documents. Each of the Company and its Subsidiaries is duly qualified to conduct business and is in good standing as a foreign corporation or other entity in each jurisdiction in which the nature of the business conducted or property owned by it makes such qualification necessary, except where the failure to be so qualified or in good standing, as the case may be, could not have or reasonably be expected to result in: (i) a material adverse effect on the legality, validity or enforceability of any Transaction Document, (ii) a material adverse effect on the results of operations, assets, business, prospects or condition (financial or otherwise) of the Company and the Subsidiaries, taken as a whole, or (iii) a material adverse effect on the Company's ability to perform in any material respect on a timely basis its obligations under any Transaction Document (any of (i), (ii) or (iii), a "Material Adverse Effect") and no Proceeding has been instituted in any such jurisdiction revoking, limiting or curtailing or seeking to revoke, limit or curtail such power and authority or qualification.

(c) Authorization; Enforcement. The Company has the requisite corporate power and authority to enter into and to consummate the transactions contemplated by this Agreement and each of the other Transaction Documents and otherwise to carry out its obligations hereunder and thereunder. The execution and delivery of this Agreement and each of the other Transaction Documents by the Company and the consummation by it of the transactions contemplated hereby and thereby have been duly authorized by all necessary action on the part of the Company and no further action is required by the Company, the Board of Directors or the Company's stockholders in connection herewith or therewith other than in connection with the Required Approvals. This Agreement and each other Transaction Document to which it is a party has been (or upon delivery will have been) duly executed by the Company and, when delivered in accordance with the terms hereof and thereof, will constitute the valid and binding obligation of the Company enforceable against the Company in accordance with its terms, except: (i) as limited by general equitable principles and applicable bankruptcy, insolvency, reorganization, moratorium and other laws of general application affecting enforcement of creditors' rights generally, (ii) as limited by laws relating to the availability of specific performance, injunctive relief or other equitable remedies and (iii) insofar as indemnification and contribution provisions may be limited by applicable law.

(d) No Conflicts. The execution, delivery and performance by the Company of this Agreement and the other Transaction Documents, the issuance and sale of the Securities and the consummation by it of the transactions contemplated hereby and thereby to which it is a party do not and will not: (i) conflict with or violate any provision of the Company's or any Subsidiary's certificate or articles of incorporation, bylaws or other organizational or charter documents, (ii) except as set forth on Schedule 3.1(d)(iii), conflict with, or constitute a default (or an event that with notice or lapse of time or both would become a default) under, result in the creation of any Lien upon any of the properties or assets of the Company or any Subsidiary, or give to others any rights of termination, amendment, acceleration or cancellation (with or without notice, lapse of time or both) of, any agreement, credit facility, debt or other instrument (evidencing a Company or Subsidiary debt or otherwise) or other understanding to which the Company or any Subsidiary is a party or by which any property or asset of the Company or any Subsidiary is bound or affected, or (iii) subject to the Required Approvals, conflict with or result in a violation of any law, rule, regulation, order, judgment, injunction, decree or other restriction of any court or governmental authority to which the Company or a Subsidiary is subject (including federal and state securities laws and regulations), or by which any property or asset of the Company or a Subsidiary is bound or affected; except in the case of each of clauses (ii) and (iii), such as could not have or reasonably be expected to result in a Material Adverse Effect.

(e) Filings, Consents and Approvals. Except as set forth on Schedule 3.1(e), the Company is not required to obtain any consent, waiver, authorization or order of, give any notice to, or make any filing or registration with, any court or other federal, state, local or other governmental authority or other Person in connection with the execution, delivery and performance by the Company of the Transaction Documents, other than: (i) the filing with the Commission pursuant to the Registration Rights Agreement and Section 4.6, (ii) the notice and/or application(s) to each applicable Trading Market, if any, for the issuance and sale of the Offering Shares and the listing of the Offering Shares for trading thereon in the time and manner required thereby, and (iii) the filing of a Form D with the Commission and such filings as are required to be made under applicable state securities laws (collectively, the "Required Approvals").

(f) Issuance of the Securities. The Securities are duly authorized and, when issued and paid for in accordance with the applicable Transaction Documents, will be duly and validly issued, fully paid and, if and as applicable, nonassessable, free and clear of all Liens imposed by the Company. The Company has reserved from its duly authorized capital stock a number of shares of Common Stock for issuance of the Offering Shares at least equal to the Required Minimum on February 12, 2019.

(g) Capitalization. The capitalization of the Company is as set forth on Schedule 3.1(g). The Company has not issued any capital stock and/or Common Stock Equivalents not set forth on Schedule 3.1(g). No Person has any right of first refusal, preemptive right, right of participation, or any similar right to participate in the transactions contemplated by the Transaction Documents. Except as a result of the purchase and sale of the Securities or as described on Schedule 3.1(g), there are no outstanding options, warrants, scrip rights to subscribe to, calls or commitments of any character whatsoever relating to, or securities, rights or obligations convertible into or exercisable or exchangeable for, or giving any Person any right to subscribe for or acquire any shares of Common Stock, or contracts, commitments, understandings or arrangements by which the Company or any Subsidiary is or may become bound to issue additional shares of Common Stock or Common Stock Equivalents. Except as set forth on Schedule 3.1(g), the issuance and sale of the Securities will not obligate the Company to issue shares of Common Stock or other securities to any Person (other than the Purchasers) and will not result in a right of any holder of securities of the Company to adjust the exercise, conversion, exchange or reset price under any of such securities. All of the outstanding shares of capital stock and other securities of the Company are duly authorized, validly issued, fully paid and nonassessable, have been issued in material compliance with all federal and state securities laws, and none of such outstanding shares was issued in violation of any preemptive rights or similar rights to subscribe for or purchase securities. No further approval or authorization of any stockholder, the Board of Directors or others is required for the issuance and sale of the Securities. Except for the Company's certificate of incorporation, there are no stockholders agreements, voting agreements or other similar agreements with respect to the Company's capital stock to which the Company is a party or, to the knowledge of the Company, between or among any of the Company's stockholders.

(h) Shell Company Status; SEC Reports; Financial Statements. The Company has never been an issuer subject to Rule 144(i) under the Securities Act. The Company has filed all reports, schedules, forms, statements and other documents required to be filed by the Company under the Securities Act and the Exchange Act, including pursuant to Section 13(a) or 15(d) thereof, for the two years preceding February 12, 2019 (or such shorter period as the Company was required by law or regulation to file such material) (the foregoing materials, including the exhibits thereto and documents incorporated by reference therein, being collectively referred to herein as the "SEC Reports") on a timely basis or has received a valid extension of such time of filing and has filed any such SEC Reports prior to the expiration of any such extension. As of their respective dates, the SEC Reports complied in all material respects with the requirements of the Securities Act and the Exchange Act, as applicable, and none of the SEC Reports, when filed, contained any untrue statement of a material fact or omitted to state a material fact required to be stated therein or necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading. The financial statements of the Company included in the SEC Reports comply in all material respects with applicable accounting requirements and the rules and regulations of the Commission with respect thereto as in effect at the time of filing. Such financial statements have been prepared in accordance with generally accepted accounting principles applied on a consistent basis during the periods involved ("GAAP"), except as may be otherwise specified in such financial statements or the notes thereto and except that unaudited financial statements may not contain all footnotes required by GAAP, and fairly present in all material respects the financial position of the Company and its consolidated Subsidiaries as of and for the dates thereof and the results of operations and cash flows for the periods then ended, subject, in the case of unaudited statements, to normal, immaterial, year-end audit adjustments.

(i) Material Changes; Undisclosed Events, Liabilities or Developments. Since the date of the latest audited financial statements included within the SEC Reports, except as specifically disclosed in a subsequent SEC Report filed prior to February 12, 2019: (i) there has been no event, occurrence or development that has had or that could reasonably be expected to result in a Material Adverse Effect, (ii) the Company has not incurred any material liabilities (contingent or otherwise) other than (A) trade payables and accrued expenses incurred in the ordinary course of business consistent with past practice and (B) liabilities not required to be reflected in the Company's financial statements pursuant to GAAP or disclosed in filings made with the Commission, (iii) the Company has not altered its method of accounting, (iv) the Company has not declared or made any dividend or distribution of cash or other property to its stockholders or purchased, redeemed or made any agreements to purchase or redeem any shares of its capital stock, and (v) the Company has not issued any equity securities to any officer, director or Affiliate, except pursuant to existing Company stock option plans. Except for the issuance of the Securities contemplated by this Agreement, no event, liability, fact, circumstance, occurrence or development has occurred or exists or is reasonably expected to occur or exist with respect to the Company or its Subsidiaries or their respective businesses, properties, operations, assets or financial condition, that would be required to be disclosed by the Company under applicable securities laws at the time this representation is made or deemed made that has not been publicly disclosed at least one (1) Trading Day prior to the date that this representation is made.

(j) Litigation. Except as described in the Memorandum or on Schedule 3.1(j), there is no action, suit, inquiry, notice of violation, proceeding or investigation pending or, to the knowledge of the Company, threatened against or affecting the Company, any Subsidiary or any of their respective properties before or by any court, arbitrator, governmental or administrative agency or regulatory authority (federal, state, county, local or foreign) (collectively, an " Action") which (i) adversely affects or challenges the legality, validity or enforceability of any of the Transaction Documents or the Securities or (ii) could, if there were an unfavorable decision, have or reasonably be expected to result in a Material Adverse Effect. Except as described on Schedule 3.1(j), since March 31, 2018, neither the Company nor any Subsidiary, nor any director or officer thereof, is or has been the subject of any Action involving a claim of violation of or liability under federal or state securities laws or a claim of breach of fiduciary duty. There has not been, and to the knowledge of the Company, there is not pending or contemplated, any investigation by the Commission or any state securities administrator involving the Company or any current or former director or officer of the Company. The Commission has not issued any stop order or other order suspending the effectiveness of any registration statement filed by the Company or any Subsidiary under the Exchange Act or the Securities Act.

(k) Compliance. Neither the Company nor any Subsidiary: (i) is in default under or in violation of and no event has occurred that has not been waived that, with notice or lapse of time or is in violation of, any indenture, loan or credit agreement or any other agreement or instrument to which it is a party or by which it or any of its properties is bound (whether or not such default or violation has been waived), (x) is in violation of any judgment, decree or order of any court, arbitrator or other governmental authority or (ii) is or has been in violation of any statute, rule, ordinance or regulation of any governmental authority, including without limitation all foreign, federal, state and local laws relating to taxes, environmental protection, occupational health and safety, product quality and safety and employment and labor matters, except in each case as could not have or reasonably be expected to result in a Material Adverse Effect.

(l) Regulatory Permits. The Company and the Subsidiaries possess all certificates, authorizations and permits issued by the appropriate federal, state, local or foreign regulatory authorities necessary to conduct their respective businesses as presently conducted, except where the failure to possess such permits could not reasonably be expected to result in a Material Adverse Effect ("Material Permits"), and neither the Company nor any Subsidiary has received any notice of proceedings relating to the revocation or modification of any Material Permit.

(m) Title to Assets. Except as described on Schedule 3.1(m), the Company and the Subsidiaries have good and marketable title in fee simple to all real property owned by them and good and marketable title in all personal property owned by them that is material to the business of the Company and the Subsidiaries, in each case free and clear of all Liens, except for (i) Liens as do not materially affect the value of such property and do not materially interfere with the use made and proposed to be made of such property by the Company and the Subsidiaries and (ii) Liens for the payment of federal, state or other taxes, for which appropriate reserves have been made in accordance with GAAP, and the payment of which is neither delinquent nor subject to penalties. Any real property and facilities held under lease by the Company and the Subsidiaries are held by them under valid, subsisting and enforceable leases with which the Company and the Subsidiaries are in compliance.

(n) Intellectual Property.

(i) The term "Intellectual Property Rights" includes:

1. the name of the Company, all fictional business names, trading names, registered and unregistered trademarks, service marks, and applications (collectively, "Marks");

2. all patents, patent applications, and inventions and discoveries that may be patentable (collectively, "Patents");

3. all copyrights in both published works and unpublished works (collectively, "Copyrights");

4. all rights in mask works (collectively, "Rights in Mask Works"); and

5. all know-how, trade secrets, confidential information, customer lists, software, technical information, data, process technology, plans, drawings, and blue prints (collectively, "Trade Secrets") owned, used, or licensed by the Company as licensee or licensor.

(ii) Agreements. Schedule 3.1(n) contains a complete and accurate list of all contracts relating to the Intellectual Property Rights to which the Company is a party or by which the Company is bound, except for any license implied by the sale of a product and perpetual, paid-up licenses for commonly available software programs with a value of less than $10,000 under which the Company is the licensee. There are no outstanding and, to the Company's knowledge, no threatened disputes or disagreements with respect to any such agreement.

(iii) Know-How Necessary for the Business. The Intellectual Property Rights are all those necessary for the operation of the Company's businesses as it is currently conducted or as represented, in writing, to the Purchasers to be conducted. The Company is the owner of all right, title, and interest in and to each of the Intellectual Property Rights, free and clear of all liens, security interests, charges, encumbrances, equities, and other adverse claims, and has the right to use all of the Intellectual Property Rights. To the Company's knowledge, no employee of the Company has entered into any contract that restricts or limits in any way the scope or type of work in which the employee may be engaged or requires the employee to transfer, assign, or disclose information concerning his work to anyone other than of the Company.

(iv) Know-How Necessary for the Business. Schedule 3.1(n) contains a complete and accurate list of all Patents. Except as set forth onSchedule 3.1(j), the Company is the owner of all right, title and interest in and to each of the Patents, free and clear of all Liens and other adverse claims. All of the issued Patents are currently in compliance with formal legal requirements (including payment of filing, examination, and maintenance fees and proofs of working or use), are valid and enforceable, and are not subject to any maintenance fees or taxes or actions falling due within ninety days after the Initial Closing Date. No Patent has been or is now involved in any interference, reissue, reexamination, or opposition proceeding. To the Company's knowledge: (1) there is no potentially interfering patent or patent application of any third party, and (2) no Patent is infringed or has been challenged or threatened in any way. To the Company's knowledge, none of the products manufactured and sold, nor any process or know-how used, by the Company infringes or is alleged to infringe any patent or other proprietary right of any other Person.

(v) Trademarks. Schedule 3.1(n) contains a complete and accurate list and summary description of all Marks. The Company is the owner of all right, title, and interest in and to each of the Marks, free and clear of all Liens and other adverse claims. All Marks that have been registered with the United States Patent and Trademark Office are currently in compliance with all formal legal requirements (including the timely post-registration filing of affidavits of use and incontestability and renewal applications), are valid and enforceable, and are not subject to any maintenance fees or taxes or actions falling due within ninety days after the Initial Closing Date. Except as set forth in Schedule 3.1(n), no Mark has been or is now involved in any opposition, invalidation, or cancellation and, to the Company's knowledge, no such action is threatened with respect to any of the Marks. To the Company's knowledge: (1) there is no potentially interfering trademark or trademark application of any third party, and (2) no Mark is infringed or has been challenged or threatened in any way. To the Company's knowledge, none of the Marks used by the Company infringes or is alleged to infringe any trade name, trademark, or service mark of any third party.

(vi) Copyrights. Schedule 3.1(n) contains a complete and accurate list of all Copyrights. The Company is the owner of all right, title, and interest in and to each of the Copyrights, free and clear of all Liens and other adverse claims. All the Copyrights have been registered and are currently in compliance with formal requirements, are valid and enforceable, and are not subject to any maintenance fees or taxes or actions falling due within ninety days after the date of the Initial Closing. No Copyright is infringed or, to the Company's knowledge, has been challenged or threatened in any way. To the Company's knowledge, none of the subject matter of any of the Copyrights infringes or is alleged to infringe any copyright of any third party or is a derivative work based on the work of a third party. All works encompassed by the Copyrights have been marked with the proper copyright notice.

(vii) Trade Secrets. With respect to each Trade Secret, the documentation relating to such Trade Secret is current, accurate, and sufficient in detail and content to identify and explain it and to allow its full and proper use without reliance on the knowledge or memory of any individual. The Company has taken all reasonable precautions to protect the secrecy, confidentiality, and value of its Trade Secrets. The Company has good title and an absolute (but not necessarily exclusive) right to use the Trade Secrets. The Trade Secrets are not part of the public knowledge or literature, and, to the Company's knowledge, have not been used, divulged, or appropriated either for the benefit of any Person (other than the Company) or to the detriment of the Company. No Trade Secret is subject to any adverse claim or has been challenged or threatened in any way.

(o) Insurance. The Company and the Subsidiaries are insured by insurers of recognized financial responsibility against such losses and risks and in such amounts as are prudent and customary in the businesses in which the Company and the Subsidiaries are engaged, including, but not limited to, directors and officers insurance coverage at least equal to the aggregate Subscription Amount. Neither the Company nor any Subsidiary has any reason to believe that it will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage from similar insurers as may be necessary to continue its business without a significant increase in cost.

(p) Transactions With Affiliates and Employees. Except as set forth in the SEC Reports, none of the officers or directors of the Company or any Subsidiary and, to the knowledge of the Company, none of the employees of the Company or any Subsidiary is presently a party to any transaction with the Company or any Subsidiary (other than for services as employees, officers and directors), including any contract, agreement or other arrangement providing for the furnishing of services to or by, providing for rental of real or personal property to or from, providing for the borrowing of money from or lending of money to or otherwise requiring payments to or from any officer, director or such employee or, to the knowledge of the Company, any entity in which any officer, director, or any such employee has a substantial interest or is an officer, director, trustee, stockholder, member or partner, in each case in excess of $100,000 other than for: (i) payment of salary or consulting fees for services rendered, (ii) reimbursement for expenses incurred on behalf of the Company and (iii) other employee benefits, including stock option agreements under any stock option plan of the Company.

(q) No General Solicitation. Neither the Company nor any person acting on behalf of the Company has offered or sold any of the Securities by any form of general solicitation or general advertising. The Company has offered the Securities for sale only to the Purchasers and certain other "accredited investors" within the meaning of Rule 501 under the Securities Act.

(r) Certain Fees. No brokerage, finder's fees, commissions or due diligence fees are or will be payable by the Company or any Subsidiary to any broker, financial advisor or consultant, finder, placement agent, investment banker, bank or other Person with respect to the transactions contemplated by the Transaction Documents except for the fees payable to the Placement Agent as set forth in the Memorandum and on Schedule 3.1(r). The Purchasers shall have no obligation with respect to any fees or with respect to any claims made by or on behalf of other Persons for fees of a type contemplated in this Section 3.1(r) that may be due in connection with the transactions contemplated by the Transaction Documents.

(s) Investment Company. The Company is not, and is not an Affiliate of, and immediately after receipt of payment for the Securities, will not be or be an Affiliate of, an "investment company" within the meaning of the Investment Company Act of 1940, as amended. The Company shall conduct its business in a manner so that it will not become an "investment company" subject to registration under the Investment Company Act of 1940, as amended.

(t) Registration Rights. Except as described in the Memorandum, no Person other than the Purchasers has any right to cause the Company or any Subsidiary to effect the registration under the Securities Act of any securities of the Company or any Subsidiary.

(u) Private Placement. Assuming the accuracy of the Purchasers' representations and warranties set forth in Section 3.2 and in the Subscription Agreement entered into by each Purchaser in connection with this Agreement, no registration under the Securities Act is required for the offer and sale of the Securities by the Company to the Purchasers as contemplated hereby.

(v) Application of Takeover Protections. The Company and the Board of Directors have taken all necessary action, if any, in order to render inapplicable any control share acquisition, business combination, poison pill (including any distribution under a rights agreement) or other similar anti-takeover provision under the Company's certificate of incorporation (or similar charter documents) or the laws of its state of incorporation that is or could become applicable to the Purchasers as a result of the Purchasers and the Company fulfilling their obligations or exercising their rights under the Transaction Documents, including without limitation as a result of the Company's issuance of the Securities and the Purchasers' ownership of the Securities.

(w) Disclosure. Except with respect to the material terms and conditions of the transactions contemplated by the Transaction Documents, the Company confirms that neither it nor any other Person acting on its behalf has provided any of the Purchasers or their agents or counsel with any information that it believes constitutes or might constitute material, non-public information. The Company understands and confirms that the Purchasers will rely on the foregoing representation in effecting transactions in securities of the Company. All of the disclosure furnished by or on behalf of the Company to the Purchasers regarding the Company and its Subsidiaries, their respective businesses and the transactions contemplated hereby, including the Disclosure Schedules to this Agreement, when taken together as a whole, is true and correct and does not contain any untrue statement of a material fact or omit to state any material fact necessary in order to make the statements made therein, in light of the circumstances under which they were made, not misleading. The Company acknowledges and agrees that no Purchaser makes or has made any representations or warranties with respect to the transactions contemplated hereby other than those specifically set forth in Section 3.2 hereof.

(x) No Integrated Offering. Assuming the accuracy of the Purchasers' representations and warranties set forth in Section 3.2, neither the Company, nor any of its Affiliates, nor any Person acting on its or their behalf has, directly or indirectly, made any offers or sales of any security or solicited any offers to buy any security, under circumstances that would cause this offering of the Securities to be integrated with prior offerings by the Company for purposes of the Securities Act which would require the registration of any such securities under the Securities Act.

(y) Solvency. Based on the consolidated financial condition of the Company as of the Closing Date, and the Company's good faith estimate of the fair market value of its assets, after giving effect to the receipt by the Company of the proceeds from the sale of the Securities hereunder: (i) the fair saleable value of the Company's assets exceeds the amount that will be required to be paid on or in respect of the Company's existing debts and other liabilities (including known contingent liabilities) as they mature, (ii) the Company's assets do not constitute unreasonably small capital to carry on its business as now conducted and as proposed to be conducted including its capital needs taking into account the particular capital requirements of the business conducted by the Company, consolidated and projected capital requirements and capital availability thereof, and (iii) the current cash flow of the Company, together with the proceeds the Company would receive, were it to liquidate all of its assets, after taking into account all anticipated uses of the cash, would be sufficient to pay all amounts on or in respect of its liabilities when such amounts are required to be paid. The Company does not intend to incur debts beyond its ability to pay such debts as they mature (taking into account the timing and amounts of cash to be payable on or in respect of its debt). The Company has no knowledge of any facts or circumstances which lead it to believe that it will file for reorganization or liquidation under the bankruptcy or reorganization laws of any jurisdiction within one year from the Initial Closing Date. Schedule 3.1(y) sets forth as of February 12, 2019 all outstanding secured and unsecured Indebtedness of the Company or any Subsidiary, or for which the Company or any Subsidiary has commitments. For the purposes of this Agreement, "Indebtedness" means (x) any liabilities for borrowed money or amounts owed in excess of $250,000 (other than trade accounts payable incurred in the ordinary course of business), (y) all guaranties, endorsements and other contingent obligations in respect of indebtedness of others, whether or not the same are or should be reflected in the Company's consolidated balance sheet (or the notes thereto), except guaranties by endorsement of negotiable instruments for deposit or collection or similar transactions in the ordinary course of business; and (z) the present value of any lease payments in excess of $250,000 due under leases required to be capitalized in accordance with GAAP. Neither the Company nor any Subsidiary is in default with respect to any Indebtedness.

(z) Tax Status. Except for matters that would not, individually or in the aggregate, have or reasonably be expected to result in a Material Adverse Effect, the Company and its Subsidiaries each (i) has made or filed all United States federal, state and local income and all foreign income and franchise tax returns, reports and declarations required by any jurisdiction to which it is subject, (ii) has paid all taxes and other governmental assessments and charges that are material in amount, shown or determined to be due on such returns, reports and declarations and (iii) has set aside on its books provision reasonably adequate for the payment of all material taxes for periods subsequent to the periods to which such returns, reports or declarations apply. There are no unpaid taxes in any material amount claimed to be due by the taxing authority of any jurisdiction, and the officers of the Company or of any Subsidiary know of no basis for any such claim.

(aa) Foreign Corrupt Practices. Neither the Company nor any Subsidiary, nor to the knowledge of the Company or any Subsidiary, any agent or other person acting on behalf of the Company or any Subsidiary, has: (i) directly or indirectly, used any funds for unlawful contributions, gifts, entertainment or other unlawful expenses related to foreign or domestic political activity, (ii) made any unlawful payment to foreign or domestic government officials or employees or to any foreign or domestic political parties or campaigns from corporate funds, (iii) failed to disclose fully any contribution made by the Company or any Subsidiary (or made by any person acting on its behalf of which the Company is aware) which is in violation of law or (iv) violated in any material respect any provision of FCPA.

(bb) Acknowledgment Regarding Purchasers' Purchase of Securities. The Company acknowledges and agrees that each of the Purchasers is acting solely in the capacity of an arm's length purchaser with respect to the Transaction Documents and the transactions contemplated thereby. The Company further acknowledges that no Purchaser is acting as a financial advisor or fiduciary of the Company (or in any similar capacity) with respect to the Transaction Documents and the transactions contemplated thereby and any advice given by any Purchaser or any of their respective representatives or agents in connection with the Transaction Documents and the transactions contemplated thereby is merely incidental to the Purchasers' purchase of the Securities. The Company further represents to each Purchaser that the Company's decision to enter into this Agreement and the other Transaction Documents has been based solely on the independent evaluation of the transactions contemplated hereby by the Company and its representatives.

(cc) Money Laundering. The operations of the Company and its Subsidiaries are and have been conducted at all times in compliance with applicable financial record-keeping and reporting requirements of the Currency and Foreign Transactions Reporting Act of 1970, as amended, applicable money laundering statutes and applicable rules and regulations thereunder (collectively, the "Money Laundering Laws"), and no action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company or any Subsidiary with respect to the Money Laundering Laws is pending or, to the knowledge of the Company or any Subsidiary, threatened.

(dd) Stock Option Plans. Each stock option granted by the Company under the Company's stock option plan was granted (i) in accordance with the terms of the Company's stock option plan and (ii) with an exercise price at least equal to the fair market value of the Common Stock on the date such stock option would be considered granted under GAAP and applicable law. No stock option granted under the Company's stock option plan has been backdated.

(ee) Sarbanes-Oxley; Internal Accounting Controls. The Company is in material compliance with all provisions of the Sarbanes-Oxley Act of 2002 which are applicable to it as of the Closing Date. The Company and the Subsidiaries maintain a system of internal accounting controls sufficient to provide reasonable assurance that: (i) transactions are executed in accordance with management's general or specific authorizations, (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with GAAP and to maintain asset accountability, (iii) access to assets is permitted only in accordance with management's general or specific authorization, and (iv) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences. The Company has established disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the Company and designed such disclosure controls and procedures to ensure that information required to be disclosed by the Company in the reports it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Commission's rules and forms. The Company's certifying officers have evaluated the effectiveness of the Company's disclosure controls and procedures as of the end of the period covered by the Company's most recently filed periodic report under the Exchange Act (such date, the "Evaluation Date"). The Company presented in its most recently filed periodic report under the Exchange Act the conclusions of the certifying officers about the effectiveness of the disclosure controls and procedures based on their evaluations as of the Evaluation Date. Since the Evaluation Date, there have been no changes in the Company's internal control over financial reporting (as such term is defined in the Exchange Act) that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting.

(ff) Listing and Maintenance Requirements. The Common Stock is registered pursuant to Section 12(b) or 12(g) of the Exchange Act, and the Company has taken no action designed to, or which to its knowledge is likely to have the effect of, terminating the registration of the Common Stock under the Exchange Act nor has the Company received any notification that the Commission is contemplating terminating such registration. The Company has not, in the 12 months preceding February 12, 2019, received notice from any Trading Market on which the Common Stock is or has been listed or quoted to the effect that the Company is not in compliance with the listing or maintenance requirements of such Trading Market. The Company is, and has no reason to believe that it will not in the foreseeable future continue to be, in compliance with all such listing and maintenance requirements.

(gg) Regulation M Compliance. The Company has not, and to its knowledge no one acting on its behalf has, (i) taken, directly or indirectly, any action designed to cause or to result in the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of any of the Securities, (ii) sold, bid for, purchased, or paid any compensation for soliciting purchases of, any of the securities of the Company, or (iii) paid or agreed to pay to any Person any compensation for soliciting another to purchase any other securities of the Company, other than, in the case of clauses (ii) and (iii), compensation paid to the Company's placement agent in connection with the placement of the Securities.

(hh) DTC Status. The Company's transfer agent (the "Transfer Agent") is a participant in and the Common Stock is eligible for transfer pursuant to the Depository Trust Company Automated Securities Transfer Program.

(ii) OFAC. Neither the Company nor, to the Company's knowledge, any director, officer, agent, employee, affiliate or person acting on its behalf, is currently subject to any U.S. sanctions administered by the Office of Foreign Assets Control of the U.S. Treasury Department ("OFAC"); and the Company will not directly or indirectly use the proceeds of the sale of the Units, or lend, contribute or otherwise make available such proceeds to any joint venture partner or other person or entity, towards any sales or operations in Cuba, Iran, Syria, Sudan, Myranmar or any other country sanctioned by OFAC or for the purpose of financing the activities of any person currently subject to any U.S. sanctions.

(jj) FDA. As to each product subject to the jurisdiction of the U.S. Food and Drug Administration ("FDA") under the Federal Food, Drug, and Cosmetic Act, as amended, and the regulations thereunder ("FDCA") that is manufactured, packaged, labeled, stored, tested, distributed, sold, and/or marketed by the Company (each such product, a "Pharmaceutical Product"), such Pharmaceutical Product is being manufactured, packaged, labeled, stored, tested, distributed, sold and/or marketed by the Company in compliance with all applicable requirements under FDCA and similar laws, rules and regulations relating to registration, investigational use, premarket application approval, good manufacturing practices, good laboratory practices, good clinical practices (GCPs), product listing, quotas, labeling, advertising, record keeping and filing of reports, except where the failure to be in compliance would not have or reasonably be expected to result in a Material Adverse Effect. All clinical trials conducted by or on behalf of the Company have been, and are being, conducted in compliance in all material respects with the applicable requirements of GCPs, informed consent and all other applicable requirements relating to protection of human subjects specifically contained in 21 CFR Parts 312, 50, 54, 56 and 11. The Company has filed with the FDA or other appropriate governmental entity all required notices, and annual or other reports, including notices of adverse experiences and reports of serious and unexpected adverse experiences, related to the use of Pharmaceutical Product in clinical trials. The Company has not received any notice that any Institutional Review Board or Ethics Committee has initiated or threatened to initiate any action to suspend any clinical trial or otherwise restrict any clinical trial of any Pharmaceutical Product. There is no pending, completed or, to the Company's knowledge, threatened, action (including any lawsuit, arbitration, or legal or administrative or regulatory proceeding, charge, complaint, or investigation) against the Company, and the Company has not received any notice, warning letter or other communication from the FDA or any other governmental entity, which (i) contests the registration, approval, uses, distribution, manufacturing or packaging, testing, sale, or the labeling and promotion of any Pharmaceutical Product, (ii) withdraws its approval of, requests the recall, suspension, or seizure of, or withdraws or orders the withdrawal of advertising or sales promotional materials relating to, any Pharmaceutical Product, (iii) imposes a clinical hold on any clinical investigation by the Company, (iv) enjoins production at any facility of the Company or any third party facility where the Pharmaceutical Product is manufactured, (v) enters or proposes to enter into a consent decree of permanent injunction with the Company, or (vi) otherwise alleges any violation of any laws, rules or regulations by the Company, and which, either individually or in the aggregate, would have or reasonably be expected to result in a Material Adverse Effect. The properties, business and operations of the Company have been and are being conducted in all material respects in accordance with all applicable laws, rules and regulations of the FDA and any other governmental entity. The Company has not been informed by the FDA or any other governmental entity that the FDA or any other governmental entity will prohibit the testing, distribution, marketing, sale, license or use of any product proposed to be developed, produced, tested, distributed or marketed by the Company nor has the FDA or any other governmental entity expressed any concern as to approving for marketing any product being developed or proposed to be developed by the Company. Neither the Company nor any of its officers, employees, agents or clinical investigators has committed any act, made any statement or failed to make any statement that would reasonably be expected to provide a basis for the FDA to invoke its policy with respect to "Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities" set forth in 56 Fed. Reg. 46191 (Sept. 10, 1991) and any amendments thereto. Neither the Company nor any officer, employee, independent contractor, or agent of the Company has been convicted of any crime or engaged in any conduct that has resulted in or would reasonably be expected to result in (i) debarment under 21 U.S.C. Section 335a or any similar state law or (ii) exclusion under 42 U.S.C. Section 1320a-7 or any similar state law or regulation.

(kk) Health Care Laws. The Company has operated and currently is in compliance in all material respects with all applicable Health Care Laws (defined herein), including, without limitation, the rules and regulations of the FDA, the U.S. Department of Health and Human Services Office of Inspector General, the Centers for Medicare & Medicaid Services, the Office for Civil Rights, the Department of Justice or any other governmental agency or body having jurisdiction over the Company or any of its properties, and has not engaged in activities which are, as applicable, cause for false claims liability, civil penalties, or mandatory or permissive exclusion from Medicare, Medicaid, or any other state or federal health care program. For purposes of this Agreement, "Health Care Laws" shall mean the federal Antikickback Statute (42 U.S.C. § 1320a- 7b(b)), the Physician Payment Sunshine Act (42 U.S.C. § 1320a-7h), the civil False Claims Act (31 U.S.C. §§ 3729 et seq.), the criminal False Claims Act (42 U.S.C. § 1320a-7b(a)), all criminal laws relating to health care fraud and abuse, including but not limited to 18 U.S.C. Sections 286 and 287, and the health care fraud criminal provisions under the Health Insurance Portability and Accountability Act of 1996 (42 U.S.C. §1320d et seq.) ("HIPAA"), the exclusion laws (42 U.S.C. § 1320a-7), the civil monetary penalties law (42 U.S.C. § 1320a-7a), HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (42 U.S.C. §§ 17921 et seq.), the patient privacy, data security and breach notification provisions under HIPAA, the Federal Food, Drug, and Cosmetic Act (21 U.S.C. §§ 301 et seq.), Medicare (Title XVIII of the Social Security Act), Medicaid (Title XIX of the Social Security Act), the regulations promulgated pursuant to such laws, and any other similar local, state or federal law and regulations. The Company has not received any FDA Form 483, notice of adverse finding, warning letter, untitled letter or other correspondence, communication or notice from the FDA or any other governmental or regulatory authority alleging or asserting noncompliance with any Health Care Laws applicable to the Company. The Company is not a party to nor has any ongoing reporting obligations pursuant to any corporate integrity agreements, deferred prosecution agreements, monitoring agreements, consent decrees, settlement orders, plans of correction or similar agreements with or imposed by any governmental or regulatory authority. Neither the Company nor any of its employees, officers, directors or, to the Company's knowledge, consultants has been excluded, suspended or debarred from participation in any U.S. state or federal health care program or human clinical research or, to the Company's knowledge, is subject to a governmental inquiry, investigation, proceeding, or other similar action that could reasonably be expected to result in debarment, suspension, or exclusion

(ll) Bad Actor Disqualification.

(i) No Disqualification Events. With respect to Securities to be offered and sold hereunder in reliance on Rule 506 under the Securities Act ("Regulation D Securities"), none of the Company, any of its predecessors, any affiliated issuer, any director, executive officer, other officer of the Company participating in the offering, any beneficial owner of 20% or more of the Company's outstanding voting equity securities, calculated on the basis of voting power, nor any promoter (as that term is defined in Rule 405 under the Securities Act) connected with the Company in any capacity at the time of sale (each, an "Issuer Covered Person" and, together, "Issuer Covered Persons") is subject to any of the "Bad Actor" disqualifications described in Rule 506(d)(1)(i) to (viii) under the Securities Act (a "Disqualification Event"), except for a Disqualification Event covered by Rule 506(d)(2) or (d)(3). The Company has exercised reasonable care to determine whether any Issuer Covered Person is subject to a Disqualification Event. The Company has complied, to the extent applicable, with its disclosure obligations under Rule 506(e), and has furnished to the Placement Agent and the Subscriber a copy of any disclosures provided thereunder.

(ii) Other Covered Persons. The Company is not aware of any person that (i) has been or will be paid (directly or indirectly) remuneration for solicitation of purchasers in connection with the sale of the Securities and (ii) who is subject to a Disqualification Event.

(iii) Notice of Disqualification Events. The Company will notify the Placement Agent in writing of (i) any Disqualification Event relating to any Issuer Covered Person and (ii) any event that would, with the passage of time, become a Disqualification Event relating to any Issuer Covered Person, prior to any Closing of this Offering.

3.2 Representations and Warranties of the Purchasers. Each of the Purchasers hereby severally, and not jointly, represents and warrants to the Company that each such Purchaser's representations and warranties in such Purchaser's Subscription Agreement entered into in connection with this Agreement are true and correct as of the applicable Closing, and such representations and warranties are deemed repeated as if contained herein.

The Company acknowledges and agrees that the representations contained in Section 3.2 shall not modify, amend or affect such Purchaser's right to rely on the Company's representations and warranties contained in this Agreement or any representations and warranties contained in any other Transaction Document or any other document or instrument executed and/or delivered in connection with this Agreement or the consummation of the transaction contemplated hereby.

ARTICLE IV.
OTHER AGREEMENTS OF THE PARTIES

4.1 Transfer Restrictions.

(a) The Securities may only be disposed of in compliance with state and federal securities laws. In connection with any transfer of Securities other than pursuant to an effective registration statement or Rule 144, to the Company or to an Affiliate of a Purchaser or in connection with a pledge as contemplated in Section 4.1(b), the Company may require the transferor thereof to provide to the Company an opinion of counsel selected by the transferor and reasonably acceptable to the Company, the form and substance of which opinion shall be reasonably satisfactory to the Company, to the effect that such transfer does not require registration of such transferred Securities under the Securities Act. As a condition of transfer, any such transferee shall agree in writing to be bound by the terms of this Agreement and the Registration Rights Agreement and shall have the rights and obligations of a Purchaser under this Agreement and the Registration Rights Agreement.

(b) The Purchasers agree to the imprinting, so long as is required by this Section 4.1, of a legend on any of the Securities in the following form:

[NEITHER] THIS SECURITY [NOR THE SECURITIES FOR WHICH THIS SECURITY IS EXERCISABLE] [HAS NOT] [HAVE] BEEN REGISTERED WITH THE SECURITIES AND EXCHANGE COMMISSION OR THE SECURITIES COMMISSION OF ANY STATE IN RELIANCE UPON AN EXEMPTION FROM REGISTRATION UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT"), AND, ACCORDINGLY, MAY NOT BE OFFERED OR SOLD EXCEPT PURSUANT TO AN EFFECTIVE REGISTRATION STATEMENT UNDER THE SECURITIES ACT OR PURSUANT TO AN AVAILABLE EXEMPTION FROM, OR IN A TRANSACTION NOT SUBJECT TO, THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT AND IN ACCORDANCE WITH APPLICABLE STATE SECURITIES LAWS AS EVIDENCED BY A LEGAL OPINION OF COUNSEL TO THE TRANSFEROR TO SUCH EFFECT, THE SUBSTANCE OF WHICH SHALL BE REASONABLY ACCEPTABLE TO THE COMPANY. THIS SECURITY [AND THE SECURITIES ISSUABLE UPON EXERCISE OF THIS SECURITY] MAY BE PLEDGED IN CONNECTION WITH A BONA FIDE MARGIN ACCOUNT WITH A REGISTERED BROKER-DEALER OR OTHER LOAN WITH A FINANCIAL INSTITUTION THAT IS AN "ACCREDITED INVESTOR" AS DEFINED IN RULE 501(a) UNDER THE SECURITIES ACT OR OTHER LOAN SECURED BY SUCH SECURITIES.

The Company acknowledges and agrees that a Purchaser may from time to time pledge pursuant to a bona fide margin agreement with a registered broker-dealer or grant a security interest in some or all of the Securities to a financial institution that is an "accredited investor" as defined in Rule 501(a) under the Securities Act and who agrees to be bound by the provisions of this Agreement and the Registration Rights Agreement and, if required under the terms of such arrangement, such Purchaser may transfer, pledge or secure Securities to the pledgees or secured parties. Such a pledge or transfer would not be subject to approval of the Company and no legal opinion of legal counsel of the pledgee, secured party or pledgor shall be required in connection therewith. Further, no notice shall be required of such pledge. At the applicable Purchaser's expense, the Company will execute and deliver such reasonable documentation as a pledgee or secured party of Securities may reasonably request in connection with a pledge or transfer of the Securities, including, if the Securities are subject to registration pursuant to the Registration Rights Agreement, the preparation and filing of any required prospectus supplement under Rule 424(b)(3) under the Securities Act or other applicable provision of the Securities Act to appropriately amend the list of selling stockholders thereunder.

(c) Certificates evidencing the Offering Shares shall not contain any legend (including the legend set forth in Section 4.1(b) hereof): (i) while a registration statement (including the Registration Statement) covering the resale of such security is effective under the Securities Act, (ii) following any sale of such Offering Shares pursuant to Rule 144, (iii) if such Offering Shares are eligible for sale under Rule 144, without the requirement for the Company to be in compliance with the current public information required under Rule 144 as to such Offering Shares and without volume or manner-of-sale restrictions, (iv) if such legend is not required under applicable requirements of the Securities Act (including judicial interpretations and pronouncements issued by the staff of the Commission) or (v) following the Effective Date. Upon the receipt by the Company of any reasonable certifications from the Purchasers requested by the Company with respect to future sales of such Offering Shares, the Company shall cause its counsel to issue a legal opinion to the Transfer Agent if required by the Transfer Agent to effect the removal of the legend hereunder. The Company agrees that following such time as such legend is no longer required under this Section 4.1(c), it will, as soon as practicable following the delivery by a Purchaser to the Company or the Transfer Agent of a certificate representing Offering Shares issued with a restrictive legend and, in each case, any reasonable certifications from the Purchaser requested by the Company or the Company's counsel in order to effectuate a legend removal, deliver or cause to be delivered to such Purchaser a certificate representing such shares that is free from all restrictive and other legends. The Company may not make any notation on its records or give instructions to the Transfer Agent that enlarge the restrictions on transfer set forth in this Section 4. Certificates for Offering Shares subject to legend removal hereunder shall be transmitted by the Transfer Agent to the Purchaser by crediting the account of the Purchaser's prime broker with the Depository Trust Company System as directed by such Purchaser if the Company is then a participant in such system.

(d) Each Purchaser, severally and not jointly with the other Purchasers, agrees with the Company that such Purchaser will sell any Securities pursuant to either the registration requirements of the Securities Act, including any applicable prospectus delivery requirements, or an exemption therefrom, and that if Securities are sold pursuant to a Registration Statement, they will be sold in compliance with the plan of distribution set forth therein, and acknowledges that the removal of the restrictive legend from certificates representing Securities as set forth in this Section 4.1 is predicated upon the Company's reliance upon this understanding.

4.2 Acknowledgment of Dilution. The Company acknowledges that the issuance of the Securities may result in dilution of the outstanding shares of Common Stock, which dilution may be substantial under certain market conditions. The Company further acknowledges that its obligations under the Transaction Documents, including, without limitation, its obligation to issue the Investor Warrant Shares pursuant to the Transaction Documents, are unconditional and absolute and not subject to any right of set off, counterclaim, delay or reduction, regardless of the effect of any such dilution or any claim the Company may have against any Purchaser and regardless of the dilutive effect that such issuance may have on the ownership of the other stockholders of the Company.

4.3 Furnishing of Information; Public Information. Commencing on the Effective Date, and until the earliest of the time that (a) no Purchaser owns Securities or (b) the Investor Warrants have expired, the Company covenants to have obtained and will thereafter maintain the registration of the Common Stock under Section 12(b) or 12(g) of the Exchange Act and to timely file (or obtain extensions in respect thereof and file within the applicable grace period) all reports required to be filed by the Company after February 12, 2019 pursuant to the Exchange Act even if the Company is not then subject to the reporting requirements of the Exchange Act.

4.4 Integration. The Company shall not sell, offer for sale or solicit offers to buy or otherwise negotiate in respect of any security (as defined in Section 2 of the Securities Act) that would be integrated with the offer or sale of the Securities in a manner that would require the registration under the Securities Act of the sale of the Securities or that would be integrated with the offer or sale of the Securities for purposes of the rules and regulations of any Trading Market such that it would require shareholder approval prior to the closing of such other transaction unless shareholder approval is obtained before the closing of such subsequent transaction.

4.5 Exercise Procedures. The form of Notice of Exercise included in the Investor Warrants sets forth the totality of the procedures required of the Purchasers in order to exercise the Investor Warrants. No additional legal opinion, other information or instructions shall be required of the Purchasers to exercise their Investor Warrants. The Company shall honor exercises of the Investor Warrants and shall deliver Investor Warrant Shares in accordance with the terms, conditions and time periods set forth in the Transaction Documents.

4.6 Securities Laws Disclosure; Publicity. The Company shall, by 5:30 p.m. (New York City time) on the fourth Trading Day immediately following February 12, 2019, file a Current Report on Form 8-K and press release disclosing the material terms of the transactions contemplated hereby, including the Transaction Documents as exhibits thereto. From and after the issuance of such press release, the Company represents to the Purchasers that it shall have publicly disclosed all material, non- public information delivered to any of the Purchasers by the Company or any of its Subsidiaries, or any of their respective officers, directors, employees or agents in connection with the transactions contemplated by the Transaction Documents. The Company and each Purchaser shall consult with each other in issuing any other press releases with respect to the transactions contemplated hereby, and neither the Company nor any Purchaser shall issue any such press release nor otherwise make any such public statement without the prior consent of the Company, with respect to any press release of any Purchaser, or without the prior consent of each Purchaser, with respect to any press release of the Company, which consent shall not unreasonably be withheld or delayed, except if such disclosure is required by law, in which case the disclosing party shall promptly provide the other party with prior notice of such public statement or communication. Notwithstanding the foregoing, the Company shall not publicly disclose the name of any Purchaser, or include the name of any Purchaser in any filing with the Commission or any regulatory agency or Trading Market, without the prior written consent of such Purchaser, except: (a) as required by federal securities law in connection with (i) any registration statement contemplated by the Registration Rights Agreement and (ii) the filing of final Transaction Documents (including conformed signature pages thereto) with the Commission and (b) to the extent such disclosure is required by law or Trading Market regulations, in which case the Company shall provide the Purchasers with prior notice of such disclosure permitted under this clause (b).

4.7 Non-Public Information. Except with respect to the material terms and conditions of the transactions contemplated by the Transaction Documents, the Company covenants and agrees that neither it, nor any other Person acting on its behalf, will provide any Purchaser or its agents or counsel with any information that the Company believes constitutes material non-public information, unless prior thereto such Purchaser shall have executed a written agreement with the Company regarding the confidentiality and use of such information or is an Affiliate of the Company. The Company understands and confirms that each Purchaser shall be relying on the foregoing covenant in effecting transactions in securities of the Company.

4.8 Use of Proceeds. The Company shall use the net proceeds from the sale of the Securities hereunder for general corporate purposes including, but not limited to, growth initiatives and capital expenditures, and shall not use such proceeds: (a) for the satisfaction of any portion of the Company's debt (other than payment of trade payables in the ordinary course of the Company's business and prior practices), (b) for the redemption of any Common Stock or Common Stock Equivalents or (c) the settlement of any outstanding litigation.

4.9 Indemnification of Purchasers. Subject to the provisions of this Section 4.9, the Company will indemnify and hold each Purchaser and its directors, officers, shareholders, members, partners, employees and agents (and any other Persons with a functionally equivalent role of a Person holding such titles notwithstanding a lack of such title or any other title), each Person who controls such Purchaser (within the meaning of Section 15 of the Securities Act and Section 20 of the Exchange Act), and the directors, officers, shareholders, agents, members, partners or employees (and any other Persons with a functionally equivalent role of a Person holding such titles notwithstanding a lack of such title or any other title) of such controlling persons (each, a "Purchaser Party") harmless from any and all losses, liabilities, obligations, claims, contingencies, damages, costs and expenses, including all judgments, amounts paid in settlements, court costs and reasonable attorneys' fees and costs of investigation that any such Purchaser Party may suffer or incur as a result of or relating to (a) any breach of any of the representations, warranties, covenants or agreements made by the Company in this Agreement or in the other Transaction Documents or (b) any action instituted against Purchaser Parties in any capacity, or any of them or their respective Affiliates, by any stockholder of the Company who is not an Affiliate of such Purchaser Party, with respect to any of the transactions contemplated by the Transaction Documents (unless such action is based upon a breach of such Purchaser Party's representations, warranties or covenants under the Transaction Documents or any agreements or understandings such Purchaser Party may have with any such stockholder or any violations by such Purchaser Party of state or federal securities laws or any conduct by such Purchaser Party which constitutes fraud, gross negligence, willful misconduct or malfeasance). If any action shall be brought against any Purchaser Party in respect of which indemnity may be sought pursuant to this Agreement, such Purchaser Party shall promptly notify the Company in writing, and the Company shall have the right to assume the defense thereof with counsel of its own choosing reasonably acceptable to the Purchaser Party. Any Purchaser Party shall have the right to employ separate counsel in any such action and participate in the defense thereof, but the fees and expenses of such counsel shall be at the expense of such Purchaser Party except to the extent that (i) the employment thereof has been specifically authorized by the Company in writing, (ii) the Company has failed after a reasonable period of time to assume such defense and to employ counsel or (iii) in such action there is, in the reasonable opinion of counsel, a material conflict on any material issue between the position of the Company and the position of such Purchaser Party, in which case the Company shall be responsible for the reasonable fees and expenses of no more than one such separate counsel. The Company will not be liable to any Purchaser Party under this Agreement (y) for any settlement by a Purchaser Party effected without the Company's prior written consent, which shall not be unreasonably withheld or delayed; or (z) to the extent, but only to the extent that a loss, claim, damage or liability is attributable to any Purchaser Party's breach of its representations, warranties or covenants under the Transaction Documents or any agreements or understandings such Purchaser Party may have with any such stockholder or any violations by such Purchaser Party of state or federal securities laws or any conduct by such Purchaser Party which constitutes fraud, gross negligence, willful misconduct or malfeasance. The indemnification required by this Section 4.9 shall be made by periodic payments of the amount thereof during the course of the investigation or defense, as and when bills are received or are incurred. The indemnity agreements contained herein shall be in addition to any cause of action or similar right of any Purchaser Party against the Company or others and any liabilities the Company may be subject to pursuant to law.

4.10 Reservation and Listing of Securities.

(a) The Company shall maintain a reserve from its duly authorized shares of Common Stock for issuance pursuant to the Transaction Documents in such amount as may then be required to fulfill its obligations in full under the Transaction Documents (the "Required Minimum").

(b) If, on any date, the number of authorized but unissued (and otherwise unreserved) shares of Common Stock is less than the Required Minimum on such date, then the Board of Directors shall use commercially reasonable efforts to amend the Company's certificate of incorporation to increase the number of authorized but unissued shares of Common Stock to at least the Required Minimum at such time, as soon as possible and in any event not later than the 60th day after such date.

(c) The Company shall take all steps necessary to cause the Offering Shares to be approved for listing and actually listed on the Company's principal Trading Market, if any.

4.11 Equal Treatment of Purchasers. No consideration (including any modification of any Transaction Document) shall be offered or paid to any Person to amend or consent to a waiver or modification of any provision of any of this Agreement unless the same consideration is also offered to all of the parties to this Agreement. For clarification purposes, this provision constitutes a separate right granted to each Purchaser by the Company and negotiated separately by each Purchaser, and is intended for the Company to treat the Purchasers as a class and shall not in any way be construed as the Purchasers acting in concert or as a group with respect to the purchase, disposition or voting of Securities or otherwise.

4.12 Certain Transactions and Confidentiality. Each Purchaser, severally and not jointly with the other Purchasers, covenants that neither it, nor any Affiliate acting on its behalf or pursuant to any understanding with it will execute any purchases or sales, including Short Sales, of any of the Company's securities during the period commencing with the execution of this Agreement and ending at such time that the transactions contemplated by this Agreement are first publicly announced pursuant to the initial press release as described in Section 4.6. Each Purchaser, severally and not jointly with the other Purchasers, covenants that until such time as the transactions contemplated by this Agreement are publicly disclosed by the Company pursuant to the initial press release as described in Section 4.6, such Purchaser will maintain the confidentiality of the existence and terms of this transaction and the information included in the Transaction Documents and the Disclosure Schedules. Notwithstanding the foregoing, and notwithstanding anything contained in this Agreement to the contrary, the Company expressly acknowledges and agrees that (i) no Purchaser makes any representation, warranty or covenant hereby that it will not engage in effecting transactions in any securities of the Company after the time that the transactions contemplated by this Agreement are first publicly announced pursuant to the initial press release as described in Section 4.6, (ii) no Purchaser shall be restricted or prohibited from effecting any transactions in any securities of the Company in accordance with applicable securities laws from and after the time that the transactions contemplated by this Agreement are first publicly announced pursuant to the initial press release as described in Section 4.6 and (iii) no Purchaser shall have any duty of confidentiality to the Company or its Subsidiaries after the issuance of the initial press release as described in Section 4.6. Notwithstanding the foregoing, in the case of a Purchaser that is a multi-managed investment vehicle whereby separate portfolio managers manage separate portions of such Purchaser's assets and the portfolio managers have no direct knowledge of the investment decisions made by the portfolio managers managing other portions of such Purchaser's assets, the covenant set forth above shall only apply with respect to the portion of assets managed by the portfolio manager that made the investment decision to purchase the Securities covered by this Agreement.

4.13 Form D; Blue Sky Filings. The Company agrees to timely file a Form D with respect to the Securities as required under Regulation D. The Company shall take such action as the Company shall reasonably determine is necessary in order to obtain an exemption for, or to qualify the Securities for, sale to the Purchasers at each Closing under applicable securities or "Blue Sky" laws of the states of the United States, and shall provide evidence of such actions promptly upon request of any Purchaser.

ARTICLE V.
MISCELLANEOUS

5.1 Termination. This Agreement may be terminated by any Purchaser, as to such Purchaser's obligations hereunder only and without any effect whatsoever on the obligations between the Company and the other Purchasers, by written notice to the other parties, if the Initial Closing has not been consummated on or before September 30, 2018; provided, however, that such date may be extended, without notice, to December 31, 2018 with the consent of the Company and the Placement Agent; provided, further, however, that such termination will not affect the right of any party to sue for any breach by any other party (or parties).

5.2 Fees and Expenses. Except as expressly set forth in the Transaction Documents to the contrary, each party shall pay the fees and expenses of its advisers, counsel, accountants and other experts, if any, and all other expenses incurred by such party incident to the negotiation, preparation, execution, delivery and performance of this Agreement. The Company shall pay all Transfer Agent fees, stamp taxes and other taxes and duties levied in connection with the delivery of any Securities to the Purchasers.

Notwithstanding the foregoing, the Company agrees to pay promptly all of the Placement Agent's legal fees reasonably incurred in connection with the negotiation, preparation, execution, delivery and performance of this Agreement and the other Transaction Documents. Subject to the following qualifications, such legal fees shall not exceed $75,000 in the aggregate, and are exclusive of disbursements and any fees incurred in connection with the contemplated Registration Statement (the "Cap"). In the event that there should be a material change in the transactions contemplated hereby, then the Placement Agent and the Company agree to a good faith upward adjustment in the Cap. Such legal fees will be due and payable as follows: fifty percent (50%) of such legal fees incurred to date shall be paid at the Initial Closing and the remainder shall be paid at each subsequent Closing together with any additional legal fees incurred from the date of the prior Closing until such subsequent Closing, subject always to the Cap. Notwithstanding the foregoing, if there be no Closing hereunder, then such legal fees shall be due and payable on demand. The Placement Agent shall deliver an invoice from the Placement Agent's counsel detailing such legal fees at least one (1) Business Day prior to the Initial Closing and each subsequent Closing.

5.3 Entire Agreement. The Transaction Documents, together with the exhibits and schedules thereto, contain the entire understanding of the parties with respect to the subject matter hereof and thereof and supersede all prior agreements and understandings, oral or written, with respect to such matters, which the parties acknowledge have been merged into such documents, exhibits and schedules.

5.4 Participation Rights. Until February 12, 2020, Purchaser shall have the right to participate in the Company's offerings of equity securities. Notwithstanding the foregoing:

(a) such Purchaser's beneficial ownership of common stock of the Company shall not exceed 4.99% of the issued and outstanding common stock of the Company, with such ownership percentage to be calculated as of the closing of such future offerings;

(b) such Purchaser acknowledges and agrees that with respect to any registered offering of securities of the Company:

(i) the forgoing right does not constitute an offer to acquire securities of the Company,

(ii) such right shall only be effective with respect to any given registered offering upon the filing by the Company with the Commission of a final prospectus with respect thereto, and

(iii) with respect to any underwritten registered offering of securities of the Company, any exercise of such rights by such Purchaser shall be contingent upon such Purchaser delivering customary indications of interest to the applicable underwriters with respect thereto; and

(c) such right shall not apply to any issuance of equity securities being issued (i) as compensation to officers, directors or consultants to the Company, or (ii) in connection with mergers, acquisitions, strategic alliances or similar transactions, the principal purpose of which is not capital raising.

The Company hereby covenants and agrees, prior to the time of consummation if any registered offering of securities of the Company, to file a final prospectus with the Commission with respect thereto.

5.5 Notices. Any and all notices or other communications or deliveries required or permitted to be provided hereunder shall be in writing and shall be deemed given and effective on the earliest of: (a) the date of transmission, if such notice or communication is delivered via facsimile at the facsimile number set forth on the signature pages attached hereto at or prior to 5:30 p.m. (New York City time) on a Trading Day, (b) the next Trading Day after the date of transmission, if such notice or communication is delivered via facsimile at the facsimile number set forth on the signature pages attached hereto on a day that is not a Trading Day or later than 5:30 p.m. (New York City time) on any Trading Day, (c) the second (2nd) Trading Day following the date of mailing, if sent by U.S. nationally recognized overnight courier service or (d) upon actual receipt by the party to whom such notice is required to be given. The address for such notices and communications shall be as set forth on the signature pages attached hereto.

5.6 Amendments; Waivers. No provision of this Agreement may be waived, modified, supplemented or amended except in a written instrument signed, in the case of an amendment, by the Company and the Purchasers holding at least 67% in interest of the Securities then outstanding, or in the case of a waiver, by the party against whom enforcement of any such waived provision is sought. No waiver of any default with respect to any provision, condition or requirement of this Agreement shall be deemed to be a continuing waiver in the future or a waiver of any subsequent default or a waiver of any other provision, condition or requirement hereof, nor shall any delay or omission of any party to exercise any right hereunder in any manner impair the exercise of any such right.

5.7 Headings. The headings herein are for convenience only, do not constitute a part of this Agreement and shall not be deemed to limit or affect any of the provisions hereof.

5.8 Successors and Assigns. This Agreement shall be binding upon and inure to the benefit of the parties and their successors and permitted assigns. The Company may not assign this Agreement or any rights or obligations hereunder without the prior written consent of each Purchaser (other than by merger). Any Purchaser may assign any or all of its rights under this Agreement to any Person to whom such Purchaser assigns or transfers any Securities, provided that such transferee agrees in writing to be bound, with respect to the transferred Securities, by the provisions of the Transaction Documents that apply to the "Purchasers."

5.9 No Third-Party Beneficiaries. This Agreement is intended for the benefit of the parties hereto and their respective successors and permitted assigns and is not for the benefit of, nor may any provision hereof be enforced by, any other Person, except as otherwise set forth in Section 4.9.

5.10 Governing Law. The Transaction Documents will be governed by and construed under the laws of the State of New York as applied to agreements among New York residents entered into and to be performed entirely within New York. The parties hereto (1) agree that any legal suit, action or proceeding arising out of or relating to this Agreement will be instituted exclusively in New York State Supreme Court, County of New York, or in the United States District Court for the Southern District of New York, (2) waive any objection which the parties may have now or hereafter to the venue of any such suit, action or proceeding, and (3) irrevocably consent to the jurisdiction of the New York State Supreme Court, County of New York, and the United States District Court for the Southern District of New York in any such suit, action or proceeding. Each of the parties hereto further agrees to accept and acknowledge service of any and all process which may be served in any such suit, action or proceeding in the New York State Supreme Court, County of New York, or in the United States District Court for the Southern District of New York and agrees that service of process upon it mailed by certified mail to its address will be deemed in every respect effective service of process upon it, in any such suit, action or proceeding. If either party shall commence an action or proceeding to enforce any provisions of the Transaction Documents, then, in addition to the obligations of the Company under Section 4.9, the prevailing party in such action, suit or proceeding shall be reimbursed by the other party for its reasonable attorneys' fees and other costs and expenses incurred with the investigation, preparation and prosecution of such action or proceeding. THE PARTIES HERETO AGREE TO WAIVE THEIR RESPECTIVE RIGHTS TO A JURY TRIAL OF ANY CLAIM OR CAUSE OF ACTION BASED UPON OR ARISING OUT OF THIS AGREEMENT OR ANY DOCUMENT OR AGREEMENT CONTEMPLATED HEREBY.

5.11 Survival. The representations and warranties contained herein shall survive the Closing and the delivery of the Securities.

5.12 Execution. This Agreement may be executed in two or more counterparts, all of which when taken together shall be considered one and the same agreement and shall become effective when counterparts have been signed by each party and delivered to each other party, it being understood that the parties need not sign the same counterpart. In the event that any signature is delivered by facsimile transmission or by e-mail delivery of a ".pdf" format data file, such signature shall create a valid and binding obligation of the party executing (or on whose behalf such signature is executed) with the same force and effect as if such facsimile or ".pdf" signature page were an original thereof.

5.13 Severability. If any term, provision, covenant or restriction of this Agreement is held by a court of competent jurisdiction to be invalid, illegal, void or unenforceable, the remainder of the terms, provisions, covenants and restrictions set forth herein shall remain in full force and effect and shall in no way be affected, impaired or invalidated, and the parties hereto shall use their commercially reasonable efforts to find and employ an alternative means to achieve the same or substantially the same result as that contemplated by such term, provision, covenant or restriction. It is hereby stipulated and declared to be the intention of the parties that they would have executed the remaining terms, provisions, covenants and restrictions without including any of such that may be hereafter declared invalid, illegal, void or unenforceable.

5.14 Rescission and Withdrawal Right. Notwithstanding anything to the contrary contained in (and without limiting any similar provisions of) any of the other Transaction Documents, whenever any Purchaser exercises a right, election, demand or option under a Transaction Document and the Company does not timely perform its related obligations within the periods therein provided, then such Purchaser may rescind or withdraw, in its sole discretion from time to time upon written notice to the Company, any relevant notice, demand or election in whole or in part without prejudice to its future actions and rights; provided, however, that in the case of a rescission of an exercise of an Investor Warrant, the applicable Purchaser shall be required to return any shares of Common Stock subject to any such rescinded exercise notice concurrently with the return to such Purchaser of the aggregate exercise price paid to the Company for such shares and the restoration of such Purchaser's right to acquire such shares pursuant to such Purchaser's Investor Warrant (including, issuance of a replacement warrant certificate evidencing such restored right).

5.15 Replacement of Securities. If any certificate or instrument evidencing any Securities is mutilated, lost, stolen or destroyed, the Company shall issue or cause to be issued in exchange and substitution for and upon cancellation thereof (in the case of mutilation), or in lieu of and substitution therefor, a new certificate or instrument, but only upon receipt of evidence reasonably satisfactory to the Company of such loss, theft or destruction. The applicant for a new certificate or instrument under such circumstances shall also pay any reasonable third-party costs (including customary indemnity) associated with the issuance of such replacement Securities.

5.16 Remedies. In addition to being entitled to exercise all rights provided herein or granted by law, including recovery of damages, each of the Purchasers and the Company will be entitled to specific performance under the Transaction Documents. The parties agree that monetary damages may not be adequate compensation for any loss incurred by reason of any breach of obligations contained in the Transaction Documents and hereby agree to waive and not to assert in any action for specific performance of any such obligation the defense that a remedy at law would be adequate.

5.17 Payment Set Aside. To the extent that the Company makes a payment or payments to any Purchaser pursuant to any Transaction Document or a Purchaser enforces or exercises its rights thereunder, and such payment or payments or the proceeds of such enforcement or exercise or any part thereof are subsequently invalidated, declared to be fraudulent or preferential, set aside, recovered from, disgorged by or are required to be refunded, repaid or otherwise restored to the Company, a trustee, receiver or any other Person under any law (including, without limitation, any bankruptcy law, state or federal law, common law or equitable cause of action), then to the extent of any such restoration the obligation or part thereof originally intended to be satisfied shall be revived and continued in full force and effect as if such payment had not been made or such enforcement or setoff had not occurred.

5.18 Independent Nature of Purchasers' Obligations and Rights . The obligations of each Purchaser under any Transaction Document are several and not joint with the obligations of any other Purchaser, and no Purchaser shall be responsible in any way for the performance or non-performance of the obligations of any other Purchaser under any Transaction Document. Nothing contained herein or in any other Transaction Document, and no action taken by any Purchaser pursuant hereto or thereto, shall be deemed to constitute the Purchasers as a partnership, an association, a joint venture or any other kind of entity, or create a presumption that the Purchasers are in any way acting in concert or as a group with respect to such obligations or the transactions contemplated by the Transaction Documents. Each Purchaser shall be entitled to independently protect and enforce its rights, including, without limitation, the rights arising out of this Agreement or out of the other Transaction Documents, and it shall not be necessary for any other Purchaser to be joined as an additional party in any proceeding for such purpose. Each Purchaser has been represented by its own separate legal counsel in its review and negotiation of the Transaction Documents. The Company has elected to provide all Purchasers with the same terms and Transaction Documents for the convenience of the Company and not because it was required or requested to do so by any of the Purchasers. It is expressly understood and agreed that each provision contained in this Agreement and in each other Transaction Document is between the Company and a Purchaser, solely, and not between the Company and the Purchasers collectively and not between and among the Purchasers.

5.19 Saturdays, Sundays, Holidays, etc. If the last or appointed day for the taking of any action or the expiration of any right required or granted herein shall not be a Business Day, then such action may be taken or such right may be exercised on the next succeeding Business Day.

5.20 Construction. The parties agree that each of them and/or their respective counsel have reviewed and had an opportunity to revise the Transaction Documents and, therefore, the normal rule of construction to the effect that any ambiguities are to be resolved against the drafting party shall not be employed in the interpretation of the Transaction Documents or any amendments thereto. In addition, each and every reference to share prices and shares of Common Stock in any Transaction Document shall be subject to adjustment for reverse and forward stock splits, stock dividends, stock combinations and other similar transactions of the Common Stock that occur after the date of this Agreement.

5.21 WAIVER OF JURY TRIAL. IN ANY ACTION, SUIT, OR PROCEEDING IN ANY JURISDICTION BROUGHT BY ANY PARTY AGAINST ANY OTHER PARTY, THE PARTIES EACH KNOWINGLY AND INTENTIONALLY, TO THE GREATEST EXTENT PERMITTED BY APPLICABLE LAW, HEREBY ABSOLUTELY, UNCONDITIONALLY, IRREVOCABLY AND EXPRESSLY WAIVES FOREVER TRIAL BY JURY.

5.22 Liquidated Damages. The Company's obligations to pay any partial liquidated damages or other amounts owing under the Transaction Documents is a continuing obligation of the Company and shall not terminate until all unpaid partial liquidated damages and other amounts have been paid notwithstanding the fact that the instrument or security pursuant to which such partial liquidated damages or other amounts are due and payable shall have been canceled.

(Signature Pages Follow)

IN WITNESS WHEREOF, the parties hereto have caused this AMENDED AND RESTATED UNIT PURCHASE AGREEMENT to be duly executed by their respective authorized signatories as of the date first indicated above.

RELMADA THERAPEUTICS, INC.

Address for Notice:

880 Third Avenue 12th Floor
New York, NY 10022

By: /s/ *Sergio Traversa*
Name: Sergio Traversa
Title: CEO

With a copy to (which shall not constitute notice):

Thomas Slusarczyk, Esq.
The Matt Law Firm, PLLC
1701 Genesee Street
Utica, NY 135011

Exhibit 10.2

AMENDMENT NO. 1 TO LICENSE AGREEMENT

This **Amendment No. 1 to License Agreement** (this "Amendment"), dated as of December 2, 2019, is made by and between **Relmada Therapeutics, Inc.**, a Nevada corporation ("Licensee") and Dr. Charles E. Inturrisi, an individual, and Dr. Paolo Manfredi, an individual, jointly and severally (collectively, "Licensor").

Whereas, the parties have previously entered into that certain License Agreement dated as of January 16, 2018 (the "License Agreement") (capitalized terms used herein but not otherwise defined shall have the meaning ascribed to such terms in the License Agreement); and

Whereas, the parties now desire to amend the License Agreement as set forth herein.

Now, Therefore, in consideration of the foregoing, of the mutual promises set forth herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto, intending legally to be bound, hereby agree as follows:

ARTICLE I

Amendment of License Agreement

1.1. Article 1, Section 1.3 of the License Agreement is hereby deleted in its entirety and replaced with the following:

"1.3 "Cause" shall mean: that the Licensee has elected to terminate Mr. Traversa's employment with Licensee either (A) because a majority of the members of Licensee's Board of Directors (the "Board") has reasonably determined in good faith (after allowing Mr. Traversa the opportunity to address the alleged wrongdoing with the Board at a duly called meeting of the Board) that Mr. Traversa has done any of the following: (i) failure by Mr. Traversa to perform his duties and responsibilities to the Licensee (or a Successor Company, as defined in Dr. Traversa's employment agreement with the Licensee, if appropriate) or gross negligence or gross incompetence in the performance of his duties, after written notice thereof and a failure to remedy such failure, if remediable, within sixty (60) days of such notice; (ii) commission by Mr. Traversa of any act of fraud, embezzlement, dishonesty or any other misconduct that has caused or is reasonably expected to cause material injury to the Licensee (or a Successor Company, if appropriate), including commission of conduct constituting a felony or crime involving fraud, moral turpitude or dishonesty; (iii) unauthorized use or disclosure by Mr. Traversa of any confidential information of the Licensee (or a Successor Company, if appropriate) or of any other party to whom Mr. Traversa owes an obligation of nonuse and nondisclosure as a result of his relationship with the Licensee (or a Successor Company, if appropriate); (iv) Mr. Traversa engaging in conduct prohibited by a Licensee (or Successor Company, if appropriate) policy governing harassment and discrimination; (v) material breach by Mr. Traversa of any of Mr. Traversa's obligations under any written agreement with the Licensee (or a Successor Company, if appropriate) after written notice thereof and a failure to remedy such breach, if remediable, within sixty (60) days of such notice; or (vi) breach of fiduciary duty or (B) because of Mr. Traversa's Disability. " Disability" shall mean that Mr. Traversa is unable due to a physical or mental condition to perform the essential functions of his position with or without reasonable accommodation for ninety (90) consecutive days or for one-hundred and eighty (180) days in the aggregate during any twelve (12) month period or based on the written certification by a licensed physician of the likely continuation of such condition for either such period."

1.2. Article 7, Section 7.1(a)(iii) is hereby deleted in its entirety and replaced with the following:

"(iii) Licensee (for the avoidance of doubt, inclusive of any successors or assigns of Licensee) terminates Mr. Traversa's employment for any reason other than for Cause prior to the later of the date five (5) years from the Effective Date or December 31, 2022 (the "Key Man Term"); provided, (A) for the avoidance of doubt, that neither the termination of Mr. Traversa's employment due to his death nor the election by Mr. Traversa to terminate his employment, regardless of reason, is a termination by Licensee for purposes of this Agreement, and (B) if Mr. Traversa is terminated due to Disability or death during the Key Man Term then Licensor shall appoint a replacement for Mr. Traversa with the consent of Licensee and the Board, which shall not be unreasonably withheld or delayed, within 30 days for the remainder of the Key Man Term, and such replacement shall have the responsibility (i) for decision-making relating to development and marketing of d-Methadone and (ii) consenting if Licensee assigns or sells its rights to the Licensed IP and/or Related Licensed IP to another Person pursuant to Section 9.2(b);"

1.3. Article 7, Section 7.1(a)(iv) is hereby deleted in its entirety and replaced with the following:

"(iv) Licensee (for the avoidance of doubt, inclusive of any successors or assigns of Licensee) prior to the later of the date five (5) years from the Effective Date or December 31, 2022: (A) removes Mr. Traversa from the position of Chief Executive Officer of Licensee without his written consent for any reason other than for Cause or his death, except in connection with or following any transaction of a type permitting Licensee to assign this Agreement to a third party without the consent of Licensor pursuant to Section 9.2(b); (B) changes Mr. Traversa's job responsibilities such that he is no longer the executive responsible for decision-making relating to development and marketing of d-Methadone without his written consent for any reason other than for Cause or his death, (C) decreases Mr. Traversa's compensation without his written consent for any reason other than for Cause or his death, or (D) assigns or sells its rights to the Licensed IP and/or Related Licensed IP to another Person pursuant to Section 9.2(b) without the written consent of Mr. Traversa, provided that, except as set forth in Section 7.1(a)(iii)(B) above), the written consent of Mr. Traversa shall not be required if Mr. Traversa has been terminated for Cause or due to his death prior to the time of such assignment or sale;"

ARTICLE II

General

2.1. **Continuation**. Except as expressly modified in Article 1, the License Agreement shall remain in full force and effect.

2.2. **Governing Law**. This Amendment shall be governed by, and construed in accordance with (A) the laws of the United States, in respect to trademark and patent issues, except that the scope and validity of any foreign Patent or trademark shall be governed by the applicable laws of the country of the Patent or trademark, and (B) in all other respects, including as to validity (except for patent and trademark issues), interpretation and effect, by the laws of the State of New York without giving effect to the conflict of laws rules thereof. The parties hereby consent to the sole and exclusive jurisdiction of the courts of the state of New York, in the county of New York, or the United States Federal District Court for the Southern District of New York for purposes of any action or proceeding brought by either of them on or in connection with this Amendment on any alleged breach thereof and waive any right to assert any rights or defenses within any other jurisdiction or to require that litigation regarding this Amendment take place elsewhere. Notwithstanding the foregoing, either party may apply to any court of competent jurisdiction for injunctive relief or any other appropriate relief.

2.3. **Headings.** The section headings contained in this Amendment are set forth for the convenience of the Parties only, do not form a part of this Amendment and are not to be considered a part hereof for the purpose of construction or interpretation hereof, or otherwise.

2.4. **Counterparts**. This Amendment may be executed and delivered in any number of counterparts including PDF, facsimile, or other electronic counterparts, each of which will be an original, but all of which together will constitute one instrument.

2.5. **Severability.** In the event any one or more of the provisions of this Amendment should for any reason be held by any court or authority having jurisdiction over this Amendment or any of the Parties to be invalid, illegal or unenforceable, such provision or provisions shall be validly reformed to as nearly as possible approximate the intent of the Parties and, if unformable, shall be divisible and deleted in such jurisdiction; elsewhere, this Amendment shall not be affected so long as the Parties are still able to realize the principal benefits bargained for in this Amendment.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the Parties hereto have caused this Amendment to be duly executed as of the Effective Date.

LICENSOR

Dr. Charles E. Inturrisi and Dr. Paolo Manfredi

By: /s/ Charles E. Inturrisi
Dr. Charles E. Inturrisi

By: /s/ Paolo Manfredi
Dr. Paolo Manfredi

LICENSEE

Relmada Therapeutics, Inc.

By: /s/ Sergio Traversa
Name: Sergio Traversa
Title: Chief Executive Officer

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Current Report on Form 8-K (this Report) contains forward looking statements that involve risks and uncertainties. All statements other than statements of historical fact contained in this Report, including statements regarding future events, our future financial performance, business strategy and plans and objectives of management for future operations, are forward-looking statements. We have attempted to identify forward-looking statements by terminology including "anticipates," "believes," "can," "continue," "could," "estimates," "expects," "intends," "may," "plans," "potential," "predicts," "should," or "will" or the negative of these terms or other comparable terminology. Although we do not make forward-looking statements unless we believe we have a reasonable basis for doing so, we cannot guarantee their accuracy. These statements are only predictions and involve known and unknown risks, uncertainties and other factors, including the risks outlined under "Risk Factors" or elsewhere in this Report, which may cause our or our industry's actual results, levels of activity, performance or achievements to differ materially from those expressed or implied by these forward-looking statements. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time and it is not possible for us to predict all risk factors, nor can we address the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause our actual results to differ materially from those contained in any forward-looking statements. All forward-looking statements included in this document are based on information available to us on the date hereof, and we assume no obligation to update any such forward-looking statements.

You should not place undue reliance on any forward-looking statement, each of which applies only as of the date of this Report. Before you invest in our securities, you should be aware that the occurrence of the events described in the section entitled "Risk Factors" and elsewhere in this Report could negatively affect our business, operating results, financial condition and stock price. Except as required by law, we undertake no obligation to update or revise publicly any of the forward-looking statements after the date of this Report to conform our statements to actual results or changed expectations.

BUSINESS

Business Overview

Relmada Therapeutics, Inc. (Relmada, the Company, we, our or us) (a Nevada corporation), is a clinical-stage biotechnology company focused on the development of d-methadone (dextromethadone, REL-1017), an N-methyl-D-aspartate (NMDA) receptor antagonist. d-methadone is a new chemical entity (NCE) that potentially addresses areas of high unmet medical need in the treatment of central nervous system (CNS) diseases and other disorders.

On October 7, 2019, our application to list our common stock on the Nasdaq Capital Market was approved. On October 10, 2019, our common stock began trading on Nasdaq under our existing symbol, "RLMD."

Our lead product candidate, d-methadone, is an NCE being developed as a rapidly acting, oral agent for the treatment of depression and other potential indications. We have previously completed Phase 1 single and multiple ascending dose studies and on October 15, 2019 we reported top-line data from study REL-1017-202, a double-blind, placebo-controlled Phase 2a clinical trial evaluating the safety, tolerability and efficacy of two doses of REL-1017, 25 mg once a day and 50 mg once a day, as an adjunctive treatment in patients with treatment resistant depression (TRD).

Subjects were adults with major depressive disorder (MDD), who did not respond to one to three courses of antidepressant treatment in their current episode and are typically classified as having TRD. 62 subjects, average age 49.2 years, with an average Hamilton Depression Rating Scale score of 25.3 and an average Montgomery-Asberg Depression Rating Scale (MADRS) score of 34.0 (severe depression), were randomized. Other demographic characteristics were balanced across all arms. After an initial screening period, subjects were randomized to one of three arms: placebo, REL-1017 25 mg or REL-1017 50 mg, in addition to stable background antidepressant therapy. Subjects in the REL-1017 treatment arms received one loading dose of either 75 mg (25 mg arm) or 100 mg (50 mg arm) of REL-1017. Subjects were treated inpatient for 7 days and discharged home at Day 9. They returned for follow-up visits at Day 14 and Day 21. Efficacy was measured on Days 2, 4 and 7 in the dosing period and on Day 14, one week after treatment discontinuation. 61 subjects received all treatment doses and were included in the per-protocol population (PPP) treatment analysis; 57 subjects completed all visits. All 62 randomized subjects were part of the intention-to-treat population (ITT) analysis. No differences were observed between the ITT and PPP analyses and results.

Key findings:

We observed that subjects in both the REL-1017 25 mg and 50 mg treatment groups experienced statistically significant improvement of on all efficacy measures tested as compared to subjects in the placebo group, including: the Montgomery-Asberg Depression Rating Scale (MADRS); the Clinical Global Impression – Severity (CGI-S) scale; the Clinical Global Impression – Improvement (CGI-I) scale; and the Symptoms of Depression Questionnaire (SDQ). SDQ scores demonstrated moderate effect size differences between subjects receiving REL-1017 and a placebo from day 4 to day 7 and demonstrated statistically significant differences and large effect size for both 25 mg (P=0.0066; d=0.9) and 50 mg (P=0.0014; d=1.1) arms at day 14.

The improvement on the MADRS appeared on Day 4 in both REL-1017 dose groups and continued through Day 7 and Day 14, seven days after treatment discontinuation, with P values< 0.03 and large effect sizes (a measure of quantifying the difference between two groups), ranging from 0.7 to 1.0. Similar findings emerged from the CGI-S and CGI-I scales.

MADRS: Analysis of Change from Baseline to Day 7 and to Day 14 ITT Population

	Day 2			Day 4			Day 7			Day 14		
	LS Means Difference	P-value	d	LS Means Difference	P-value	d	LS Means Difference	P-value	D	LS Means Difference	P-value	d
REL-1017 25mg vs Placebo	-1.9	0.4340	0.3	-7.9	0.0087	0.9	-8.7	0.0122	0.8	-9.4	0.0103	0.9
REL-1017 50mg vs Placebo	-0.3	0.9092	0.0	-7.6	0.0096	0.8	-7.2	0.0308	0.7	-10.4	0.0039	1.0

LS = Least Squares; d = Cohen's effect size

The study also supported the favorable tolerability profile of REL-1017, which was also observed in the Phase 1 studies. Subjects experienced mild and moderate adverse events (AEs), and no serious adverse events, without significant differences between placebo and treatment groups. The AEs observed in the Phase 2a clinical study were of the same nature as those observed in the Phase 1 clinical studies in d-Methadone, and there was no evidence of either treatment induced psychotomimetic and dissociative AEs or withdrawal signs and symptoms upon treatment discontinuation.

NMDA receptors are present in many parts of the central nervous system and play important roles in regulating neuronal activity. We believe that d-methadone acting as a NMDA receptor antagonist can have potential applications in a number of disease indications which mitigates risk and offers significant upside.

In addition to REL-1017, we have a portfolio of three Section 505(b)(2) product candidates at various stages of development. These product candidates are: LevoCap ER (REL-1015), a sustained release dosage form of the opioid analgesic levorphanol designed to be abuse deterrent; BuTab (oral buprenorphine, REL-1028), an oral dosage form of the opioid analgesic buprenorphine; and MepiGel (topical mepivacaine, REL-1021), an orphan drug designated, topical formulation of the local anesthetic mepivacaine. These products are not currently in active development.

Key Upcoming Anticipated Milestones

We expect multiple key milestones over the next 12-18 months (our fiscal year ends June 30; however, the anticipated milestones set forth below refer to calendar year periods). These include:

- Presentation of full details of the Phase 2a data for REL-1017 in TRD in the first half of 2020.
- Meeting with the U.S. Food and Drug Administration (FDA) in an End-of-Phase 2 meeting for REL-1017 in TRD at the end of the first half of 2020.
- Start of pivotal studies for TRD. We intend to propose a Phase 3 study design of REL-1017 in TRD at the End-of-Phase 2 meeting with the FDA.
- Start of Phase 2 study in MDD. At the End-of-Phase 2 meeting with the FDA, we intend to also propose a Phase 2 study design of REL-1017 in MDD. We plan to start both the Phase 3 TRD and Phase 2 MDD studies in the second half of 2020, though development plans may be delayed based on the FDA's feedback and other factors.

Our Development Programs

Our four development projects are briefly described below:

d-methadone (dextromethadone, REL-1017) and Treatment-Resistant Depression (TRD)

Background

In 2014, the National Institute of Mental Health (NIMH) estimated that 15.7 million adults aged 18 or older in the United States had at least one major depressive episode in the past year. According to data from nationally representative surveys supported by NIMH, only about half of Americans diagnosed with major depression in a given year receive treatment. Of those receiving treatment with as many as four different standard antidepressants, 33% of drug-treated depression patients do not achieve adequate therapeutic benefits according to the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial published in the American Journal of Psychiatry. In 2017, approximately 17.3 million people in the United States suffered from MDD and approximately 10 to 30% of patients suffered from TRD.

In addition to the high failure rate, none of the marketed products for depression can demonstrate rapid antidepressant effects and currently approved products can take two to four weeks to show activity. The urgent need for improved, faster acting antidepressant treatments is underscored by the fact that severe depression can be life-threatening, due to heightened risk of suicide.

Recent studies have shown that ketamine, a drug known previously as an anesthetic, can lift depression in many patients within hours. However, we believe it is unlikely that ketamine itself will become a practical treatment for most cases of depression. It must be administered through intravenous infusion, requiring a hospital setting, and more importantly can potentially trigger adverse side effects including psychedelic symptoms (hallucinations, memory defects, panic attacks), nausea/vomiting, somnolence, cardiovascular stimulation and, in a minority of patients, hepatoxicity. Ketamine also has not been thoroughly studied for long-term safety and effectiveness, and the FDA has not approved it to treat depression.

d-methadone Overview and Mechanism of Action

d-methadone's mechanism of action, as a non-competitive NMDA channel blocker or antagonist, is fundamentally differentiated from all currently FDA-approved antidepressants, as well as all atypical antipsychotics used adjunctively with standard, FDA-approved antidepressants. Working through the same brain mechanisms as ketamine but potentially lacking its adverse side effects, d-methadone is being developed as a rapidly acting, oral agent for the treatment of depression, neuropathic pain, and/or other potential CNS pathological conditions.

In chemistry an enantiomer, also known as an optical isomer, is one of two stereoisomers that are mirror images of each other that are non-superposable (not identical), much as one's left and right hands are the same except for being reversed along one axis. A racemic compound, or racemate, is one that has equal amounts of left- and right-handed enantiomers of a chiral molecule. For racemic drugs, often only one of a drug's enantiomers is responsible for the desired physiologic effects, while the other enantiomer is less active or inactive.

Methadone is a highly lipophilic molecule that is suitable for a variety of administration routes, with oral bioavailability close to 80%.

As a single isomer of racemic methadone, d-methadone has been shown to possess NMDA antagonist properties with virtually no traditional opioid effect or ketamine-like adverse events at the expected therapeutic doses. In contrast, racemic methadone is associated with common opioid activity and side effects that include anxiety, nervousness, restlessness, sleep problems (insomnia), nausea, vomiting, constipation, diarrhea, drowsiness, and others. It has been shown that the left (levo) isomer, l-methadone, is largely responsible for methadone's opioid activity, while the right (dextro) isomer, d-methadone, at the currently therapeutic doses used in development is virtually inactive as an opioid while maintaining affinity for the NMDA receptor.

NMDA receptors are present in many parts of the central nervous system and play important roles in regulating neuronal activity and promoting synaptic plasticity in brain areas important for cognitive functions such as executive function, learning and memory. Based on these premises, we believe d-methadone could show benefits in several different CNS indications.

d-Methadone Phase 1 Clinical Safety Studies

The safety data from two Company-funded d-methadone Phase 1 clinical safety studies and a third study conducted by researchers at Memorial Sloan-Kettering Cancer Center indicate that d-methadone was well tolerated in both healthy subjects and cancer patients at all therapeutic doses tested.

In November 2014, Health Canada approved a Clinical Trial Application (CTA) to conduct the first Phase 1 study with d-methadone. This was a Single Ascending Dose (SAD) study and was followed by a Multiple Ascending Dose (MAD) study, both in healthy volunteers. The two studies were designed to assess the safety, tolerability and pharmacokinetics of d-methadone in healthy, opioid-naïve subjects. The SAD study included single escalating oral doses of d-methadone to determine the maximum tolerated dose, defined as the highest dose devoid of unacceptable adverse events. In the MAD study, healthy subjects received daily oral doses of d-methadone for several days to assess its safety, pharmacokinetics and tolerability. In March 2015, we reported that d-methadone demonstrated an acceptable safety profile with no dose limiting side effects after four cohorts were exposed to increasing higher doses. In April 2015, we received clearance from Health Canada to continue with dose escalation and explore even higher single doses of d-methadone. In June 2015, we successfully completed the SAD study identifying the maximum tolerated dose and subsequently received a No Objection Letter (NOL) from Health Canada to conduct the MAD clinical study in August 2015. The MAD study was completed in January 2016 and the results successfully demonstrated a potential therapeutic dosing regimen for d-methadone with a favorable side effect and tolerability profile. The data from these studies were used to design the Phase 2a study in patients with TRD.

d-Methadone In Vivo Animal Study for Depression

In May 2016, we announced the results of an in vivo study showing that administration of d-methadone resulted in antidepressant-like effects in a well-validated animal model of depression, known as the forced swim test (FST), providing preclinical support for its potential as a novel treatment of depression.

According to the Journal of Visualized Experiments, the FST is based on the assumption that when placing an animal in a container filled with water, it will first make efforts to escape by swimming or climbing, but eventually will exhibit "immobility" that may be considered to reflect a measure of behavioral despair. This test has been extensively used because it involves the exposure of the animals to stress, which was shown to have a role in the tendency for major depression. Additionally, the FST has been shown to be influenced by some of the factors that are altered by or worsen depression in humans, including changes in food consumption and sleep abnormalities. The main advantages of the FST is that it is relatively easy to perform and its results are easily and quickly analyzed. Importantly, the FST's sensitivity to a broad range of antidepressant drugs makes it a suitable screening test and is one of the most important features leading to its high predictive validity.

In our FST study, male Sprague Dawley rats were administered single doses of placebo, ketamine, or d-methadone on day one (after habituation; 24 hours prior to forced swim testing). At all doses tested, d-methadone induced statistically significant decrease of immobility of the rats compared to the placebo, suggesting antidepressant-like activity. In addition, the effect of d-methadone on immobility at the two highest doses tested was larger than the effect seen with ketamine. Moreover, the effects of d-methadone in the forced swim test were not caused by a stimulant effect on spontaneous locomotor activity of the rats. Locomotor activity of lab animals is often monitored to assess the behavioral effects of drugs.

In September 2017, we completed two additional in vivo studies to further assess the antidepressant-like effect of d-methadone in validated animal models, the Novelty Suppressed Feeding Test (NSFT) and the Female Urine-Sniffing test (FUST) test. The studies were performed by Professor Ronald S. Duman, Ph.D. at Yale University School of Medicine.

For FUST, rats are first exposed to a cotton tip dipped in tap water and later exposed to another cotton tip infused with fresh female urine. Male behavior was video recorded and total time spent sniffing the cotton-tipped applicator is determined. For NSFT, rats were food deprived for 24 hours and then placed in an open field with food pellets in the center; latency to eat is recorded in seconds. As a control, food consumption in the home cage is quantified. Rats were administered vehicle, ketamine or d-methadone.

The results of the FUST demonstrate that administration of ketamine induced a statistically significant increase of the time male rats spent engaged in sniffing female urine compared to vehicle group. Similarly, a single dose of d-methadone produced a statistically significant increase of the time spent sniffing female urine compared to vehicle. In contrast, ketamine or d-methadone had no effect on time sniffing water, demonstrating that the effect of drug treatment was specific to the rewarding effects of female urine. The results of the NSFT demonstrate that a single dose of ketamine significantly decreased the latency to eat in a novel open field. Similarly, a single dose of d-methadone also significantly decreased the latency to enter and eat in the novel feed. In contrast, neither ketamine nor methadone influenced latency to feed in the home cage.

These findings demonstrate that ketamine and d-methadone produce rapid antidepressant actions in the FUST and NSFT, effects that are only observed after chronic administration of an SSRI antidepressant.

A separate in vitro electrophysiology study of d-methadone was conducted using 2 subtypes of cloned human NMDA receptors.

The results of this study demonstrated functional antagonist activity with d-methadone comparable to that of both racemic ketamine and the isomer S-ketamine.

Phase 2a Study for d-Methadone

Combined with the results of our Phase 1 studies, the encouraging results of in vivo and in vitro studies supported further evaluation of d-methadone. We submitted an Investigational New Drug (IND) application for the Phase 2a study in TRD with the FDA, which was accepted on January 25, 2017.

In April 2017, we announced that the FDA granted Fast Track designation for d-methadone (REL-1017; dextromethadone) for the adjunctive treatment of major depressive disorder. Fast Track designation is a process designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need. The purpose, according to the FDA, is to get important new drugs to the patient earlier. Drugs that receive Fast Track designation may be eligible for more frequent meetings and written communications with the FDA, priority review and priority approval, and rolling New Drug Application (NDA) review.

In January 2018, we announced that we had acquired the global rights to develop and market d-methadone for the treatment of neurological conditions including certain rare diseases with symptoms affecting the CNS.

In February 2018, we initiated our Phase 2a study of d-methadone in patients with TRD who did not respond to one to three courses of antidepressant treatment in their current episode.

In July 2019, we announced the completion of dosing of the last patient in our Phase 2a study of d-methadone in patients with TRD.

In October 2019, we reported top-line data from the Phase 2a study of d-methadone in adults with TRD. Subjects in both dose groups experienced statistically significant improvement of their depression compared to subjects in the placebo group on all efficacy measures used in the study, including: the MADRS, the CGI-S, the CGI-I and the SDQ. The improvement on the MADRS appeared on Day 4 in both REL-1017 dose groups and continued through Day 7 and Day 14, seven days after treatment discontinuation, with P values< 0.03 and large effect sizes (a measure of quantifying the difference between two groups), ranging from 0.7 to 1.0. Similar findings emerged from the CGI-S and CGI-I scales. The study also supported the favorable tolerability profile of d-methadone, which was also observed in the Phase 1 studies. Subjects experienced mild and moderate AEs, and no serious adverse events, without significant differences between placebo and treatment groups. The AEs observed in the Phase 2a clinical study were of the same nature as those observed in the Phase 1 clinical studies in d-Methadone, and there was no evidence of either treatment induced psychotomimetic and dissociative AEs or withdrawal signs and symptoms upon treatment discontinuation.

d-methadone (dextromethadone, REL-1017) in other indications

In addition to developing d-methadone in TRD, we are initiating work in additional indications that include MDD and Rett syndrome. Rett syndrome is an X-linked neurodevelopmental disorder with high unmet need caused by Mecp2 gene mutation. Loss of Mecp2 disrupts synaptic function and structure and neuronal networks. Rett syndrome is an Orphan Disease affecting ~15,000 in U.S., primarily girls, with no approved therapy. The disease begins with a short period of developmental stagnation, then rapid regression in language and motor skills, followed by long-term stability.

Studies of ketamine, a NMDAR antagonist with a mechanism of action similar to that of d-methadone, in Rett Syndrome mouse models showed that low-dose ketamine acutely reverses multiple disease manifestations and chronic administration of ketamine improved Rett Syndrome progression, providing a solid rationale to pursue this indication with d-methadone.

Restless leg syndrome is another potential indication we may pursue in the future.

LevoCap ER (REL-1015)

LevoCap ER (REL-1015) is a novel formulation of an approved drug product. LevoCap ER is an extended release, proprietary formulation of levorphanol (levo-3-hydroxy-N-methyl-morphinan), a unique, broad spectrum opioid with additional “non-opioid” mechanisms of action. LevoCap ER is designed to be abuse deterrent. In particular, levorphanol binds to all three opioid receptor subtypes involved in analgesia (mu, kappa, and delta), the NMDA receptor, and the norepinephrine and serotonin reuptake pumps, whereas morphine, oxycodone, hydrocodone, and other opioids are highly selective for the mu receptor subtype. Due to its multi-modal mechanism of action, levorphanol could achieve analgesia in patients resistant to other strong opioids. In clinical studies, levorphanol demonstrated a broad spectrum of analgesic activity against many different types of pain including neuropathic pain, post-surgical pain, and chronic pain in patients refractory to other opioids.

Levorphanol is a potent opioid analgesic first introduced in the United States around 1953 for the treatment of moderate to severe pain where an opioid analgesic is appropriate. Extended-release (long-acting opioid) agents may be preferable to immediate release formulations due to better patient adherence, less dose-watching, and result in improved sleep. Both immediate- and extended-release opioids can potentially be crushed to produce concentrated drug with greater appeal to abusers. Intentional crushing or extracting the active ingredient from the extended-release dosage form can destroy the timed-release mechanism and result in a rapid surge of drug into the bloodstream for the purpose of achieving a high or euphoric feeling. Serious side effects and death have been reported from such misuse.

LevoCap ER is the first product candidate utilizing SECUREL™, our proprietary abuse deterrent extended release technology for opioid drugs. According to data on the formulation characteristics contained in the patent, SECUREL™ dosage forms cannot be easily crushed for inhalation or to obtain rapid euphoria from high blood levels when swallowed. It is also difficult for intravenous abusers to extract the active drug from the dosage form using common solvents, including alcohol.

We believe LevoCap ER can be developed under the Section 505(b)(2) regulatory pathway. Following a meeting with the FDA in January 2017, we believe we have defined a path forward for a Phase 3 clinical study for LevoCap ER and an NDA submission. In light of the promising data generated by our d-methadone research program, and our focus on the d-methadone program, we are currently limiting our investments in LevoCap ER.

BuTab (REL-1028)

BuTab (REL-1028) represents a novel formulation of oral, modified release buprenorphine as a potential therapeutic for both chronic pain and opioid dependence. Buprenorphine has been widely used by the sublingual and transdermal routes of administration, but was believed to be ineffective by the oral route because of poor oral bioavailability. We have completed a preclinical study to better define the pharmacokinetic profile of BuTab and to assess the time course of systemic absorption of buprenorphine using several different oral modified release formulations of buprenorphine in dogs, compared to an intravenous administration. Based on the results of this work, we obtained approval from Health Canada and initiated a Phase 1 pharmacokinetic study in healthy volunteers in the second quarter of 2015. This trial was completed in the fourth quarter of 2015. The absolute bioavailability of BuTab relative to intravenous (IV) administration exceeded published data with non-modified buprenorphine when administered orally and compares favorably with a currently marketed transdermal patch. There were no tolerability issues observed. The data generated by this study will guide formulation optimization and inform the design of subsequent clinical pharmacology studies. BuTab can be developed under the Section 505(b)(2) regulatory pathway. In light of the promising data generated by our d-methadone research program, and our focus on the d-methadone program, we are currently limiting our investments in BuTab.

MepiGel (REL-1021)

MepiGel (REL-1021), is a proprietary topical dosage form of the local anesthetic mepivacaine for the treatment of painful peripheral neuropathies, such as painful diabetic neuropathy, postherpetic neuralgia and painful HIV-associated neuropathy. Mepivacaine is an anesthetic (numbing medicine) that blocks the nerve impulses that send pain signals to the brain. It is chemically related to bupivacaine but pharmacologically related to lidocaine. Mepivacaine is currently indicated for infiltration, nerve block and epidural anesthesia. We have received two FDA Orphan Drug Designations for mepivacaine, one each for “the treatment of painful HIV-associated neuropathy” and for “the management of postherpetic neuralgia” (PHN). We have selected the formulations to be advanced into clinical studies for MepiGel after the evaluation of results from in vitro and ex vivo studies comparing various topical prototypes of mepivacaine that were conducted by MedPharm Ltd, a specialist formulation development company recognized internationally for its expertise in topical and transdermal products. Multiple toxicology studies were successfully conducted and completed in 2015. We believe MepiGel can be developed under the Section 505(b)(2) regulatory pathway. In light of the promising data generated by our d-methadone research program, and our focus on the d-methadone program, we are currently limiting our investments in MepiGel.

Overview of the 505(b)(2) Pathway

Part of our strategy is the utilization of FDA’s Section 505(b)(2) NDA for approval. The Section 505(b)(2) NDA is one of three drug approval pathways and represents an appealing regulatory strategy for many companies. The pathway was created by the Hatch-Waxman Amendments of 1984, with Section 505(b)(2) referring to a section of the Federal Food, Drug, and Cosmetic Act. The provisions of Section 505(b)(2) were created, in part, to help avoid unnecessary duplication of studies already performed on a previously approved drug; the section enables the applicant to rely on FDA’s prior findings in approving a similar product or published literature in support of its application.

A Section 505(b)(2) NDA contains full safety and effectiveness reports but permits the submission of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference. If the Section 505(b)(2) applicant can establish that reliance on the FDA's prior findings of safety and/or effectiveness is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. This can result in a less expensive and faster development program, compared with a traditional development path, while creating new, differentiated products with tremendous commercial value.

Overview of Orphan Drug Status

A sponsor may request that a regulatory agency designate a drug intended to treat a rare disease or condition as an Orphan Drug. For example, in the United States, a rare disease or condition is defined as one which affects less than 200,000 people in the United States, or which affects more than 200,000 people but for which the cost of developing and making available the product is not expected to be recovered from sales of the product in the United States. Upon the approval of the first NDA for a drug designated as an orphan drug for a specified indication, the sponsor of that NDA is entitled to 7 years of exclusive marketing rights in the United States unless the sponsor cannot assure the availability of sufficient quantities to meet the needs of persons with the disease. In Europe, this exclusivity is 10 years, and in Australia it is 5 years. However, orphan drug status is particular to the approved indication and does not prevent another company from seeking approval of a drug that has other labeled indications that are not protected by orphan drug or other exclusivities. Orphan drugs may also be eligible for federal income tax credits for costs associated with such as the disease state, the strength and complexity of the data presented, the novelty of the target or compound, risk-management approval and whether multiple rounds of review are required for the agency to evaluate the submission. There is no guarantee that a potential treatment will receive marketing approval or that decisions on marketing approvals or treatment indications will be consistent across geographic areas.

Our Corporate History and Background

We are a clinical-stage biotechnology company developing NCEs and novel versions of proven drug products that potentially address areas of high unmet medical need in the treatment of depression and other CNS diseases.

Currently, none of our product candidates have been approved for sale in the United States or elsewhere. We have no commercial products nor do we have a sales or marketing infrastructure. In order to market and sell our products we must conduct clinical trials on patients and obtain regulatory approvals from appropriate regulatory agencies, like the FDA in the United States, and similar organizations elsewhere in the world.

We have not generated revenues and do not anticipate generating revenues for the foreseeable future. We had net loss of $17,318,000 and $8,961,000 for the years ended June 30, 2019 and June 30, 2018, respectively. At June 30, 2019, we have an accumulated deficit of $111,662,000.

Business Strategy

Our strategy is to leverage our industry experience, understanding of CNS markets and development expertise to identify, develop and commercialize product candidates with significant market potential that can fulfill unmet medical needs in the treatment of CNS diseases. We have assembled a management team along with both scientific and business advisors, including recognized experts in the fields of depression, with significant industry and regulatory experience to lead and execute the development and commercialization of d-methadone.

We plan to further develop d-methadone as our priority program. As the drug d-methadone is an NCE, the regulatory pathway required to support and NDA submission will consist of conducting a full clinical development program. Depending on the resources available to us, we may also develop REL-1028, REL-1015, REL-1021 via the Section 505(b)(2) regulatory pathway. We would anticipate, if approved, obtaining three-year exclusivity under the Hatch-Waxman Act for the new indications for those products and also orphan drug exclusivity in certain indications. We plan to also generate intellectual property (IP) that will further protect our products from competition. We will continue to prioritize our product development activities after taking into account the resources we have available, market dynamics and potential for adding value. We plan to continue to outsource development of our product candidates, while retaining scientific, operational and financial oversight and control.

Market Opportunity

We believe that the market for addressing areas of high unmet medical need in the treatment of CNS diseases will continue to be large for the foreseeable future and that it will represent a sizable revenue opportunity for us. For example, the World Health Organization (WHO) has estimated that CNS diseases affect nearly 2 billion people globally, making up approximately 40% of total disease burden (based on disability adjusted life years), compared with 13% for cancer and 12% for cardiovascular disease. We also believe that each of our product candidates is designed to have value added features that will provide product related competitive advantages versus the existing drugs available on the market.

The depression treatment market is segmented on the basis of antidepressants drugs, devices, and therapies. Antidepressants are the largest and most popular market segment. The antidepressants segment consists of large pharmaceutical and generic companies, such as Eli Lily, Pfizer, GlaxoSmithKline, Allergan, Sage Therapeutics and Johnson & Johnson. Some of the popular drugs produced by these companies are Cymbalta® (Eli Lily), Effexor® (Pfizer), Pristiq® (Pfizer), Zulresso (Sage) and Spravato (Johnson & Johnson).

Intellectual Property Portfolio and Market Exclusivity

We have secured three Orphan Drug Designations from the FDA: 1) d-methadone for "the treatment of postherpetic neuralgia"; 2) MepiGel for "the treatment of painful HIV-associated neuropathy"; and MepiGel for "the management of postherpetic neuralgia." Each would, upon NDA approval, carry 7-year FDA Orphan Drug marketing exclusivity. In the European Union, some of our products may be eligible up to 10 years of market exclusivity, which includes 8 years data exclusivity and 2 years market exclusivity. In addition to any granted patents, our products will be eligible for market exclusivity to run concurrently with the term of the patent for 3 years in the U.S. (Hatch Waxman plus pediatric exclusivity) and up to 10 years of in the E.U. We believe an extensive intellectual property estate of several patents will protect our technology and products once our patent applications for our products are approved.

The following is a summary of our patents and patent applications:

Levorphanol:

US Patent No. 9,125,833, filed 4/26/08, granted on 9/8/15. Multimodal Abuse Resistant and Extended Release Opioid Formulations. Owned by Relmada. Estimated expiry in 2029. This patent may cover the SECUREL technology platform and Relmada's lead product candidate, LevoCap ER (REL-1015, levorphanol extended-release, abuse deterrent capsules) as well as providing additional coverage for multiple opioid molecules that are prone to abuse.

EU patent No. 2,448,406, filed 2/26/10, granted on 4/20/16. Extended Release Oral Pharmaceutical Compositions of 3-Hydroxy-N-Methylmorphinan and Method of Use. Owned by Relmada. Estimated expiry in 2030.

U.S. Patent application 12/223,327 filed 1/29/07, Abuse Resistant and Extended Release Formulations and Method of Use Thereof. Owned by Relmada. Currently pending.

U.S. Patent application 13/320,989 filed 2/26/10 Extended Release Oral Pharmaceutical Compositions of 3-Hydroxy-N-Methylmorphinan and Method of Use. Owned by Relmada. Currently pending.

EP Patent Application No. 16158311.7 filed 2/26/10, Extended Release Oral Pharmaceutical. Owned by Relmada. Currently pending.

d-Methadone:

U.S. Patent No. 9,468,611 issued on 10/18/2016 (filed 3/14/2013), “d-Methadone for the Treatment of Psychiatric Symptoms.” Licensed to Relmada. Estimated expiry in 2033.

U.S. Patent No. 9,855,226 issued on 1/2/2018 (filed 7/7/2016), “d-Methadone for the Treatment of Psychiatric Symptoms.” Licensed to Relmada. Estimated expiry in 2033.

U.S. Patent Application No. 15/884,915 (filed 1/31/2018), “Compounds for the treatment or prevention of disorders of the Nervous system and symptoms and manifestations thereof, and for cyto-protection against diseases and aging of cells and symptoms and manifestations thereof.”

Australian Patent No. 2013323645 issued on 2/15/2018 (filed 9/25/2013), “d-Methadone for the Treatment of Psychiatric Symptoms.” Licensed to Relmada. Estimated expiry in 2033.

European Patent No. 2,906,209 granted on 6/20/2018 (filed 9/25/2013), “d-Methadone for the Treatment of Psychiatric Symptoms.” Licensed to Relmada. Estimated expiry in 2033.

Australian Patent Application No. 2017276189 (filed 9/25/2013), “d-Methadone for the Treatment of Psychiatric Symptoms.” Licensed to Relmada.

Canadian Patent Application No. 2,893,238 (filed 9/25/2013), “d-Methadone for the Treatment of Psychiatric Symptoms.” Licensed to Relmada.

Chinese Patent No. ZL201380061197.3 issued on 9/14/2019 (filed 9/25/2013), “d-Methadone for the Treatment of Psychiatric Symptoms.” Licensed to Relmada.

Hong Kong Patent Application No. 16101841.1 (filed 9/25/2013), “d-Methadone for the Treatment of Psychiatric Symptoms.” Licensed to Relmada. Currently allowed and awaiting issuance.

Indian Patent Application No. 3481/DELNP/2015 (filed 9/25/2013), “d-Methadone for the Treatment of Psychiatric Symptoms.” Licensed to Relmada.

Mexican Patent Application No. 2015/006720 (filed 9/25/2013), “d-Methadone for the Treatment of Psychiatric Symptoms.” Licensed to Relmada.

South Korean Patent No. 1969667 issued 4/10/2019 (filed 9/25/2013), “d-Methadone for the Treatment of Psychiatric Symptoms.” Licensed to Relmada.

Taiwanese Patent Application No. 107108987 (filed 3/16/2018), “Compounds for the treatment or prevention of disorders of the Nervous system and symptoms and manifestations thereof, and for cyto-protection against diseases and aging of cells and symptoms and manifestations thereof.”

Australian Patent Application No. 2018215056 (filed 1/31/2018), “Compounds for the treatment or prevention of disorders of the Nervous system and symptoms and manifestations thereof, and for cyto-protection against diseases and aging of cells and symptoms and manifestations thereof.” Licensed to Relmada.

Brazilian Patent Application No. BR112019015286-5 (filed 1/31/2018), “Compounds for the treatment or prevention of disorders of the Nervous system and symptoms and manifestations thereof, and for cyto-protection against diseases and aging of cells and symptoms and manifestations thereof.” Licensed to Relmada.

Canadian Patent Application No. 3052273 (filed 1/31/2018), “Compounds for the treatment or prevention of disorders of the Nervous system and symptoms and manifestations thereof, and for cyto-protection against diseases and aging of cells and symptoms and manifestations thereof.” Licensed to Relmada.

Chinese Patent Application No. 201880020508.4 (filed 1/31/2018), “Compounds for the treatment or prevention of disorders of the Nervous system and symptoms and manifestations thereof, and for cyto-protection against diseases and aging of cells and symptoms and manifestations thereof.” Licensed to Relmada.

EP Patent Application No. 18706021.5 (filed 1/31/2018), “Compounds for the treatment or prevention of disorders of the Nervous system and symptoms and manifestations thereof, and for cyto-protection against diseases and aging of cells and symptoms and manifestations thereof.” Licensed to Relmada.

Indian Patent Application No. 201917033638 (filed 1/31/2018), “Compounds for the treatment or prevention of disorders of the Nervous system and symptoms and manifestations thereof, and for cyto-protection against diseases and aging of cells and symptoms and manifestations thereof.” Licensed to Relmada.

Japanese Patent Application No. (appl’n no. not yet assigned) (filed 1/31/2018), “Compounds for the treatment or prevention of disorders of the Nervous system and symptoms and manifestations thereof, and for cyto-protection against diseases and aging of cells and symptoms and manifestations thereof.” Licensed to Relmada.

Mexican Patent Application No. 2019/009038 (filed 1/31/2018), “Compounds for the treatment or prevention of disorders of the Nervous system and symptoms and manifestations thereof, and for cyto-protection against diseases and aging of cells and symptoms and manifestations thereof.” Licensed to Relmada.

South Korean Patent Application No. 2019-7025398 (filed 1/31/2018), “Compounds for the treatment or prevention of disorders of the Nervous system and symptoms and manifestations thereof, and for cyto-protection against diseases and aging of cells and symptoms and manifestations thereof.” Licensed to Relmada.

U.S. Provisional Patent Application No. 62/852,537 (filed 5/24/2019), “Dextromethadone for the Prevention and Treatment of Diseases and Conditions in Asian Subjects.” Licensed to Relmada.

U.S. Provisional Patent Application No. 62/798,709 (filed 1/31/2019), “Structurally Modified Opioids for the Prevention and Treatment of Diseases and Conditions,” Licensed to Relmada.

International (PCT) Patent Application No. PCT/US2019/055590 (filed 10/10/2019), “Structurally Modified Opioids for the Prevention and Treatment of Diseases and Conditions,” Licensed to Relmada.

Buprenorphine:

U.S. Patent application 12/988,209 (filed 3/9/2009), “Oral Pharmaceutical Compositions of Buprenorphine and Method of Use.” Owned by Relmada.

U.S. Patent Application No. 13/229,505 (filed 9/9/2011), “Oral Pharmaceutical Compositions of Buprenorphine.” Owned by Relmada.

U.S. Patent Application No. 15/057,358 (filed 3/1/2016), “Oral Pharmaceutical Compositions of Buprenorphine.” Owned by Relmada.

EP Patent Application No. 9719755.2 (filed 3/9/2009), “Oral Pharmaceutical Compositions of Buprenorphine and Method of Use.” Owned by Relmada.

EP Patent Application No. 09841608.4 (filed 9/28/2009), “Modified Release Pharmaceutical Compositions of Buprenorphine.” Owned by Relmada.

Mepivacaine:

Canadian Patent No. 2,796,575 issued on 5/15/2018 (filed 4/13/2011), “Dermal Pharmaceutical Compositions of 1-Methyl-2,6-Pipecoloxylidide and Method of Use.” Owned by Relmada. Estimated expiry in 2031.

Chinese Patent No. ZL201180027559.8 issued on 5/31/2017 (filed 4/13/2011), “Dermal Pharmaceutical Compositions of 1-Methyl-2,6-Pipecoloxylidide and Method of Use.” Owned by Relmada. Estimated expiry in 2031.

Japanese Patent No. 5927506 issued on 5/13/2016 (filed 4/13/2011), “Dermal Pharmaceutical Compositions of 1-Methyl-2,6-Pipecoloxylidide and Method of Use.” Owned by Relmada. Estimated expiry in 2031.

U.S. Patent Application No. 13/641,240 (filed 4/13/2011), “Dermal Pharmaceutical Compositions of 1-Methyl-2,6-Pipecoloxylidide and Method of Use.” Owned by Relmada.

Australian Patent No. 2016259348 issued 2/21/2019 (filed 4/13/2011), “Dermal Pharmaceutical Compositions of 1-Methyl-2,6-Pipecoloxylidide and Method of Use.” Owned by Relmada.

European Patent No. 2557924 issued 6/12/2019 (filed 4/13/2011), “Dermal Pharmaceutical Compositions of 1-Methyl-2,6-Pipecoloxylidide and Method of Use.” Owned by Relmada.

Indian Patent Application No. 9424/CHENP/2012 (filed 4/13/2011), “Dermal Pharmaceutical Compositions of 1-Methyl-2,6-Pipecoloxylidide and Method of Use.” Owned by Relmada.

South Korean Patent Application No. 10-2018-7017167 (filed 4/13/2011), “Dermal Pharmaceutical Compositions of 1-Methyl-2,6-Pipecoloxylidide and Method of Use.” Owned by Relmada.

Chinese Patent Application No. 20171323695.0 (filed 4/13/2011), “Dermal Pharmaceutical Compositions of 1-Methyl-2,6-Pipecoloxylidide and Method of Use.” Owned by Relmada.

Hong Kong Patent Application No. 18102952.2 (filed 4/13/2011), “Dermal Pharmaceutical Compositions of 1-Methyl-2,6-Pipecoloxylidide and Method of Use.” Owned by Relmada.

d-Methadone License Agreement

In January 2018 we entered into an Intellectual Property Assignment Agreement (the "Assignment Agreement") and License Agreement (the License Agreement and together with the Assignment Agreement, the Agreements), with Dr. Charles E. Inturrisi and Dr. Paolo Manfredi (collectively, the "Licensor"). Pursuant to the Assignment Agreement, we assigned our existing rights, including patents and patent applications, to d-methadone in the context of psychiatric use to Licensor, and pursuant to the License Agreement, Licensor then granted us an exclusive, perpetual, worldwide license under the assigned intellectual property rights as well as patents and know-how covering certain new inventions developed by Licensor and relating to d-methadone in neurological and other uses, to develop and commercialize d-methadone in all fields of use . The License Agreement also grants to us rights in all future inventions developed by Licensor, whether or not in collaboration with us, that relate in any way to d-methadone or the use thereof. The License Agreement was amended in December 2019 to modify certain termination rights relating to the Chief Executive Officer, which are described further below.

In consideration of the rights granted to us under the License Agreement, we paid Licensor an upfront license fee of $180,000. Additionally, we are required to pay Licensor a quarterly license maintenance fee of $45,000 until the earliest to occur of the following events: (i) the first commercial sale of a licensed product anywhere in the world, (ii) the expiration or invalidation of the last to expire or be invalidated of the patent rights anywhere in the world, or (iii) the termination of the License Agreement. We will also pay Licensor royalties in the very low single digits on net sales of licensed products covered by the licensed intellectual property rights, including future licensed products, subject to certain reductions following expiration of the patent rights covering the licensed products, and a percentage of all consideration received by us for sublicenses granted under the License Agreement ranging from twenty percent down to the mid-teens, depending on the extent of patent coverage of the licensed products. We will be required to pay royalties and sublicensing revenue to Licensor as long as we continue to receive income derived from the intellectual property rights licensed to us under the License Agreement.

If we develop any new inventions relating to d-methadone, we are required to do so in collaboration with Licensor, and to file patents covering such inventions jointly in the name of the Company and Licensor. All such future inventions or patents shall be jointly owned by us and Licensor, and will be included in and subject to the financial and other terms of the License Agreement.

The License Agreement includes standard termination rights for Licensor in the event of our insolvency, challenge of the licensed patents and uncured material breach of our obligations under the License Agreement. In addition, the License Agreement contains certain "Key Man" provisions such that Licensor may terminate the License Agreement if we terminate the employment of our Chief Executive Officer Mr Sergio Traversa for any reason other than for specified causes determined by a majority of our Board of Directors (including fraud, gross negligence, unauthorized use of our confidential information, conduct including harassment or discrimination, breach of fiduciary duty or uncured material breach), or if we (a) substantially modify Mr Traversa's job responsibilities or decision-making rights in connection with the development and commercialization of d-methadone, (b) remove him from the role of Chief Executive Officer other than in connection with a permitted change-of-control transaction, (c) materially reduce his compensation, or (d) assign or transfer our rights under the License Agreement or the d-methadone intellectual property without Mr Traversa's consent, in each case (termination or the events in (a) through (d)) during the period commencing on the effective date and ending on the later of five years from the original effective date of the License Agreement or December 31, 2022 (the "Key Man Term"). The December 2019 amendment to the License Agreement made certain clarifications to the nature of a termination for Cause, including to clarify that termination due to Mr Traversa's death or disability does not give Licensor the right to terminate the License Agreement.

Wonpung License Agreement

In 2007, we entered into a License Development and Commercialization Agreement with Wonpung Mulsan Co (Wonpung), a shareholder of ours. Wonpung has exclusive territorial rights in countries it selects in Asia to market up to two drugs we are currently developing, as well as a right of first refusal (ROFR) for up to an additional five drugs that we may develop in the future and selected by Wonpung, as defined in more detail in the license agreement. In January 2018, Wonpung exercised its ROFR with respect to d-methadone for South Korea, Japan, the People's Republic of China, Taiwan, Singapore and Hong Kong.

We received an upfront license fee of $1,500,000 and will earn royalties of up to 12% of net sales for up to two licensed products we are currently developing. The licensing terms for products for which Wonpung may exercise the ROFR will be subject to future negotiations on a product-by-product basis, and are subject to binding arbitration if we are unable to agree upon the licensing terms. The terms of each licensing agreement will expire on the earlier of any time from 15 years to 20 years after licensing or on the date of commercial availability of a generic product to such licensed product in the licensed territory. Our current focus is on developing and marketing our products in the United States and not Asia.

Key Strengths

We believe that the key elements for our success include:

- Compelling lead product opportunity, d-methadone completed Phase 2a trial for treatment of TRD.
- Successful Phase 1 safety studies of d-methadone and strong clinical activity signal in depression established in three independent animal models.
- Potential in additional indications in underserved markets with large patient population and rare diseases such as Restless Leg Syndrome and Rett Syndrome.
- Scientific support of leading experts: Our scientific advisors include clinicians and scientists who are affiliated with a number of highly regarded medical institutions such as Harvard, Cornell, Yale, Penn and John Hopkins Universities.
- Substantial IP portfolio and market protection: approved and filed patent applications provide coverage beyond 2030. In addition, some of our drugs, including d-methadone have also been designated as Orphan Drugs by the FDA, thereby providing seven years of market exclusivity at launch.

Competition Overview

The pharmaceutical and biotechnology industry is characterized by intense competition, rapid product development and technological change. Competition is intense among manufacturers of prescription pharmaceuticals and other product areas where we may develop and market products in the future. Most of our competitors are large, well-established pharmaceutical or healthcare companies with considerably greater financial, marketing, sales and technical resources than are available to us. Additionally, many of our competitors have research and development capabilities that may allow such competitors to develop new or improved products that may compete with our products. Our products could be rendered obsolete or made uneconomical by the development of new products.

Regarding our competitive position in the industry, none of our products have been approved for sale.

Currently, there are no oral FDA-approved therapies for TRD with the mechanism of action of d-methadone. Johnson & Johnson's Spravato (esketamine nasal spray) has been recently approved for the treatment of TRD however it needs to be taken under the supervision of a healthcare provider in a healthcare setting. Products approved for other indications, for example, low doses of the anesthetic ketamine, are being or may be increasingly used off-label for treating depression, as well as other CNS indications for which d-methadone may have therapeutic potential. Additionally, other treatment options, such psychotherapy and electroconvulsive therapy, are sometimes used instead of and before antidepressant medications to treat patients with TRD.

In the field of new generation antidepressants focused on specifically blocking the NMDA receptor channel, our principal competitor is intranasal esketamine, an isomer of ketamine, developed by Johnson & Johnson subsidiary Janssen Pharmaceuticals and approved in the United States in March 2019. Other potential competitors focused on modulation of the NMDA receptor at its glycine co-agonist site include VistaGen Therapeutics, Inc. that is developing AV-101, an orally available prodrug candidate that gains access to the CNS after systemic administration and is rapidly converted in the brain into its active metabolite, 7-chlorokynurenic acid (7-Cl-KYNA), a well-characterized, potent and highly selective antagonist of the NMDA receptor at the glycine co-agonist site. Vistagen is currently conducting a multicenter Phase 2 study for the adjunctive use of oral AV-101 for MDD in patients with an inadequate response to standard antidepressant therapy.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

FDA Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act (FD&C Act) and other federal and state statutes and regulations govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling and import and export of pharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending new drug applications (NDAs), warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties and criminal prosecution.

Pharmaceutical product development for a new product or certain changes to an approved product in the U.S. typically involves preclinical laboratory and animal tests, the submission to FDA of an investigational new drug application (IND) which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease.

Preclinical tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements, including good laboratory practices. The results of preclinical testing are submitted to FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long-term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted. A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin. Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with good clinical practice, or GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to FDA as part of the IND.

FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board (IRB) for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence of effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the drug for a particular indication, dosage tolerance and optimum dosage, and to identify common adverse effects and safety risks. If a drug demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug. In most cases, FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug. A single Phase 3 trial with other confirmatory evidence may be sufficient in rare instances, such as where the study is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible.

The manufacturer of an investigational drug in a Phase 2 or 3 clinical trial for a serious or life-threatening disease is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for expanded access.

After completion of the required clinical testing, an NDA is prepared and submitted to FDA. FDA approval of the NDA is required before marketing of the product may begin in the U.S. The NDA must include the results of all preclinical, clinical and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture and controls. The cost of preparing and submitting an NDA is substantial. The submission of most NDAs is additionally subject to a substantial application user fee, and the applicant under an approved NDA is also subject to an annual program fee for each prescription product. These fees are typically increased annually. Sponsors of applications for drugs granted Orphan Drug Designation are exempt from these user fees.

FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, FDA begins an in-depth review. FDA has agreed to certain performance goals in the review of NDAs to encourage timeliness. Applications for most standard review drug products are reviewed within twelve months from submission of NDAs for new molecular entities (NMEs) and ten months from submission of NDAs for non-NMEs. Priority review can be applied to drugs that FDA determines offer major advances in treatment or provide a treatment where no adequate therapy exists. The review process for both standard and priority review may be extended by FDA for three additional months to consider certain late-submitted information or information intended to clarify information already provided in the submission.

FDA may also refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an outside advisory committee – typically a panel that includes clinicians and other experts – for review, evaluation and a recommendation as to whether the application should be approved. FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving an NDA, FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, FDA will inspect the facility or the facilities at which the drug is manufactured. FDA will not approve the product unless compliance with current good manufacturing practices (cGMPs) is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

After FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for FDA to reconsider the application. If, or when, those deficiencies have been addressed to FDA's satisfaction in a resubmission of the NDA, FDA will issue an approval letter. FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, FDA may require a risk evaluation and mitigation strategy (REMS) to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use (ETASU). ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Fast Track Designation

FDA is required to facilitate the development, and expedite the review, of drugs that are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Under the Fast Track program, the sponsor of a new drug candidate may request that FDA designate the drug candidate for a specific indication as a Fast Track drug concurrent with, or after, the filing of the IND for the drug candidate. FDA must determine if the drug candidate qualifies for Fast Track Designation within 60 days of receipt of the sponsor's request.

If a submission is granted Fast Track Designation, the sponsor may engage in more frequent interactions with FDA, and FDA may review sections of the NDA before the application is complete. This rolling review is available if the applicant provides, and FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, FDA's time period goal for reviewing an application does not begin until the last section of the NDA is submitted. Additionally, Fast Track Designation may be withdrawn by FDA if FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Orphan Drugs

Under the Orphan Drug Act, FDA may grant Orphan Drug Designation to drugs intended to treat a rare disease or condition – generally a disease or condition that affects fewer than 200,000 individuals in the U.S. Orphan Drug designation must be requested before submitting an NDA. After FDA grants Orphan Drug Designation, the generic identity of the drug and its potential orphan use are disclosed publicly by FDA. Orphan Drug Designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA Orphan Drug Designation is entitled to a seven-year exclusive marketing period in the U.S. for that product, for that indication. During the seven-year exclusivity period, FDA may not approve any other applications to market the same drug for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of Orphan Drug Designation are tax credits for certain research and an exemption from the NDA application user fee.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in certain circumstances for up to two years after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Pediatric Information

Under the Pediatric Research Equity Act (PREA), NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. FDA may grant full or partial waivers, or deferrals, for submission of data. With certain exceptions, PREA does not apply to any drug for an indication for which orphan designation has been granted.

The Best Pharmaceuticals for Children Act (BPCA) provides NDA holders a six-month extension of any exclusivity – patent or nonpatent – for a drug if certain conditions are met. Conditions for exclusivity include FDA's determination that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, FDA making a written request for pediatric studies, and the applicant agreeing to perform, and reporting on, the requested studies within the statutory timeframe. Applications under the BPCA are treated as priority applications, with all of the benefits that designation confers.

Post-Approval Requirements

Once an NDA is approved, a product will be subject to certain post-approval requirements. For instance, FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling.

Adverse event reporting and submission of periodic reports are required following FDA approval of an NDA. FDA also may require post-marketing testing, known as Phase 4 testing, REMS and surveillance to monitor the effects of an approved product, or FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, drug manufacture, packaging and labeling procedures must continue to conform to cGMPs after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with FDA and certain state agencies. Registration with FDA subjects entities to periodic unannounced inspections by FDA, during which the Agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality-control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

The Hatch-Waxman Amendments

Orange Book Listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant's product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an abbreviated new drug application (ANDA). An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, preclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the applicant must certify that (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a section viii statement certifying that its proposed ANDA label does not contain (or carve out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

Exclusivity

Upon NDA approval of a new chemical entity (NCE), which is a drug that contains no active moiety that has been approved by FDA in any other NDA, that drug receives five years of marketing exclusivity during which FDA cannot receive any ANDA seeking approval of a generic version of that drug. An ANDA may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period. Certain changes to a drug, such as the addition of a new indication to the package insert, can be the subject of a three-year period of exclusivity if the application contains reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the sponsor that were essential to approval of the application. FDA cannot approve an ANDA for a generic drug that includes the change during the period of exclusivity.

In the case of a non-racemic drug containing as an active ingredient a single enantiomer that is contained in a racemic drug approved in another NDA, the NDA for the non-racemic drug may elect to have the single enantiomer not be considered the same active ingredient as that contained in the approved racemic drug and therefore eligible for NCE exclusivity, if certain conditions are met. These conditions include: (1) the single enantiomer has not been previously approved except in the approved racemic drug, (2) the NDA for the non-racemic drug includes full reports of new clinical investigations necessary for the approval of the product conducted or sponsored by the applicant and not submitted for approval of the racemic drug, and (3) the NDA for the non-racemic drug is not submitted for approval of a condition of use in a therapeutic category in which the approved racemic drug has been approved or for which any other enantiomer of the racemic drug has been approved. In addition, FDA will not approve the non-racemic drug for any condition of use in the therapeutic category in which the racemic drug has been approved for a period of 10 years after approval of the non-racemic drug, and the labeling of the non-racemic drug will include a statement in the indication that the non-racemic drug is not approved, and has not been shown to be safe and effective, for any condition of use of the racemic drug. The applicant for the non-racemic drug may make this election only in an application submitted before October 1, 2022.

Patent Term Extension

After NDA approval, owners of relevant drug patents may apply for up to a five-year patent extension. The allowable patent term extension is calculated as half of the drug's testing phase (the time between IND application and NDA submission) and all of the review phase (the time between NDA submission and approval up to a maximum of five years). The time can be shortened if FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years, and only one patent can be extended. For patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the United States Patent and Trademark Office must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug for which an NDA has not been submitted.

Section 505(b)(2) NDAs

A special type of NDA, commonly referred to as a Section 505(b)(2) NDA, enables the applicant to rely, in part, on the FDA's prior findings in approving a similar product or published literature in support of its application. A Section 505(b)(2) NDA may provide an alternate path to FDA approval for a new or improved formulation, a new route of administration, or a new use of a previously approved product. Section 505(b)(2) permits the submission of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference. If the Section 505(b)(2) applicant can establish that reliance on the FDA's prior findings of safety and/or effectiveness is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all, or some, of the indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

To the extent that the Section 505(b)(2) applicant is relying on the FDA's prior findings of safety or effectiveness for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an abbreviated new drug application, or ANDA, applicant would. Thus, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Controlled Substances

The federal Controlled Substances Act of 1970, or CSA, and its implementing regulations establish a closed chain of distribution for entities handling controlled substances. The CSA and regulations enforced by the United States Drug Enforcement Administration, or DEA, impose registration, security, recordkeeping and reporting, storage, manufacturing, distribution, importation, exportation, and other requirements on entities handling controlled substances. The DEA requires those individuals or entities that handle controlled substances to comply with these requirements in order to ensure legitimate use and prevent the diversion of controlled substances to illicit channels of commerce.

Facilities that manufacture, distribute, import or export any controlled substance must register annually with the DEA. The DEA registration is specific to a particular location, activity, and controlled substance schedule. For example, separate registrations are required for importation and manufacturing activities, and the authority granted under each registration determines which schedules of controlled substances the registrant may handle. However, certain DEA registrations permit coincident activities without obtaining a separate DEA registration, such as authorizing a manufacturer to also distribute controlled substances produced by that registrant.

The CSA categorizes controlled substances into one of five schedules – Schedule I, II, III, IV, or V – depending on the potential for abuse and physical or psychological dependence. Schedule I substances by definition have a high potential for abuse, have no currently accepted medical use in treatment in the U.S. and lack accepted safety for use under medical supervision. They may not be marketed or sold for dispensing to patients in the U.S. Pharmaceutical products having a currently accepted medical use and that are otherwise approved for marketing may be listed as Schedule II, III, IV, or V substances, with Schedule II substances presenting the highest potential for abuse and physical or psychological dependence, and Schedule V substances presenting the lowest relative potential for abuse and dependence. Schedule II substances (as well as substances defined as narcotics in any Schedule) are subject to most regulatory requirements and restrictions, such as recordkeeping, reporting and security. For example, all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist in most situations unless they are electronically prescribed pursuant to DEA regulations, and cannot be refilled. Schedules III, IV and V controlled substances are subject to fewer restrictions.
The DEA inspects manufacturers, distributors, importers, and exporters to review compliance with the CSA and DEA regulations including security, record keeping and reporting prior to issuing a controlled substance registration. The specific security requirements vary by the type of business activity and the schedule and quantity of controlled substances handled by the registrant. The most stringent requirements apply to manufacturers of Schedule I and Schedule II substances. Physical security for controlled substances includes storage in approved vaults, safes, and cages, and the use of alarm systems and surveillance cameras. Other security measures include restricted employee access to controlled substances. Once registered, manufacturing, distribution, exporting or importing facilities must maintain records documenting the manufacture, receipt, distribution, import, or export of all controlled substances. Manufacturers and distributors must also submit regular reports to the DEA of the distribution of Schedule I and II controlled substances, Schedule III narcotic substances, and other designated substances. All DEA registrants must report any controlled substance thefts or significant losses and must obtain authorization to destroy or dispose of controlled substances. In addition to maintaining an importer and/or exporter registration, importers and exporters of controlled substances must obtain a permit for every import or export of a Schedule I or II substance and a narcotic substance in Schedule III, IV and V. For all other drugs in Schedule III, IV and V, importers and exporters must submit an import or export declaration.

Practitioners such as pharmacies and physicians, as well as other types of entities that handle controlled substances, such as researchers and analytical laboratories, are also subject to DEA registration, recordkeeping, reporting, and security requirements on the receipt, storage, and dispensing of controlled substances.

The DEA establishes annually an aggregate production quota for the amount of substances within Schedules I and II and certain Schedule III substances, that may be produced in the U.S. based on the DEA's estimate of the quantity needed to meet legitimate medical, scientific, research and industrial needs. The aggregate quota for each controlled substance is allocated among the various individual manufacturers through an application process. Manufacturers may not exceed the manufacturing or procurement quota granted in a given year. The quotas apply equally to the manufacturing of the active pharmaceutical ingredient and production of dosage forms. The DEA may adjust aggregate production quotas and individual manufacturing or procurement quotas from time to time during the year, although the DEA has substantial discretion concerning whether or not to make such adjustments.

Failure to maintain compliance with applicable DEA requirements, particularly as manifested in the loss or diversion of controlled substances, can result in an enforcement action. The DEA may seek civil penalties, refuse to renew necessary registrations, or initiate administrative proceedings to revoke those registrations. In certain circumstances, violations could lead to criminal prosecution.

The various states, commonwealths, and the District of Columbia, also regulate controlled substances and impose similar licensing, recordkeeping, and reporting requirements on entities that handle controlled substances. Entities must independently comply with the various state requirements in addition to the federal controlled substance requirements.

Other Healthcare Laws

In the United States, biotechnology company activities are subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, the Centers for Medicare & Medicaid Services (CMS), other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General and the Office for Civil Rights), the U.S. Department of Justice (DOJ) and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, research, sales, marketing and scientific/educational grant programs have to comply with the anti-fraud and abuse provisions of the Social Security Act, the federal false claims laws, the privacy and security provisions of the Health Insurance Portability and Accountability Act (HIPAA) and similar state laws, each as amended, as applicable.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering, recommending or arranging for the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. The Anti- Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and/or formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor. In addition, the statutory exceptions and regulatory safe harbors are subject to change.

Additionally, the intent standard under the Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act (discussed below).

The civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

Federal false claims laws, including the federal civil False Claims Act, prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes “any request or demand” for money or property presented to the U.S. government. In addition, manufacturers can be held liable under the civil False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. Pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies’ marketing of the product for unapproved, and thus generally non-reimbursable, uses and purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes.

HIPAA created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Data privacy and security regulations by both the federal government and the states in which business is conducted may also be applicable. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, imposes requirements relating to the privacy, security and transmission of individually identifiable health information. HIPAA requires covered entities to limit the use and disclosure of protected health information to specifically authorized situations and requires covered entities to implement security measures to protect health information that they maintain in electronic form. Among other things, HITECH made HIPAA's security standards directly applicable to business associates, independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Additionally, the federal Physician Payments Sunshine Act within the ACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report to CMS information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members. The information is reported annually, and the reported data are made available in searchable form on a public website. Failure to submit required information may result in civil monetary penalties. Effective January 1, 2022, reporting on transfers of value to physician assistants, nurse practitioners or clinical nurse specialists, certified registered nurse anesthetists, and certified nurse-midwives will also be required.

Commercial distribution of products requires compliance with state laws that require the registration of manufacturers and wholesale distributors of drug and biological products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. In addition, several states have enacted legislation requiring pharmaceutical and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. Certain local jurisdictions also require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. Sales and marketing activities are also potentially subject to federal and state consumer protection and unfair competition laws.

Violation of any of the federal and state healthcare laws described above or any other governmental regulations may result in penalties, including without limitation, significant civil, criminal and/or administrative penalties, damages, fines, disgorgement, exclusion from participation in government programs, such as Medicare and Medicaid, imprisonment, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, refusal to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings.

U.S. Healthcare Reform

In March 2010, President Obama enacted the ACA, which substantially changed healthcare financing and delivery by both governmental and private insurers and has significantly impacted the pharmaceutical and biotechnology industry.

Among the ACA provisions of importance to the pharmaceutical and biotechnology industries, in addition to those otherwise described above, are the following:

- an annual, nondeductible fee on any entity that manufacturers or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price, or AMP;
- a Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Some of the provisions of the ACA have yet to be implemented, and there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA such as removing penalties, starting January 1, 2019, for not complying with the ACA's individual mandate to carry health insurance, and delaying the implementation of certain ACA-mandated fees, and increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D. On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017. While the Texas U.S. District Court Judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA.

There has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the Trump administration's budget proposals for fiscal years 2019 and 2020 contain further drug price control measures that could be enacted during the budget process or in other future legislation. Further, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. HHS has started soliciting feedback on some of these measures and implementing others under its existing authority. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent the generation revenue, attainment profitability, or commercialization of products.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the United States, sales of any product candidates for which regulatory approval for commercial sale is obtained will depend in part on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government authorities and health programs in the United States such as Medicare and Medicaid, managed care providers, private health insurers and other organizations. These third-party payors are increasingly reducing reimbursements for medical products and services. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the reimbursement rate that the payor will pay for the drug product. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of FDA-approved drugs for a particular indication. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

Corporate Information

Our principal executive offices are located at 880 Third Avenue, 12th Floor, New York, New York 10022 and our telephone number is (646) 876 3459. Our website address is *www.relmada.com.* The information contained in, or that can be accessed through, our website is not part of, and is not incorporated in, this Report.

Available Information

Reports we file with the Securities and Exchange Commission (SEC) pursuant to the Exchange Act of 1934, as amended (the Exchange Act), including annual and quarterly reports, and other reports we file, can be inspected and copied at the public reference facilities maintained by the SEC at 100 F Street NE, Washington, D.C. 20549.

DIRECTORS AND EXECUTIVE OFFICERS

Directors and Officers

The following sets forth information about our directors and executive officers as of December 3, 2019:

Name	Age	Position
Sergio Traversa, PharmD.	59	Chief Executive Officer, and Director
Charles Ence	59	Chief Financial Officer
Ottavio Vitolo	47	Senior Vice President, Head of R&D and Chief Medical Officer
Charles J. Casamento	74	Chairman of the Board and Director
Paul Kelly	62	Director
Maged Shenouda, R.Ph, MBA	55	Director

Sergio Traversa, PharmD, MBA has been our Chief Executive Officer and director since April 2012. Mr. Traversa was our Interim Chief Financial Officer from February 2017 to July 2019. Previously, from January 2010 to April 2012 he was the Chief Executive Officer of Medeor Inc., a spinoff pharmaceutical company from Cornell University. From January 2008 to January 2010. Dr. Traversa was a partner at Ardana Capital. Dr. Traversa has over thirty years of experience in the healthcare sector in the United States and Europe, ranging from management positions in the pharmaceutical industry to investing and strategic advisory roles. He has held financial analyst, portfolio management and strategic advisory positions at large U.S. investment firms specializing in healthcare, including Mehta & Isaly and Mehta Partners, ING Barings, Merlin BioMed and Rx Capital. In Europe, he held the position of Area Manager for Southern Europe of Therakos Inc., a cancer and immunology division of Johnson & Johnson. Prior to Therakos, Dr. Traversa was at Eli Lilly, where he served as Marketing Manager of the Hospital Business Unit. He was also a member of the CNS (Central Nervous System) team at Eli Lilly, where he participated in the launch of Prozac and the early development of Zyprexa and Cymbalta. Dr. Traversa started his career as a sales representative at Farmitalia Carlo Erba, the largest pharmaceutical company in Italy, now part of Pfizer. Dr. Traversa served as a board member and previously as interim Chief Executive Officer and Chief Financial Officer of Actinium Pharmaceuticals. Dr. Traversa holds a Laurea degree in Pharmacy from the University of Turin (Italy) and an MBA in Finance and International Business from the New York University Leonard Stern School of Business. As our Chief Executive Officer, Dr. Traversa is our most senior executive and as such provides our Board of Directors with the greatest insight into our business and the challenges and material risks it faces. Dr. Traversa has approximately 30 years of healthcare industry experience and is especially qualified to understand the risks and leadership challenges facing a growing pharmaceutical company from a senior management and financial expertise perspective led us to conclude that Dr. Traversa should serve as Chief Executive Officer and Director of the Company.

Charles Ence was appointed as our Chief Financial Officer on July 29, 2019. From October 2018 until June 2019, Mr. Ence was Corporate Controller of New Age Beverages Corp/Xing Beverages, LLC (“New Age”) located in Denver, Colorado. From August 2003 until October 2018, Mr. Ence was Chief Financial Officer of New Age. He managed all the financial affairs of New Age and their other portfolio companies helping lead the firm into becoming one of the top 100 non-alcoholic beverage companies worldwide. He helped guide the expansion of the business to ultimately penetration of 46 states domestically and 10 countries internationally, with consistent growth and profitability throughout his tenure. Prior to New Age, Mr. Ence was a senior executive, Planning Manager and Director of Finance for Quantum Corp. Following Quantum he served as a Director of Finance and Investor Relations at On Command Corp. Mr. Ence began his career at PepsiCo. During his 12 years at PepsiCo, Mr. Ence served as a financial analyst, planning supervisor, planning and analysis manager and ultimately controller.

He received his Bachelor of Arts in Business Administration and Accounting from Southern Utah University in 1984, and obtained a Master’s in Business Administration in Finance from Arizona State University School of Business in 1985.

Ottavio V. Vitolo, M.D., M.M.Sc. has been our Senior Vice President, Head of R&D and Chief Medical Officer since April 2018. Dr. Vitolo is a neuropsychiatrist and clinical researcher with 20 years of preclinical and clinical research experience both in academia and industry. His expertise includes psychiatric and neurological disorders, such as depression, schizophrenia, Alzheimer’s disease, Parkinson’s disease, and rare diseases, such as Duchenne’s muscular dystrophy, Huntington’s disease, Friedreich’s ataxia and phenylketonuria.

Prior to joining us, from January 2017 to March 2018, Dr. Vitolo was Vice President of Clinical Development at Homology Medicines, Inc., a gene therapy and gene editing company, where he led the clinical development for the company lead gene therapy program and built the clinical strategy for the company portfolio. From May 2013 to January 2017, he held positions of increasing responsibility at Pfizer Inc., overseeing studies and programs ranging from small molecules to biologics to gene therapy, first in the Neuroscience Research Unit and later in the Rare Disease Research Unit, where he served as Senior Medical Director and Head of Neuromuscular Clinical Research. Prior to Pfizer, from July 2012 to April 2013, he was an Associate Medical Director in Discovery Research at Shire Human Genetic Therapies (HGT). Since 2011, Dr. Vitolo has held a position as an Assistant Psychiatrist at Massachusetts General Hospital and has been an Instructor in Psychiatry at Harvard Medical School since 2009.

Dr. Vitolo received a master of medical sciences in clinical investigation (M.M.Sc.) from Harvard Medical School, and a medical degree (M.D.),*summa cum laude*, in medicine and surgery from the University of Rome - La Sapienza. He trained in psychiatry at Barnes Jewish Hospital and Washington University in St. Louis Medical School and in behavioral neurology and neuropsychiatry at Brigham and Women's Hospital and Harvard Medical School.

Board of Directors

Charles J. Casamento, MBA has been our Chairman of the Board since June 2017 and a director since July 2015. Mr. Casamento is also Chairman of our Audit Committee and a member of Compensation Committee and Corporate Governance and Nominating Committee. Since 2007 Mr. Casamento is Executive Director and Principal of The Sage Group, a health care advisory group specializing in business development strategies and transactions. Prior to The Sage Group he was President and CEO of Osteologix from October 2004 until April 2007. Originally a private VC funded company in Copenhagen, Denmark which had discovered a new drug for the treatment of Osteoporosis, Mr. Casamento commenced operations and initiated clinical trials in the US, completed a financing with Rodman & Renshaw and Roth Capital Partners and took the company public through a merger with a public shell company. The product was eventually acquired by Servier a major French pharmaceutical company. Osteologix was Mr. Casamento's fifth startup company, all of which were successfully taken public, during his tenure, either through IPOs or through reverse mergers.

He was Senior Vice President & General Manager for Pharmaceuticals and Biochemicals at Genzyme. He joined Genzyme in 1985 while it was an early stage venture backed company and was there during the time Genzyme was taken public. In 2011 Genzyme was acquired by Sanofi for an estimated $20 Billion. In 1989 he co-founded and later took public, Interneuron Pharmaceuticals (Indevus) which eventually reached a $1.6 billion market valuation after a weight loss product that was developed during his tenure was approved by FDA. Indevus was acquired in 2009 by Endo for nearly $1 Billion. In 1993 Mr. Casamento joined RiboGene as Chairman, President and CEO. He took the Company public and completed several major corporate collaborations and R&D collaboration agreements as well as a merger with a public corporation in 1998 to form Questcor Pharmaceuticals, where he was Chairman, CEO and President until August 2004. He acquired Acthar, a product for West Syndrome and MS, for a $100,000 cash payment plus a 1% royalty. Questcor was acquired by Mallinckrodt in 2014 at a valuation of $6 Billion and Acthar has revenue at a run rate of $1 Billion for 2014.

Prior to joining Genzyme in 1985 Mr. Casamento has held a number of marketing, sales, finance and business development positions with Novartis, Hoffmann-LaRoche, Johnson & Johnson and American Hospital Supply Corporation where he was Vice President of Business Development and Strategic Planning for the Critical Care Division from January 1983 until May 1985. During his career he has completed well over 100 major business development/M&A deals which had the effect of enhancing and expediting the growth and development of his businesses. He took four biotechnology companies public and secured pubic and VC financing for five biotechnology companies.

Mr. Casamento currently serves as an Independent Director for AzurRx Biopharma. During his career he has served on the boards of twelve public companies and two private companies. Mr. Casamento also served as Chairman of the Audit Committee of Astex Pharmaceuticals and is a SOX defined financial expert. He is a member of the Fordham University Science Council and has been a guest lecturer at Fordham University. He was previously Vice Chairman of the Catholic Medical Mission Board, a large not for profit organization providing health care services to third world countries. A graduate of Fordham University in New York City and Iona College in New Rochelle, New York. Mr. Casamento has a degree in Pharmacy and an MBA. That Mr. Casamento brings over 35 years of biotechnology experience to our Board of Directors, having served in various senior positions over the course of his career, and that he has developed significant management and leadership skills relating to the pharmaceutical industry, led us to conclude that Mr. Casamento should serve as a director.

Maged Shenouda, R.Ph, MBA, Maged Shenouda, R.Ph, MBA, has been our director since November 2015. Mr. Shenouda is also a member of the Audit Committee and Compensation Committee, and is Chairman of the Corporate Governance and Nominating Committee. Mr. Shenouda has over 25 years of biotechnology and equity research experience. Mr. Shenouda served as the Chief Financial Officer of AzurRx Biopharma where he also served as a Director. Prior to this Mr. Sheouda was the Head of Business Development and Licensing at Retrophin, Inc. from January 2014 to November 2014. Prior to that, he spent the bulk of his career as an equity analyst. He has held senior level positions at UBS, JP Morgan and Stifel Nicolaus, covering a broad range of small and large capitalization biotechnology companies. Mr. Shenouda started his sell-side equity research career at Citigroup and Bear Stearns where his coverage universe focused on U.S and European pharmaceutical companies. Before entering Wall Street, he was a management consultant with PricewaterhouseCoopers Pharmaceutical Consulting practice and also spent time in pharmaceutical sales, having worked as a hospital representative and managed care specialist for Abbott Laboratories Pharmaceutical Products Division. He earned a B.S. in Pharmacy from St. John's University and is a registered pharmacist in New Jersey and California. He also received an M.B.A from Rutgers Graduate School of Management. That Mr. Shenouda brings over 25 years of biotechnology and equity research experience to our Board of Directors, having served in various executive-level positions over the course of his career, and that Mr. Shenouda has developed significant management and leadership skills relating to the pharmaceutical industry, led us to conclude that Mr. Shenouda should serve as a director.

Paul Kelly has been a director of the Company since November 2015. Mr. Kelly is also Chairman of the Compensation Committee, and a member of the Audit Committee and Corporate Governance and Nominating Committee. Mr. Kelly has been actively involved as an analyst, consultant and investor in the biotechnology sector for the past twenty years. He began as an equity analyst at Mabon Securities in 1993, and served in the same capacity at UBS Securities, Volpe, Brown, Whalen, ING Securities and Merrill Lynch. Mr. Kelly was named to the inaugural Fortune magazine All Star Analyst team in 2000. Subsequently, since 2007 Mr. Kelly has engaged in consulting for both private and public biotechnology companies and for hedge funds. He currently manages his own investments and continues his industry consulting activities. Mr. Kelly has advised Spring Bank Pharmaceuticals, Inc. and VisionGate, Inc. Mr. Kelly holds an A.B. in Biochemistry from Brown University, from which he was graduated magna cum laude, Sigma Xi and Phi Beta Kappa. He attended the University of Rochester School of Medicine and received an MBA in Finance from the William E. Simon School at the University of Rochester. That Mr. Kelly brings over 25 years of biotechnology experience to our Board of Directors, having served in various executive-level positions over the course of his career, and that he has developed significant management and leadership skills relating to the pharmaceutical industry, led us to conclude that Mr. Kelly should serve as a director.

CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

The following is a summary of each transaction or series of similar transactions since June 30, 2017 or any currently proposed transaction, to which we were or are a party in which:

- the amount involved exceeded or exceeds $120,000 or one percent of our total assets at June 30, 2018; and
- any of our directors or executive officers or any beneficial owners of 5% of any class of our voting capital stock or and affiliate or immediate family member thereof, had or will have a direct or indirect material interest, other than compensation and other arrangements that are described under the section titled "Executive Compensation" or that were approved by our compensation committee.

Beneficial ownership is determined in accordance with the rules of the SEC and generally includes voting or investment power with respect to such securities.

Related Party Transactions

License Agreement

See "Business—Intellectual Property Portfolio and Market Exclusivity—D-Methadone License Agreement" regarding our Intellectual Property Assignment Agreement and License Agreement with Dr. Charles E. Inturrisi and Dr. Paolo Manfredi, as it relates to our Chief Executive Officer, Sergio Traversa.

Exhibit 99.2

RISK FACTORS

Our business faces significant risks. You should carefully consider the risks described below, together with all of the other information included in our filings with the United States Securities and Exchange Commission (SEC) when evaluating our business. If any of the following risks actually occurs, our business, financial condition or results of operations could be materially adversely affected and the trading price of shares of our common stock could decline. The occurrence of any of the following risks could cause our actual results to differ materially from those contained in forward-looking statements we have made in this report and those we may make from time to time.

Risk Related to Our Business

Our business depends on the success of d-methadone (dextromethadone, REL-1017), our only product candidate currently under clinical development, which is in the early stages of clinical development and has not initiated pivotal clinical trials. If we are unable to obtain regulatory approval for and successfully commercialize REL-1017 or other future product candidates, or we experience significant delays in doing so, our business will be materially harmed.

To date, the primary focus of our product development has been d-methadone (dextromethadone, REL-1017) for the treatment of patients with TRD. Currently, d-methadone is our only product candidate under clinical development. This may make an investment in our company riskier than similar companies that have multiple product candidates in active development and that therefore may be able to better sustain a failure of a lead candidate. Successful continued development and ultimate regulatory approval of d-methadone for the treatment of MDD, TRD or other indications is critical to the future success of our business. We have invested, and will continue to invest, a significant portion of our time and financial resources in the clinical development of d-methadone. If we cannot successfully develop, obtain regulatory approval for and commercialize d-methadone, we may not be able to continue our operations. The future regulatory and commercial success of d-methadone is subject to a number of risks, including the following:

- we may not have sufficient financial and other resources to complete the necessary clinical trials for d-methadone, including, but not limited to, the clinical trials needed to obtain drug approval;
- the mechanism of action of d-methadone is complex, and we do not know the degree to which it will translate into a therapeutic benefit, if any, in MDD, TRD or any other indication, and we do not know the degree to which the complex mechanism of action may contribute to long-term safety issues or adverse events, if any, when d-methadone is taken for prolonged periods such as in the treatment of MDD, TRD or any other indication;
- we may not be able to obtain adequate evidence from clinical trials of efficacy and safety for d-methadone for the treatment of MDD, TRD or other indications;
- we may not be able to demonstrate that the benefits of d-methadone for the treatment of TRD, MDD or other indications outweigh the risks;
- in our clinical trials for d-methadone, we may need additional clinical trial sites, which could delay our clinical trial progress;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory authorities for marketing approval;
- patients in our clinical trials may suffer serious adverse effects for reasons that may or may not be related to d-methadone, which could delay or prevent further clinical development;
- the standards implemented by clinical or regulatory agencies may change at any time and we cannot be certain what efficacy endpoints the FDA or foreign clinical or regulatory agencies may require in pivotal clinical trials with respect to MDD, TRD or any other indication for the approval of d-methadone;
- the results of later stage clinical trials may not be as favorable as the results we have observed to date in our preclinical studies and Phase 1 and 2a clinical trials;
- we cannot be certain of the number and type of clinical trials and preclinical or toxicology studies that the FDA or other regulatory agencies will require in order to approve d-methadone for the treatment of TRD, MDD or any other indication;
- if approved for TRD or MDD, d-methadone will likely compete with products that may reach approval for the treatment of TRD or MDD prior to d-methadone, products that are currently approved for the treatment of TRD or MDD and the off-label use of currently marketed products for TRD or MDD; and
- we may not be able to obtain, maintain or enforce our patents and other intellectual property rights.

d-methadone and any future product candidates will be subject to rigorous and extensive clinical trials and extensive regulatory approval processes implemented by the FDA and comparable foreign regulatory authorities before obtaining marketing approval from these regulatory authorities, if at all. The drug development and approval process is lengthy and expensive, and approval is never certain. Investigational new drugs, such as d-methadone, may not prove to be safe and effective in clinical trials. We have no direct experience as a company in conducting later stage clinical trials required to obtain regulatory approval. We may be unable to conduct clinical trials at preferred sites, enlist clinical investigators, enroll sufficient numbers of participants or begin or successfully complete clinical trials in a timely fashion, if at all. In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. Because we have limited experience as a company designing clinical trials, we may be unable to design and execute a clinical trial to support regulatory approval.

There is a high failure rate for drugs and biological products proceeding through clinical trials. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of d-methadone or any future product candidate may not be predictive of the results of later-stage clinical studies or trials and the results of studies or trials in one set of patients or line of treatment may not be predictive of those obtained in another. In fact, many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late stage clinical trials even after achieving promising results in preclinical studies and earlier stage clinical trials. In addition, data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. It is impossible to predict when or if d-methadone or any future product candidate will prove effective or safe in humans or will receive regulatory approval. Owing in part to the complexity of biological pathways, d-methadone or any future product candidate may not demonstrate in patients the biochemical and pharmacological properties we anticipate based on laboratory studies or earlier stage clinical trials, and they may interact with human biological systems or other drugs in unforeseen, ineffective or harmful ways. The number of patients exposed to product candidates and the average exposure time in the clinical development programs may be inadequate to detect rare adverse events or findings that may only be detected once a product candidate is administered to more patients and for greater periods of time. To date, our Phase 2a clinical study has involved a small population of subjects with TRD, and, because of the small sample size in such trial, the results of this clinical trial may be subject to substantial variability and may not be indicative of either future top-line results or final results. If we are unable to successfully demonstrate the safety and efficacy of d-methadone or other future product candidates and receive the necessary regulatory approvals, our business will be materially harmed.

Even if we do receive regulatory approval to market d-methadone, any such approval may be subject to limitations on the indicated uses or patient populations for which we may market the products. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we may be unable to successfully develop or commercialize d-methadone. If we or any of our future development collaborators are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize d-methadone, we may not be able to generate sufficient revenue to continue our business.

Top-line results may not accurately reflect the complete results of the clinical study.

In October 2019, we reported top-line data from our Phase 2a study of d-methadone in adults with MDD who did not respond to one to three courses of antidepressant treatment in their current episode (TRD). Although the top-line data indicated that subjects experienced statistically significant improvement of their depression compared to subjects in the placebo group, as well as a favorable safety and tolerability profile, the top-line data are based on preliminary analysis of key pharmacokinetic, safety and efficacy data, and such data may change following a more comprehensive review of the data and may not accurately reflect the complete results of the study. Preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data. As a result, preliminary data should be viewed with caution until the final data are available.

Our license agreement for d-methadone, our only product candidate currently under clinical development, could terminate under certain circumstances, including if we terminate our chief executive officer except for cause, and we would be unable to conduct our business as planned.

In January 2018, we entered into an Intellectual Property Assignment Agreement (the "Assignment Agreement") and License Agreement (the License Agreement and together with the Assignment Agreement, the Agreements), with Dr. Charles E. Inturrisi and Dr. Paolo Manfredi (collectively, the "Licensor"). Pursuant to the Assignment Agreement, we assigned our existing rights, including patents and patent applications, to d-methadone in the context of psychiatric use to Licensor, and pursuant to the License Agreement, Licensor then granted us an exclusive perpetual, worldwide license under the assigned intellectual property rights as well as patents and know-how covering certain new inventions developed by Licensor and relating to d-methadone in neurological and other uses, to develop and commercialize d-methadone in all fields of use. The License Agreement also grants to us rights in all future inventions developed by Licensor, whether or not in collaboration with us that relate in any way to d-methadone or the use thereof. The License Agreement was amended in December 2019 to modify certain termination rights relating to the Chief Executive Officer, which are described further below.

If we develop any new inventions relating to d-methadone, we are required to do so in collaboration with Licensor, and to file patents covering such inventions jointly in the name of the Company and Licensor. All such future inventions or patents shall be jointly owned by us and Licensor and, will be included in and subject to the financial and other terms of the License Agreement.

The License Agreement includes standard termination rights for Licensor in the event of our insolvency, challenge of the licensed patents and uncured material breach of our obligations under the License Agreement. In addition, the License Agreement contains certain "Key Man" provisions such that the Licensor may terminate the License Agreement if we terminate the employment of our Chief Executive Officer Mr. Sergio Traversa for any reason other than for specified causes determined by a majority of our Board of Directors (including fraud, gross negligence, unauthorized use of our confidential information, conduct including harassment or discrimination, breach of fiduciary duty or uncured material breach), or if we (a) substantially modify Mr. Traversa's job responsibilities or decision-making rights in connection with the development and commercialization of d-methadone, (b) remove him from the role of Chief Executive Officer other than in connection with a permitted change-of-control transaction, (c) materially reduce his compensation, or (d) assign or transfer our rights under the License Agreement or the d-methadone intellectual property without Mr. Traversa's consent, in each case (termination or the events in (a) through (d) during the period commencing on the effective date and ending on the later of five years from the original effective date of the License Agreement on December 31, 2022 (the "Key Man Term"). The December 2019 amendment to the License Agreement made certain clarifications to the nature of a termination for Cause, including to clarify that termination due to Mr. Traversa's death or disability does not give Licensor the right to terminate the License Agreement.

As a result of the provisions described above, we are limited in our ability to terminate, as well as to decrease the salary or authority of, our Chief Executive Officer until December 31, 2022. In addition, the agreement provides that any assignor that we assign the agreement to must agree in writing to all terms of the license, including the key man provisions, and as noted above, our Chief Executive Officer has the right to consent to any such assignment of the agreement unless previously terminated for cause or due to death. As the license agreement relates to our only product candidate currently under clinical development, these provisions may be deemed to have an anti-takeover effect and may delay, deter or prevent a tender offer or takeover attempt that a stockholder might consider to be in its best interests, including attempts that might result in a premium being paid over the market price for the shares held by stockholders. If we fail to comply with the terms of the License Agreement, our rights to those patents may be terminated, and we will be unable to conduct our business.

We have generated no revenue from commercial sales to date and our future profitability is uncertain.

We have a limited operating history and our business is subject to all of the risks inherent in the establishment of a new business enterprise. Our likelihood of success must be considered in light of the problems, expenses, difficulties, complications and delays frequently encountered in connection with this. Since we began our business, we have focused on research, development and clinical trials of product candidates, and have incurred significant losses since inception and generated no product revenues. If we continue to incur operating losses and fail to become a profitable company, we may be unable to continue our operations. We expect to continue to operate at a net loss for at least the next several years as we continue our research and development efforts, continue to conduct clinical trials and develop manufacturing, sales, marketing and distribution capabilities. There can be no assurance that the products under development by us will be approved for sales in the US or elsewhere. Furthermore, there can be no assurance that if such products are approved they will be successfully commercialized, and the extent of our future losses and the timing of our profitability are highly uncertain.

International commercialization of our product candidates faces significant obstacles.

We may plan to commercialize some of our products internationally through collaborative relationships with foreign partners. We have limited foreign regulatory, clinical and commercial resources. Future partners are critical to our international success. We may not be able to enter into collaboration agreements with appropriate partners for important foreign markets on acceptable terms, or at all. Future collaborations with foreign partners may not be effective or profitable for us. We will need to obtain approvals from the appropriate regulatory, pricing and reimbursement authorities to market any of our proposed products internationally, and we may be unable to obtain foreign regulatory approvals. Pursuing foreign regulatory approvals will be time-consuming and expensive. The regulations can vary among countries and foreign regulatory authorities may require different or additional clinical trials than we conducted to obtain FDA approval for our product candidates. In addition, adverse clinical trial results, such as death or injury due to side effects, could jeopardize not only regulatory approval, but if approval is granted, may also lead to marketing restrictions. Our product candidates may also face foreign regulatory requirements applicable to controlled substances.

We need to raise additional capital to operate our business.

We are a company focused on product development and have not generated any product revenues to date. Until, and if, we receive approval from the FDA and other regulatory authorities for our product candidates, we cannot sell our drugs and will not have product revenues. Based on our current development plans, we believe that our existing cash and cash equivalents will only enable us to fund our operating expenses and capital expenditure requirements for at least the next six months unless we halt research and development activities. Therefore, for the foreseeable future, we will have to fund all of our operations and capital expenditures from the net proceeds of future offerings. For our lead product candidate, REL-1017, we anticipate commencing in the second half of 2020 (i) a Phase 3 trial in TRD, which we cannot assure you that we can complete, or we will need to halt our research and development activities, and (ii) a Phase 2 trial for MDD. We currently do not have enough funds to fund these anticipated milestones. Our actual capital requirements will depend on many factors, including FDA feedback. We also have one additional payment of $250,000 in connection with the settlement of the Babul ligation in 2018 (see – “We may be subject to litigation for a variety of claims, which could adversely affect our business, financial condition or results of operations.” for more information). If we experience unanticipated cash requirements, we may need to seek additional sources of financing, which may not be available on favorable terms, if at all. If we do not succeed in raising additional funds on acceptable terms, we will be unable to complete planned clinical trials or obtain approval of our product candidates from the FDA and other regulatory authorities. In addition, we could be forced to discontinue research and development activities, product development, reduce or forego attractive business opportunities, or discontinue operations.

We have a history of losses and we may never achieve or sustain profitability.

We have incurred substantial losses since our inception, and we may not achieve profitability for the foreseeable future, if at all. Since inception, we have an accumulated deficit of approximately $5.977 million at September 30, 2019. The Company has cash and cash equivalents of approximately $7.85 million at September 30, 2019. Even if we succeed in developing and commercializing one or more of our product candidates, we expect to incur substantial net losses and negative cash flows for the foreseeable future due in part to increasing research and development expenses, including clinical trials, and increasing expenses from leasing additional facilities and hiring additional personnel. As a result, we will need to generate significant revenues in order to achieve and maintain profitability. We may not be able to generate these revenues or achieve profitability in the future. Even if we do achieve profitability, we may not be able to sustain or increase profitability.

We have a limited operating history upon which to base an investment decision.

Our limited operating history may limit your ability to evaluate our prospects due to our limited historical financial data and our unproven potential to generate profits. You should evaluate the likelihood of financial and operational success in light of the risks, uncertainties, expenses and difficulties associated with an early-stage business, many of which may be beyond our control, including:

- our potential inability to continue to undertake preclinical studies, pharmaceutical development and clinical trials,
- our potential inability to obtain regulatory approvals, and
- our potential inability to manufacture, sell and market our products.

Our operations have been limited to organizing and staffing, on a limited basis, our company, acquiring, developing and securing our proprietary technology and undertaking preclinical studies and early stage clinical trials of our principal product candidates. These operations provide a limited basis for you to assess our ability to commercialize our product candidates and the advisability of investing in our common stock.

If we fail to obtain the capital necessary to fund our operations, we will be unable to continue or complete our product development and you will likely lose your entire investment.

We had cash and cash equivalents of approximately $7.8 million at September 30, 2019, which will not be sufficient to capitalize the development and commercialization of d-methadone and we will need to continue to seek capital from time to time to continue the development and to acquire and develop other product candidates. Our first product candidate is not expected to be commercialized for at least several years, if ever, and the revenues it will generate, if any, may not be sufficient to fund our ongoing operations. Accordingly, we believe that we will need to raise substantial additional capital to fund our continuing operations and the development and commercialization of our product candidates. Our business or operations may change in a manner that would consume available funds more rapidly than anticipated and substantial additional funding may be required to maintain operations, fund expansion, develop new or enhanced products, acquire complementary products, business or technologies or otherwise respond to competitive pressures and opportunities, such as a change in the regulatory environment or a change in preferred depression treatment modalities. In addition, we may need to accelerate the growth of our sales capabilities and distribution beyond what is currently envisioned and this would require additional capital. However, we may not be able to secure funding when we need it or on favorable terms. If we cannot raise adequate funds to satisfy our capital requirements, we will have to delay, scale-back or eliminate our research and development activities, clinical studies or future operations. We may also be required to obtain funds through arrangements with collaborators, which arrangements may require us to relinquish rights to certain technologies or products that we otherwise would not consider relinquishing, including rights to future product candidates or certain major geographic markets. We may further have to license our technology to others. This could result in sharing revenues which we might otherwise retain for ourselves. Any of these actions may harm our business, financial condition and results of operations.

The amount of capital we may need depends on many factors, including the progress, timing and scope of our product development programs; the progress, timing and scope of our nonclinical studies and clinical trials; the time and cost necessary to obtain regulatory approvals; the time and cost necessary to further develop manufacturing processes and arrange for contract manufacturing; our ability to enter into and maintain collaborative, licensing and other commercial relationships; and our partners' commitment of time and resource to the development and commercialization of our products.

We have limited access to the capital markets and even if we can raise additional funding, we may be required to do so on terms that are dilutive to you.

We have limited access to the capital markets to raise capital. The capital markets have been unpredictable in the recent past for unprofitable companies such as ours. In addition, it is generally difficult for companies to raise capital under current market conditions. The amount of capital that a company such as ours is able to raise often depends on variables that are beyond our control. As a result, we may not be able to secure financing on terms attractive to us, or at all. If we are able to consummate a financing arrangement, the amount raised may not be sufficient to meet our future needs. If adequate funds are not available on acceptable terms, or at all, our business, results of operations, financial condition and our continued viability will be materially adversely affected.

We may be subject to litigation for a variety of claims, which could adversely affect our business, financial condition or results of operations.

In addition to product liability claims, we and our directors and officers may be subject to claims arising from our normal business activities. These may include claims, suits, and proceedings involving shareholder and fiduciary matters, intellectual property, labor and employment, wage and hour, commercial and other matters. For example, in 2014, we dismissed with prejudice a lawsuit we had brought against Najib Babul, our former President, which had sought to compel Dr. Babul to account for questionable expenditures of our funds. Dr. Babul subsequently brought a lawsuit against us, including claims for breach of contract, intentional infliction of emotional distress, defamation and wrongful use of civil process. We settled this litigation, agreeing, among other things, to pay Dr. Babul as a consulting fee a $500,000 initial payment and four subsequent payments of $250,000, the last installment of which is due on December 31, 2019.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

As of June 30, 2019, we had Federal, New York State and New York City net operating loss (NOL) carryforwards of approximately $64,546,000, $60,892,000 and $60,509,000, which begin expiring in 2027, 2032 and 2032, respectively. Under U.S. federal tax legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act, or Tax Act, federal NOLs incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal NOLs is limited. It is uncertain if and to what extent various states will conform to the Tax Act. Under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change" (generally defined as a greater than 50 percentage-point cumulative change (by value) in the equity ownership of certain stockholders over a rolling three-year period), the corporation's ability to use its pre-change NOLs and other pre-change tax attributes to offset its post-change taxable income or taxes may be limited. We may also experience ownership changes as a result of stock offerings or as a result of subsequent shifts in our stock ownership, some of which are outside our control. We have not completed an analysis to determine whether any such limitations have been triggered. If any were determined to be triggered, our ability to use our current NOLs and other pre-change tax attributes to offset post-change taxable income or taxes would be subject to limitation. We will be unable to use our NOLs if we do not attain profitability sufficient to offset our available NOLs prior to their expiration.

We may not be successful in hiring and retaining key employees.

Our future operations and successes depend in large part upon the continued service of key members of our senior management team whom we are highly dependent upon to manage our business, specifically Dr. Sergio Traversa, our Chief Executive Officer. If he terminates employment with us, such a departure would have a material adverse effect on our business.

Our future success also depends on our ability to identify, attract, hire or engage, retain and motivate other well-qualified managerial, technical, clinical and regulatory personnel. We currently only have 4 full time employees and may need to hire additional qualified personnel with expertise in nonclinical pharmacology and toxicology, pharmaceutical development, clinical research, regulatory affairs, manufacturing, sales and marketing. We compete for qualified individuals with numerous biopharmaceutical companies, universities and other research institutions. Competition for such individuals, particularly in the United States, is intense, and we may not be able to hire sufficient personnel to support our efforts. There can be no assurance that these professionals will be available in the market, or that we will be able to retain existing professionals or to meet or to continue to meet their compensation requirements. Furthermore, the cost base in relation to such compensation, which may include equity compensation, may increase significantly, which could have a material adverse effect on us. Failure to establish and maintain an effective management team and work force could adversely affect our ability to operate, grow and manage our business.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to:

- comply with FDA regulations or similar regulations of comparable foreign regulatory authorities; provide accurate information to the FDA or comparable foreign regulatory authorities;
- comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities;
- report financial information or data accurately; or
- disclose unauthorized activities to us.

In particular, research, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

Managing our growth as we expand operations may strain our resources.

We expect to need to grow rapidly in order to support additional, larger, and potentially international, pivotal clinical trials of our drug candidates, which will place a significant strain on our financial, managerial and operational resources. In order to achieve and manage growth effectively, we must continue to improve and expand our operational and financial management capabilities. Moreover, we will need to increase staffing and to train, motivate and manage our employees. All of these activities will increase our expenses and may require us to raise additional capital sooner than expected. Failure to manage growth effectively could harm our business, financial condition or results of operations.

We may expand our business through the acquisition of rights to new drug candidates that could disrupt our business, harm our financial condition and may also dilute current stockholders' ownership interests in our company.

Our business strategy includes expanding our products and capabilities, and we may seek acquisitions of drug candidates or technologies to do so. Acquisitions involve numerous risks, including substantial cash expenditures; potentially dilutive issuance of equity securities; incurrence of debt and contingent liabilities, some of which may be difficult or impossible to identify at the time of acquisition; difficulties in assimilating the acquired technologies or the operations of the acquired companies; diverting our management's attention away from other business concerns; risks of entering markets in which we have limited or no direct experience; and the potential loss of our key employees or key employees of the acquired companies.

We cannot assure you that any acquisition will result in short-term or long-term benefits to us. We may incorrectly judge the value or worth of an acquired product, company or business. In addition, our future success would depend in part on our ability to manage the rapid growth associated with some of these acquisitions. We cannot assure you that we will be able to make the combination of our business with that of acquired products, businesses or companies work or be successful. Furthermore, the development or expansion of our business or any acquired products, business or companies may require a substantial capital investment by us. We may not have these necessary funds or they might not be available to us on acceptable terms or at all. We may also seek to raise funds by selling shares of our preferred or common stock, which could dilute each current stockholder's ownership interest in us.

If we cannot compete successfully for market share against other drug companies, we may not achieve sufficient product revenues and our business will suffer.

The market for our drug candidates is characterized by intense competition and rapid technological advances. If our drug candidates receive FDA approval, they will compete with a number of existing and future drugs and therapies developed, manufactured and marketed by others. Existing or future competing products may provide greater therapeutic convenience or clinical or other benefits for a specific indication than our products, or may offer comparable performance at a lower cost. If our products are unable to capture and maintain market share, we may not achieve sufficient product revenues and our business will suffer.

We and our collaborators will compete for market share against fully integrated pharmaceutical companies or other companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors have drugs already approved or drug candidates in development that will or may compete against our approved drug candidates. In addition, many of these competitors, either alone or together with their collaborative partners, operate larger research and development programs and have substantially greater financial resources than we do, as well as significantly greater experience in:

- developing drugs;
- conducting preclinical testing and human clinical trials;
- obtaining FDA and other regulatory approvals of drugs;
- formulating and manufacturing drugs; and
- launching, marketing, distributing and selling drugs.

Media stories regarding the diversion of opioids and other controlled substances are commonplace. Law enforcement agencies or regulatory agencies may apply policies that seek to limit the availability of opioids. Such efforts may adversely affect the regulatory approval and commercialization of our drug candidates.

Developments by competitors may render our products or technologies obsolete or non-competitive.

Alternative technologies and products are being developed to improve or replace the use of opioids for pain management, several of which are in clinical trials or are awaiting approval from the FDA. In addition, the active ingredients in nearly all opioid drugs are available in generic form. Drug companies that sell generic opioid drugs represent substantial competition. Many of these organizations competing with us have substantially greater capital resources, larger research and development staffs and facilities, greater experience in drug development and in obtaining regulatory approvals and greater manufacturing and marketing capabilities than we do. Our competitors may market less expensive or more effective drugs that would compete with our drug candidates or reach market with competing drugs before we are able to reach market with our drug candidates. These organizations also compete with us to attract qualified personnel and partners for acquisitions, joint ventures or other collaborations.

Business interruptions could limit our ability to operate our business.

Our operations as well as those of our collaborators on which we depend are vulnerable to damage or interruption from computer viruses, human error, natural disasters, electrical and telecommunication failures, international acts of terror and similar events. We have not established a formal disaster recovery plan and our back-up operations and our business interruption insurance may not be adequate to compensate us for losses we may suffer. A significant business interruption could result in losses or damages incurred by us and require us to cease or curtail our operations.

Unfavorable media coverage of opioid pharmaceuticals could negatively affect our business.

Opioid drug abuse receives a high degree of media coverage. Unfavorable publicity regarding, for example, the use or misuse of oxycodone or other opioid drugs, the limitations of abuse-deterrent or resistant formulations, public inquiries and investigations into prescription drug abuse, litigation or regulatory activity, or the independent actions regarding the sales, marketing, distribution or storage of our drug products, could adversely affect our reputation. Such negative publicity could have an adverse effect on the potential size of the market for our drug candidates and decrease revenues and royalties, which would adversely affect our business and financial results.

Risks Related to Clinical and Regulatory Matters

If we or our potential collaborators fail to obtain the necessary regulatory approvals, or if such approvals are limited, we and our potential collaborators will not be allowed to commercialize our drug candidates, and we will not generate product revenues.

Satisfaction of all regulatory requirements for commercialization of a drug candidate typically takes many years, is dependent upon the type, complexity and novelty of the drug candidate, and requires the expenditure of substantial resources for research and development. Our research and clinical approaches may not lead to drugs that the FDA considers safe for humans and effective for indicated uses we are studying. The FDA may require studies in addition to those we plan to conduct, in which case we or our collaborators would have to expend additional time and resources and would likely delay the date of potentially receiving regulatory approval. The approval process may also be delayed by changes in government regulation, future legislation or administrative action or changes in FDA policy that occur prior to or during our regulatory review. Delays in obtaining regulatory approvals would:

- delay commercialization of, and product revenues from, our drug candidates; and
- diminish the competitive advantages that we may have otherwise enjoyed, which would have an adverse effect on our operating results and financial condition.

Even if we or our collaborators comply with all FDA regulatory requirements, our drug candidates may never obtain regulatory approval. If we or our collaborators fail to obtain regulatory approval for any of our drug candidates we will have fewer commercial products, if any, and corresponding lower product revenues, if any. Even if our drug candidates receive regulatory approval, such approval may involve limitations on the indications and conditions of use or marketing claims for our products. Further, later discovery of previously unknown problems or adverse events could result in additional regulatory restrictions, including withdrawal of products. The FDA may also require us or our collaborators to commit to perform lengthy Phase 4 post-approval clinical efficacy or safety studies. Our expending additional resources on such trials would have an adverse effect on our operating results and financial condition.

In jurisdictions outside the United States, we or our collaborators must receive marketing authorizations from the appropriate regulatory authorities before commercializing our drugs. Regulatory approval processes outside the United States generally include all of the aforementioned requirements and risks associated with FDA approval.

If we or our collaborators are unable to design, conduct and complete successful clinical trials, our drug candidates will not be able to receive regulatory approval.

Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex and expensive nonclinical testing and clinical trials that the product is both safe and effective for use in each target indication.

Results from early clinical trials may not support moving a drug candidate to later-stage clinical trials. Phase 3 clinical trials may not demonstrate the safety or efficacy of our drug candidates. Success in preclinical studies and early clinical trials does not ensure that later clinical trials will be successful. Results of later clinical trials may not replicate the results of prior clinical trials and preclinical studies. Even if the results of Phase 3 clinical trials are positive, we or our collaborators may have to commit substantial time and additional resources to conducting further preclinical studies and clinical trials before obtaining FDA approval for any of our drug candidates.

Clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous requirements. The clinical trial process also consumes a significant amount of time. Furthermore, if participating patients in clinical trials suffer drug-related adverse reactions during the course of such clinical trials, or if we, our collaborators or the FDA believe that participating patients are being exposed to unacceptable health risks, such clinical trials will have to be suspended or terminated. Failure can occur at any stage of the clinical trials, and we or our collaborators could encounter problems that cause abandonment or repetition of clinical trials.

Our clinical trials and our future clinical trials for d-methadone measure clinical symptoms, such as depression that are not biologically measurable. The primary measure of depression is subjective and can be influenced by factors outside of our control, and can vary widely from day to day for a particular patient, and from patient to patient and site to site within a clinical study. The results we have obtained in completed animal studies or we have observed in published clinical trials conducted by third parties of other dosage forms of the same drug (e.g., immediate release oral, parenteral) may not be predictive of results from our future clinical trials. In addition, clinical trial results from the study of depression, chronic pain (e.g., osteoarthritis and chronic low back pain) and neuropathic pain (e.g., painful diabetic neuropathy, postherpetic neuralgia and painful HIV-associated neuropathy) are inherently difficult to predict. Additionally, we may suffer significant setbacks in advanced clinical trials, even after promising results in earlier studies.

We have no history of developing drug candidates. We do not know whether any of our planned clinical trials will result in marketable drugs.

In addition, completion of clinical trials can be delayed by numerous factors, including:

- delays in identifying and agreeing on acceptable terms with prospective clinical trial sites;
- slower than expected rates of patient recruitment and enrollment;
- unanticipated patient dropout rates;
- increases in time required to complete monitoring of patients during or after participation in a clinical trial; and

Any of these delays could significantly impact the timing, approval and commercialization of our drug candidates and could significantly increase our overall costs of drug development.

We cannot predict whether regulatory agencies will determine that the data from our clinical trials support marketing approval.

The FDA's and other regulatory agencies' decision to approve our depression product candidates will depend on our ability to demonstrate with substantial clinical evidence through adequate well-controlled clinical trials, that the product candidates are effective, as measured statistically by comparing the overall improvement in depression in actively-treated patients against improvement in depression in the control group (usually a placebo control). However, there is a possibility that our data may fail to show a statistically significant difference from the placebo control or the active control. Alternatively, there is a possibility that our data may be statistically significant, but that the actual clinical benefit of the product candidates may not be considered to be clinically significant, clinically relevant or clinically meaningful. Consequently, we believe that the FDA may consider additional data, such as a "responder" analysis, secondary efficacy endpoints and even safety when evaluating whether our product can be approved. We cannot predict whether the regulatory agencies will find that our clinical trial results provide compelling "responder" or other secondary endpoint data. Even if we believe that the data from our trials will support marketing approval in the United States or in Europe, we cannot predict whether the agencies will agree with our analysis and approve our applications.

We may not receive royalty or milestone revenue under our collaboration and license agreements for several years, or at all.

Certain of our license agreements provide for payments on achievement of development or commercialization milestones and for royalties on product sales. However, because none of our drug candidates has been approved for commercial sale, many of our drug candidates are at early stages of development and drug development entails a high risk of failure, we may never realize much of the milestone revenue provided for in our collaboration and license agreements and we do not expect to receive any royalty revenue for several years, if at all. Similarly, drugs we select to commercialize ourselves or partner for later stage co-development and commercialization may not generate revenue for several years, or at all.

Developments by competitors may establish standards of care that affect our ability to conduct our clinical trials as planned.

Changes in standards related to clinical trial design could affect our ability to design and conduct clinical trials as planned. For example, regulatory authorities may not allow us to compare our drug candidates to placebo in a particular clinical indication where approved products are available. In that case, both the cost and the amount of time required to conduct a clinical trial could increase.

The DEA through its quota system limits the availability of the active ingredients in certain of our current drug candidates and, as a result, the Company's quotas for these ingredients may not be sufficient to complete clinical trials, or to meet commercial demand or may result in clinical delays.

The U.S. Drug Enforcement Administration, or DEA, regulates certain controlled substance chemical compounds as Schedule I, II, III, IV or V substances, with Schedule I substances considered to present the highest risk of abuse and Schedule V substances the lowest risk. Certain active ingredients in our current drug candidates, such as oxycodone, are listed by the DEA as Schedule II. Consequently, their handling (including manufacture, research, shipment, storage, sale and use) are subject to a high degree of federal and state oversight and regulation. For example, all Schedule II drug prescriptions other than electronic prescriptions must be signed by a physician, physically presented to a pharmacist and may not be refilled. A new prescription is necessary to receive additional amounts of the drug product. Furthermore, the amount of Schedule II substances that can be obtained for clinical trials and commercial distribution is limited by the DEA through its quota system. Quotas for these substances may not be sufficient to complete clinical trials or meet commercial demand. There is a risk that federal statutes and DEA regulations concerning applicable quotas may interfere with the supply of the drugs used in clinical trials for our product candidates, and, in the future, the ability to manufacture and distribute our products in the volume needed to meet commercial demand.

Conducting clinical trials of our drug candidates or commercial sales of a drug candidate may expose us to expensive product liability claims and we may not be able to maintain product liability insurance on reasonable terms or at all.

The risk of product liability is inherent in the testing of pharmaceutical products. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or terminate testing of one or more of our drug candidates. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against product liability claims could prevent or inhibit the commercialization of our drug candidates. We currently carry clinical trial insurance but do not carry product liability insurance. If we successfully commercialize one or more of our drug candidates, we may face product liability claims, regardless of FDA approval for commercial manufacturing and sale. We may not be able to obtain such insurance at a reasonable cost, if at all. Even if our agreements with any current or future corporate collaborators entitle us to indemnification against product liability losses, such indemnification may not be available or adequate should any claim arise.

If our drug candidates receive regulatory approval, we and our collaborators will also be subject to ongoing FDA obligations and continued regulatory review, such as continued safety reporting requirements, and we and our collaborators may also be subject to additional FDA post-marketing obligations or new regulations, all of which may result in significant expense and limit our and our collaborators' ability to commercialize our drugs.

Any regulatory approvals that our drug candidates receive may also be subject to limitations on the indicated uses for which the drug may be marketed or contain requirements for costly post-marketing follow-up studies. In addition, if the FDA approves any of our drug candidates, the manufacturing processes, labeling, packaging, distribution, post-approval monitoring and adverse event reporting, storage, import, export, advertising, promotion and record keeping for the drug will be subject to extensive and ongoing regulatory requirements. The FDA has significant post-market authority, including the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials to evaluate safety risks related to the use of a product or to require withdrawal of the product from the market. The manufacturing facilities used to manufacture our product candidates will also be subject to periodic review and inspection by the FDA and other regulatory agencies, including for continued compliance with current good manufacturing practices (cGMPs) requirements. The discovery of any new or previously unknown problems with our third-party manufacturers, manufacturing processes or facilities may result in restrictions on the product, manufacturer or facility, including withdrawal of the product from the market. Any product promotion and advertising will also be subject to regulatory requirements and continuing regulatory review. The FDA imposes stringent restrictions on manufacturers' communications regarding use of their products. If we promote our product candidates in a manner inconsistent with FDA-approved labeling or otherwise not in compliance with FDA regulations, we may be subject to enforcement action. If we or our collaborators, manufacturers or service providers fail to comply with applicable continuing regulatory requirements in the United States or foreign jurisdictions in which we seek to market our products, we or they may be subject to, among other things, fines, warning or untitled letters, holds on clinical trials, delay of approval or refusal by the FDA or similar foreign regulatory bodies to approve pending applications or supplements to approved applications, suspension or withdrawal of regulatory approval, product recalls and seizures, administrative detention of products, refusal to permit the import or export of products, operating restrictions, injunction, civil penalties and criminal prosecution.

The FDA's policies may change and additional government regulations may be enacted that could prevent or delay regulatory approval of our drug candidates. For example, on July 9, 2012, the FDA approved a risk management program, known as a Risk Evaluation and Mitigation Strategy, or REMS, for extended-release and long-acting opioid analgesics, or ER/LA opioid analgesics. This REMS will require companies affected by the REMS to make available training for health care professionals who prescribe ER/LA opioid analgesics on proper prescribing practices and also to distribute educational materials to prescribers and patients on the safe use of ER/LA opioid analgesics. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the United States or abroad.

We may not succeed at in-licensing drug candidates or technologies to expand our product pipeline.

We may not successfully in-license drug candidates or technologies to expand our product pipeline. The number of such candidates and technologies is limited. Competition among large pharmaceutical companies and biopharmaceutical companies for promising drug candidates and technologies is intense because such companies generally desire to expand their product pipelines through in-licensing. If we fail to carry out such in-licensing and expand our product pipeline, our potential future revenues may suffer.

Fast Track Designation may not lead to a faster development or regulatory review or approval process.

We have obtained Fast Track Designation for d-methadone for the adjunctive treatment of MDD. Fast Track Designation is granted if a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition. Fast Track Designation does not guarantee a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program.

We may not be able to obtain or maintain orphan drug exclusivity for our products.

The FDA has granted orphan drug designation for mepivacaine for postherpetic neuralgia (PHN) and painful HIV neuropathy. We have also received orphan designation for d-methadone for PHN. If a product that has orphan drug designation subsequently receives FDA approval for the indication for which it has such designation, the product is entitled to orphan drug exclusivity, which means that for seven years, the FDA may not approve any other applications to market the same drug for the same indication, except in limited circumstances. We may be unable to obtain orphan drug designations for any additional product candidates or orphan drug exclusivity for any of our product candidates, or our potential competitors may obtain orphan drug exclusivity for d-methadone or mepivacaine product candidates for the orphan indications we are pursuing before we do, in which case our product candidates may not be approved during the exclusivity period. Even if we obtain orphan drug exclusivity for any of our product candidates, we may not be able to maintain it if a competitive product is shown to be clinically superior to our product. Although obtaining FDA approval to market a product with orphan drug exclusivity can be advantageous, there can be no assurance that it would provide us with a significant commercial advantage.

We may not be able to obtain marketing exclusivity under the Hatch-Waxman Amendments or equivalent regulatory data exclusivity protection in other jurisdictions for our products.

We intend to rely, in part, on Hatch-Waxman exclusivity for the commercialization of our products in the United States, if approved. The Hatch-Waxman Amendments provide marketing exclusivity to the first applicant to gain approval of an NDA under specific provisions of the Federal Food, Drug, and Cosmetic Act. For d-methadone, which we intend to elect to have not be considered the same active ingredient as methadone and therefore an NCE, we anticipate obtaining 5-year exclusivity. If FDA were to determine that we do not meet the requirements to make the election, we may not be able to obtain 5-year exclusivity for the product. In addition, under the statute, this election currently may only be made in an NDA submitted before October 1, 2022. If we do not submit an NDA before that date or if the statute is not amended to extend the election, we may not obtain 5-year exclusivity for d-methadone, if approved. For d-methadone, which is an NCE, we anticipate obtaining 5-year exclusivity for a product containing an active moiety that the FDA has not previously approved. For our other products, we anticipate obtaining 3-year exclusivity because the NDAs for those products will contain reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by us that were essential to approval of the application. These market exclusivities will not prevent the FDA from approving a competitor's NDA if the competitor's NDA is based on studies it has performed

There can be no assurance that European authorities will grant data exclusivity for our products, because it does not contain a new active molecule. Even if European data exclusivity is granted for our products, that may not protect us from direct competition. Given the well-established use of our product candidates as pain relievers, a competitor with a generic version of our products may be able to obtain approval of their product during our product's period of data exclusivity, by submitting a marketing authorization application (MAA) with a less than full package of nonclinical and clinical data.

We may need to focus our future efforts in new therapeutic areas where we have little or no experience.

Although our primary strategic interest is in the areas of depression, d-methadone has potential benefits in other therapeutic areas. If our drug development efforts in depression fails, or if the competitive landscape or investment climate for antidepressant drug development is less attractive, we may need to change the company's strategic focus to include development of our product candidates, or of newly acquired product candidates, for therapeutic areas other than depression. We have very limited drug development experience in other therapeutic areas and we may be unsuccessful in making this change from a depression company to a company with a focus in areas other than depression or a company with a focus in multiple therapeutic areas including depression.

Our product candidates contain controlled substances, the supply of which may be limited by U.S. statutes and regulations, and the use of which may generate public controversy.

The active ingredients in our current product candidates, including levorphanol, buprenorphine and d-methadone are listed by the DEA as controlled substances under the Controlled Substances Act of 1970. The DEA regulates certain drug substances in Schedule I, II, III, IV or V, with Schedule I substances considered to present the highest risk of substance abuse and Schedule V substances the lowest risk. These product candidates are also subject to DEA regulations relating to their handling (i.e., manufacturing, storage, distribution, prescribing and dispensing procedures).

Some of our drug products (e.g., buprenorphine, REL-1041) have a less restrictive controlled substance schedule (i.e., within the Schedule III to V range) than Schedule II drugs. According to the DEA, drugs are scheduled according to their decreasing threat of risk of diversion and abuse. For example, Schedule V drugs have lower abuse potential than Schedule II, III and IV drugs. Despite the foregoing reduced risk of abuse from Schedule III, IV and V drugs, when compared to Schedule II drugs, there is no assurance that such reduced risk can be demonstrated in well controlled nonclinical and/or clinical studies in models of physical dependence, psychic dependence, addiction or precipitated withdrawal, or in studies of addiction or abuse liability in opioid addicts, opioid ex-addicts or recreational drug users. In the event that a reduced risk of abuse from Schedule III, IV and V drugs, when compared to Schedule II drugs is demonstrated in well controlled nonclinical and/or clinical studies, there is no assurance that the FDA will agree to incorporation of such favorable language in the products prescribing information, or that DEA will incorporate such information when scheduling the drug product after FDA approval of the same.

Our LevoCap ER is a Schedule II drug in a dosage form designed to be abuse deterrent. Although the dosage form may be referred to as abuse resistant, abuse deterrent or tamper resistant, a determined or persistent abuser can defeat, wholly or partially, the tamper resistance within the dosage form. In addition, opioid addicts and recreational opioid users can over time find new methods to defeat the tamper resistance mechanism within the dosage form.

Although our LevoCap ER is designed to be an abuse deterrent dosage form, we may elect to not seek specific language in the prescribing information to describe this feature in order to reduce the amount of data required for our NDA, the time it will take to gather such data, and/or the probability of a protracted review process. The absence of such language in the prescribing information may reduce the commercial value of the product. Even if we do seek specific language in the prescribing information to describe the abuse deterrent feature, there is no assurance that FDA will agree to any such language.

Products containing controlled substances may generate public controversy. Opponents of these products may seek restrictions on marketing and withdrawal of any regulatory approvals. In addition, these opponents may seek to generate negative publicity in an effort to persuade the medical community to reject these products. Political pressures and adverse publicity could lead to delays in, and increased expenses for, and limit or restrict the introduction and marketing of our product candidates.

Failure to comply with the Controlled Substances Act or DEA regulations, or the cost of compliance with these regulations, may adversely affect our business.

A number of our products are opioids and subject to extensive regulation by the DEA, due to their status as opioid controlled substances. Although d-methadone is substantially devoid of opioid activity, the DEA may elect to designate it as a controlled substance falling under a DEA controlled substance Schedule, including Schedule II. Any level of DEA scheduling for d-methadone, particularly in Schedules II, III or IV, would substantially reduce commercial interest in d-methadone. Additionally, d-Methadone is produced by separation from racemic methadone, a scheduled drug subject to extensive regulation by the DEA.

The manufacture, shipment, storage, sale and use of controlled substances are subject to a high degree of regulation, including security, record-keeping and reporting obligations enforced by the DEA. For example, all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist and may not be refilled. This high degree of regulation can result in significant costs in order to comply with the required regulations, which may have an adverse effect on the development and commercialization of our product candidates.

The DEA limits the availability and production of all scheduled substances, including d-methadone, through a quota system. The DEA requires substantial evidence and documentation of expected legitimate medical and scientific needs before assigning quotas to manufacturers. In future years, we may need greater amounts of controlled substances to sustain our Phase 3 development program, and we will need significantly greater amounts to implement our commercialization plans if the FDA approves our proposed formulations. Any delay or refusal by the DEA in establishing the procurement quota or a reduction in our quota for scheduled controlled substances or a failure to increase it over time as we anticipate could delay or stop the clinical development or commercial sale of some of our products or product candidates. This could have a material adverse effect on our business, results of operations, financial condition and prospects.

Some of our products for clinical trials are manufactured outside the United States, including Schedule II controlled substances.

DEA regulations require Scheduled II controlled substances to be manufactured in the United States if the products are to be marketed in the United States. There is no guarantee that we will secure a commercial supply agreement with a manufacturer based in the United States. Switching or adding commercial manufacturing capability can involve substantial cost and require extensive management time and focus, as well as additional regulatory filings. In addition, there is a natural transition period when a new manufacturing facility commences work. As a result, delays may occur, which can materially impact our ability to meet our desired commercial timelines, thereby increasing our costs and reducing our ability to generate revenue.

We manufacture some products outside the United States for development and to conduct human clinical studies either in the US or outside the US. These products are for development purposes only, and not for commercial manufacturing.

If a supplier of an active pharmaceutical ingredient (API) or a pharmaceutical excipient fails to provide us sufficient quantities, we may not be able to obtain an alternative supply on a timely or acceptable basis.

We currently rely on a single source for our supply of levorphanol. There are presently no alternative sources of pharmaceutical grade levorphanol. We may also not be able to find alternative suppliers in a timely manner that would provide levorphanol at acceptable quantities and prices. Any interruption in the supply of levorphanol would disrupt our ability to manufacture LevoCap ER and could have a material adverse effect on our business. Currently this single source supplies the API for research and development purposes only. There is no material agreement for commercial supply at this time.

Our pharmaceutical excipients and other APIs are multisource, although not all sources have an active Drug Master File (DMF) with the FDA. (A DMF is a submission to the FDA used to provide confidential detailed information about facilities, processes, or articles used in the manufacturing, processing, packaging, and storing of drugs to support drug development and approval). In addition, some of the countries for our multisource APIs are not the same as our drug manufacturing locations. Thus, any disruption in supply from our preferred vendor could result in significant delays with our pharmaceutical development, clinical trials, NDA submission, NDA approval or commercial sale of the finished product due to contract delays, the need to manufacture a new batch of API, out of specification API, the need for import and export permits, and the failure of the newly sourced API to perform to the standards of the previously sourced API.

Modifications to our products may require new NDA approvals.

After a product candidate receives FDA approval, expanded uses or uses in new indications of our products may require additional clinical trials and new regulatory approvals, including additional IND submissions before we can begin clinical development and supplemental NDA approval prior to marketing and sales. If we are required to conduct additional clinical studies, itwould require additional expenditures and harm our operating results. Delays in obtaining required future approvals could adversely affect our ability to introduce new or enhanced products in a timely manner, which in turn would harm our future growth.

Moving from a powder dose formulation to a tablet formulation for future Phase 3 and Phase 2 REL-1017 trials could result in product development delays.

We are currently collaborating with Patheon/ThermoFisher to manufacture REL-1017 tablets for the clinical development program. We will propose to the FDA that we include a pharmacokinetic (PK) analysis of the tablets as part of the anticipated Phase 3 TRD study expected to commence in the second half of 2020. If, however, the FDA requests that we run a separate PK bridging study prior to the initiation of our Phase 3 TRD study, the start of the anticipated Phase 3 TRD and Phase 2 MDD studies could be delayed to the first quarter of 2021 or beyond.

Delays in the commencement or completion of pharmaceutical development, manufacturing or clinical testing could result in increased costs to us and delay our ability to generate revenues.

We do not know whether our pharmaceutical development, manufacturing or clinical testing will begin on time or be completed on schedule, if at all. For example, we may encounter delays during the manufacture of pilot scale batches including delays with our contract development or manufacturing organization, sourcing satisfactory quantities of APIs, narcotic import and export permits, sourcing of excipients, contract disputes with our third party vendors and manufacturers, or failure of the product to meet specification. Similar delays may occur a during our cGMP manufacture of the product.

The commencement and completion of clinical trials can be disrupted for a variety of reasons, including difficulties in:

- recruiting and enrolling patients to participate in a clinical trial;
- obtaining regulatory approval to commence a clinical trial;

- reaching agreement on acceptable terms with prospective clinical research organizations and trial sites;
- obtaining approval of the institutional review board (IRB) at each site selected for participation in our clinical trials;
- manufacturing sufficient quantities of a product candidate;
- investigator fraud, including data fabrication by clinical trial personnel;
- diversion of controlled substances by clinical trial personnel; and

A clinical trial may also be suspended or terminated by us, the FDA or other regulatory authorities due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements or in accordance with our clinical protocols;
- inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- unforeseen safety issues; or
- inadequate patient enrollment or lack of adequate funding to continue the clinical trial.

In addition, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes, which could impact the cost, timing or successful completion of a clinical trial. If we experience delays in the commencement or completion of our clinical trials, the commercial prospects for our product candidates will be harmed, and our ability to generate product revenues will be delayed. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also lead to the denial of regulatory approval of a product candidate.

Conducting successful clinical studies may require the enrollment of large numbers of patients, and suitable patients may be difficult to identify and recruit.

Patient enrollment in clinical trials and completion of patient participation and follow-up depends on many factors, including the size of the patient population; the nature of the trial protocol; the attractiveness of, or the discomforts and risks associated with, the treatments received by enrolled subjects; the availability of appropriate clinical trial investigators; support staff; the number of ongoing clinical trials in the same indication that compete for the same patients; and proximity of patients to clinical sites and ability to comply with the eligibility and exclusion criteria for participation in the clinical trial and patient compliance. For example, patients may be discouraged from enrolling in our clinical trials if the trial protocol requires them to undergo extensive post-treatment procedures or follow-up to assess the safety and effectiveness of our products or if they determine that the treatments received under the trial protocols are not attractive or involve unacceptable risks or discomforts. Patients may also not participate in our clinical trials if they choose to participate in contemporaneous clinical trials of competitive products.

Adverse safety outcomes could affect our ability to conduct our clinical trials or obtain approval of our product candidates.

Serious injury or death resulting from a failure of one of our drug candidates during current or future clinical trials could result in the FDA delaying our clinical trials or denying or delaying clearance or approval of a product. Even though an adverse event may not be the result of the failure of our drug candidate, FDA or an IRB could delay or halt a clinical trial for an indefinite period of time while an adverse event is reviewed, and likely would do so in the event of multiple such events. Any delay or termination of our current or future clinical trials as a result of the risks summarized above, including delays in obtaining or maintaining required approvals from IRBs, delays in patient enrollment, the failure of patients to continue to participate in a clinical trial, and delays or termination of clinical trials as a result of protocol modifications or adverse events during the trials, may cause an increase in costs and delays in the submission of any NDAs to the FDA, delay the approval and commercialization of our products or result in the failure of the clinical trial, which could adversely affect our business, operating results and prospects. Lengthy delays in the completion of clinical trials of our products would adversely affect our business and prospects and could cause us to cease operations.

On November 29, 2006, the FDA required a boxed warning to be added to the Prescribing Information for racemic methadone, a parent compound to our d-methadone related to cardiac death. Although the decision was based on case reports and not on a controlled clinical trial, as part of the development of d-methadone we will likely have to conduct a specific study to evaluate the effects of d-methadone on QTc interval prolongation. QT interval is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle. Drugs that prolong the corrected QT interval (QTc) are associated with an increased risk of serious disturbances in heart rhythm, potentially leading to sudden death. QT interval studies can be costly and there is no assurance that we will have funds to undertake such a study. In addition, even if we do a QT interval prolongation study in accordance with regulatory guidelines, there is no assurance that the results of the study will demonstrate an absence of QT interval prolongation with d-methadone. An adverse safety outcome from such study could result in a similar bolded warning on the label of d-methadone or in a decision not to approve d-methadone, either one of which could have serious consequences for our continued operation.

Our products may never achieve market acceptance.

Products that we may develop, if approved, may never gain market acceptance among physicians, patients and the medical community. The degree of market acceptance of any of our products will depend on a number of factors, including the actual and perceived effectiveness and reliability of our products; the results of any long−term clinical trials relating to use of our products; the availability, relative cost and perceived advantages and disadvantages of alternative technologies; the degree to which treatments using our products are approved for reimbursement by public and private insurers; the strength of our marketing and distribution infrastructure; and the level of education and awareness among physicians and hospitals concerning our products. Failure of any of our products to significantly penetrate current or new markets would negatively impact our business, financial condition and results of operations.

To be commercially successful, physicians must determine that using our products for treatment of depression are effective alternatives to existing therapies and treatments.

We believe that doctors and other physicians will not widely adopt our products, if approved, unless they determine, based on experience, clinical data, and published peer reviewed journal articles, that the use of our products provides an effective alternative to other means of treating depression. Patient studies or clinical experience may indicate that treatment with our products does not provide patients with sufficient benefits in depression relief and/or quality of life. We believe that recommendations and support for the use of our products from influential physicians will be essential for widespread market acceptance. Our products are still in the development stage and it is premature to attempt to gain support from physicians at this time. We can provide no assurance that such support will ever be obtained. If our products do not receive such support from these physicians and from long-term data, physicians may not use or continue to use, and hospitals may not purchase or continue to purchase, our products.

Some of our product candidates will require Risk Evaluation and Mitigation Strategies (REMS).

Some of our product candidates, the controlled substance-based and maybe others, will require REMS. The REMS may include requirements for special labeling or medication guides for patients, special communication plans to health care professionals and restrictions on distribution and use. We cannot predict the specific REMS to be required as part of the FDA's approval of any of our products. Depending on the extent of the REMS requirements, our costs to commercialize our products may increase significantly. Furthermore, controlled substances risks that are not adequately addressed through proposed REMS for our product candidates may also prevent or delay their approval for commercialization.

Our revenue stream will depend upon third party reimbursement.

The commercial success of our products in both domestic and international markets will be substantially dependent on whether third-party coverage and reimbursement is available for patients that use our products. However, the availability of insurance coverage and reimbursement for newly approved drugs to treat depression is uncertain, and therefore, third-party coverage may be particularly difficult to obtain even if our products are approved by the FDA as safe and efficacious. Many patients using existing approved therapies are generally reimbursed all or part of the product cost by Medicare or other third-party payors. Medicare, Medicaid, health maintenance organizations and other third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement of new drugs, and, as a result, they may not cover or provide adequate payment for these products. Submission of applications for reimbursement approval generally does not occur prior to the filing of an NDA for that product and may not be granted for as long as many months after NDA approval. In order to obtain reimbursement arrangements for these products, we or our commercialization partners may have to agree to a net sales price lower than the net sales price we might charge in other sales channels. The continuing efforts of government and third-party payors to contain or reduce the costs of healthcare may limit our revenue. Initial dependence on the commercial success of our products may make our revenues particularly susceptible to any cost containment or reduction efforts.

We may have conflicts with our partners that could delay or prevent the development or commercialization of our product candidates.

We may have conflicts with our partners, such as conflicts concerning the interpretation of nonclinical or clinical data, the achievement of milestones, the interpretation of contractual obligations, payments for services, development obligations or the ownership of intellectual property developed during our collaboration. If any conflicts arise with any of our partners, such partner may act in a manner that is adverse to our best interests. Any such disagreement could result in one or more of the following, each of which could delay or prevent the development or commercialization of our product candidates, and in turn prevent us from generating revenues: unwillingness on the part of a partner to pay us milestone payments or royalties we believe are due to us under a collaboration; uncertainty regarding ownership of intellectual property rights arising from our collaborative activities, which could prevent us from entering into additional collaborations; unwillingness by the partner to cooperate in the development or manufacture of the product, including providing us with product data or materials; unwillingness on the part of a partner to keep us informed regarding the progress of its development and commercialization activities or to permit public disclosure of the results of those activities; initiating of litigation or alternative dispute resolution options by either party to resolve the dispute; or attempts by either party to terminate the agreement.

Our products will face significant competition in the markets for such products, and if they are unable to compete successfully, our business will suffer.

Our products candidates face, and will continue to face, intense competition from large pharmaceutical companies, specialty pharmaceutical and biotechnology companies as well as academic and research institutions. We compete in an industry that is characterized by: (i) rapid technological change, (ii) evolving industry standards, (iii) emerging competition and (iv) new product introductions. Our competitors have existing products and technologies that will compete with our products and technologies and may develop and commercialize additional products and technologies that will compete with our products and technologies. Because several competing companies and institutions have greater financial resources than us, they may be able to: (i) provide broader services and product lines, (ii) make greater investments in research and development, (R&D), and (iii) carry on larger R&D initiatives. Our competitors also have greater development capabilities than we do and have substantially greater experience in undertaking nonclinical and clinical testing of products, obtaining regulatory approvals, and manufacturing and marketing pharmaceutical products. They also have greater name recognition and better access to customers than us. Our chief competitors include companies such as Johnson and Johnson, Allergan, Pfizer, Eli Lilly, Sage Therapeutics, Vistagen among others.

We are faced with intense competition and rapid technological change, which may make it more difficult for us to achieve significant market penetration. If we cannot compete successfully for market share against other drug companies, we may not achieve sufficient product revenues and our business will suffer.

The market for our product candidates is characterized by intense competition and rapid technological advances. If our product candidates receive FDA approval, they will compete with a number of existing and future drugs and therapies developed, manufactured and marketed by others. If our competitors' existing products or new products are more effective than or considered superior to our future products, the commercial opportunity for our product candidates will be reduced or eliminated. Existing or future competing products may provide greater therapeutic convenience or clinical or other benefits for a specific indication than our products, or may offer comparable performance at a lower cost. We face competition from fully integrated pharmaceutical companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. If we are successful in penetrating the relevant markets for pain treatment with our product candidates, other companies may be attracted to the market. Many of our competitors have products already approved or in development. In addition, many of these competitors, either alone or together with their collaborative partners, are larger than we are and have substantially greater financial, technical, research, marketing, sales, distribution and other resources than we do. Our competitors may develop or market products that are more effective or commercially attractive than any that we are developing or marketing. Our competitors may obtain regulatory approvals, and introduce and commercialize products before we do. These developments could have a significant negative effect on our financial condition. Even if we are able to compete successfully, we may not be able to do so in a profitable manner.

We may be exposed to liability claims associated with the use of hazardous materials and chemicals.

Our research and development activities involve the controlled use of hazardous materials and chemicals. Although we believe that our safety procedures for using, storing, handling and disposing of these materials comply with federal, state and local laws and regulations, we cannot completely eliminate the risk of accidental injury or contamination from these materials. In the event of such an accident, we could be held liable for any resulting damages and any liability could materially adversely affect our business, financial condition and results of operations. In addition, the federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous or radioactive materials and waste products may require us to incur substantial compliance costs that could materially adversely affect our business and financial condition.

We may incur substantial liabilities and may be required to limit commercialization of our products in response to product liability lawsuits.

The testing and marketing of medical products entail an inherent risk of product liability. We may be held liable if serious adverse reactions from the use of our product candidates occur. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of pharmaceutical products we develop, alone or with corporate collaborators. We currently do not carry product liability insurance. We, or any corporate collaborators, may not be able to obtain insurance at a reasonable cost, if at all. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate if any claim arises.

Risks Related to Our Intellectual Property

Our business depends upon securing and protecting critical intellectual property.

Our commercial success will depend in part on our obtaining and maintaining patent, trade secret, copyright and trademark protection of our technologies in the United States and other jurisdictions as well as successfully enforcing this intellectual property and defending this intellectual property against third-party challenges. We will only be able to protect our technologies from unauthorized use by third parties to the extent that valid and enforceable intellectual property protection, such as patents or trade secrets, cover them. In particular, we place considerable emphasis on obtaining patent and trade secret protection for significant new technologies, products and processes. Furthermore, the degree of future protection of our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. Moreover, the degree of future protection of our proprietary rights is uncertain for products that are currently in the early stages of development because we cannot predict which of these products will ultimately reach the commercial market or whether the commercial versions of these products will incorporate proprietary technologies.

Our patent position is highly uncertain and involves complex legal and factual questions.

Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. For example, we or our licensors might not have been the first to make the inventions covered by each of our pending patent applications and issued patents; we or our licensors might not have been the first to file patent applications for these inventions; others may independently develop similar or alternative technologies or duplicate any of our technologies; it is possible that none of our pending patent applications or the pending patent applications of our licensors will result in issued patents; our issued patents and issued patents of our licensors may not provide a basis for commercially viable technologies, or may not provide us with any competitive advantages, or may be challenged and invalidated by third parties; and, we may not develop additional proprietary technologies that are patentable.

As a result, our owned and licensed patents may not be valid and we may not be able to obtain and enforce patents and to maintain trade secret protection for the full commercial extent of our technology. The extent to which we are unable to do so could materially harm our business.

We or our licensors have applied for and will continue to apply for patents for certain products. Such applications may not result in the issuance of any patents, and any patents now held or that may be issued may not provide us with adequate protection from competition. Furthermore, it is possible that patents issued or licensed to us may be challenged successfully. In that event, if we have a preferred competitive position because of such patents, any preferred position held by us would be lost. If we are unable to secure or to continue to maintain a preferred position, we could become subject to competition from the sale of generic products. Failure to receive, inability to protect, or expiration of our patents would adversely affect our business and operations.

Patents issued or licensed to us may be infringed by the products or processes of others. The cost of enforcing our patent rights against infringers, if such enforcement is required, could be significant, and the Company does not currently have the financial resources to fund such litigation. Further, such litigation can go on for years and the time demands could interfere with our normal operations. There has been substantial litigation and other proceedings regarding patent and other intellectual property rights in the pharmaceutical industry. We may become a party to patent litigation and other proceedings. The cost to us of any patent litigation, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the costs of such litigation more effectively than we can because of their substantially greater financial resources. Litigation may also absorb significant management time.

Unpatented trade secrets, improvements, confidential know-how and continuing technological innovation are important to our scientific and commercial success. Although we attempt to and will continue to attempt to protect our proprietary information through reliance on trade secret laws and the use of confidentiality agreements with our corporate partners, collaborators, employees and consultants and other appropriate means, these measures may not effectively prevent disclosure of our proprietary information, and, in any event, others may develop independently, or obtain access to, the same or similar information.

Certain of our patent rights are licensed to us by third parties. If we fail to comply with the terms of these license agreements, our rights to those patents may be terminated, and we will be unable to conduct our business.

If we are found to be infringing on patents or trade secrets owned by others, we may be forced to cease or alter our product development efforts, obtain a license to continue the development or sale of our products, and/or pay damages.

Our manufacturing processes and potential products may violate proprietary rights of patents that have been or may be granted to competitors, universities or others, or the trade secrets of those persons and entities. As the pharmaceutical industry expands and more patents are issued, the risk increases that our processes and potential products may give rise to claims that they infringe the patents or trade secrets of others. These other persons could bring legal actions against us claiming damages and seeking to enjoin clinical testing, manufacturing and marketing of the affected product or process. If any of these actions are successful, in addition to any potential liability for damages, we could be required to obtain a license in order to continue to conduct clinical tests, manufacture or market the affected product or use the affected process. Required licenses may not be available on acceptable terms, if at all, and the results of litigation are uncertain. If we become involved in litigation or other proceedings, it could consume a substantial portion of our financial resources and the efforts of our personnel.

Our ability to protect and enforce our patents does not guaranty that we will secure the right to commercialize our patents.

A patent is a limited monopoly right conferred upon an inventor, and his successors in title, in return for the making and disclosing of a new and non-obvious invention. This monopoly is of limited duration but, while in force, allows the patent holder to prevent others from making and/or using his invention. While a patent gives the holder this right to exclude others, it is not a license to commercialize the invention, where other permissions may be required for permissible commercialization to occur. For example, a drug cannot be marketed without the appropriate authorization from the FDA, regardless of the existence of a patent covering the product. Further, the invention, even if patented itself, cannot be commercialized if it infringes the valid patent rights of another party.

Changes in U.S. patent law or the patent law of other countries or jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

The United States has enacted and implemented wide-ranging patent reform legislation. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on actions by Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce patents that we have licensed or that we might obtain in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions or changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we have licensed or that we may obtain in the future.

We may not be able to protect our intellectual property rights throughout the world, which could impair our business.

Filing, prosecuting, and defending patents covering our product candidates and any future product candidate throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may have or obtain patent protection, but where patent enforcement is not as strong as that in the United States. These unauthorized products may compete with our products in such jurisdictions and take away our market share where we do not have any issued or licensed patents and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

If our future trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We intend to use registered or unregistered trademarks or trade names to brand and market ourselves and our products. Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make product that is similar to our current and future product candidates we intend to commercialize that is not covered by the patents that we own or license and have the right to enforce;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our future patent applications will not lead to issued patents;
- issued patents that we own or license may not provide us with any competitive advantages, or may be held invalid or unenforceable as a result of legal challenges;
- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; and we may not develop additional proprietary technologies that are patentable.

We rely on confidentiality agreements to protect our trade secrets. If these agreements are breached by our employees or other parties, our trade secrets may become known to our competitors.

We rely on trade secrets that we seek to protect through confidentiality agreements with our employees and other parties. If these agreements are breached, our competitors may obtain and use our trade secrets to gain a competitive advantage over us. We may not have any remedies against our competitors and any remedies that may be available to us may not be adequate to protect our business or compensate us for the damaging disclosure. In addition, we may have to expend resources to protect our interests from possible infringement by others.

If we are unable to obtain the statutory patent extension related to the review time in the United States, we may need to rely on marketing exclusivity under the Hatch-Waxman Amendments, the six month pediatric exclusivity, any 7- year Orphan Drug exclusivity, potential future formulation patents and up to ten years of data exclusivity in Europe.

Risks Related to Government Regulation

We may undertake international operations, which will subject us to risks inherent with operations outside of the United States.

Although we do not have any foreign operations at this time, we intend to seek to obtain market clearances in foreign markets that we deem to generate significant opportunities. However, even with the cooperating of a commercialization partner, conducting drug development in foreign countries involves inherent risks, including, but not limited to: difficulties in staffing, funding and managing foreign operations; unexpected changes in regulatory requirements; export restrictions; tariffs and other trade barriers; difficulties in protecting, acquiring, enforcing and litigating intellectual property rights; fluctuations in currency exchange rates; and potentially adverse tax consequences.

If we were to experience any of the difficulties listed above, or any other difficulties, any international development activities and our overall financial condition may suffer and cause us to reduce or discontinue our international development and registration efforts.

We depend on our information technology systems and those of our third-party collaborators, service providers, contractors or consultants. Our internal computer systems, or those of our third-party collaborators, service providers, contractors or consultants, may fail or suffer security breaches, disruptions, or incidents, which could result in a material disruption of our development programs or loss of data or compromise the privacy, security, integrity or confidentiality of sensitive information related to our business and have a material adverse effect on our reputation, business, financial condition or results of operations.

In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. Our internal technology systems and infrastructure, and those of our current or future third-party collaborators, service providers, contractors and consultants are vulnerable to damage from computer viruses, unauthorized access or use resulting from malware, natural disasters, terrorism, war and telecommunication and electrical failures, denial-of-service attacks, cyber-attacks or cyber-intrusions over the Internet, hacking, phishing and other social engineering attacks, persons inside our organizations (including employees or contractors), loss or theft, or persons with access to systems inside our organization. Attacks on information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and they are being conducted by increasingly sophisticated and organized foreign governments, groups and individuals with a wide range of motives and expertise. In addition to extracting or accessing sensitive information, such attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the security, confidentiality, integrity and availability of information. The prevalent use of mobile devices that access sensitive information also increases the risk of data security incidents which could lead to the loss of confidential information or other intellectual property. While to our knowledge we have not experienced any material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations or the operations of third-party collaborators, service providers, contractors and consultants, it could result in a material disruption of our development programs and significant reputational, financial, legal, regulatory, business or operational harm. The costs to us to mitigate, investigate and respond to potential security incidents, breaches, disruptions, network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position.

For example, the loss of clinical trial data from completed, ongoing or planned clinical trials for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any real or perceived security breach affects our systems (or those of our third-party collaborators, service providers, contractors or consultants), or results in the loss of or accidental, unlawful or unauthorized access to, use of, release of, or other processing of personally identifiable information or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed. Such a breach may require notification to governmental agencies, the media or individuals pursuant to various foreign, domestic (federal and state) privacy and security laws, if applicable, including the U.S. Health Insurance Portability and Accountability Act of 1996 (HIPAA), as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH), and its implementing rules and regulations, as well as regulations promulgated by the Federal Trade Commission and state breach notification laws. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyberattacks and other related incidents.

Any failure or perceived failure by us or any third-party collaborators, service providers, contractors or consultants to comply with our privacy, confidentiality, data security or similar obligations, or any data security incidents or other security breaches that result in the accidental, unlawful or unauthorized access to, use of, release of, processing of, or transfer of sensitive information, including personally identifiable information, may result in negative publicity, harm to our reputation, governmental investigations, enforcement actions, regulatory fines, litigation or public statements against us, could cause third parties to lose trust in us or could result in claims by third parties, including those that assert that we have breached our privacy, confidentiality, data security or similar obligations, any of which could have a material adverse effect on our reputation, business, financial condition or results of operations. To the extent we maintain individually identifiable health information, we could be subject to fines and penalties (including civil and criminal) under HIPAA for any failure by us or our business associates to comply with HIPAA's requirements. Moreover, data security incidents and other security breaches can be difficult to detect, and any delay in identifying them may lead to increased harm. While we have implemented data security measures intended to protect our information, data, information technology systems, applications and infrastructure, there can be no assurance that such measures will successfully prevent service interruptions or data security incidents.

Failure to comply with existing or future laws and regulations related to privacy or data security could lead to government enforcement actions (which could include civil or criminal fines or penalties), private litigation, other liabilities, and/or adverse publicity. Compliance or the failure to comply with such laws could increase the costs of our products and services, could limit their use or adoption, and could otherwise negatively affect our operating results and business.

Regulation of data processing is evolving, as federal, state, and foreign governments continue to adopt new, or modify existing, laws and regulations addressing data privacy and security, and the collection, processing, storage, transfer, and use of data. We and our partners may be subject to current, new, or modified federal, state, and foreign data privacy and protection laws and regulations (e.g., laws and regulations that address data privacy and data security including, without limitation, health data). These new or proposed laws and regulations are subject to differing interpretations and may be inconsistent among jurisdictions, and guidance on implementation and compliance practices are often updated or otherwise revised, which adds to the complexity of processing personal data. These and other requirements could require us or our partners to incur additional costs to achieve compliance, limit our competitiveness, necessitate the acceptance of more onerous obligations in our contracts, restrict our ability to use, store, transfer, and process data, impact our or our partners' ability to process or use data in order to support the provision of our products or services, affect our or our partners' ability to offer our products and services in certain locations, or cause regulators to reject, limit or disrupt our clinical trial activities.

In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. Furthermore, in June 2018, California enacted the California Consumer Privacy Act of 2018, or CCPA, which takes effect on January 1, 2020. The CCPA gives California residents certain rights related to their personal information, including the right to access and require deletion of their personal information, the right to opt out of certain personal information sharing, and the right to detailed information about how their personal information is collected, used and shared. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Although the CCPA includes exemptions for certain clinical trials data, the law may increase our compliance costs and potential liability with respect to other personal information we collect about California residents. The CCPA has prompted a wave of proposals for new federal and state privacy legislation that, if passed, could increase our potential liability, increase our compliance costs and adversely affect our business.

International data protection laws, including, without limitation, the General Data Protection Regulation ((EU) 2016/679)) (the "GDPR"), that took effect in May 2018, and member state data protection legislation, may also apply to health-related and other personal information obtained outside of the United States. These laws impose strict obligations on the ability to process health-related and other personal information of data subjects in the EU, including in relation to use, collection, analysis, and transfer of such personal information. These laws include several requirements relating to obtaining the consent of the individuals to whom the personal data relates, limitations on data processing, establishing a legal basis for processing, notification of data processing obligations or security incidents to appropriate data protection authorities or data subjects, the security and confidentiality of the personal data and various rights that data subjects may exercise.

The GDPR prohibits the transfer, without an appropriate legal basis, of personal data to countries outside of the European Economic Area, or EEA, such as the United States, which are not considered by the European Commission to provide an adequate level of data protection. Switzerland has adopted similar restrictions. Although there are legal mechanisms to allow for the transfer of personal data from the EEA and Switzerland to the United States, uncertainty about compliance with EU data protection laws remains and such mechanisms may not be available or applicable with respect to the personal data processing activities necessary to research, develop and market our products and services. For example, ongoing legal challenges in Europe to the mechanisms allowing companies to transfer personal data from the EEA to the United States could result in further limitations on the ability to transfer personal data across borders, particularly if governments are unable or unwilling to reach new or maintain existing agreements that support cross-border data transfers, such as the European Union-U.S. and Swiss-U.S. Privacy Shield framework. Additionally, other countries have passed or are considering passing laws requiring local data residency and/or restricting the international transfer of data.

Under the GDPR, regulators may impose substantial fines and penalties for non-compliance. Companies that violate the GDPR can face fines of up to the greater of 20 million Euros or 4% of their worldwide annual turnover (revenue). The GDPR has increased our responsibility and liability in relation to personal data that we process, requiring us to put in place additional mechanisms to ensure compliance with the GDPR and other EU and international data protection rules.

Failure to comply with U.S. and international data privacy and protection laws and regulations could result in government enforcement actions (which could include civil or criminal penalties, fines or sanctions), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, patients about whom we or our partners obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations related to security or privacy, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business. Compliance with data protection laws may be time-consuming, require additional resources and could result in increased expenses, reduce overall demand for our products and services and make it more difficult to meet expectations of or commitments to customers or partners.

Any of these matters could materially adversely affect our business, financial condition, or operational results.

Our relationships with customers and payors will be subject to applicable anti-kickback, fraud and abuse, transparency, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens, and diminished profits and future earnings.

Healthcare providers, physicians and payors play a primary role in the recommendation and prescription of any product candidates for which we may obtain marketing approval. Our arrangements with healthcare providers, payors, customers and others may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, market, sell and distribute any product candidates for which we may obtain marketing approval. Restrictions under applicable federal, state and foreign healthcare laws and regulations may affect our ability to operate, including:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;

- the federal False Claims Act, which imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- state and foreign anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and its implementing regulations, which also imposes obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- State and local laws which require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restricting payments that may be made to healthcare providers and report certain information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and drug pricing; and

- federal laws requiring drug manufacturers to report information related to payments and other transfers of value made to physicians and other healthcare providers, as well as ownership or investment interests held by physicians and their immediate family members, including under the federal Open Payments program, as well as other state and foreign laws regulating marketing activities.

If our operations are found to be in violation of any of the federal and state laws described above or any other government laws that apply to us, we may be subject to significant civil, criminal, and administrative penalties, including, without limitation, damages, fines, imprisonment, exclusion from participation in government healthcare programs, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment of restricting of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Healthcare legislative reform measures may have a negative impact on our business and results of operations.

The U.S. and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our future products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. For example, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, or collectively the ACA, was passed in March 2010 and substantially changed the way healthcare is financed and continues to significantly impact the U.S. pharmaceutical industry. Since the ACA's enactment, there have been, and continue to be, Congressional, executive branch, judicial, and regulatory challenges to the ACA. In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted, and we expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products.

Risks Related to Our Reliance on Third Parties

We have no manufacturing capabilities and depend on other parties for our manufacturing operations. If these manufacturers fail to meet our requirements and strict regulatory requirements, our product development and commercialization efforts may be materially harmed.

We do not own or operate facilities for drug manufacturing, storage, distribution or quality testing. We currently rely, and may continue to rely, on third-party contract manufacturers to manufacture APIs, drug products and other components of our product candidates. Reliance on third-party manufacturers may expose us to different risks than if we were to manufacture product candidates ourselves.

The manufacturing process for a product candidate is subject to FDA and foreign regulatory authority review. We, and our suppliers and manufacturers, must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as cGMPs. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA and foreign regulatory authorities. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or comparable foreign regulatory authorities, we may not be able to rely on their manufacturing facilities for the manufacture of our product candidates. Moreover, we do not control the manufacturing process at our contract manufacturers and are completely dependent on them for compliance with current regulatory requirements. In the event that any of our manufacturers fails to comply with such requirements or to perform its obligations in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty transferring such to another third party. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to enable us, or to have another third party, manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines; and we may be required to repeat some of the development program. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

We expect to continue to rely on third-party manufacturers if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. Any manufacturing facilities used to produce our products will be subject to periodic review and inspection by the FDA and foreign regulatory authorities, including for continued compliance with cGMP requirements, quality control, quality assurance and corresponding maintenance of records and documents. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements, comply with cGMPs or maintain a compliance status acceptable to the FDA or foreign regulatory authorities could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;
- loss of the cooperation of existing or future collaborators;
- subjecting third-party manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

Additionally, our contract manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our contract manufacturers were to encounter any of these difficulties, our ability to provide our product candidates to patients in preclinical and clinical trials, or to provide product for treatment of patients once approved, would be jeopardized.

We intend to rely on third parties to conduct our preclinical studies and clinical trials. If these third parties do not perform as contractually required or otherwise expected, we may not be able to obtain regulatory approval for our product candidates.

We do not currently intend to conduct preclinical studies or clinical trials on our own, and instead will rely on third parties, such as contract research organizations (CROs), medical institutions, clinical investigators and contract laboratories, to assist us with our preclinical studies and clinical trials. Accordingly, we will have less control over the timing, quality and other aspects of preclinical studies and clinical trials than we would have had we conducted them on our own. These investigators, CROs and consultants will not be our employees and we will have limited control over the amount of time and resources that they dedicate to our programs. These third parties may have contractual relationships with other entities, some of which may be our competitors, which may draw time and resources from our programs. The third parties with which we may contract might not be diligent, careful or timely in conducting our preclinical studies or clinical trials, resulting in the preclinical studies or clinical trials being delayed or unsuccessful.

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we will be responsible for ensuring that each of our preclinical studies and clinical trials are conducted in accordance with the general investigational plan and protocols for the trial as well as applicable legal and regulatory requirements. The FDA generally requires preclinical studies to be conducted in accordance with good laboratory practices and clinical trials to be conducted in accordance with good clinical practices, including for designing, conducting, recording and reporting the results of preclinical studies and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. Our reliance on third parties that we do not control will not relieve us of these responsibilities and requirements. Any adverse development or delay in our preclinical studies or clinical trials as a result of our reliance on third parties could have a material and adverse effect on our business, financial condition, results of operations and prospects.

We must enter into an agreement, including an existing agreement with a large shareholder, with, and depend upon, one or more partners to assist us in commercializing our product candidates.

Because of our limited financial and other resources, we must actively seek and enter into a collaboration with one or more partners to assist us in our product launch, if marketing approval is granted. Any collaboration agreement we enter into may contain unfavorable terms, for example, with respect to product candidates covered, control over decisions and responsibilities, termination rights, payment, and other significant terms. Our ability to receive any significant revenue from our product candidates covered by the collaboration agreement will be dependent on the efforts of our collaboration partner and may result in lower levels of income to us than if we marketed our product candidates entirely on our own. The collaboration partner may not fulfill its obligations or commercialize our product candidates as quickly as we would like. We could also become involved in disputes with our partner, which could lead to delays in or termination of our commercialization programs and time-consuming and expensive litigation or arbitration. If a collaboration partner terminates or breaches its agreement with us, or otherwise fails to complete its obligations in a timely manner, the chances of successfully developing or commercializing our product candidates would be materially and adversely affected.

We also currently have an existing agreement with our largest shareholder where they have a right of first refusal to commercialize certain of our products in Asia, including d-methadone. If the parties do not agree to the terms of such a license then they could force binding arbitration to protect their rights to commercialize in Asia. Accordingly, the terms of such a license could be on unfavorable terms to us.

Additionally, depending upon the collaboration partner that we choose, other companies that might otherwise be interested in developing products with us could be less inclined to do so because of our relationship with the collaboration partner. If our ability to work with present or future strategic partners or collaborators is adversely affected as a result of our collaboration agreement, our business prospects may be limited and our financial condition may be adversely affected.

If we are unable to develop our own sales, marketing and distribution capabilities, or if we are not successful in contracting with third parties for these services on favorable terms, or at all, our product revenues could be disappointing.

We currently have no sales, marketing or distribution capabilities. In order to commercialize our products, if any are approved by the FDA, we will either have to develop such capabilities internally or collaborate with third parties who can perform these services for us. If we decide to commercialize any of our drugs ourselves, we may not be able to hire the necessary experienced personnel and build sales, marketing and distribution operations which are capable of successfully launching new drugs and generating sufficient product revenues. In addition, establishing such operations will take time and involve significant expense.

If we decide to enter into new co-promotion or other licensing arrangements with third parties, we may be unable to locate acceptable collaborators because the number of potential collaborators is limited and because of competition from others for similar alliances with potential collaborators. Even if we are able to identify one or more acceptable new collaborators, we may not be able to enter into any collaborative arrangements on favorable terms, or at all.

In addition, any revenues we receive would depend upon our collaborators' efforts which may not be adequate due to lack of attention or resource commitments, management turnover, change of strategic focus, business combinations or other factors outside of our control. Depending upon the terms of our collaboration, the remedies we have against an under-performing collaborator may be limited. If we were to terminate the relationship, it may be difficult or impossible to find a replacement collaborator on acceptable terms, or at all.

Risks Related to Ownership of Our Common Stock

There is a limited market for our common stock that may make it more difficult to dispose of your stock.

Our common stock is currently listed on the Nasdaq Capital Market under the symbol "RLMD". There is a limited trading market for our common stock. Accordingly, there can be no assurance as to the liquidity of any markets that may develop for our common stock, the ability of holders of our common stock to sell shares of our common stock, or the prices at which holders may be able to sell their common stock.

A sale of a substantial number of shares of our common stock may cause the price of the common stock to decline.

If our stockholders sell substantial amounts of our common stock in the public market, the market price of our common stock could fall. These sales also may make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem reasonable or appropriate. Stockholders who have held their shares for at least six months are be able to sell their shares pursuant to Rule 144 under the Securities Act of 1933, as amended (the Securities Act). We have registered under separate registration statements in aggregate up to 10,894,658 shares of our common stock for sale into the public market by certain selling stockholders named therein. These shares represent a large number of shares of our common stock, and if sold in the market all at once or at about the same time, could depress the market price of our common stock during the period the registration statement remains effective and could also affect our ability to raise equity capital.

We are subject to the reporting requirements of federal securities laws, which can be expensive and may divert resources from other projects, thus impairing our ability grow.

We are a public reporting company and, accordingly, subject to the information and reporting requirements of the Exchange Act and other federal securities laws, including compliance with the Sarbanes-Oxley Act of 2002 (the Sarbanes-Oxley Act). The costs of preparing and filing annual and quarterly reports, proxy statements and other information with the SEC and furnishing audited reports to stockholders would cause our expenses to be higher than they would be if we remained privately held.

It may be time consuming, difficult and costly for us to develop and implement the internal controls and reporting procedures required by the Sarbanes-Oxley Act. We may need to hire additional financial reporting, internal controls and other finance personnel in order to develop and implement appropriate internal controls and reporting procedures. If we are unable to comply with the internal controls requirements of the Sarbanes-Oxley Act, then we may not be able to obtain the independent accountant certifications required by such act, which may preclude us from keeping our filings with the SEC current.

If we fail to establish and maintain an effective system of internal control, we may not be able to report our financial results accurately or to prevent fraud. Any inability to report and file our financial results accurately and timely could harm our reputation and adversely impact the trading price of our common stock.

Effective internal control is necessary for us to provide reliable financial reports and prevent fraud. If we cannot provide reliable financial reports or prevent fraud, we may not be able to manage our business as effectively as we would if an effective control environment existed, and our business and reputation with investors may be harmed. As a result, our small size and any current internal control deficiencies may adversely affect our financial condition, results of operation and access to capital. We have not performed an in-depth analysis to determine if historical un-discovered failures of internal controls exist, and may in the future discover areas of our internal control that need improvement. In addition, as a smaller reporting company, our independent registered public accounting firm is not required to formally attest to the effectiveness of our internal control over financial reporting so long as we remain a smaller reporting company, which could increase the likelihood of undiscovered errors in our internal controls or reported financial statements as compared to issuers whose independent registered public accounting firms have provided such attestations.

Public company compliance may make it more difficult to attract and retain officers and directors.

The Sarbanes-Oxley Act and new rules subsequently implemented by the SEC have required changes in corporate governance practices of public companies. As a public company these new rules and regulations to increase our compliance costs and make certain activities more time consuming and costly. As a public company, these new rules and regulations may make it more difficult and expensive for us to obtain director and officer liability insurance in the future and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified persons to serve on our board of directors or as executive officers.

Our stock price may be volatile.

The market price of our common stock is likely to be highly volatile and could fluctuate widely in price in response to various factors, many of which are beyond our control, including the following:

- changes in our industry;
- competitive pricing pressures;
- our ability to obtain working capital financing;
- additions or departures of key personnel;
- limited "public float" in the hands of a small number of persons whose sales or lack of sales could result in positive or negative pricing pressure on the market price for our common stock;
- sales of our common stock;
- our ability to execute our business plan;
- operating results that fall below expectations;
- loss of any strategic relationship;
- regulatory developments;
- economic and other external factors;
- period-to-period fluctuations in our financial results; and
- inability to develop or acquire new or needed technology or products.

In addition, the securities markets have from time to time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. These market fluctuations may also materially and adversely affect the market price of our common stock.

The Nevada Revised Statutes and our articles of incorporation and bylaws contain provisions that could discourage, delay or prevent a change in control of our Company, prevent attempts to replace or remove current management and reduce the market price of our stock.

Provisions in our articles of incorporation and bylaws may discourage, delay or prevent a merger or acquisition involving us that our stockholders may consider favorable. For example, our articles of incorporation authorize our board of directors to issue up to 200,000,000 shares of "blank check" preferred stock. As a result, without further stockholder approval, the board of directors has the authority to attach special rights, including voting and dividend rights, to this preferred stock. With these rights, preferred stockholders could make it more difficult for a third party to acquire us.

We are also subject to the anti-takeover provisions of the Nevada Revised Statutes (NRS). Depending on the number of residents in the state of Nevada who own our shares, we could be subject to the provisions of Sections 78.378 et seq. of the Nevada Revised Statutes, which, unless otherwise provided in the Company's articles of incorporation or by-laws, restricts the ability of an acquiring person to obtain a controlling interest of 20% or more of our voting shares. Our articles of incorporation and by-laws do not contain any provision which would currently keep the change of control restrictions of Section 78.378 from applying to us.

In addition, our articles of incorporation and amended and restated bylaws provide that our board of directors is classified into three classes of directors with staggered three-year terms. Only one class of directors will be elected at each annual meeting of stockholders, with the other classes continuing for the remainder of their respective three-year terms. A third party may be discouraged from making a tender offer or otherwise attempting to obtain control of us as it is more difficult and time consuming for stockholders to replace a majority of the directors on a classified board of directors.

Our bylaws provides that a Nevada court and the federal district courts of the United States will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Pursuant to our bylaws, to the fullest extent permitted by law, and unless we consent in writing to the selection of an alternative forum, the Eighth Judicial District Court of Clark County, Nevada, is the sole and exclusive forum for any stockholder (including a beneficial owner of stock) to bring (a) any derivative action or proceeding brought in the name or right of the Company or on our behalf, (b) any action asserting a claim of, or a claim based on, breach of any fiduciary duty owed by any current or former director, officer, employee, agent or stockholder of the Company to the Company or the Company's stockholders, (c) any action arising or asserting a claim arising pursuant to any provision of NRS Chapters 78 or 92A or any provision of the articles of incorporation or our bylaws or (d) any action asserting a claim against us or any current or former director, officer, employee or stockholder (including a beneficial owner of stock) governed by the internal affairs doctrine, including, without limitation, any action to interpret, apply, enforce or determine the validity of our articles of incorporation or bylaws. By its terms, to the fullest extent permitted by law, our forum selection provision applies to actions arising under the Securities Act or Exchange Act. (However, Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder, and the Company does not intend for its exclusive forum jurisdiction provision to apply to Exchange Act claims.) These choice of forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees. If a court were to find the choice of forum provision contained in our bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business.

Our common stock was formerly deemed a "penny stock," which imposes certain limitations on us.

Prior to our 1-for-4 reverse stock split on September 30, 2019, and the listing of our common stock on the Nasdaq Capital Market on October 10, 2019, our common stock was considered a "penny stock" under the Exchange Act. The penny stock rules generally apply to companies whose common stock is not listed on a national securities exchange and trades at less than $5.00 per share, other than companies that have had average revenue of at least $6,000,000 for the last three years or that have tangible net worth of at least $5,000,000 ($2,000,000 if the company has been operating for three or more years). These rules imposed certain investor suitability and other requirements on brokers who traded our stock. Although currently our common stock is not subject to such limitations, because we offered and sold a "penny stock" in the past, we are considered an "ineligible issuer" under rule 405 of the Securities Act and remain subject to certain limitations until three years after our last offering of penny stock, including limitations on our ability to use free writing prospectuses and on the ability of brokers to publish research reports on us.

You may have difficulty trading our common stock.

There is a limited trading market for our common stock. As a result, investors may find it difficult to dispose of shares of our common stock. Accordingly, investors may therefore bear the economic risk of an investment in our common stock, for an indefinite period of time. Even if an active market develops for the common stock, Rule 144 promulgated under the Securities Act (Rule 144), which provides for an exemption from the registration requirements under the Securities Act under certain conditions, requires, among other conditions, a one-year holding period prior to the resale (in limited amounts) of securities acquired in a non-public offering without having to satisfy the registration requirements under the Securities Act. There can be no assurance that we will fulfill any reporting requirements in the future under the Exchange Act or disseminate to the public any current financial or other information concerning us, as is required by Rule 144 as part of the conditions of its availability.

Exhibit 99.3


RELMADA
THERAPEUTICS
Targeting Major Advances in Treatment of CNS Disorders
December 2019
Nasdaq: RLMD

Disclosures

Certain statements contained in this presentation or in other documents of Relmada Therapeutics, Inc. (the "Company"), along with certain statements that may be made by management of the Company orally in presenting this material, may contain "forward-looking statements." These statements can be identified by the fact that they do not relate strictly to historic or current facts. They use words such as "estimate," "expect," "intend," "believe," "plan," "anticipate," "projected" and other words and terms of similar meaning in connection with any discussion of future operating or financial performance or condition. These statements are based upon the current beliefs and expectations of the Company's management and are subject to significant risks and uncertainties. Statements regarding future action, future performance and/or future results including, without limitation, those relating to the timing for completion, and results of, scheduled or additional clinical trials and the FDA's or other regulatory review and/or approval and commercial launch and sales results (if any) of the Company's formulations and products and regulatory filings related to the same may differ from those set forth in the forward-looking statements. Peak sales and market size estimates have been determined on the basis of market research and comparable product analysis, but no assurances can be given that such sales levels will be achieved, if at all, or that such market size estimates will prove accurate.

Because actual results are affected by these and other potential risks, contingencies and uncertainties, the Company cautions investors that actual results may differ materially from those expressed or implied in any forward-looking statement. It is not possible to predict or identify all such risks, contingencies and uncertainties. The Company identifies some of these factors in its Securities and Exchange Commission ("SEC") filings on Forms 10-K, 10-Q and 8-K, and investors are advised to consult the Company's filings for a more complete listing of risk factors, contingencies and uncertainties affecting the Company and its business and financial performance.

The Company assumes no obligation to update forward-looking statements as circumstances change. Investors are advised to consult further disclosures that the Company makes or has made on related subjects in the Company's Form 10-K, 10-Q and 8-K reports.

Investment Highlights

Highly-compelling lead product opportunity w/ REL-1017

Phase 2a TRD trial completed with positive results

Statistically significant and rapid anti-depressant effects observed with favorable safety and tolerably profile

Fast track designation from FDA

Strong IP position around REL-1017 with protection to the mid-2030s

Management team and scientific advisors have considerable CNS expertise

Johnson & Johnson, Eli Lilly, Pfizer, Shire,

Harvard, Yale, Cornell

REL-1017 has potential in multiple underserved markets[1]

Significant potential in multiple additional indications including Major Depressive Disorders (MDD)

~ 17.3M Americans suffered from MDD in 2017[1]

~ 10 to 30% of MDD patients suffer from Treatment Resistant Depression[2]

Multiple key catalysts expected over next 12-18 months*

Presentation of REL-1017 Phase 2 TRD study full data H1 2020

End of TRD Phase 2 meeting with the FDA H1 2020

Start of pivotal program in TRD H2 2020

Start of Phase 2 study in MDD H2 2020

1. https://www.nimh.nih.gov/health/statistics/major-depression.shtml
2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3363299/

* Our fiscal year end is June 30. However the periods referred to in this slide are calendar years and quarters


d-Methadone (REL-1017)
as a Potential Treatment for Depression

REL-1017 Program Overview

Relmada is focused on advancing d-methadone (REL-1017) as a rapid-acting oral treatment for depression and other CNS disorders.

Compelling Lead Product Candidate: REL-1017

- REL-1017 is a non-competitive N-methyl-D-aspartate Receptor (NMDAR) antagonist
- REL-1017 has the potential to be the first oral NMDAR antagonist for the treatment of depression and treatment resistant depression
- Completed Phase 1 and Phase 2 trial for treatment of Treatment Resistant Depression (TRD)
- In a Phase 2a trial, both doses of REL-1017 25 mg and 50 mg demonstrated rapid onset and sustained antidepressant effects with statistically significant differences compared to placebo on all efficacy measures
    - Study demonstrated rapid onset and long-lasting antidepressant effects
    - Only mild and moderate AEs - no serious AEs
    - No evidence of treatment induced dissociative and psychotomimetic AEs
    - No evidence of opiate withdrawal symptoms in treatment groups vs placebo

d-Methadone is an NMDAR antagonist with Significant Potential Advantages in the Treatment of Depression

Novel mechanism of action

d-Methadone and other NMDA antagonists represent a new approach to treating depression with MOA markedly different from currently approved drugs (SSRIs, SNRIs, TCAs, MAOIs, etc.)

Rapid onset

Faster onset of antidepressant activity – statistically significant difference in MADRS score vs placebo after 4 days of treatment

Long lasting effect – statistically significant difference in MADRS score vs placebo seven days after termination of a 7-day treatment

Most of the currently approved products take up to a month to show antidepressant activity

d-Methadone has the potential to address a high unmet need in MDD [1]

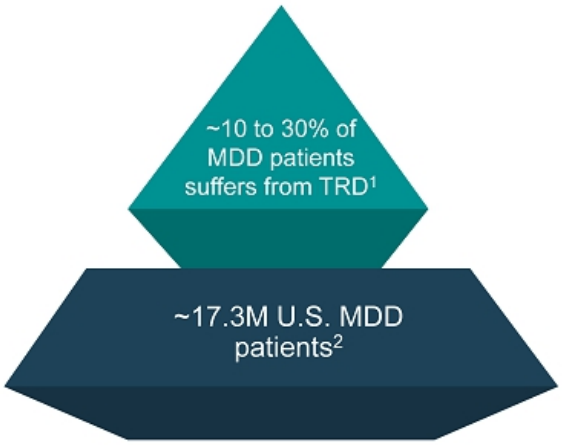
~65% MDD patients do not respond to first antidepressant treatment

~30% MDD patients do not respond to up to 4 different antidepressant treatments

Potentially equal or superior antidepressant effects with better safety profile than ketamine

1 Source: Am J Psychiatry. 2006 Nov;163(11):1905-17, https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHDetailedTabs2017/NSDUHDetailedTabs2017.htm#tab8-10A

An Effective Treatment for Treatment-Resistant Depression (TRD) Remains a High Unmet Need



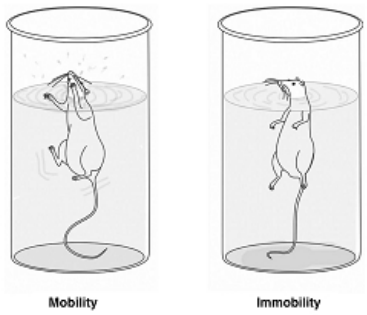
1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3363299/
2. https://www.nimh.nih.gov/health/statistics/major-depression.shtml

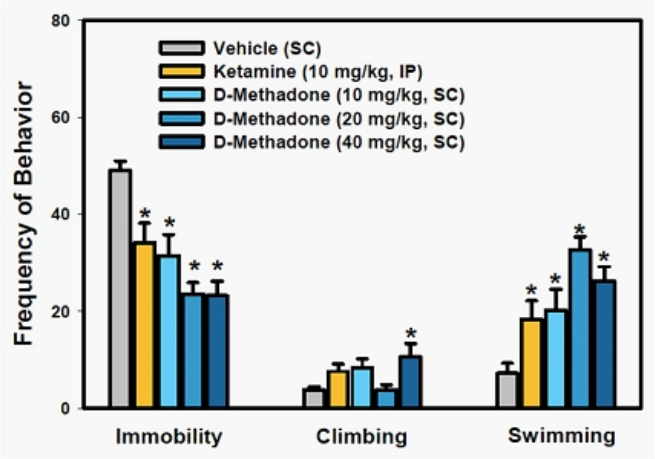
Expanding Focus on NMDAR's Role in Treatment of Depression

Strong Anti-Depressant Effects Observed in Three Animal Models of Depression

Improved performance on the rat forced swim test 24 hours after d-methadone treatment

Forced Swim Test





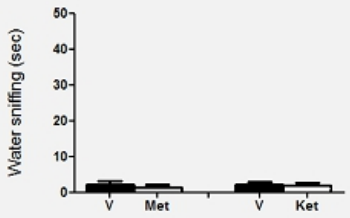
* = p<0.05 compared to placebo group

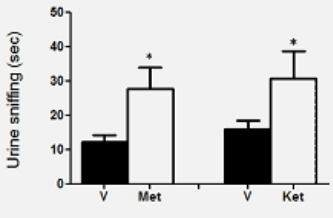
PsychoGenics – Dr. Taleen Hanania
Data published: Hanania, T. et al., Exp Clin Psychopharmacol. 2019 Aug 1.

Strong Anti-Depressant Effects Observed in Three Animal Models of Depression

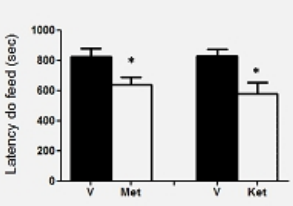
Improved performance on the rat FUST and the NSFT 24 hours after d-methadone treatment

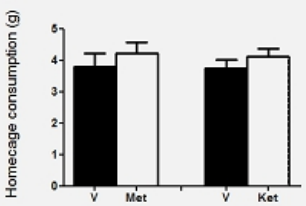
Female Urine Smell Test





Novelty Suppressed Feeding Test





* = p<0.05 compared to placebo group - Dr. Ron Duman's laboratory - Yale Medical School
Data published: Fogaça, MV et al., Neuropsychopharmacology. 2019 Dec;44(13):2230-2238.

Phase 1 SAD and MAD Study Showed Favorable Safety and Tolerability Profile

Single Ascending Dose (SAD) Study Design

Parallel group, double-blind, placebo controlled

Objectives

- Establish PK, PD and safety of single dose administration

Treatment Administration

- Cohorts 5, 20, 60, 100, 150, 200 mg
- N = 42

Study Conclusions

- MTD = 150 mg (single dose)
- PK demonstrated linear proportionality of C_{max} and $AUC_{0\text{-}inf}$ vs. dose
- No clinically significant opioid effects of dextromethadone up to 150 mg

Multiple Ascending Dose (MAD) Study Design

Parallel group, double-blind, placebo controlled

Objectives

- Establish PK, PD and safety of once daily, 10 day administration

Treatment Administration

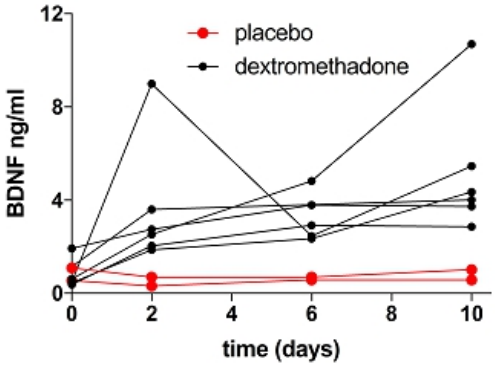
- Cohorts 25, 50, 75 mg
- N = 24

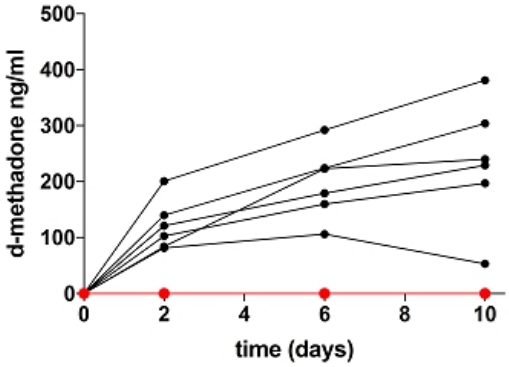
Study Conclusions

- Doses up to 75mg per day well tolerated
- Dose proportionality was demonstrated for the single-dose parameters Cmax and AUC_τ on Day 1 and for the steady state parameters Cmax, AUC_τ, and Css on Day 10

PK: pharmacokinetics; PD: pharmacodynamics; MTD: maximum tolerated dose; Cmax: maximum plasma concentration; AUC: area under the curve 0 to infinite time; AUC_τ : area under the curve to the end of dosing period
Data published: Bernstein, G. et al., J. Clin. Psychopharmacology 2019 May/Jun;39(3):226-237.

d-Methadone Significantly Increased BDNF Plasma Levels Compared to Placebo in Phase 1 MAD Study in Healthy Volunteers



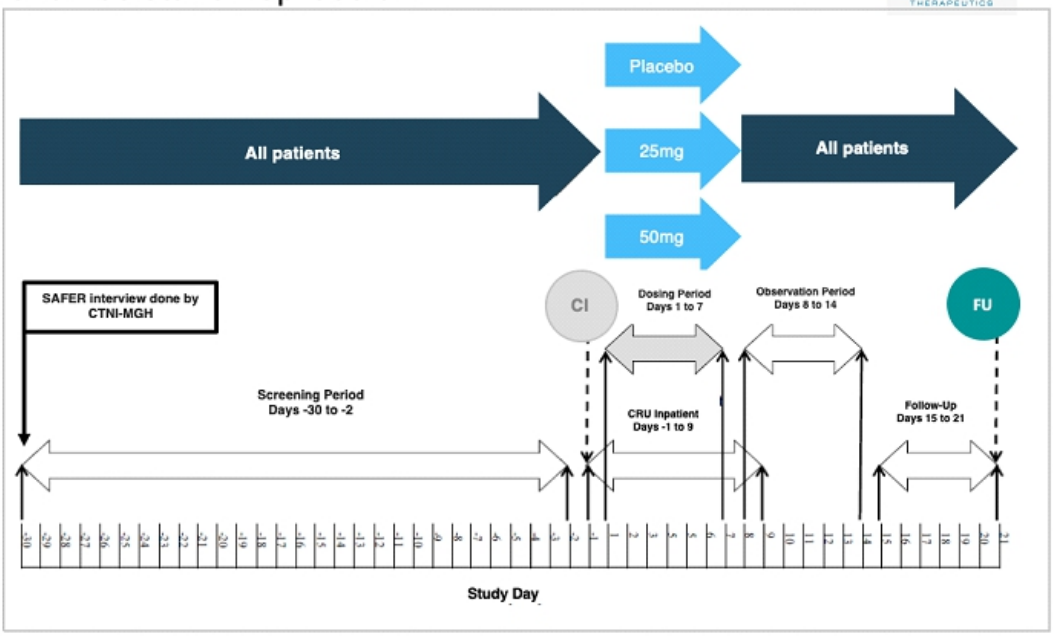


Treatment Arm	Average Plasma BDNF ng/ml (±SD)	
	Pre-treatment	Post-treatment
d-Methadone	0.84 (0.60)	5.84 (2.83)
Placebo	0.81 (0.38)	0.79 (0.30)

BDNF: Brain Derived Neutrophic Factor; SD: standard deviation

REL-1017 – Phase 2a Study Evaluated Safety and Tolerability, PK and Efficacy in Treatment Resistant Depression

- RDPC study of 7-day dosing at 25 mg and 50 mg QD as adjunctive therapy in MDD subjects who did not respond to adequate antidepressant treatments (TRD)
- 11 U.S. sites
- Dose selection based on effect measured in pre-clinical studies
- 62 subjects randomized to three arms:
  - placebo, 25 mg/day, 50 mg/day
- **Primary Endpoints**
  - safety and tolerability
- **Secondary Endpoints**
  - efficacy (MADRS, SDQ, CGIs)
  - pharmacokinetic (PK) profile



RDPC = randomized double-blind placebo controlled; MADRS = Montgomery-Asberg Depression Rating Scale; SDQ = Symptoms of Depression Questionnaire; CGIs = Clinical Global Impression scales

Study REL-1017-202 Was Designed to Provide Data on Safety, PK and Efficacy of REL-1017 in Treatment Resistant Depression

Primary Objectives	Primary Endpoints
Safety and tolerability of 25 mg and 50 mg of REL-1017 vs placebo as adjunctive treatment	PE, Laboratory studies, ECG, AEs CADSS (dissociative symptoms) 4-item PSRS (psychotomimetic symptoms) COWS (opiate withdrawal symptoms) C-SSRS (suicidality)
Secondary Objectives	**Secondary Endpoints**
To characterize pharmacokinetic (PK) profile of REL-1017 25 mg and 50 mg x 7 days	PK parameters for both 25 and 50 mg qday
To explore the efficacy of 25 mg and 50 mg of REL-1017 as adjunctive treatment in patients with TRD	Change from BSL at Day 2, 4, 7 and 14 on: • MADRS • SDQ • CGI-S Difference in CGI-I score placebo vs treatment groups Day 2 to 14

PE: Physical exam; ECG: Electrocardiogram; AEs: Adverse Events; CADSS: Clinician Administered Dissociative States Scale;
PSRS: Positive Symptom Rating Scale; COWS: Clinical Opiate Withdrawal Scale; C-SSRS: Columbia-Suicide Severity Rating Scale;
MADRS: Montgomery Asberg Depression Rating Scale; SDQ: Symptoms of Depression Questionnaire; CGI-S and CGI-I: Clinical Global Impression- Severity and Improvement

Subjects' Disposition, Demographic Characteristics and Depression Severity Were Homogeneously Distributed Across Arms

	Placebo	REL-1017 25 mg	REL-1017 50 mg	All Subjects
Randomized Subjects	22	19	21	62
Completed all visits (Day 21)	20	18	19	57
Received all doses	21	19	21	61
Age: mean years (SD)	49.7 (11.1)	49.4 (12.4)	48.6 (10.9)	49.2 (11.3)
Females	11 (50%)	8 (42.1%)	9 (42.9%)	28 (45.2%)
Subjects ITT	22	19	21	62
Subjects PPP	21	19	21	61
Screening HAMD - Mean (SD)	25.6 (3.5)	25.1 (3.5)	25.0 (3.8)	25.3 (3.6)
Baseline MADRS - Mean (SD)	33.8 (4.0)	32.9 (6.0)	35.2 (3.9)	34.0 (4.7)

ITT: Intent-To-Treat; PPP: Per-Protocol-Population; HAMD: Hamilton Depression Rating Scale; MADRS: Montgomery-Asberg Depression Rating Scale

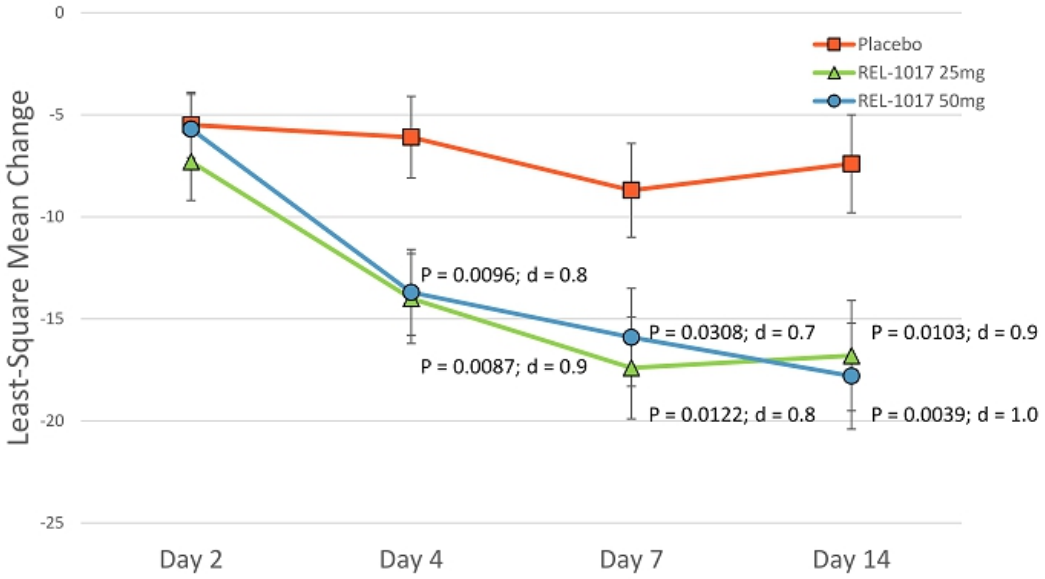
Study REL-1017 Phase 2a Key Safety Findings

REL-1017-202 results confirm the favorable tolerability and safety profile observed in the Phase 1 SAD and MAD studies
Only Mild and Moderate AEs - no SAEs
No increased prevalence of specifically relevant organ group AEs in treatment groups vs placebo
No evidence of treatment induced dissociative symptoms in the treatment groups vs placebo
No evidence of treatment induced psychotomimetic symptoms in treatment groups vs placebo
No evidence of opiate withdrawal symptoms in treatment groups vs placebo

Study REL-1017 Phase 2a Key Efficacy Findings

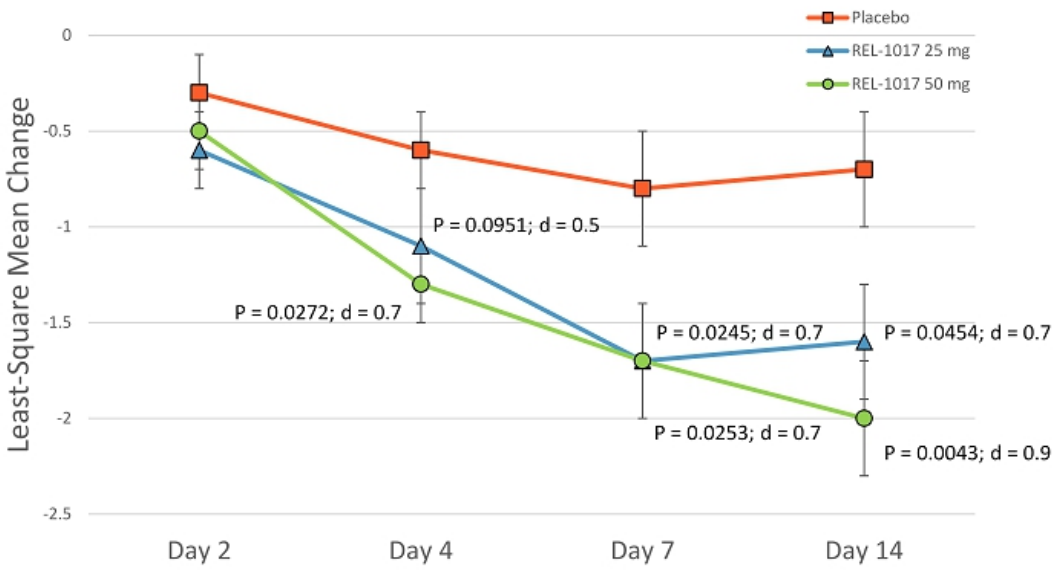
REL-1017 25 mg and 50 mg show rapid onset and sustained antidepressant effects with statistically significant differences compared to placebo on all efficacy measures
Solid effects observed on MADRS with P values < 0.03 and large effect sizes (0.7- 1.0) from Day 4 to Day 14
CGI-S and CGI-I solid findings consistent with MADRS results with P-values and effect sizes of similar magnitude
SDQ scores with moderate effect size differences (d = 0.4 and 0.5) from Day 4 to Day 7 and with both statistically significant differences and large effect size for both 25 mg (P = 0.0066; d = 0.9) and 50 mg (P= 0.0014; d = 1.1) arms at Day 14
Study demonstrates rapid onset and long-lasting antidepressant effects
Findings support continuing clinical development and larger pivotal study

MADRS Scores in the Treatment Groups Achieved Statistically Significant Difference vs Placebo from Day 4 through Day 14



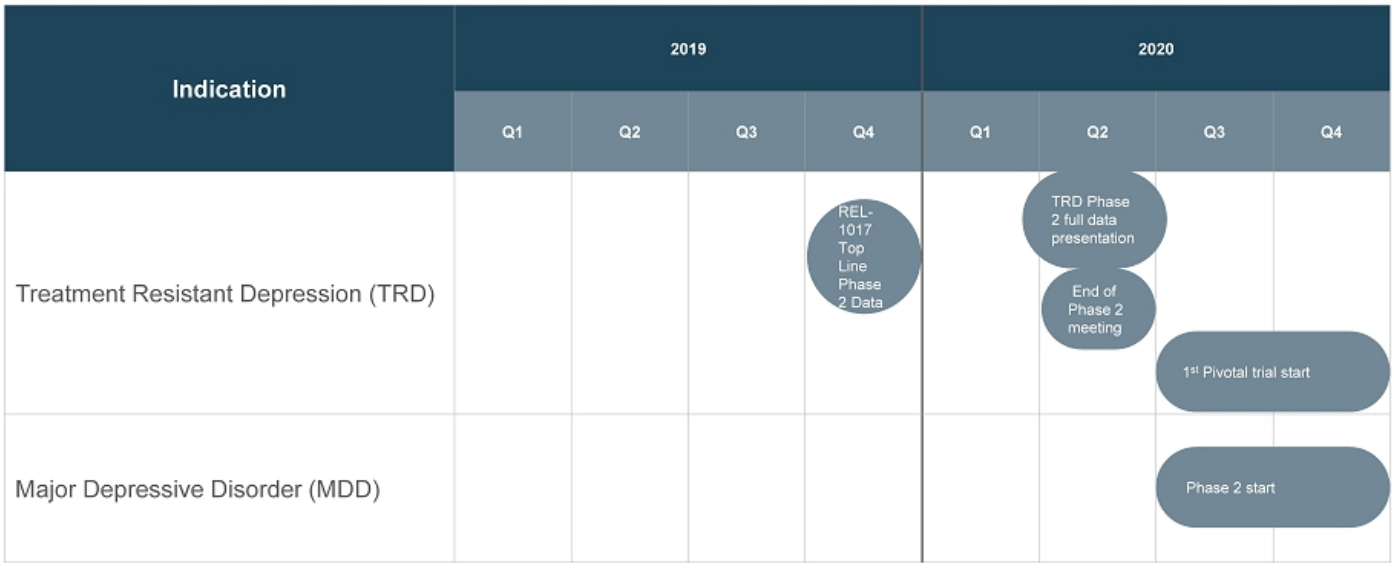
MADRS: Montgomery-Asberg Depression Rating Scale; ITT: Intent-To-Treat; Error Bars: Standard Errors; P and d values as Treatment vs Placebo

CGI-S Scores Achieved Statistically Significant Difference vs Placebo from Day 4 for REL-1017 50 mg and for both Doses on Day 7 and Day 14



CGI-S: Clinical Global Impression of Severity; ITT: Intent-To-Treat; Error Bars = Standard Errors; P and d values as Treatment vs Placebo

Anticipated Development Timeline REL-1017*



* May be delayed based on FDA feedback and other factors .

Our fiscal year end is June 30. However the periods referred to in this slide are calendar years and quarters

Potential Competitive Advantages of d-Methadone

Compound (Company)	Mechanism of Action	Delivery	Current Clinical Stage	Dosing Regimen
Dextromethadone (Relmada)	Non-competitive NMDA channel blocker	Oral	Completed Phase 2	Once Daily
Esketamine (Janssen/J&J)		Nasal (administered in clinic)	Approved and launched	Biweekly
AXS-05 DM 45 mg + BUP 105 mg (Axsome)	Multimodal (NMDA+others)	Oral	Phase 3	Twice daily
Sage-217	GABA receptor allosteric modulator	Oral	Phase 3	Once Daily

Corporate Information

Financial Overview

Cash & Cash Equivalents (as of 9/30/19)	**$7.8 million**
Common Shares Outstanding (as of 11/8/19)	**~10.3 million**

Investment Highlights

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Johnson & Johnson, Eli Lilly, Pfizer, Shire,

Harvard, Yale, Cornell

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2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3363299/

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Management Team and Key Scientific Advisors

Management

Sergio Traversa	PharmD, MBA, Chief Executive Officer	Johnson & Johnson, Lilly
Ottavio Vitolo	Senior Vice President, Head of R&D and Chief Medical Officer	Pfizer, Shire, Massachusetts General Hospital, Harvard University
Chuck Ence	Chief Financial Officer	PepsiCo, NewAge

Advisors

Maurizio Fava	Scientific Advisor	Harvard University, Massachusetts General Hospital
Charles Inturrisi	Scientific Advisor	Cornell University
Paolo Manfredi	Scientific Advisor	Memorial Sloan Kettering Cancer Center, MD Anderson Cancer Network, Massachusetts General Hospital, Mount Sinai


RELMADA
THERAPEUTICS
Targeting Major Advances in Treatment of CNS Disorders
December 2019
Nasdaq: RLMD