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

FORM 10-K

☒ ANNUAL REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

□ TRANSITION REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2023

Commission file number: 000-55347

Relmada Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Nevada	**45-5401931**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

2222 Ponce de Leon Blvd., Floor 3
Coral Gables, FL 33134
(Address of principal executive offices) (Zip Code)

(786) 629 1376
(Registrant's telephone number, including area code)

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

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock ($.001 par value)	RLMD	The NASDAQ Global Select Market

Securities registered pursuant to section 12(g) of the Act:
None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes □ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes □ No ☒

Indicate by checkmark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No □

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No □

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	□	Accelerated filer	□
Non-accelerated filer	☒	Smaller reporting company	☒
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. □

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. □

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. □

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). □

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes □ No ☒

As of June 30, 2023 (the last business day of the registrant's most recently completed second fiscal quarter), the aggregate market value of the registrant's common stock held by non-affiliates of the registrant was $72,952,616, based on the closing price on that date as reported on the NASDAQ.

As of March 15, 2024, there were 30,174,202 shares of common stock, $0.001 par value per share, outstanding.

Documents Incorporated by Reference

Portions of the registrant's definitive proxy statement for its 2024 Annual Meeting of Stockholders (the "Proxy Statement"), to be filed within 120 days of the registrant's fiscal year ended December 31, 2023, are incorporated by reference in Part III of this Annual Report on Form 10-K. Except with respect to information specifically incorporated by

reference in this Annual Report on Form 10-K, the Proxy Statement is not deemed to be filed as part of this Annual Report on Form 10-K.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (this Report) contains forward looking statements that involve risks and uncertainties, principally in the sections entitled "Description of Business," "Risk Factors," and "Management's Discussion and Analysis of Financial Condition and Results of Operations." 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 on Form-10-K. 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 on Form-10-K to conform our statements to actual results or changed expectations.

PART I

All brand names or trademarks appearing in this report are the property of their respective holders. Unless the context requires otherwise, references in this report to "Relmada," the "Company," "we," "us," and "our" refer to Relmada Therapeutics, Inc., a Nevada corporation.

ITEM 1. BUSINESS

Business Overview

Relmada Therapeutics, Inc. (Relmada, the Company, we or us) (a Nevada corporation), is a clinical-stage biotechnology company focused on the development of esmethadone (d-methadone, dextromethadone, REL-1017), an N-methyl-D-aspartate (NMDA) receptor antagonist. Esmethadone, an isomer of 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.

Our lead product candidate, esmethadone, is being developed as a rapidly acting, oral agent for the treatment of depression and other potential indications. On October 15, 2019, we reported top-line data from study REL-1017-202. During late 2022, we announced RELIANCE I and III, both Phase 3 trials, did not achieve their primary endpoints. Relmada has completed its long term, open label study and plans to complete two additional ongoing adjunctive Phase 3 trials (RELIANCE II and RELIGHT).

Relmada also intends, in 2024, to enter human studies of its proprietary, modified-release formulation of psilocybin (REL-P11) in doses that we believe are lower than those associated with psychedelic effects for metabolic indications.

Phase 2 Clinical Trial

In the REL-1017-202 study, 62 subjects, with an average age of 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 (ITT) analysis. No differences were observed between the ITT and PPP analyses and results.

We observed that subjects in both the REL-1017 25 mg and 50 mg treatment groups experienced statistically significant improvement on all efficacy measures tested as compared to subjects in the placebo group, including: MADRS; the Clinical Global Impression – Severity (CGI-S) scale; the Clinical Global Impression – Improvement (CGI-I) scale; and the Symptoms of Depression Questionnaire (SDQ).

Improvements on the MADRS endpoint 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 confirmed the tolerability profile of REL-1017, which was observed in the Phase 1 studies. Subjects experienced only 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 of d-Methadone, and there was no evidence of either treatment induced psychotomimetic and dissociative AEs or withdrawal signs and symptoms upon treatment discontinuation.

Phase 3 Program

On December 20, 2020, Relmada announced that the first patient had been enrolled in the first Phase 3 clinical trial (RELIANCE I) for the Company's lead product candidate, REL-1017, as an adjunctive treatment for Major Depressive Disorder (MDD).

On April 1, 2021, Relmada announced the initiation of RELIANCE II, the second of two sister pivotal Phase 3 clinical trials (RELIANCE I and RELIANCE II) for the Company's lead product candidate, REL-1017, as an adjunctive treatment for MDD.

On October 4, 2021, Relmada announced the initiation of RELIANCE III study, a monotherapy trial for the Company's lead product candidate, REL-1017.

In addition, on October 4, 2021, Relmada announced that in order to support potential regulatory submissions seeking approval for REL-1017 as adjunctive and monotherapy treatment, the Food and Drug Administration (FDA) confirmed that, based on what was known at the time, Relmada would not be required to conduct a two-year carcinogenicity study of REL-1017, as sufficient clinical data had been generated to date. The FDA also confirmed that Relmada would not need to conduct a TQT cardiac study in humans to support cardiac safety in potential regulatory submissions for REL-1017, as the data already provided and the data to be generated by the Phase 3 program would be adequate to evaluate the cardiac safety profile of REL-1017.

On August 9, 2022, Relmada announced that the FDA granted Fast Track designation to REL-1017 as a monotherapy for the treatment of MDD.

On October 13, 2022, Relmada announced that its RELIANCE III study, evaluating REL-1017 in the monotherapy setting for MDD, did not achieve its primary endpoint, which was a statistically significant improvement in depression symptoms compared to placebo as measured by MADRS on Day 28. In the study, the REL-1017 treatment arm showed a MADRS reduction of 14.8 points at Day 28 versus 13.9 points for the placebo arm, a higher than expected placebo response.

On December 7, 2022, Relmada announced that its RELIANCE I study, evaluating REL-1017 as an adjunctive treatment for MDD, did not achieve its primary endpoint, which was a statistically significant improvement in depression symptoms compared to placebo as measured by MADRS on Day 28. In the study, the REL-1017 treatment arm (n= 113) showed a MADRS reduction of 15.1 points at Day 28 versus 12.9 points for the placebo arm (n=114), which is a clinically meaningful difference of 2.3 points on the MADRS. The study also showed a nominally statistically significant difference in the response rate, with a response rate of 39.8% in the REL-1017 arm vs 27.2% in the placebo arm ($p<0.05$). Additionally, in a prespecified per protocol population analysis, the REL-1017 treatment arm (n=101) showed a MADRS reduction of 15.6 points at Day 28 versus 12.5 points for the placebo arm (n=97), a difference of 3.1 points, with nominal p=0.051.

Patients who completed the RELIANCE trials were eligible to rollover into the long-term, open-label study, Study 310, which also included subjects who had not previously participated in a REL-1017 clinical trial. This rollover study completed subject visits on July 11, 2023. On September 20, 2023, Relmada announced efficacy results for the de novo (or new to treatment) patients (204 patients) and safety results for all subjects (627 patients) from Study 310 of REL-1017 in patients with MDD. Patients treated daily with REL-1017 for up to one year experienced rapid, clinically meaningful, and sustained improvements in depressive symptoms and associated functional impairment. REL-1017 was well-tolerated with long-term dosing, showing low rates of adverse events and discontinuations due to adverse events. The most commonly reported adverse events deemed to be treatment-related all occurred included headache, nausea and dizziness. No new safety signals were detected.

On August 23, 2023, Relmada announced the dosing of the first patient in RELIGHT, a Phase 3 clinical trial for REL-1017, as an adjunctive treatment for MDD.

Human Abuse Potential (HAP) Studies

Top-line Results - Oxycodone:

On July 27, 2021, Relmada announced top-line results that showed that all three doses of REL-1017 (25 mg, 75 mg and 150 mg, the therapeutic, supratherapeutic and maximum tolerated doses (MTD), respectively) tested in recreational opioid users, demonstrated a highly statistically significant difference vs. the active control drug, oxycodone 40 mg. The study's primary endpoint was a measure of "likability" with the subjects rating the maximum effect (or Emax) for Drug Liking "at the moment", using a 1-100 bipolar rating scale (known as a visual analog scale or VAS), with 100 as the highest likability, 50 as neutral (placebo-like), and 0 the highest dislike. In summary, all tested doses of REL-1017, including the 150 mg MTD, showed a highly statistically significant difference in abuse potential versus oxycodone with p-values less than 0.05. Consistent results were seen for the secondary endpoints. Additionally, all REL-1017 doses including 150 mg (6 times the therapeutic dose and MTD) were statistically equivalent to placebo ($p<0.05$). These results support the lack of opioid effects of REL-1017.

Top-line Results - Ketamine:

On February 23, 2022, Relmada announced top-line results that showed that all three doses of REL-1017 (25 mg, 75 mg, and 150 mg, the therapeutic, supratherapeutic and MTD, respectively) tested in recreational drug users, demonstrated a substantial (30+ points) and statistically significant difference vs. the active control drug, intravenous ketamine 0.5 mg/kg over 40 minutes, and, importantly, were statistically equivalent to placebo. The study's primary endpoint was a measure of "likability" with the subjects rating the maximum effect (or Emax) for Drug Liking "at this moment", using a 1-100 bipolar rating scale (known as a visual analog scale or VAS), with 100 as the highest likability, 50 as neutral (placebo-like), and 0 the highest dislike. Consistent results are seen for the secondary endpoints.

Psilocybin Program (REL-P11):

On October 11, 2023, Relmada announced that it intends to enter human studies of its proprietary, modified-release formulation of psilocybin (REL-P11) for metabolic indications in doses that we believe are lower than those associated with psychedelic effects. The Company plans to commence a single-ascending dose Phase 1 trial in obese patients in the first half of 2024 to define the pharmacokinetic, safety and tolerability profile of Relmada's modified-release psilocybin formulation (REL-P11) in this population, followed by a Phase 2a trial to establish clinical proof-of-concept.

Pre-clinical data in a rodent model of metabolic dysfunction-associated steatotic liver disease (MASLD) demonstrated beneficial effects of psilocybin, on multiple metabolic parameters, including reduced hepatic steatosis, reduced body weight gain, and fasting blood glucose levels.

Key Upcoming Anticipated Milestones

We expect multiple key milestones over the next 12 months. These include:

- Complete enrollment in the ongoing RELIANCE II study, which is planned to enroll approximately 300 patients, with top-line data in the second half of 2024.
- Complete enrollment in the RELIGHT study (study 304), which is planned to enroll approximately 300 patients, by the end of 2024.
- Initiate Phase 1 trial in obese patients with the modified-release formulation of psilocybin (REL-P11) in the first half of 2024.

Our Development Program

Esmethadone (d-Methadone, dextromethadone, REL-1017) as a treatment for MDD

Background

In 2021, the National Institute of Mental Health (NIMH) estimated that 21.0 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, about 61% of adult Americans diagnosed with major depression received treatment in 2021. 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 addition to the high failure rate, only two of the marketed products for depression, esketamine (marketed by Johnson and Johnson as Spravato®), an in-clinic nasal spray treatment, and dextromethorphan-bupropion (marketed by Axsome as Auvelityä), can demonstrate rapid antidepressant effects, while the other currently approved products can take two to eight 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.

Esmethadone Overview and Mechanism of Action

Esmethadone's mechanism of action, as a low affinity, non-competitive NMDA channel blocker or antagonist, is fundamentally differentiated from most 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 and esketamine but potentially lacking their adverse side effects, esmethadone is being developed as a rapidly acting, oral agent for the treatment of depression and potentially other CNS 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-superimposable (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.

As a single isomer of racemic methadone, esmethadone has been shown to possess NMDA antagonist properties with virtually no traditional opioid or ketamine-like adverse events at the expected therapeutic doses. In contrast, racemic methadone is associated with common opioid 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, esmethadone, 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 CNS 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, esmethadone could show benefits in several different CNS indications.

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

While our current strategy is currently to focus on the further development of esmethadone as an adjunctive treatment for MDD, we are evaluating other indications that Relmada may explore in the future, including restless leg syndrome and other glutamatergic system activation related diseases.

Psilocybin Program

Relmada acquired the development and commercial rights to a novel psilocybin and derivative program from Arbormentis LLC in July of 2021. The original focus of the program was limited to neurodegenerative diseases. Psilocybin has neuroplastogen™ effects that have the potential to ameliorate the consequences of multiple neurodegenerative conditions. The pleiotropic metabolic effects of low-dose psilocybin were discovered while studying its neuroplastogen™ potential in a rodent model deficient in neurogenesis – obese rodents maintained on a high fructose, high fat diet (HFHFD). Specifically, in a rodent model of metabolic dysfunction-associated steatotic liver disease (MASLD), beneficial effects of psilocybin were observed on multiple metabolic parameters, including reduced hepatic steatosis, reduced body weight gain, and fasting blood glucose levels.

Our Corporate History and Background

We are a clinical-stage, publicly traded biotechnology company developing NCEs and novel versions of drug products that potentially address areas of high unmet medical need in the treatment of depression and other CNS diseases. We are also developing a novel modified release formulation of psilocybin for the treatment of metabolic indications.

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 approximately $98,791,700 and $157,043,800 for the years ended December 31, 2023 and 2022, respectively. At December 31, 2023, we had an accumulated deficit of approximately $560,902,700.

Business Strategy

Our strategy is to leverage our considerable 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 advisors, including recognized experts in the fields of depression, and business advisors with significant industry and regulatory experience to lead and execute the development and commercialization of esmethadone.

We plan to further develop esmethadone as our priority program. As the drug esmethadone is an NCE, the regulatory pathway required to support a new drug application (NDA) submission involves a full clinical development program. We plan to continue to generate intellectual property (IP) that will further protect our products from competition. We will also continue to prioritize our product development activities after taking into account the resources we have available, market dynamics and potential for adding value.

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.

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 Lilly, Pfizer, GlaxoSmithKline, Allergan, Sage Therapeutics and Johnson & Johnson. Some of the notable drugs produced by these companies are Cymbalta® (Eli Lilly), Effexor® (Pfizer), Pristiq® (Pfizer), ZURZUVANE™ (Sage), Spravato® (Johnson & Johnson) and Auvelity™ (Axsome).

Intellectual Property Portfolio and Market Exclusivity

We have over 50 issued patents and pending patent applications related to REL-1017 for multiple uses, including psychological and neurological conditions, potentially provide coverage beyond 2033. We have also secured an Orphan Drug Designation from the FDA for d-methadone for "the treatment of postherpetic neuralgia" (postherpetic neuralgia is lasting pain in areas of skin affected by previous outbreaks of shingles, caused by the varicella-zoster, or herpes zoster, virus) which, upon potential NDA approval, carries 7-year FDA Orphan Drug marketing exclusivity. In the European Union, some of our prospective 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, REL-1017 will be eligible for market exclusivity to run concurrently with the term of the patent for 5 years in the U.S. (Hatch Waxman Act) and may be eligible for an additional 6 months of pediatric exclusivity and up to 10 years of exclusivity in the European Union. We believe an extensive intellectual property estate of US and foreign patents and applications, once approved, will protect our technology and products.

Esmethadone License Agreement

As a result of a prior acquisition, the Company assumed an obligation to pay third parties (Dr. Charles E. Inturrisi and Dr. Paolo Manfredi – see below): (A) royalty payments up to 2% on net sales of licensed products that are not sold by sublicensee and (B) on each and every sublicense earned royalty payment received by licensee from its sublicensee on sales of license product by sublicensee, the higher of (i) 20% of the royalties received by licensee; or (ii) up to 2% of net sales of sublicensee. The Company will also make milestone payments of up to $4 or $2 million, for the first commercial sale of product in the field that has a single active pharmaceutical ingredient, and for the first commercial sale of product in the field of product that has more than one active pharmaceutical ingredient, respectively. As of December 31, 2023, the Company has not generated any revenue related to this license agreement.

Inturrisi / Manfredi

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 Agreements, Relmada assigned its existing rights, including patents and patent applications, to esmethadone in the context of psychiatric use (the Existing Invention) to Licensor. Licensor then granted Relmada under the License Agreement a perpetual, worldwide, and exclusive license to commercialize the Existing Invention and certain further inventions regarding esmethadone. In consideration of the rights granted to Relmada under the License Agreement, Relmada paid the Licensor an upfront, non-refundable license fee of $180,000. Additionally, Relmada will pay Licensor $45,000 every three months 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. Relmada will also pay Licensor tiered royalties with a maximum rate of 2%, decreasing to 1.75%, and 1.5% in certain circumstances, on net sales of licensed products covered under the License Agreement. Relmada will also pay Licensor tiered payments up to a maximum of 20%, and decreasing to 17.5%, and 15% in certain circumstances, of all consideration received by Relmada for sublicenses granted under the License Agreement. As of December 31, 2023, no events have occurred, and the Company continues to pay Licensor $45,000 every three months.

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, Dr 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 Dr. Traversa's job responsibilities or decision-making rights in connection with the development and commercialization of esmethadone, (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 esmethadone intellectual property without Dr. 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 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 Dr. Traversa's death or disability does not give Licensor the right to terminate the License Agreement. On December 27, 2022, the Licensor and the Company entered into a new amendment extending the "Key Man" provision period until December 31, 2027. The License Agreement was not otherwise modified.

Wonpung License Agreement

In 2007, the Company entered into a License Development and Commercialization Agreement with Wonpung Mulsan Co, a shareholder of the Company. Wonpung has exclusive territorial rights in countries it selects in Asia to market up to two drugs the Company is currently developing and a right of first refusal (ROFR) for up to an additional five drugs that the Company may develop in the future as defined in more detail in the license agreement. If the parties cannot agree to terms of a license agreement then the Company shall be able to engage in discussions with other potential licensors. As of March 19, 2024, no discussions are active between the Company and Wonpung.

The Company 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 it is currently developing. The licensing terms for the ROFR products are subject to future negotiations and binding arbitration. 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.

Psilocybin License Agreement

In July 2021, we executed a License Agreement with Arbormentis, LLC which gives us the development and commercial rights to a novel psilocybin and derivate program. Under the terms of the agreement, we paid Arbormentis, LLC an up-front fee of $12.7 million consisting of a mix of cash and warrants to purchase the Company's common stock, in addition to potential milestone payments totaling up to approximately $160 million related to pre-specified development and commercialization milestones. Arbormentis, LLC is also eligible to receive a low single digit percentage royalty on net sales of any commercialized therapy resulting from this agreement. The license agreement is terminable by us but is perpetual and not terminable by the licensor absent material breach of its terms by us. We will collaborate with Arbormentis, LLC on the development of new therapies targeting neurological, psychiatric and metabolic disorders. We will leverage Arbormentis' understanding of neuroplasticity, and focusing on this emerging new class of drugs targeting the neuroplastogen mechanism of action. Importantly, neuroplasticity also plays a key role in the activity of REL-1017, Relmada's lead program. Dr. Paolo Manfredi, our Acting Chief Scientific Officer and co-inventor of REL-1017, and Dr. Marco Pappagallo, Safety/Adjudication Officer, are among the scientists affiliated with Arbormentis, LLC.

Key Strengths

We believe that the key elements for our market success include:

- Compelling lead product opportunity, REL-1017 currently in two Phase 3 trials for the adjunctive treatment of MDD (RELIANCE II and RELIGHT) that build on the knowledge gleaned from RELIANCE I, which did not meet its primary endpoint.
- Robust and highly statistically significant, efficacy seen with esmethadone in a randomized Phase 2 trial with the primary endpoint at 7 days, with onset of action seen at 4 days, and the effect carrying through to 14 days (7 days post treatment).
- Successful Phase 1 safety studies of esmethadone and strong clinical activity signal in depression established in three independent animal models in preclinical studies.
- Potential in additional multiple indications in underserved markets with large patient population in other affective disorders, and cognitive disorders.
- Substantial esmethadone IP portfolio and market protection: approved and filed patent applications provide coverage beyond 2033.
- Portfolio diversification with the development of a novel psilocybin (REL-P11) for the treatment of metabolic indications. This program is expected to enter human studies, to define its pharmacokinetic, safety and tolerability profile, in first half of 2024.
- 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, and University of Pennsylvania.

Competition

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 more 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, we currently have no products approved for sale.

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 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 not permit a clinical trial to begin, or 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, each convincing on its own, to demonstrate the efficacy of the drug. A single Phase 3 trial with other confirmatory evidence may be sufficient in rare instances, such as (i) 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 or (ii) when in conjunction with other confirmatory evidence.

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 submission 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 the active ingredient in 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.

FDA strictly regulates marketing, labeling, advertising and promotion of drugs that are placed on the market. Advertising and promotion of drugs must be in compliance with the Federal Food, Drug, and Cosmetic Act (FDCA) and its implementing regulations and only for the approved indications and in a manner consistent with the approved labeling. FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including investigation by federal and state authorities.

Generic Competition

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 (a Paragraph IV certification). 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 or certifies that the listed patents will not be infringed by the new product, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. If the ANDA applicant has provided a Paragraph IV certification, the NDA and patent holders may then initiate a patent infringement lawsuit in response. The filing of a patent infringement lawsuit within 45 days of the receipt of a such 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.

Exclusivity

Upon NDA approval of a NCE such as esmethadone, 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 applicant for the non-racemic drug may elect, in the NDA, 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 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, 2027.

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.

Controlled Substances

The active ingredients in esmethadone are regulated as controlled substances pursuant to the Comprehensive Drug Abuse Prevention and Control Act of 1970 (CSA) and regulations promulgated by the United States Drug Enforcement Administration (DEA). The CSA and its implementing regulations establish a closed chain of distribution for entities handling controlled substances. The DEA is responsible for enforcing the law and regulations that impose registration, security, inventory, recordkeeping, reporting and storage requirements on entities that manufacture, distribute, import and export, prescribe, dispense or otherwise physically handle controlled substances. The law and regulations require 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.

The CSA classifies 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 depending on the comparative abuse potential of the drug or substance, with Schedule II substances classified as having the highest potential for abuse and physical or psychological dependence, and Schedule V substances classified as having the lowest relative potential for abuse and dependence. Schedule II substances are subject to the strictest regulatory requirements involving registration, storage, recordkeeping, reporting and security. Schedule II drugs are subject to manufacturing quotas and the distribution and dispensing of Schedule II drugs are more limited and tightly controlled. For example, Schedule II drug prescriptions cannot be refilled and must contain a written or electronic signature of a practitioner when presented to a pharmacy. Schedules III, IV and V controlled substances are subject to registration, recordkeeping, reporting and security requirements, but these requirements are less restrictive than Schedule II drugs.

Esmethadone is the single isomer of methadone, is currently classified as a Schedule II substance, and psilocybin is currently classified as a Schedule I substance. Any Schedule I substance, such as psilocybin, that is FDA-approved for marketing in the United States will need to be rescheduled from Schedule I to Schedule II-V by the DEA before it can be commercially marketed, distributed, and sold. Rescheduling is dependent on FDA approval and the FDA must make a recommendation to the DEA on the appropriate schedule. The DEA must conduct notice and comment rulemaking to reschedule any controlled substance. Such action is subject to public comment and potential requests for an administrative hearing objecting to, or supporting, any such action. In addition, because each state has its own statutory and regulatory requirements related to controlled substances, each state or jurisdiction must also take appropriate administrative or legislative action to reschedule a controlled substance within that state based on federal rescheduling.

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 and DEA regulations impose certain security, recordkeeping and reporting requirements on DEA registrants. The DEA conducts cyclic inspections of manufacturers, distributors, importers, and exporters to review compliance with these requirements. 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. For example, manufacturers and distributors must store Schedule I and II drugs in secure vault with specific structural requirements. Other physical security requirements that apply to all controlled substances include safes and cages, and the use of alarm systems and surveillance cameras. Regulations also require that registrants restrict 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 certain 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. DEA conducts cyclic inspections to determine whether registrants are complying with these requirements.

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 also established annual aggregate quotas for manufacturing of certain controlled substances and companies are subject to quarterly individual manufacturing and procurement quotas. 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 bulk manufacturers through an application process. Manufacturers of dosage forms are also subject to procurement quotas to obtain the bulk active pharmaceutical ingredients to make finished drugs. Manufacturers may not exceed the manufacturing or procurement quota granted in a given quarter or 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 of the CSA and DEA regulations 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.

The United States and the majority of countries are signatories to the United Nations (UN) international drug control treaties which dictate certain scheduling, licensing, restrictions and other requirements involving controlled substances. Because psilocybin is classified as a Schedule I controlled substance under the UN Convention on Psychotropic Substances, 1971 most countries maintain laws and regulations comparable to those in the United Stated related to methadone, psilocybin and other controlled substances.

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 (HHS) (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.

The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully offering, soliciting or receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers, among others, on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. In addition, a person or entity does not need to have actual knowledge of the Anti-Kickback Statute or specific intent to violate it in order to commit a violation.

Federal civil and criminal false claims laws, including the federal civil False Claims Act, prohibit any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. This includes claims made to programs where the federal government reimburses, such as Medicare and Medicaid, as well as programs where the federal government is a direct purchaser, such as when it purchases off the Federal Supply Schedule. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. Additionally, the government may assert 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 civil False Claims Act. Most states also have statutes or regulations similar to the federal Anti-Kickback Statute and civil False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Other federal statutes pertaining to healthcare fraud and abuse include the civil monetary penalties statute, which prohibits, among other things, the offer or payment of remuneration to a Medicaid or Medicare beneficiary that the offeror or payor knows or should know is likely to influence the beneficiary to order a receive a reimbursable item or service from a particular supplier.

Further, pursuant to the federal Physician Payment Sunshine Act, CMS, has issued a final rule that requires manufacturers of prescription drugs to collect and report information on certain payments or transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), physician assistants, certain types of advance practice nurses and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. The reported data is made available in searchable form on a public website on an annual basis. Failure to submit required information may result in civil monetary penalties.

In addition, several states now require prescription drug companies to report certain expenses relating to the marketing and promotion of drug products and to report gifts and payments to individual healthcare practitioners in these states. Other states prohibit various marketing-related activities, such as the provision of certain kinds of gifts or meals. Still other states require the posting of information relating to clinical studies and their outcomes. Some states require the reporting of certain drug pricing information, including information pertaining to and justifying price increases and new high-cost drug introductions. In addition, certain states require pharmaceutical companies to implement compliance programs and/or marketing codes. Certain states and local jurisdictions also require the registration of pharmaceutical sales and medical representatives. Compliance with these laws is difficult and time consuming, and companies that do not comply with these state laws may face civil penalties.

Data privacy and security regulations by both the federal government and the states in which business is conducted may also be applicable. Health Insurance Portability and Accountability Act of 1996 (HIPAA), as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH), and its implementing regulations, imposes requirements relating to the privacy, security and transmission of individually identifiable health information. HIPAA prohibits, among other things, knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program or obtain by means of false or fraudulent pretenses, representations or promises of any money or property owned by or under the control of any healthcare benefit program in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal 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 commit a violation. 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, may not have the same effect, and often are not preempted by HIPAA, thus complicating compliance efforts. For example, the California Consumer Privacy Act (CCPA), which went into effect on January 1, 2020, creates new data privacy obligations for covered companies and provides new privacy rights to California residents. On January 1, 2023, the California Privacy Rights Act (CPRA), which substantially amends the CCPA, went into effect. The CCPA and CPRA provide for unlimited civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Virginia's Consumer Data Protection Act, which took effect on January 1, 2023, requires businesses subject to the legislation to conduct data protection assessments in certain circumstances and requires opt-in consent from consumers to acquire and process their sensitive personal information, which includes information revealing a consumer's physical and mental health diagnosis and genetic and biometric information that can identify a consumer. Colorado enacted the Colorado Privacy Act, and Connecticut enacted the Connecticut Data Privacy Act, each of which took effect on July 1, 2023, and Utah enacted the Consumer Privacy Act, which became effective on December 31, 2023, and each of these laws may increase the complexity, variation in requirements, restrictions, and potential legal risks.

Healthcare Reform

Healthcare reforms that have been adopted, and that may be adopted in the future, could result in further reductions in coverage and levels of reimbursement for pharmaceutical products, increases in rebates payable under U.S. government rebate programs and additional downward pressure on pharmaceutical product prices. Healthcare reform proposals recently culminated in the enactment of the Inflation Reduction Act (IRA) in August 2022, which, among other things, allows the HHS to directly negotiate the selling price of statutorily specified number of drugs and biologics each year that CMS reimburses under Medicare Part B and Part D. Only high-expenditure single-source drugs that have been approved for at least 7 years (11 years for biologics) can be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. Negotiations for Medicare Part D products take place in 2024 with the negotiated price taking effect in 2026, and negotiations for Medicare Part B products will begin in 2026 with the negotiated price taking effect in 2028. In August 2023, HHS announced the ten Medicare Part D drugs and biologics that it selected for negotiations. HHS will announce the negotiated maximum fair prices by September 1, 2024, and this price cap, which cannot exceed a statutory ceiling price, will go into effect on January 1, 2026. A drug or biological product that has an orphan drug designation for only one rare disease or condition will be excluded from the IRA's price negotiation requirements, but will lose that exclusion if it receives designations for more than one rare disease or condition, or if it is approved for an indication that is not within that single designated rare disease or condition, unless such additional designation or such disqualifying approvals are withdrawn by the time CMS evaluates the drug for selection for negotiation. The IRA also imposes rebates on Medicare Part D and Part B drugs whose prices have increased at a rate greater than the rate of inflation. In addition, the IRA extends enhanced subsidies for individuals purchasing health insurance coverage in Patient Protection and Affordable Care Act (ACA) marketplaces through plan year 2025. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. It is unclear to what extent other statutory, regulatory, and administrative initiatives will be enacted and implemented.

Insurance Coverage and Reimbursement

Significant uncertainty exists as to the insurance 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 2222 Ponce de Leon Blvd., Floor 3, Coral Gables, Florida 33134 and our telephone number is (786) 629-1376. 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.

Human Capital

As of December 31, 2023, we had a total of 20 employees. We understand people are our greatest asset and that our innovation and operational excellence are ultimately noted in our human capital. Our success depends in large part on our ability to recruit, develop and retain a qualified, productive, and engaged workforce.

Inclusion & Diversity

Inclusion and diversity is a focus of our corporate human capital strategy. By embracing inclusion and diversity, we enhance our work environment and drive business success. We endeavor to create a culture of inclusion in which our employees feel empowered to bring their full, authentic selves to work and pursue their professional goals in a setting of equality. Fostering such a culture welcomes different perspectives and generates innovation and growth. We honor the diversity of our employees—in gender, race/ethnicity, age, gender identity, sexual orientation, socio-economic status, language, nationality, abilities and life experiences. As of December 31, 2023, our employee population was approximately 60% female.

Total Rewards and Employee Engagement

We maintain a competitive compensation and benefits package including incentive compensation tied to both company and individual performance, and retirement benefits. Our performance-based compensation strategy is designed to recognize and reward employees for their contribution to our success, and we strive to provide strong, equitable incentives for performance. Compensation is comprised of two elements: base compensation, which is determined based upon a number of factors, including size, scope and impact of the employee's role, the market value associated with the employee's role, leadership skills, length of service and individual performance; and an annual bonus, which is a cash award determined based on a combination of individual and company performance during the period to which the bonus relates. We seek to determine compensation on the basis of merit and without regard to demographic characteristics. During 2023, we employed a third-party consultant to assist us in evaluating our pay practices. In conducting this exercise, we found no meaningful difference in compensation based upon gender, race or any other defining characteristic examined.

ITEM 1A. 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.

Summary of Risks

This section provides a summary of the risks that may impact our performance in the future. For details of our various risk factors and their impacts, see "Risk Factors Discussion."

Our risk factors are organized into the following categories: 1) Risks related to our business, 2) Risks related to clinical and regulatory matters, 3) Risks related to our intellectual property, 4) Risks related to government regulations, 5) Risks related to our reliance on third parties, and 6) Risks related to ownership of our common stock.

Risks related to our business

Business risks include risks associated with our products and regulatory approval, licensing agreements, historical losses, managing growth, and acquisitions. In general, the risks related to our business can cause variability in the future profits of the Company.

Risks related to clinical and regulatory matters

Clinical and regulatory matters include risks associated with clinical trials and the future ability to commercially market the product. In order for any of our products to be commercialized and produce future profits, successful trials need to be completed with supporting data to receive regulatory approval. Failing to complete the trial will significantly increase our cost of doing business. In addition, the active ingredient in our products is a controlled substance which can affect the supply available for clinical trials, as well as commercial sales. A limited supply could increase the time needed to complete clinical trials and overall costs including product liability claims. We could also face potential fines or reputational risk if we do not comply. Developments from competitors and the ability to obtain market exclusivity could also negatively impact future profits.

Risks related to our intellectual property

Our products depend upon securing and protecting critical intellectual property. Patent positions are highly uncertain and involve complex legal and factual questions. Infringing upon patents or trade secrets could force us to cease or alter our product development efforts or obtain a license to continue to develop or sale our products. These risks could not only impact the future profits of the company but also create adverse publicity for us.

Risks related to government regulations

We are required to comply with various federal and state pharmaceutical and healthcare laws and regulations, and to maintain secure systems to protect sensitive confidential information. Complying with the various regulations can increase our cost of doing business. We could also face potential fines or reputational risk if we do not comply. Litigation or investigations can increase costs, negatively affect our operating results and create adverse publicity for us.

Risks related to our reliance on third parties

The Company relies on third parties to conduct preclinical and clinical studies, as well as to manufacture our product candidates. Third parties' failure to perform the trials as contractually required could impact our ability to obtain regulatory approval. If our third-party manufacturers fail to meet our requirements and strict regulatory requirements, our product development and commercialization efforts may be materially harmed.

Risks related to ownership of our common stock

Common stocks risks include risks associated with the limited market for our common stock, a potential issuance of a substantial number of additional shares, stock price volatility, and reporting requirements of federal securities laws. The net effect of these risks can include reductions in future profits, additional operating expenses, inability to meet liquidity needs, inability to access capital and increased cost of capital.

Risk Factors Discussion

Risks Related to Our Business

Our business depends on the success of esmethadone (d-methadone, dextromethadone, REL-1017), our only product candidate currently in clinical development, which is in a pivotal clinical trial for the adjunctive treatment of MDD. 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 esmethadone (d-methadone, dextromethadone, REL-1017) for the adjunctive treatment of patients with MDD. Currently, esmethadone is our only product candidate under clinical development. We intend, in 2024, to enter human studies of our proprietary, low dose modified-release formulation of psilocybin (REL-P11) for metabolic indications, but there can be no assurance that such studies will be commenced or completed. 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 setback of a lead candidate. Successful continued development and ultimate regulatory approval of esmethadone for the adjunctive treatment of MDD 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 esmethadone. If we cannot successfully develop, obtain regulatory approval for and commercialize esmethadone, we may not be able to continue our operations. The future regulatory and commercial success of esmethadone is subject to a number of risks, including the following:

- we may not be able to obtain adequate evidence from clinical trials to support the efficacy and safety for esmethadone for the adjunctive treatment of MDD or other indications;
- we may not be able to demonstrate that the benefits of esmethadone for the adjunctive treatment of MDD or other indications outweigh the risks;
- in our clinical trials for esmethadone, enrollment may be slower than anticipated and we may need additional clinical trial sites than originally planned, 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 esmethadone, 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 the adjunctive treatment of MDD or any other indication for the approval of esmethadone;
- 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 2 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 esmethadone for the adjunctive treatment of MDD or any other indication;
- we may not have sufficient financial and other resources to complete the necessary clinical trials for esmethadone, including, but not limited to, the clinical trials needed to obtain drug approval;
- if approved for the adjunctive treatment of MDD, esmethadone will likely compete with products that may reach approval prior to esmethadone, products that are currently approved for the adjunctive treatment of MDD and the off-label use of currently marketed products for MDD; and
- we may not be able to obtain, maintain or enforce our patents and other intellectual property rights.

Esmethadone, psilocybin 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, if at all, from these regulatory authorities. The drug development and approval process is lengthy and expensive, and approval is never certain. Investigational new drugs, such as esmethadone, may not prove to be safe and effective in clinical trials. We have limited experience as a company in conducting later stage clinical trials required to obtain regulatory approval. We may be unable, if at all, to conduct future clinical trials at preferred sites, enlist clinical investigators, enroll sufficient numbers of participants or begin or successfully complete clinical trials in a timely fashion. 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 clinical trials 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 esmethadone, psilocybin 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. Owing in part to the complexity of biological pathways, esmethadone, psilocybin 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. Our Phase 2 clinical study of REL-1017 involved a small population of subjects with MDD, 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. In addition, results from open-label trials, such as our open-label trial of REL-1017, may not predict results in placebo-controlled trials for a number of reasons, including biases that may exaggerate therapeutic effect. On October 13, 2022, we announced that the RELIANCE III study, evaluating REL-1017 in the monotherapy setting for MDD, did not achieve its primary endpoint, which was a statistically significant improvement in depression symptoms compared to placebo as measured by the MADRS on Day 28. On December 7, 2022, we announced that the RELIANCE I study, evaluating REL-1017 in the adjunctive setting for MDD, did not achieve its primary endpoint, which was a statistically significant improvement in depression symptoms compared to placebo as measured by the MADRS on Day 28. With these findings, even if RELIANCE II, RELIGHT, or any additional Phase 3 studies achieve their primary endpoints, we may not have sufficient evidence to demonstrate the efficacy of REL-1017 as an adjunctive treatment of MDD. If we are unable to successfully demonstrate the safety and efficacy of esmethadone, psilocybin 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 esmethadone, psilocybin or other future product candidates, 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 esmethadone, psilocybin or other future product candidates. If we or any of our future development collaborators are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize esmethadone, psilocybin or other future product candidates, we may not be able to generate sufficient revenue to continue our business.

Preliminary or top-line results may not accurately reflect the complete results of the clinical study.

Preliminary or top-line data remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary or top-line data. As a result, preliminary or top-line data should be viewed with caution until the final data are available.

Our license agreement for esmethadone, 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 esmethadone 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 esmethadone in neurological and other uses, to develop and commercialize esmethadone 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 esmethadone 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 esmethadone, 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 esmethadone, (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 esmethadone 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 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. On December 27, 2022, the Licensor and the Company entered into a new amendment extending the "Key Man" provision period until December 31, 2027. The License Agreement was not otherwise modified.

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, 2027. 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 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 $560.9 million at December 31, 2023. The Company had cash, cash equivalents and short-term investments of approximately $96.3 million at December 31, 2023. 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 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.

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

As of December 31, 2023, we had Federal, New York State and New York City net operating loss (NOL) carryforwards of approximately $100,077,000, $15,016,000 and $14,998,000, respectively, 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 to 80% of taxable income in the year. 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, and Dr. Paolo Manfredi, Acting Chief Scientific Officer. If either 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 16 full time employees and are likely 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.

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

We expect to need to grow rapidly in order to support ongoing and 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.

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.

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.

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 are conducting, 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. For example, our RELIANCE I study did not achieve its primary endpoint, statistically significant improvements in depression symptoms compared to placebo on Day 28, even though our Phase 2 study was positive. Further, our monotherapy Phase 3 study, RELIANCE III, also did not meet its primary endpoint, statistically significant improvements in depression symptoms compared to placebo on Day 28. Even if our RELIANCE II, RELIGHT or other potential 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 trial results from the study of depression are inherently difficult to predict. In addition, our clinical trials and our future clinical trials for esmethadone 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 our clinical trials conducted to date may not be predictive of results from our future clinical trials. For example, our RELIANCE III and RELIANCE I studies did not achieve their primary endpoints, statistically significant improvements in depression symptoms compared to placebo on Day 28.

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.

We have a limited history of developing drug candidates. We do not know whether any of our ongoing or 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; and
- increases in time required to complete monitoring of patients during or after participation in a clinical trial.

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' decisions to approve our product candidates will depend on our ability to demonstrate through adequate well-controlled clinical trials, that the product candidate is effective. For esmethadone product candidate, efficacy is measured statistically by comparing the overall improvement in depression in actively-treated patients against improvement in depression in the control group (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. For example, our RELIANCE III and RELIANCE I studies did not achieve their primary endpoints, statistically significant improvements in depression symptoms compared to placebo on Day 28. 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. 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.

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. In that case, both the cost and the amount of time required to conduct a clinical trial could increase.

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 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 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, 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. 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.

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

We have obtained Fast Track Designation for esmethadone 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.

Even though we have obtained orphan drug designation in the United States for esmethadone for the treatment of postherpetic neuralgia, we may not obtain or maintain orphan drug exclusivity for that product candidate, and we may not obtain orphan drug designation or exclusivity for any of our other product candidates or indications.

The FDA may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the active ingredient is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same active ingredient for the same disease for seven years. Orphan drug exclusivity may be lost if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

We have obtained orphan drug designation for esmethadone for the treatment of postherpetic neuralgia. If the product candidate were to obtain orphan drug exclusivity upon approval, such exclusivity would prevent the FDA from approving another application to market a drug containing the same active moiety for the same orphan indication, except in very limited circumstances, including when the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use, such as MDD, that is broader than the indication for which it received orphan designation.

Even though we have received orphan drug designation for esmethadone for the treatment of postherpetic neuralgia, we may not be the first to obtain marketing approval for this active moiety for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical product candidates. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition or a drug with the same active moiety can be approved for a different indication. Orphan drug designation by the FDA neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. In addition, even if we intend to seek orphan drug designation for other product candidates or indications, we may never receive such designations or obtain orphan drug exclusivity.

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 FDCA. For esmethadone, 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, 2027.

There can be no assurance that European authorities will grant data exclusivity for esmethadone, because it does not contain a new active molecule. Even if European data exclusivity is granted for esmethadone, this may not protect us from direct competition. A competitor(s) with a generic version of our product may be able to obtain approval of its 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, esmethadone has potential benefits in other therapeutic areas. If our drug development efforts in depression fail, 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, such as metabolic disorders with psilocybin, 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 esmethadone and psilocybin are listed by the CSA and regulations promulgated by the DEA as controlled substances. The CSA and regulations promulgated by the DEA regulate 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 the CSA and DEA regulations relating to their handling (i.e., manufacturing, storage, distribution, prescribing and dispensing procedures). Furthermore, the amount of controlled substances that can be obtained for clinical trials and commercial distribution is limited by the DEA through its quota system. Quotas 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 the ability to manufacture and distribute our product candidates, if approved, in the volume needed to meet commercial demand.

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 CSA or DEA regulations, or the cost of compliance with these regulations, may adversely affect our business.

Esmethadone and psilocybin are subject to extensive regulation by the DEA. Although esmethadone is substantially devoid of opioid activity, and psychotomimetic effects, it is currently classified as a Schedule II drug. Upon approval, the DEA may continue to designate it as a controlled substance falling under a DEA controlled substance schedule. Esmethadone is produced by separation from racemic methadone, a scheduled drug subject to extensive regulation by the DEA. Any psilocybin-containing product candidate we develop is also subject to extensive regulation by the DEA as a Schedule I substance.

The manufacture, shipment, storage, sale and use of controlled substances are highly regulated, including security, recordkeeping and reporting obligations enforced by the DEA. Schedule I substances by definition have a high potential for abuse, have no currently "accepted medical use" in the United States, lack accepted safety for use under medical supervision, and may not be prescribed, marketed or sold in the United States. Schedule I and II substances (as well as substances defined as narcotics in any Schedule) are subject to the strictest regulatory requirements and restrictions involving registration, storage, security, recordkeeping and reporting. In particular, distribution and dispensing of Schedule II drugs are strictly controlled. For example, all Schedule II drug prescriptions cannot be refilled and must contain a written or electronic signature of a practitioner when presented to a pharmacy. 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 esmethadone and psilocybin, 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 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.

Psilocybin is currently classified as a Schedule I drug in the United States, and any product containing this substance must be rescheduled to be marketed. There can be no assurance that the DEA will make a favorable scheduling decision. Even assuming categorization as a Schedule II or lower controlled substance (i.e., Schedule III, IV or V) at the federal level, such substances would also require scheduling determinations under state laws and regulations.

If approved by FDA, and if the finished dosage form of a future psilocybin-containing drug product is listed by the DEA as a Schedule II, III, or IV controlled substance, its manufacture, importation, exportation, domestic distribution, storage, sale, prescribing, and dispensing will continue to be subject to a significant degree of regulation by the DEA. In addition, the final scheduling process may take significantly longer than the 90-day deadline set forth in the CSA, especially if there are objections to such scheduling, thereby delaying the launch of our psilocybin-containing product candidate in the United States. Furthermore, the FDA, DEA or any comparable foreign regulatory authority could require us to generate more clinical or other data than we currently anticipate to establish whether or to what extent the substance has an abuse or misuse potential, which could increase the cost and/or delay the launch of any future psilocybin-containing product candidates. In addition, product candidates containing controlled substances are subject to regulations relating to manufacturing, storage, distribution, prescribing, and dispensing, including:

- *State-controlled substances laws*. Individual U.S. states have also established controlled substance laws and regulations. Though state-controlled substances laws often mirror federal law, because the states are separate jurisdictions, they will need to separately reschedule any future psilocybin-containing drug products we develop, if approved by FDA. State scheduling may delay commercial sale of any product for which we obtain federal regulatory approval and adverse scheduling would have a material adverse effect on the commercial attractiveness of such product. We or our vendors must also obtain separate state registrations, permits or licenses in order to be able to obtain, handle, and distribute controlled substances for clinical trials or, if approved, commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions by the states in addition to those from the DEA or otherwise arising under federal law.

- *Clinical trials*. Because we plan to conduct clinical trials of a psilocybin-containing product candidate in the United States prior to approval, each of our research sites must submit a research protocol to the DEA and obtain and maintain a DEA Schedule I researcher registration that will allow those sites to handle and dispense this product candidate and to obtain the product from our importer. If the DEA delays or denies the grant of a researcher registration or approval of the research protocol to one or more research sites, the clinical trial could be significantly delayed, and we could lose clinical trial sites. The importer for the clinical trials must also obtain a Schedule I importer registration and an import permit for each import. We do not currently conduct any manufacturing or repackaging/relabeling of either psilocybin or the psilocybin-containing product candidate in the United States.

The potential reclassification of psilocybin in the United States could create additional regulatory burdens on our operations and negatively affect our results of operations.

If psilocybin, rather than just a specific FDA-approved formulation, is rescheduled under the CSA as a Schedule II or lower controlled substance (i.e., Schedule III, IV or V), the ability to conduct research on psilocybin would most likely be improved. However, rescheduling psilocybin may materially alter enforcement policies across many federal and state agencies, primarily FDA and DEA. FDA's responsibilities include regulating the ingredients as well as the marketing and labeling of drugs sold in interstate commerce. Because it is currently illegal under federal law to produce and sell psilocybin, and because there are no federally recognized medical uses, FDA has historically deferred enforcement related to psilocybin to the DEA. If psilocybin were to be rescheduled to a federally controlled, yet legal, substance, FDA would likely play a more active regulatory role. The DEA would continue to be active in regulating manufacturing, distribution and dispensing of such substances. The potential for multi-agency enforcement post-rescheduling, including state agencies, e.g., Boards of Pharmacy, could threaten or have a materially adverse effect on our business. In addition, if the psilocybin-containing product candidate is scheduled as Schedule II, III, IV or V, we would also need to identify wholesale distributors with the appropriate DEA registrations and authority to distribute the psilocybin-containing product candidate. The failure to obtain, or delay in obtaining, or the loss of any of those registrations could result in increased costs to us. If the psilocybin-containing product candidate is classified as a Schedule II drug, participants in our supply chain may have to maintain enhanced security including specially constructed vaults at manufacturing and distribution facilities. This additional security may also discourage some pharmacies from carrying the product.

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.

Our APIs and pharmaceutical excipients 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 may not be same as our drug manufacturing locations. Thus, any disruption in supply from our preferred vendors 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, if approved, 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, it would require additional expenditures and impact 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.

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 be 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 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; and
- diversion of controlled substances by clinical trial personnel.

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 halting or 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 related to cardiac death for racemic methadone, a parent compound to our esmethadone. Although the decision was based on case reports and not on a controlled clinical trial, as part of the development of esmethadone, we currently assess (and have actively assessed) the cardiac safety profile of esmethadone in our Phase 3 clinical trials. There is no assurance that the results of our clinical studies will demonstrate an absence of cardiac adverse events with esmethadone. An adverse safety outcome could result in a similar bolded warning on the label of esmethadone or in a decision not to approve esmethadone, either one of which could have serious consequences for our continued operation.

If approved, esmethadone and any psilocybin-containing drug product we successfully develop may require Risk Evaluation and Mitigation Strategies (REMS).

Esmethadone and any psilocybin-containing drug product we successfully develop, may 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 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, Abbvie, Pfizer, Eli Lilly, Axsome Therapeutics, and Neumora Therapeutics, Inc. among others.

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.

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 guarantee 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.

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 a 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 current and 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; and
- 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.

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 cooperation 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.

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.

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.

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

Healthcare providers and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with providers, third-party payors and customers will subject 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 market, sell and distribute any product candidates for which we obtain marketing approval.

Restrictions under applicable U.S. federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons and entities from 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 healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation;

- federal false claims laws, including the federal False Claims Act, 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. In addition, the government may assert that a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;

- HIPAA, as amended by HITECH, imposes criminal and civil liability for, among other things, knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal 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;

- the federal Physician Payment Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report payments and other transfers of value provided during the previous year to physicians, as defined by such law, physician assistants, certain types of advance practice nurses, and teaching hospitals, as well as certain ownership and investment interests held by such physicians and their immediate family, which includes annual data collection and reporting obligations; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures or drug pricing.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of product candidates from government-funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

Enacted and future legislation may affect the prices we may set. The full effect of recent United States healthcare reform and other changes in the healthcare industry, laws, and regulations and in healthcare spending is currently unknown, and the reform and other changes may adversely affect our business model.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, affect our ability to profitably sell any products for which we obtain marketing approval.

The commercial potential for our products, if any, could also be affected by changes in healthcare spending and policy in the United States and abroad. New laws, regulations, or judicial decisions or new interpretations of existing laws, regulations, or decisions, related to healthcare availability, the method of delivery, or payment for healthcare products and services could adversely affect our business, operations, and financial condition, if and when we are able to obtain marketing approval and commercialize our products. For example, the ACA was enacted in 2010 with a goal, among others, of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. The ACA, among other things, expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program, imposed a significant annual, nondeductible fee on companies that manufacture or import certain branded prescription drug products, and enacted substantial provisions affecting compliance, which may affect our business practices with healthcare practitioners.

There have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs in general and the cost of pharmaceuticals in particular. These initiatives recently culminated in the enactment of the IRA in August 2022, which, among other things, allows HHS to directly negotiate the selling price of a statutorily speficied number of drugs and biologics each year that CMS reimburses under Medicare Part B and Part D. Only high-expenditure single-source biologics that have been approved for at least 11 years (7 years for single-source drugs) can be selected by CMS for negotiation, with the negotiated price taking effect two years after the selection year. Negotiations for Medicare Part D products begin in 2024 with the negotiated price taking effect in 2026, and negotiations for Medicare Part B products begin in 2026 with the negotiated price taking effect in 2028. In August 2023, HHS announced the ten Medicare Part D drugs and biologics that it selected for negotiations. HHS will announce the negotiated maximum fair prices by September 1, 2024, and this price cap, which cannot exceed a statutory ceiling price, will come into effect on January 1, 2026. A drug or biological product that has an orphan drug designation for only one rare disease or condition will be excluded from the IRA's price negotiation requirements, but will lose that exclusion if it has designations for more than one rare disease or condition, or if is approved for an indication that is not within that single designated rare disease or condition, unless such additional designation or such disqualifying approvals are withdrawn by the time CMS evaluates the drug for selection for negotiation. The IRA also imposes rebates on Medicare Part D and Part B drugs whose prices have increased at a rate greater than the rate of inflation. In addition, the law eliminates, beginning in 2025, the coverage gap under Medicare Part D by significantly lowering the beneficiary maximum out-of-pocket cost and requiring manufacturers to subsidize, through a newly established manufacturer discount program, 10% of Part D enrollees' prescriptions costs for brand drugs below the out-of-pocket maximum, and 20% once the out-of-pocket maximum has been reached. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Manufacturers that fail to comply with the IRA may be subject to various penalties, including civil monetary penalties. These provisions will take effect progressively starting in 2023, although they may be subject to legal challenges. For example, the provisions related to the negotiation of selling prices of high-expenditure single-source drugs and biologics have been challenged in multiple lawsuits brought by pharmaceutical manufacturers. Thus, while it is unclear how the IRA will implemented, it will likely have a significant impact on the pharmaceutical industry.

Further, at the U.S. state level, legislatures are increasingly enacting laws and implementing regulations designed to control pharmaceutical and biological product pricing, including price or reimbursement constraints, discount requirements, marketing cost disclosure, price gouging prohibitions, and price transparency reporting. 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 and services or otherwise negatively impact our business model.

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 fail to comply with such requirements or to perform their 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 other third parties, 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 original manufacturers and we may have difficulty transferring such to other third parties. These factors would increase our reliance on such manufacturers or require us to obtain a license from such manufacturers in order to enable us, or to have other third parties, manufacture our product candidates.

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. Or a third parties' 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.

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 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 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 have less control over the timing, quality and other aspects of preclinical studies and clinical trials than if we conducted them on our own. These investigators, CROs and consultants are not 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.

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 Global Select 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 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 21,041,717 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 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 undiscovered 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.

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;
- negative or poor clinical results;
- 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.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 1C. CYBERSECURITY

To respond to the threat of security breaches and cyberattacks, we have developed a cybersecurity risk management program designed to identify, assess, manage, mitigate, and respond to cybersecurity threats to all information and systems owned by us. We maintain certain risk management processes intended to identify cybersecurity threats, determine their likelihood of occurring, and assess potential material impacts to our business. Based on our assessment, we implement and maintain risk management processes designed to protect the confidentiality, integrity, and availability of our information systems and the information residing therein.

Cybersecurity is reviewed as part of our overall enterprise risk management program, led by our Chief Compliance Officer (CCO), which assesses our significant enterprise risks, provides a summary of those risks and primary mitigations, identifies control improvement projects for our significant risks, and regularly reports on the progress of control improvement projects for those risks to the Audit Committee of our Board of Directors. Cybersecurity risks are reviewed by the Board of Directors, at least annually, as part of the Company's corporate risk mapping exercise.

The Company's processes are designed to identify such threats by, among other things, monitoring the threat environment using manual and automated tools, subscribing to services that identify cybersecurity threats, analyzing reports of threats, conducting scans of the threat environment, evaluating threats reported to us and conducting vulnerability assessments to identify vulnerabilities.

We rely on a multidisciplinary team (including from management and third-party service providers) to assess how identified cybersecurity threats could impact our business. These assessments may leverage, among other processes, industry tools and metrics designed to assist in the assessment of risks from such cybersecurity threats. Management also conducts periodic and on-demand assessments of our cybersecurity risks.

Our CCO, is responsible for developing and implementing the cybersecurity risk management program and reporting on cybersecurity matters to the Board. Additionally, members of the third-party service providers have cybersecurity experience and/or certifications. We view cybersecurity as a shared responsibility across our management team and periodically perform simulations and incorporate external resources and advisors as needed. All employees are required to complete cybersecurity training at least annually and have access to more frequent cybersecurity training through online events.

The CCO is responsible for continuously monitoring and assessing the Company's cybersecurity risk management program, informing senior management regarding the prevention, detection and mitigation and remediation of cybersecurity incidents and supervising such efforts.

To operate our business, we utilize certain third-party service providers to perform a variety of functions, such as outsourced business critical functions, clinical research, professional services, SaaS platforms, cloud-based infrastructure, encryption and other functions. We have certain vendor management processes designed to help to manage cybersecurity risks associated with our use of these providers. Depending on the nature of the services provided, and the sensitivity and quantity of information processed, our vendor management process may include reviewing the cybersecurity practices of such provider, contractually imposing obligations on the provider related to the services they provide and/or the information they process, conducting security assessments, conducting on-site inspections, requiring their completion of written questionnaires regarding their services and data handling practices, and conducting periodic re-assessments during their engagement.

We have not experienced any material cybersecurity incidents in the past, and we believe no cybersecurity events have occurred that have materially affected the Company or its business strategy, results of operations or financial condition. We continue to invest in the cybersecurity of our infrastructure and the enhancement of our internal controls and processes, which are designed to help protect our systems and data, and the information they contain. We carry insurance in amounts that we believe are reasonable for our business that provides protection against potential losses arising from a cybersecurity incident. However, there is no assurance that our insurance coverage will cover or be sufficient to cover all losses or claims that may arise from a cybersecurity incident.

ITEM 2. PROPERTIES

We do not own any property.

The Company's corporate headquarters are located at 2222 Ponce de Leon Blvd., Floor 3, Coral Gables, Florida 33134.

Pursuant to a lease agreement, dated August 1, 2021, and renewed in 2022, 2023 and 2024, the Company leased office space at 2222 Ponce de Leon Blvd, Floor 3, Coral Gables, FL 33134. Under the 2021 lease agreement the average monthly rent expense was approximately $11,000. For 2022, 2023 and 2024, the renewed lease agreement was for an average monthly rent expense of approximately $9,000, $7,000 and $7,000, respectively.

On June 8, 2017, the Company entered into an Amended and Restated License Agreement (the Actinium License) with Actinium Pharmaceuticals, Inc. (Actinium) for office space located at 275 Madison Avenue, 7th Floor, New York, New York 10016, our former corporate headquarters. This agreement amends and restates the license agreement entered into between the parties on March 10, 2016 (the Lease Agreement). Pursuant to the terms of the Actinium License, Actinium will continue to license the furniture, fixtures, equipment and tenant improvements located in its office (the FFE) for a license fee of $7,529 per month until December 8, 2022. On July 7, 2022, Actinium exercised its right to purchase the FFE for $52,698.

Beginning on January 1, 2023, the Company also leased office space at 880 Third Avenue, 12th Floor, New York, NY 10022 for approximately $15,000 per month, this lease was terminated on November 30, 2023.

Beginning on December 1, 2023, the Company leased office space at 12 E 49th Street, New York, NY 10022 for approximately $12,000 per month, that expires on July 31, 2024.

ITEM 3. LEGAL PROCEEDINGS

From time to time, the Company may become involved in lawsuits and other legal proceedings that arise in the course of business. Litigation is subject to inherent uncertainties, and it is not possible to predict the outcome of litigation with total confidence. The Company is currently not aware of any legal proceedings or potential claims against it whose outcome would be likely, individually or in the aggregate, to have a material adverse effect on the Company's business, financial condition, operating results, or cash flows.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock is listed on Nasdaq Global Select Market, under the symbol "RLMD".

Holders

As of March 15, 2024, 30,174,202shares of common stock were issued and outstanding, which were held by 129 holders of record. These stockholders held their stock either individually or in nominee or "street" names through various brokerage firms. There are no shares of our Class A convertible preferred stock outstanding. Our transfer agent is:

Empire Stock Transfer
1859 Whitney Mesa Drive
Henderson, NV 89014
Telephone (702) 818-5898
www.empirestock.com

Inquiries regarding stock transfers, lost certificates or address changes should be directed to the above address.

Dividends

We plan to retain any earnings for the foreseeable future for our operations. We have never paid any cash dividends on our stock and do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay cash dividends will be at the discretion of our Board of Directors and will depend on our financial condition, operating results, capital requirements and such other factors as our Board of Directors deems relevant.

Securities Authorized for Issuance under Equity Compensation Plans

Relmada has a 2014 Option and Equity Incentive Plan, as amended (the 2014 Plan) in which its directors, officers, employees and consultants shall be eligible to participate. The 2014 Plan allows for the granting of common stock awards, stock appreciation rights, and incentive and nonqualified stock options to purchase shares of the Company. On May 20, 2021, at the annual shareholders meeting, our shareholders approved our 2021 Equity Incentive Plan (the 2021 Plan) which allows for the granting of incentive and nonqualified stock options, stock appreciation rights, restricted stock awards, performance share awards and other equity-based awards for up to 1,500,000 options or stock awards. At the annual shareholders meeting on May 25, 2022, our shareholders approved an amendment to the 2021 Plan to increase the shares of the Company's common stock available for issuance thereunder by 3,900,000 shares. At the annual shareholders meeting on May 25, 2023, our shareholders approved an amendment to the 2021 Plan to increase the shares of the Company's common stock available for issuance thereunder by 2,500,000 shares. At the annual shareholders meeting (currently anticipated for May 24, 2024), our shareholders will vote on a management proposal to increase the shares authorized for awards under the 2021 Plan by an additional 4,500,000 shares, but there can be no assurance such amendment will be approved. With these grants and approvals, as of December 31, 2023, the Company had 136,750 shares available to be issued pursuant to awards under the 2021 Plan.

The following table summarizes our equity compensation plan information as of December 31, 2023:

Equity Compensation Plan Information

Plan Category	Number of securities to be issued upon exercise of outstanding options and stock appreciation rights	Weighted-average exercise price of outstanding options and stock appreciation rights	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
	(a)	(b)	(c)
Equity compensation plans approved by security holders (1)	17,416,192	$ 12.99	136,750
Equity compensation plans not approved by security holders	-	-	-
Total	17,416,192	$ 12.99	136,750

(1) The 2021 Equity Incentive Plan, as amended.

ITEM 6. [RESERVED]

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The information and financial data discussed below is derived from the consolidated financial statements of Relmada for the years ended December 31, 2023 and 2022. The consolidated financial statements of Relmada were prepared and presented in accordance with generally accepted accounting principles in the United States. The information and financial data discussed below is only a summary and should be read in conjunction with the historical financial statements and related notes of Relmada contained elsewhere in this Report. The consolidated financial statements contained elsewhere in this Report fully represent Relmada's financial condition and operations; however, they are not indicative of the Company's future performance. See "Cautionary Note Regarding Forward Looking Statements" above for a discussion of forward-looking statements and the significance of such statements in the context of this Annual Report.

This discussion contains forward-looking statements reflecting our current expectations that involve risks and uncertainties. Actual results may differ materially from those discussed in these forward-looking statements due to a number of factors, including those set forth in the section entitled "**Risk Factors**" and elsewhere herein. The information and financial data discussed below is only a summary and should be read in conjunction with the historical financial statements and related notes of Relmada Therapeutics, Inc. contained elsewhere in this document. Relmada's current consolidated financial position and consolidated results of operations; are not necessarily indicative of the Company's future performance. See "Cautionary Note Regarding Forward Looking Statements" above for a discussion of forward-looking statements and the significance of such statements in the context of this document.

Our Corporate History and Background

Relmada Therapeutics, Inc. is a clinical-stage, publicly traded biotechnology company developing NCEs that potentially address areas of high unmet medical need in the treatment of depression and other CNS diseases.

The Company's lead product candidate, esmethadone, is being developed as a rapidly acting, oral agent for the treatment of depression and other potential indications.

On October 15, 2019, we reported top-line data from study REL-1017-202. This was a double-blind, placebo-controlled Phase 2 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 MDD, who experienced an inadequate response to 1 to 3 treatments with an antidepressant medication.

On December 20, 2020, the Company announced that the first patient had been enrolled in the first Phase 3 clinical trial (RELIANCE I) of REL-1017, as an adjunctive treatment for MDD.

On April 1, 2021, Relmada announced the initiation of RELIANCE II, the second of two sister pivotal Phase 3 clinical trials (RELIANCE I and RELIANCE II) of REL-1017, as an adjunctive treatment for MDD.

On October 4, 2021, Relmada announced the initiation of the RELIANCE III study, the monotherapy trial for the Company's lead product candidate, REL-1017.

In addition, on October 4, 2021, Relmada announced that in order to support potential regulatory submissions seeking approval for REL-1017 as adjunctive and monotherapy treatment, the FDA confirmed that, based on what was known at the time, Relmada would not be required to conduct a two-year carcinogenicity study of REL-1017, as sufficient clinical data had been generated to date. The FDA also confirmed that Relmada would not need to conduct a TQT cardiac study in humans to support cardiac safety in potential regulatory submissions for REL-1017, as the data already provided and the data to be generated by the Phase 3 program would be adequate to evaluate the cardiac safety profile of REL-1017.

On October 13, 2022, Relmada announced that the RELIANCE III study, evaluating REL-1017 in the monotherapy setting for MDD, did not achieve its primary endpoint, which was a statistically significant improvement in depression symptoms compared to placebo as measured by the Montgomery-Asberg Depression Rating Scale (MADRS) on Day 28.

On December 7, 2022, Relmada announced that the RELIANCE I, evaluating REL-1017 as an adjunctive treatment for MDD, did not achieve its primary endpoint, which was a statistically significant improvement in depression symptoms compared to placebo as measured by the Montgomery-Asberg Depression Rating Scale (MADRS) on Day 28

Patients who completed the RELIANCE trials were eligible to rollover into a long-term, open-label study (Study 310), which also included subjects who had not previously participated in a REL-1017 clinical trial. This rollover study completed subject visits on July 11, 2023.

On August 23, 2023, Relmada announced the dosing of the first patient in RELIGHT, a Phase 3 clinical trial for REL-1017, as an adjunctive treatment for MDD.

On September 20, 2023, Relmada announced efficacy results for the de novo (or new to treatment) patients (204 patients) and safety results for all subjects (627 patients) from the Phase 3, long-term, open-label, safety trial (Study 310) of REL-1017 in patients with Major Depressive Disorder (MDD). Patients treated daily with REL-1017 for up to one year experienced rapid, clinically meaningful, and sustained improvements in depressive symptoms and associated functional impairment. REL-1017 was well-tolerated with long-term dosing, showing low rates of adverse events and discontinuations due to adverse events. No new safety signals were detected.

We have not generated revenues and do not anticipate generating revenues for the foreseeable future. We had a net loss of approximately $98,791,700 and $157,043,800 for the years ended December 31, 2023 and 2022, respectively. At December 31, 2023, we have an accumulated deficit of approximately $560,902,700.

Results of Operations

For the Year Ended December 31, 2023 vs the Year Ended December 31, 2022

Research and Development Expense

Total research and development expense for the year ended December 31, 2023 was approximately $54,807,400, as compared to $113,323,000 for the same period of 2022, a decrease of $58,515,600. The decrease in research and development expense was primarily due to:

- Decrease in study costs of $45,506,500 associated with the completion execution of two Phase 3 trials and the long-term, open-label, safety study (Study 310);
- Decrease in other research expenses of $12,919,100 primarily associated with additional consultants contracted to assist in the execution of our Phase 3 trials;
- Decrease in manufacturing and drug storage costs of $924,800 related to materials needed to complete the Phase 3 program;
- Decrease in stock-based compensation expense of $658,700;
- Decrease in pre-clinical and toxicology expenses of $131,000; and
- Increase in compensation expense of $1,624,500 due to higher employee-related costs.

General and Administrative Expense

Total general and administrative expense for the year ended December 31, 2023 was approximately $48,894,900, as compared to $47,926,100 for the same period of 2022, an increase of $968,800. The increase in general and administrative expenses was primarily due to:

- Increase in compensation expense of $2,242,000 due to higher employee-related costs;
- Increase in stock-based compensation expense of $275,000 primarily related to options granted to employees and the board of directors during 2023; and
- Decrease in other general and administrative expenses of $1,548,200 due to decreases in professional fees and consulting expenses during 2023.

Other Income, Net

Gain on settlement fees was approximately $6,351,600 received from a settlement during 2022. There was no gain on settlement of fees during 2023.

Interest/investment income was approximately $5,151,700 for the year ended December 31, 2023 compared to approximately $2,659,400 for the same period of 2022, an increase of $2,492,300. The increase was primarily related to higher returns from higher interest rates, offset by lower average investment balance during 2023 as compared to 2022.

Realized loss on short-term investments was approximately $4,064,400 compared to approximately $585,500 for the same period of 2022, an increase of $3,478,900. The increase was related to the timing of the sales of short-term investments along with market conditions.

Unrealized gain on short-term investments was approximately $3,823,200 compared to an unrealized loss of approximately $4,220,300 for the same period of 2022, an increase of $8,043,500. The increase was related to the market conditions.

Income Taxes

The Company did not provide for income taxes for the years ended December 31, 2023 and 2022, since there was a loss and a full valuation allowance against all deferred tax assets.

Net Loss

The Company recorded a net loss of approximately $98,791,700 and $157,043,800 or $3.28 and $5.30 per common share, basic and diluted, during the years ended December 31, 2023 and 2022, respectively, based on the factors described above.

Liquidity

As shown in the accompanying financial statements, the Company incurred negative operating cash flows of $51,659,206 for the year ended December 31, 2023 and has an accumulated deficit of $560,902,681 from inception through December 31, 2023.

Relmada has funded its past operations through equity raises and warrant and stock option exercises.

Management believes that due to previous equity raises completed and exercises of options and warrants and the resulting cash position on its balance sheet, it has sufficient funding, based on its budgeted cash flow requirements, to continue ongoing operations for at least 12 months from the filing of this annual report.

The following table sets forth selected cash flow information for the periods indicated below:

	For the Year Ended December 31, 2023	For the Year Ended December 31, 2022
Cash used in operating activities	$ (51,659,206)	$ (103,801,617)
Cash provided by investing activities	50,453,332	19,733,609
Cash provided by (used in) financing activities	(98,463)	45,020,474
Net decrease in cash and cash equivalents	$ (1,304,337)	$ (39,047,534)

For the year ended December 31, 2023, cash used in operating activities was $51,659,206 primarily due to the net loss of $98,791,746. This was offset by non-cash expenses which primarily consisted of stock-based compensation of $43,811,149. There were realized losses and unrealized gains on short term investments of $4,064,391 and $3,823,234, respectively. In addition, there were increases in operating assets and liabilities for the year ended December 31, 2023 of $3,080,234.

For the year ended December 31, 2022, cash used in operating activities was $103,801,617 primarily due to the net loss of $157,043,823. This was offset by non-cash expenses which primarily consisted of stock-based compensation of $44,194,765 and a gain on settlement of $6,351,606. There were realized and unrealized losses on short term investments of $585,522 and $4,220,255, respectively. In addition, there were increases in operating assets and liabilities for the year ended December 31, 2022 of $10,593,270.

For the year ended December 31, 2023, cash provided by investing activities was $50,453,332, due to $90,463,532 of purchases of short term investments offset by $140,916,864 of sales of short term investments.

For the year ended December 31, 2022, cash provided by investing activities was $19,733,609, due to $47,293,763 of purchases of short term investments offset by $67,027,372 of sales of short term investments.

Net cash used in financing activities for the year ended December 31, 2023, was $98,463 due to ATM reactivation fees.

Net cash provided by financing activities for the year ended December 31, 2022, was $45,020,474 due to proceeds from issuance of common stock of $42,728,599, proceeds from warrants exercised for common stock of $1,264,523, proceeds from options exercised for common stock of $703,720, proceeds from Section 16b short swing profit of $373,632 offset by the payment of fees for warrants issued for common stock of $50,000.

Effects of Inflation

Our assets are primarily monetary, consisting of cash and cash equivalents. Because of their liquidity, these assets are not directly affected by inflation. Because we intend to retain and continue to use our equipment, we believe that the incremental inflation related to replacement costs of such items will not materially affect our operations. However, the rate of inflation affects our expenses, such as those for employee compensation and contract services, which could increase our level of expenses and the rate at which we use our resources.

Lease Obligations

The Company is obligated to pay approximately $171,800 under 2 leases for office space over the next year.

Seasonality

We do not have a seasonal business cycle.

Critical Accounting Policies and Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses for the reporting period. Management bases its estimates on historical experience and on various assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. On a continual basis, management reviews its estimates utilizing currently available information, changes in facts and circumstances, historical experience, and reasonable assumptions. After such reviews, and if deemed appropriate, managements estimates are adjusted accordingly. Actual results could differ from those estimates and assumptions under different and/or future circumstances. Management considers an accounting estimate to be critical if:

- it requires assumptions to be made that were uncertain at the time the estimate was made; and
- changes in the estimate, or the use of different estimating methods that could have been selected, could have a material impact on results of operations or financial condition.

We evaluate our estimates and assumptions on an ongoing basis and none of the Company's estimates and assumptions used within the consolidated financial statements involve a high level of estimation uncertainty. For additional discussion regarding the application of the significant accounting policies, see Note 2 to the Company's consolidated financial statements included in this report.

Recent Accounting Pronouncements

The Company lists material recent accounting pronouncements in Note 2 of the consolidated financial statements.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest rate risk

Our cash and cash equivalents include all highly liquid investments with an original maturity of three months or less. Our cash equivalents are in a money market account. Because of the short-term maturities of our cash and cash equivalents, we do not believe that an increase in market rates would have a significant impact on the realized value of our investments. We place our cash and cash equivalents on deposit with financial institutions in the United States. The Federal Deposit Insurance Corporation limits coverage for all depository accounts. Our cash and cash equivalents at times may exceed covered limits.

Foreign currency exchange risk

We currently have limited, but may in the future have increased, clinical and commercial manufacturing agreements which are denominated in Euros or other foreign currencies. As a result, our financial results could be affected by factors such as a change in the foreign currency exchange rate between the U.S. dollar and the Euro or other applicable currencies, or by weak economic conditions in Europe or elsewhere in the world. We are not currently engaged in any foreign currency hedging activities.

Market indexed security risk

We have issued warrants to various holders underlying shares of our common stock. These warrants are re-measured to their fair value at each reporting period with changes in their fair value recorded as derivative gain (loss) in the accompanying consolidated statement of operations. We use the Black-Scholes model for valuation of the warrants.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Our audited consolidated financial statements as of December 31, 2023 and 2022 for the years then ended are included beginning on Page F-1 immediately following the signature page to this report. See Item 15 for a list of the financial statements included herein.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we carried out an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, at December 31, 2023, such disclosure controls and procedures were effective.

Disclosure controls and procedures are controls and other procedures that are designed to ensure that information required to be disclosed in our reports filed or submitted under the Exchange Act is recorded, processed, summarized and reported within the time periods specified by the SEC. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed in our reports filed or submitted under the Exchange Act is accumulated and communicated to management, including our Chief Executive Officer and Chief Financial Officer, or persons performing similar functions, as appropriate, to allow timely decisions regarding required disclosure.

This Annual Report on Form 10-K does not include an attestation report from our registered public accounting firm regarding internal control over financial reporting. Our internal control over financial reporting was not subject to such attestation as we are a non-accelerated filer.

Limitations on the Effectiveness of Controls

Our disclosure controls and procedures are designed to provide reasonable, not absolute, assurance that the objectives of our disclosure control system are met. Because of inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues, if any, within a company have been detected. Our Chief Executive Officer and Chief Financial Officer have concluded, based on their evaluation as of the end of the period covered by this Report that our disclosure controls and procedures were effective to provide reasonable assurance that the objectives of our disclosure control system were met.

Changes in Internal Control Over Financial Reporting

There were no changes in the Company's internal controls over financial reporting that occurred during the fourth quarter of the fiscal year covered by this Annual Report on Form 10-K that have materially affected, or are reasonably likely to materially affect, the Company's internal control over financial reporting.

Management's Report on Internal Control Over Financial Reporting

As required by the SEC rules and regulations for the implementation of Section 404 of the Sarbanes-Oxley Act, our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our consolidated financial statements for external reporting purposes in accordance with United States Generally Accepted Accounting Principles (GAAP). Our internal control over financial reporting includes those policies and procedures that:

(1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of our company,

(2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of consolidated financial statements in accordance with accounting principles generally accepted in the United States of America, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors, and

(3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the consolidated financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect errors or misstatements in our consolidated financial statements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree or compliance with the policies or procedures may deteriorate. Management assessed the effectiveness of our internal control over financial reporting at December 31, 2023. In making these assessments, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission COSO (2013 framework). Based on our assessments and those criteria, management determined that we did maintain effective internal control over financial reporting at December 31, 2023.

ITEM 9B. OTHER INFORMATION

On March 14, 2024, our Board of Directors unanimously approved, subject to stockholder approval, an amendment to the Company's 2021 Equity Incentive Plan (the "2021 Plan"), increasing by 4,500,000 shares the number of shares of our common stock that will be available for issuance of awards under the 2021 Plan. The 2021 Plan as adopted and approved by our shareholders originally authorized awards for up to 1,500,000 shares of our common stock. On May 25, 2022, shareholders approved an amendment to the 2021 Plan to increase the shares of the Company's common stock available for issuance thereunder by 3,900,000 shares. On May 25, 2023, shareholders approved an amendment to the 2021 Plan to increase the shares of the Company's common stock available for issuance thereunder by 2,500,000.

The purpose of the 2021 Plan is to (a) enable the Company and its affiliates to attract and retain the types of employees, directors and consultants who will contribute to the Company's long range success; (b) provide incentives that align the interests of employees, consultants and directors with those of the stockholders of the Company; and (c) promote the success of the Company's business, thus enhancing the value of the Company for the benefit of its stockholders.

Administration. The 2021 Plan will be administered by a committee (the "Committee"), or in the Board's sole discretion by the Board. In case no Committee has been appointed, the Board may appoint one or more members of the Board appointed by the Board to administer the 2021 Plan in accordance with the terms of the 2021 Plan. The Board has appointed the Compensation Committee of the Board to administer the 2021 Plan.

Shares Available for Awards. Subject to shareholder approval of the most recent amendment to the 2021 Plan, and to adjustment in certain circumstances in accordance with the terms of the 2021 Plan, we will reserve for issuance under the 2021 Plan no more than 12,400,000 shares of common stock (subject to adjustment in certain circumstances as provided in the 2021 Plan). Shares of Common Stock available for distribution under the 2021 Plan may consist, in whole or in part, of authorized and unissued shares, treasury shares or shares reacquired by the Company in any manner. Shares of Common Stock subject to an award that expires or is canceled, forfeited, or terminated without issuance of the full number of shares of Common Stock to which the award related, as well as any shares of common stock subject to an award that are (a) tendered in payment of an option, (b) delivered or withheld by the company to satisfy any tax withholding obligation, or (c) covered by a stock-settled stock appreciation right or other awards that were not issued upon the settlement of the award, shall be added back to the shares of common stock available for issuance of awards or delivery under the 2021 Plan.

Available Awards. Awards that may be granted under the 2021 plan include: (a) incentive stock options, (b) non-qualified stock options, (c) stock appreciation rights, (d) restricted awards, (e) performance share awards, (f) cash awards, and (g) other equity-based awards.

Recipients of Grants. Incentive stock options may be granted only to employees. Awards other than incentive stock options may be granted to employees, consultants and directors and those individuals whom the Committee or the Board determines are reasonably expected to become employees, consultants and directors following the grant date. Our principal executive officer, principal financial officer and other named executive officers are eligible to participate in and receive awards under the 2021 Plan.

Term.

The 2021 Plan has a term of ten years.

This summary of the 2021 Plan is qualified in its entirety by the full text of the 2021 Plan, which is filed as Exhibit 10.33 to this Report and is incorporated by reference herein.

The proposed amendment to the 2021 Plan will be submitted for the approval of our shareholders at our 2024 Annual Meeting of Stockholders. If the proposed amendment is not approved by the shareholders, the 2021 Plan will remain effective with respect to the number of shares of common stock originally authorized. Options for 4,363,250 shares of commons stock were issued in December 2023 subject to approval by the shareholders of this amendment. If the amendment is not approved, such options will be void, but the recipients thereof will receive identical options for a pro-rata share of any shares available for issuance of awards under the 2021 Plan immediately after the shareholder meeting.

Insider Trading Arrangements

On November 15, 2023, Charles Ence, our Chief Accounting and Compliance Officer, adopted a Rule 10b5-1 trading arrangement that was intended to satisfy the affirmative defense of Rule 10b5-1(c) under the Exchange Act for the sale of up to 137,110 shares of the Company's common stock, with such transactions to occur during sale periods beginning on or after April 23, 2024 and ending on the earlier of December 20, 2024, or the date on which all shares authorized for sale have been sold in conformance with the terms of the arrangement. On November 22, 2023, Mr. Ence terminated this trading arrangement.

No other officers, as defined in Rule 16a-1(f), or directors adopted and/or terminated a "Rule 10b5-1 trading arrangement" or a "non-Rule 10b5-1 trading arrangement," as defined in Item 408 of Regulation S-K, during the fourth fiscal quarter of 2023.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

The information required for the Items contained in Part III is incorporated herein by reference from our definitive proxy statement for our 2024 Annual Meeting of Stockholders (the "Proxy Statement"), which will be filed with the SEC no later than 120 days after December 31, 2023.

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS, AND CORPORATE GOVERNANCE

ITEM 11. EXECUTIVE COMPENSATION

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

Financial Statement Schedules

Our consolidated financial statements are listed on the Index to Financial Statements on this annual report on Form 10-K beginning on page F-1.

All financial statement schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

Our independent registered public accounting firm is Marcum LLP (PCAOB ID #688) of Houston, Texas.

RELMADA THERAPEUTICS, INC.
(INDEX TO FINANCIAL STATEMENTS)

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and Board of Directors of
Relmada Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Relmada Therapeutics, Inc. (the "Company") as of December 31, 2023 and 2022, the related consolidated statements of operations, changes in stockholders' equity and cash flows for each of the two years in the period ended December 31, 2023, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2023, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

Critical audit matters are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. We determined that there are no critical audit matters.

/s/ Marcum LLP

Marcum LLP

We have served as the Company's auditor since 2014**.**

Houston, Texas
March 19, 2024

Relmada Therapeutics, Inc.
Consolidated Balance Sheets

	As of December 31, 2023	As of December 31, 2022
Assets		
Current assets:		
Cash and cash equivalents	$ 4,091,568	$ 5,395,905
Short-term investments	92,232,292	142,926,781
Other receivables	-	512,432
Prepaid expenses	1,185,057	4,035,186
Total current assets	97,508,917	152,870,304
Other assets	43,125	34,875
Total assets	$ 97,552,042	$ 152,905,179
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 3,506,009	$ 5,261,936
Accrued expenses	8,688,791	7,206,941
Total current liabilities	12,194,800	12,468,877
Total liabilities	12,194,800	12,468,877
Commitments and Contingencies (Note 7)		
Stockholders' Equity:		
Preferred stock, $0.001 par value, 200,000,000 shares authorized, none issued and outstanding	-	-
Class A convertible preferred stock, $0.001 par value, 3,500,000 shares authorized, none issued and outstanding	-	-
Common stock, $0.001 par value, 150,000,000 shares authorized, 30,099,203 and 30,099,203 shares issued and outstanding, respectively	30,099	30,099
Additional paid-in capital	646,229,824	602,517,138
Accumulated deficit	(560,902,681)	(462,110,935)
Total stockholders' equity	85,357,242	140,436,302
Total liabilities and stockholders' equity	$ 97,552,042	$ 152,905,179

The accompanying notes are an integral part of these consolidated financial statements.

Relmada Therapeutics, Inc.
Consolidated Statements of Operations
For the Years Ended December 31, 2023 and 2022

	2023	2022
Operating expenses:		
Research and development	$ 54,807,348	$ 113,322,999
General and administrative	48,894,945	47,926,077
Total operating expenses	103,702,293	161,249,076
Loss from operations	(103,702,293)	(161,249,076)
Other income (expenses):		
Gain on settlement of fees	-	6,351,606
Interest/investment income, net	5,151,704	2,659,424
Realized loss on short-term investments	(4,064,391)	(585,522)
Unrealized gain (loss) on short-term investments	3,823,234	(4,220,255)
Total other income (expenses), net	4,910,547	4,205,253
Net loss	$ (98,791,746)	$ (157,043,823)
Net loss per common share – basic and diluted	$ (3.28)	$ (5.30)
Weighted average number of common shares outstanding – basic and diluted	30,099,203	29,628,664

The accompanying notes are an integral part of these consolidated financial statements.

Relmada Therapeutics, Inc.
Consolidated Statements of Changes in Stockholders' Equity
For the Years Ended December 31, 2023 and 2022

	Common Stock		Additional Paid-in	Accumulated	
	Shares	Par Value	Capital	Deficit	Total
Balance – December 31, 2021	27,740,147	$ 27,740	$ 513,304,258	$ (305,067,112)	$ 208,264,886
Stock-based compensation expense	-	-	44,194,765	-	44,194,765
ATM offering, net	2,094,243	2,094	42,726,505	-	42,728,599
Share exchange – Prefunded warrants, net of fees	(1,452,016)	(1,452)	(48,548)	-	(50,000)
Net exercise – Prefunded warrants	1,451,795	1,452	(1,452)	-	-
Warrants exercised	181,336	181	1,264,342	-	1,264,523
Options exercised	83,698	84	703,636	-	703,720
Short swing profit, net	-	-	373,632	-	373,632
Net loss	-	-	-	(157,043,823)	(157,043,823)
Balance – December 31, 2022	30,099,203	30,099	602,517,138	(462,110,935)	140,436,302
Stock-based compensation expense	-	-	43,811,149	-	43,811,149
ATM fees	-	-	(98,463)	-	(98,463)
Net loss	-	-	-	(98,791,746)	(98,791,746)
Balance – December 31, 2023	30,099,203	$ 30,099	$ 646,229,824	$ (560,902,681)	$ 85,357,242

The accompanying notes are an integral part of these consolidated financial statements.

Relmada Therapeutics, Inc.
Consolidated Statements of Cash Flows
For the Years Ended December 31, 2023 and 2022

	2023	2022
Cash flows from operating activities		
Net loss	$ (98,791,746)	$ (157,043,823)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	43,811,149	44,194,765
Gain on settlement	-	(6,351,606)
Realized loss on short-term investments	4,064,391	585,522
Unrealized (gain) loss on short-term investments	(3,823,234)	4,220,255
Change in operating assets and liabilities:		
Lease payment receivable	-	86,377
Other receivable	512,432	(512,432)
Prepaid expenses and other assets	2,841,879	7,259,767
Accounts payable	(1,755,927)	421,040
Accrued expenses	1,481,850	3,338,518
Net cash used in operating activities	(51,659,206)	(103,801,617)
Cash flows from investing activities		
Purchase of short-term investments	(90,463,532)	(47,293,763)
Sale of short-term investments	140,916,864	67,027,372
Net cash provided by investing activities	50,453,332	19,733,609
Cash flows from financing activities		
Payment of ATM fees	(98,463)	-
Payment of fees for warrants issued for common stock	-	(50,000)
Proceeds from issuance of common stock	-	42,728,599
Proceeds from options exercised for common stock	-	703,720
Proceeds from warrants exercised for common stock	-	1,264,523
Proceeds from short swing profit, net	-	373,632
Net cash (used in) provided by financing activities	(98,463)	45,020,474
Net decrease in cash and cash equivalents	(1,304,337)	(39,047,534)
Cash and cash equivalents at beginning of the year	5,395,905	44,443,439
Cash and cash equivalents at end of the year	$ 4,091,568	$ 5,395,905

	2023	2022
Supplemental disclosure of cash flow information:		
Non-cash operating transactions:		
Forgiveness of accounts payable related to gain	$ -	$ 3,212,583
Non-cash investing and financing transactions:		
Share exchange for Pre-funded warrants	$ -	$ 1,452
Net exercise of Pre-funded warrants	$ -	$ (1,452)

The accompanying notes are an integral part of these consolidated financial statements.

NOTE 1 - BUSINESS

Relmada Therapeutics Inc. (Relmada or the Company) (a Nevada corporation) is a clinical-stage, publicly traded biotechnology company focused on the development of esmethadone (d-methadone, dextromethadone, REL-1017), an N-methyl-D-aspartate (NMDA) receptor antagonist. Esmethadone 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. The Company is also developing a novel psilocybin (REL-P11) in doses that we believe are lower than those associated with psychedelic effects for the treatment of metabolic indications.

In addition to the normal risks associated with a new business venture, there can be no assurance that the Company's research and development will be successfully completed or that any product will be approved or commercially viable. The Company is subject to risks common to companies in the biotechnology industry including, but not limited to, dependence on collaborative arrangements, development by the Company or its competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, and compliance with the Food and Drug Administration (FDA) and other governmental regulations and approval requirements.

NOTE 2 - SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation and Principles of Consolidation

The accompanying consolidated financial statements and related notes have been prepared in accordance with accounting principles generally accepted in the United States of America (U.S. GAAP). The consolidated financial statements include the Company's accounts and those of the Company's wholly-owned subsidiary. All significant intercompany accounts and transactions have been eliminated in consolidation.

Liquidity

As shown in the accompanying consolidated financial statements, the Company incurred negative operating cash flows of $51,659,206 for the year ended December 31, 2023 and has an accumulated deficit of $560,902,681 from inception through December 31, 2023.

Relmada has funded its past operations through equity raises. There were no equity raises in the year ended December 31, 2023.

Management believes that the Company's existing cash and cash equivalents will enable them to fund operating expenses and capital expenditure requirements for at least 12 months from the issuance of these consolidated financial statements. Beyond that point management will evaluate the size and scope of any subsequent operations and clinical trials that will affect the timing of additional financings through public or private sales of equity or debt securities or from bank or other loans or through strategic collaboration and/or licensing agreements. Any such expenditures related to any subsequent clinical trials will not be incurred until such additional financing is raised. Further, additional financing related to subsequent trials does not affect the Company's conclusion that based on the cash on hand and the budgeted cash flow requirements, the Company has sufficient funds to maintain operations for at least 12 months from the issuance of these consolidated financial statements.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses for the reporting period. Actual results could differ from those estimates. The significant estimates are stock-based compensation expenses, and recorded amounts related to income taxes.

Cash and Cash Equivalents

The Company considers cash deposits and all highly liquid investments with a maturity of three months or less when purchased to be cash and cash equivalents. The Company's cash and cash equivalents are held at two high-credit-quality financial institutions. The Company's cash and cash equivalents of $4,091,568 at December 31, 2023 at these institutions exceed federally insured limits.

Short-term Investments

The Company's investments consist entirely of mutual funds. The securities are measured at fair value based on the net asset value ("NAV"). The Company adopted FASB ASU 2016-01, Financial Instruments, which requires substantially all equity investments in nonconsolidated entities to be measured at fair value with recurring changes recognized in earnings, except for those accounted for using equity method accounting. Changes in fair value of the securities are recorded as part of other income on the consolidated statement of operations. Short term investment activity is presented in the investing activities section on the consolidated statement of cash flows.

Short-term investments at December 31, 2023 consisted of mutual funds with a fair value of $92,232,292.

Patents

Costs related to filing and pursuing patent applications are recorded as general and administrative expense and expensed as incurred since recoverability of such expenditures is uncertain.

Leases

The Company recognizes its leases with a term of greater than a year on the balance sheet by recording right-of-use assets and lease liabilities. Leases can be classified as either operating leases or finance leases. Operating leases will result in straight-line lease expense, while finance leases will result in front-loaded expense. The Company's lease consists of an operating leases for office space. The Company does not recognize a lease liability or right-of-use asset on the balance sheet for short-term leases. Instead, the Company recognizes short-term lease payments as an expense on a straight-line basis over the lease term. A short-term lease is defined as a lease that, at the commencement date, has a lease term of 12 months or less and does not include an option to purchase the underlying asset that the lessee is reasonably certain to exercise.

Gain on Settlement

The Company recognizes a gain when cash (or other assets, such as claims to cash) has been received without the expectation of repayment. A gain is recorded when the assets are readily convertible to know amounts of cash or claims to cash. Gains are reported as part of other income (expense) on the consolidated statement of operations. The Company recorded a gain on settlement of $0 and $6,351,606 included in other income (expense) for the years ended December 31, 2023 and 2022, respectively.

Fair Value of Financial Instruments

The Company's financial instruments primarily include cash, short term investments derivative liabilities and accounts payable. Due to the short-term nature of cash and accounts payable the carrying amounts of these assets and liabilities approximate their fair value. Derivatives are recorded at fair value at each period end.

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the reporting date. A fair value hierarchy has been established for valuation inputs that gives the highest priority to quoted prices in active markets for identical assets or liabilities and the lowest priority to unobservable inputs. The fair value hierarchy is as follows:

Level 1 Inputs - Unadjusted quoted prices in active markets for identical assets or liabilities that the reporting entity has the ability to access at the measurement date.

Level 2 Inputs - Inputs other than quoted prices included in Level 1 that are observable for the asset or liability, either directly or indirectly. These might include quoted prices for similar assets or liabilities in active markets, quoted prices for identical or similar assets or liabilities in markets that are not active, inputs other than quoted prices that are observable for the asset or liability (such as interest rates, volatilities, prepayment speeds, credit risks, etc.) or inputs that are derived principally from or corroborated by market data by correlation or other means.

Level 3 Inputs - Prices or valuation techniques that require inputs that are both significant to the fair value measurement and unobservable (supported by little or no market activity).

The Company's short-term investment instruments of $92,232,292 at December 31, 2023 are classified using Level 1 inputs within the fair value hierarchy because they are valued using NAV. Unrealized gains and losses are recorded in the consolidated statement of operations as unrealized gain on short-term investments. The Company recorded an unrealized gain of $3,823,234 and an unrealized loss of $4,220,255, included in other income (expense) for the years ended December 31, 2023 and 2022, respectively.

Fair Value on a Recurring Basis

As required by Accounting Standard Codification (ASC) Topic No. 820 - 10 *Fair Value Measurement*, financial assets and liabilities are classified based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement requires judgment and may affect the valuation of the fair value of assets and liabilities and their placement within the fair value hierarchy levels.

Income Taxes

The Company accounts for income taxes using the asset and liability method. Accordingly, deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in the tax rate is recognized in income or expense in the period that the change is effective. Tax benefits are recognized when it is probable that the deduction will be sustained. A valuation allowance is established when it is more likely than not that all or a portion of a deferred tax asset will either expire before the Company is able to realize the benefit, or that future deductibility is uncertain. At December 31, 2023 and 2022, the Company had recorded a valuation allowance to the full extent of the Company's net deferred tax assets since the likelihood of realization of the benefit does not meet the more likely than not threshold.

The Company files a U.S. Federal income tax return and various state returns. Uncertain tax positions taken on our tax returns will be accounted for as liabilities for unrecognized tax benefits. The Company will recognize interest and penalties, if any, related to unrecognized tax benefits in general and administrative expenses in the statements of operations. There were no liabilities recorded for uncertain tax positions at December 31, 2023 and 2022. The open tax years, subject to potential examination by the applicable taxing authority, for the Company are from June 30, 2018 forward.

Research and Development

Research and development costs primarily consist of research contracts for the advancement of product development, salaries and benefits, stock-based compensation, and consultants. The Company expenses all research and development costs in the period incurred. The Company makes an estimate of costs in relation to clinical study contracts. The Company analyzes the progress of studies, including the progress of clinical studies and phases, invoices received and contracted costs when evaluating the adequacy of the amount expensed and the related prepaid asset and accrued liability.

Stock-Based Compensation

The Company measures the cost of employee services received in exchange for an award of equity instruments based on the grant-date fair value of the award. That cost is recognized over the period during which an employee is required to provide service in exchange for the award - the requisite service period. The grant-date fair value of employee share options is estimated using the Black-Scholes option pricing model adjusted for the unique characteristics of those instruments.

Net Loss per Common Share

Basic net loss per common share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted net loss per common share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common share equivalents outstanding for the period determined using the treasury-stock method. Dilutive common stock equivalents are comprised of Class A convertible preferred stock, Series A preferred stock, options and warrants to purchase common stock. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted shares outstanding due to the Company's net losses in each period.

The potentially dilutive securities that would be anti-dilutive due to the Company's net loss are not included in the calculation of diluted net loss per share attributable to common stockholders. The anti-dilutive securities are as follows (in common stock equivalent shares):

	Year ended December 31, 2023	Year ended December 31, 2022
Common stock warrants	2,381,366	3,027,441
Common stock options	17,416,192	12,122,606
Total	19,797,558	15,150,047

Recent Accounting Pronouncements

In October 2021, the FASB issued ASU 2021-08, "*Business Combinations (Topic 805): Accounting for Contract Assets and Contract Liabilities from Contracts with Customers*". The amendments in this ASU require that an entity (acquirer) recognize, and measure contract assets and contract liabilities acquired in a business combination, including contract assets and contract liabilities arising from revenue contracts with customers, as if it had originated the contracts as of the acquisition date. The amendments in this ASU were effective for annual and interim periods beginning after December 15, 2022. The Company adopted this standard effective January 1, 2023 and the standard did not have a significant impact on our consolidated financial statements.

In November 2023, The FASB issued ASU 2023-07, "*Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures*" which expands annual and interim disclosures for reportable segments, primarily through enhanced disclosures about significant segment expenses. ASU 2023-07 is effective for our annual periods beginning January 1, 2024, and for interim periods beginning January 1, 2025, with early adoption permitted. The Company is currently evaluating the potential effect that the updated standard will have on our financial statement disclosures.

In December 2023, the FASB issued ASU 2023-09, "*Income Taxes (Topic 740): Improvements to Income Tax Disclosures*" to expand the disclosure requirements for income taxes, specifically related to the rate reconciliation and income taxes paid. ASU 2023-09 is effective for our annual periods beginning January 1, 2025, with early adoption permitted. The Company is currently evaluating the potential effect that the updated standard will have on our financial statement disclosures.

NOTE 3 - PREPAID EXPENSES

Prepaid expenses consisted of the following (rounded to nearest $00):

	December 31, 2023	December 31, 2022
Insurance	$ 365,100	$ 313,200
Research and Development	695,000	3,619,800
Other	125,000	102,200
Total	$ 1,185,100	$ 4,035,200

NOTE 4 - ACCRUED EXPENSES

Accrued expenses consisted of the following (rounded to nearest $00):

	December 31, 2023	December 31, 2022
Research and development	$ 5.394,700	$ 5,809,800
Professional fees	174,000	116,500
Accrued bonus	2,632,400	492,100
Accrued vacation	372,200	529,800
Other	115,500	258,700
Total	$ 8,688,800	$ 7,206,900

NOTE 5 - STOCKHOLDERS' EQUITY

Common Stock

During the year ended December 31, 2023, the Company did not issue any shares of common stock for the exercise of warrants. During the year ended December 31, 2022, the Company issued 181,336 shares of common stock for the exercise of warrants for proceeds of $1,264,523.

During the year ended December 31, 2023, the Company did not issue any shares of common stock for the exercise of options. During the year ended December 31, 2022, the Company issued 83,698 shares of common stock for the exercise of options for proceeds of $703,720.

On May 15, 2020, the Company entered into an Open Market Sale Agreement with Jefferies LLC, as sales agent ("Jefferies"), pursuant to which the Company offered to sell, from time to time, through Jefferies, shares of the Company's common stock, having an aggregate offering price of up to $75,000,000. The Company was not obligated to sell any shares under the agreement. During the years ended December 31, 2023 and 2022, the Company issued 0 and 2,094,243 shares of common stock for net cash proceeds of $0 and $42,728,599 under the agreement, respectively. As of December 31, 2023, no shares were available to be issued under this agreement.

On April 6, 2022, the Company entered into a new Open Market Sale Agreement with Jefferies, as sales agent, pursuant to which we may offer and sell, from time to time, through Jefferies, shares of our common stock, having an aggregate offering price of up to $100,000,000. We are not obligated to sell any shares under the agreement. As of December 31, 2023, no shares have been issued under this agreement.

During the years ended December 31, 2023 and 2022, there were no common stock shares issued for issuances of restricted common stock.

Stock-based compensation - options

In December 2014, the Board of Directors adopted and the shareholders approved Relmada's 2014 Stock Option and Equity Incentive Plan, as amended (the "2014 Plan"), which allows for the granting of 5,152,942 common stock awards, stock appreciation rights, and incentive and nonqualified stock options to purchase shares of the Company's common stock to designated employees, non-employee directors, and consultants and advisors.

In May 2021, the Company's Board of Directors adopted and shareholders approved the Company's 2021 Equity Incentive Plan (the "2021 Plan"), which allowed for the granting of 1,500,000 options or other stock awards.

In May 2022, the Company's Board of Directors adopted, and shareholders approved an amendment to the 2021 Plan to increase the shares of the Company's common stock available for issuance thereunder by 3,900,000 shares.

In May 2023, the Company's Board of Directors adopted and shareholders approved an amendment to the 2021 Plan to increase the shares of the Company's common stock available for issuance thereunder by 2,500,000 shares.

These combined plans allowed for the granting of up to 13,052,942 options or other stock awards.

Stock options are exercisable generally for a period of 10 years from the date of grant and generally vest either over four years or upon achievement of certain specified corporate or other milestones. As of December 31, 2023, there were no shares available to be granted under either the 2014 or 2021 Plan. The shareholders will vote at their annual meeting in 2024 on a management proposal to increase the shares available to be issued under the 2021 Plan. There can be no assurance such amendment will be approved. As of December 31, 2023, options for 4,363,250 shares of common stock had been issued subject to approval by the shareholders of this amendment. If the amendment is not approved, such options will be forfeited.

The Company uses the simplified method for share-based compensation to estimate the expected term for employee option awards for share-based compensation in its option-pricing model.

From November 13, 2023 through December 15, 2023, the Company awarded a total of 5,010,000 options to consultants and employees with an exercise price ranging from $2.48 to $2.82 and a 10-year term vesting over a 4-year period. The options granted include time-based vesting grants. The options have an aggregate fair value of approximately $10,703,070 calculated using the Black Scholes option-pricing model. Variables used in the Black-Scholes option-pricing model include: (1) discount rate of 3.93 – 4.68% (2) expected life of 6.25 years, (3) expected volatility of 113-114%, and (4) zero expected dividends.

From August 1, 2023 through September 18, 2023, 10,000 options were issued to various employees with an exercise price ranging from $2.56 to $2.96 and a 10-year term, vesting over a 4-year period. The options granted include time-based vesting grants. The options have an aggregate fair value of approximately $23,840 calculated using the Black-Scholes option-pricing model. Variables used in the Black-Scholes option-pricing model include: (1) discount rate of 4.20– 4.44% (2) expected life of 6.25 years, (3) expected volatility of 113-114%, and (4) zero expected dividends.

From April 10, 2023 through June 20, 2023, 60,000 options were issued to various employees with an exercise price ranging from $2.28 to $3.32 and a 10-year term, vesting over a 4-year period. The options granted include time-based vesting grants. The options have an aggregate fair value of approximately $148,420 calculated using the Black-Scholes option-pricing model. Variables used in the Black-Scholes option-pricing model include: (1) discount rate of 3.43 – 3.91% (2) expected life of 6.25 years, (3) expected volatility of 114%, and (4) zero expected dividends.

From January 6, 2023 through February 21, 2023, 620,000 options were issued to various consultants and employees with an exercise price ranging from $3.18 to $4.30 and a 10-year term, vesting over a 4-year period. The options have an aggregate fair value of approximately $1,933,613 calculated using the Black-Scholes option-pricing model. Variables used in the Black-Scholes option-pricing model include: (1) discount rate of 3.46 – 4.12% (2) expected life of 6.25 years, (3) expected volatility of 115-116%, and (4) zero expected dividends.

From December 16, 2022 through December 21, 2022, the Company awarded a total of 2,800,000 options to consultants and employees with an exercise price ranging from $3.20 to $3.37 and a 10-year term vesting over a 4-year period. The options granted include time-based vesting grants. The options have an aggregate fair value of $8,169,325 calculated using the Black Scholes option-pricing model. Variables used in the Black-Scholes option-pricing model include: (1) discount rate of 3.60 – 3.78% (2) expected life of 6.25 years, (3) expected volatility of 115%, and (4) zero expected dividends.

On December 16, 2022, the Company awarded a total of 199,432 options to employees with an exercise price of $3.37 and a 10-year term vesting immediately. The options have an aggregate fair value of $561,902 calculated using the Black Scholes option-pricing model. Variables used in the Black-Scholes option-pricing model include: (1) discount rate of 3.61% (2) expected life of 5 years, (3) expected volatility of 120%, and (4) zero expected dividends.

From July 1, 2022 through September 29, 2022, 260,000 options were issued to various consultants with an exercise price ranging from $18.30 to $36.19 and a 10-year term, vesting over a 4 year period. The options granted include time-based vesting grants. The options have an aggregate fair value of approximately $5.0 million calculated using the Black-Scholes option-pricing model. Variables used in the Black-Scholes option-pricing model include: (1) discount rate of 2.9 – 3.94% (2) expected life of 6.25 years, (3) expected volatility of 93-94%, and (4) zero expected dividends.

From April 25, 2022 through May 5, 2022, 260,000 options were issued to various consultants with an exercise price ranging from $22.40 to $25.52 and a 10-year term, vesting over a 4-year period. The options granted include time-based vesting grants. The options have an aggregate fair value of approximately $4.6 million, calculated using the Black-Scholes option-pricing model. Variables used in the Black-Scholes option-pricing model include: (1) discount rate of 2.85 – 3.04% (2) expected life of 6.25 years, (3) expected volatility of 95%, and (4) zero expected dividends.

On March 28, 2022, the Company awarded a total of 15,000 options to an employee with an exercise price of $25.76 and a 10-year term vesting over a 4-year period. The options granted include time-based vesting grants. The options have an aggregate fair value of $307,845 calculated using the Black Scholes option-pricing model. Variables used in the Black-Scholes option-pricing model include: (1) discount rate of 2.55% (2) expected life of 6.25 years, (3) expected volatility of 98%, and (4) zero expected dividends.

From January 5, 2022 through March 14, 2022, 110,000 options were issued to various consultants with an exercise price ranging from $18.00 to $21.46 and a 10-year term, vesting over a 4-year period. The options granted include time-based vesting grants. The options have an aggregate fair value of approximately $1.6 million, calculated using the Black-Scholes option-pricing model. Variables used in the Black-Scholes option-pricing model include: (1) discount rate of 1.53 – 2.00% (2) expected life of 6.25 years, (3) expected volatility of 98%, and (4) zero expected dividends.

On January 1, 2022, 50,000 options were issued to a consultant with an exercise price of $22.53 and a 10-year term, vesting over a 1-year period. The options granted include performance vesting based on the Company's achievement of performance metrics. The options have an aggregate fair value of $847,583, calculated using the Black-Scholes option-pricing model. Variables used in the Black-Scholes option-pricing model include: (1) discount rate of 1.53% (2) expected life of 5.5 years, (3) expected volatility of 96%, and (4) zero expected dividends.

Options

A summary of the changes in options outstanding for the years ended December 31, 2023 and 2022 is as follows:

	Number of Shares	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding and expected to vest at December 31, 2021	10,330,622	$ 22.52	9.0	$ 46,088,534
Granted	3,744,432	7.40	9.8	-
Exercised	(83,698)	-	-	-
Forfeited	(1,868,750)	-	-	-
Outstanding and expected to vest at December 31, 2022	12,122,606	$ 18.19	8.5	$ 417,998
Granted	5,700,000	$ 2.61	9.9	-
Forfeited	(406,414)	-	-	-
Outstanding and expected to vest at December 31, 2023	17,416,192	$ 12.99	8.3	$ 11,183,370
Options exercisable at December 31, 2023	7,161,748	$ 20.25	7.0	$ 1,015,520

On September 5, 2023, Dr. Eric Schmidt, a member of the Board of Directors (the "Board"), notified the Company that he would resign from the Board, effective immediately. On September 22, 2023, the Board voted and approved that all of Dr. Schmidt's unvested options would vest immediately and be exercisable through the original term of the respective grants. In addition, the Board approved the extension of the exercise period for the options which were vested on September 5, 2023 from 90 days to the original term of the respective options. As a result of the modifications, the Company recorded approximately $1.2 million of stock-based compensation during the year ended December 31, 2023.

At December 31, 2023, the Company has unrecognized stock-based compensation expense of approximately $62,386,500 related to unvested stock options over the weighted average remaining service period of 2.5 years. The weighted average fair value of options granted during the years ended December 31, 2023 and 2022 was approximately $2.61 and $7.40 per share, respectively, on the date of grant using the Black-Scholes option pricing model with the following assumptions:

	Years Ended December 31, 2023	Years Ended December 31, 2022
Risk free interest rate	3.43 to 4.68%	1.53 to 3.94%
Dividend yield	0%	0%
Volatility	113-116%	93-120%
Expected term (in years)	6.25	5 to 6.25

Warrants

A summary of the changes in outstanding warrants during the years ended December 31, 2023 and 2022 is as follows:

	Number of Shares	Weighted Average Exercise Price Per Share
Outstanding at December 31, 2021	3,208,777	$ 16.45
Issued	1,452,016	0.001
Exercised	(1,633,352)	0.77
Outstanding at December 31, 2022	3,027,441	$ 17.02
Forfeited	(646,075)	$ 1.50
Outstanding at December 31, 2023	2,381,366	$ 20.02
Warrants exercisable at December 31, 2023	2,235,366	$ 19.20

There were no warrants issued during the year ended December 31, 2023.

On September 20, 2022, the Company entered into an agreement with an investor to exchange 1,452,016 shares of outstanding common stock for 1,452,016 prefunded warrants. The 1,452,016 shares of common stock were returned. These warrants have an exercise price of $0.001 and a 9.99% beneficial ownership limitation. On October 19, 2022 a cashless exercise of the 1,452,016 prefunded warrants was transacted with 1,451,795 shares of common shares issued and the remaining 221 warrants being cancelled.

At December 31, 2023, the Company had approximately $3,200,000 of unrecognized stock-based compensation expense related to outstanding warrants. At December 31, 2023, the aggregate intrinsic value of warrants vested and outstanding was approximately $19,000.

Stock-based compensation by class of expense

The following summarizes the components of stock-based compensation expense which includes common stock, stock options, warrants and restricted stock in the consolidated statements of operations (rounded to nearest $00):

	Year Ended December 31, 2023	Year Ended December 31, 2022
Research and development	$ 7,224,000	$ 7,882,700
General and administrative	36,587,100	36,312,100
Total	$ 43,811,100	$ 44,194,800

NOTE 6 - INCOME TAXES

No provision or benefit for federal or state income taxes has been recorded because the Company has incurred net losses for all periods presented and has recorded a valuation allowance against its deferred tax assets.

The components of the Company's deferred tax assets are as follows at:

	December 31, 2023	December 31, 2022
Deferred tax assets:		
Federal net operating loss	$ 21,016,000	$ 24,964,000
State net operating loss	3,771,000	13,781,000
Research and development tax credits	2,238,000	7,902,000
Capitalized R&D	49,581,000	45,666,000
Nonqualified Stock Options	29,305,000	19,803,000
Accruals	1,616,000	1,546,000
Intangibles and Fixed Assets	2,599,000	2,732,000
Other	11,000	2,000
Less: valuation allowance	(110,137,000)	(116,396,000)
Total	$ -	$ -

The Company has maintained a full valuation allowance against its deferred tax assets at December 31, 2023 and 2022. A valuation allowance is required to be recorded when it is more likely than not that some portion or all of the net deferred tax assets will not be realized. Since the Company cannot be assured of realizing the net deferred tax asset, a full valuation allowance has been provided. The valuation allowance (decreased)/increased for the years ended December 31, 2023 and 2022 by approximately $(6,259,000) and $20,201,000, respectively. Deferred tax asset for net operating loss carryforwards at December 31, 2023 was adjusted with the corresponding offset to valuation allowance.

At December 31, 2023, the Company had federal, New York State and New York City net operating loss (NOL) carryforwards of approximately $100,077,000, $15,016,000 and $14,998,000 respectively, which begin expiring in 2027, 2032 and 2032, respectively. Approximately $88,611,000 federal NOL can be carried forward indefinitely but it is limited to 80% of future taxable income. The Company also has federal research and development tax credit carryforwards of approximately $2,237,600 that will begin to expire in 2042. The Company's ability to use its NOL carryforwards may be limited if it experiences an "ownership change" as defined in Section 382 ("Section 382") of the Internal Revenue Code of 1986, as amended. An ownership change generally occurs if certain stockholders increase their aggregate percentage ownership of a corporation's stock by more than 50 percentage points over their lowest percentage ownership at any time during the testing period, which is generally the three-year period preceding any potential ownership change.

Sections 382 and 383 of the Internal Revenue Code of 1986 subject the future utilization of net operating losses and certain other tax attributes, such as research and development tax credits, to an annual limitation in the event of certain ownership changes, as defined. The Company has undergone and ownership change and has determined that various "changes in ownership" as defined by IRS Section 382 did occur. Accordingly, about $111,168,000 of the Company's NOL carryforwards are limited. Approximately, $41,562,000 of NOLs and $7,346,000 of R&D Credits are expected to expire unused. The deferred tax assets associated with the attributes that will expire without utilization have been written-off. There are $1,109,000 of NOLs available for use after the October 13, 2022 change in 2023. In subsequent years, the NOLs available from the October 13, 2022 change under section 382 are $740,000, annually.

A reconciliation of the statutory tax rate to the effective tax rate is as follows:

	Year Ended December 31, 2023	Year Ended December 31, 2022
Statutory federal income tax rate	21.00%	21.00%
State (net of federal benefit)	(6.56)%	(9.46)%
Non-deductible expenses	(5.34)%	(0.53)%
R&D Credit	1.70%	1.64%
NOL and R&D adjustment due to 382	(16.27)%	0.00%
Permanent true-ups	(0.89)%	0.00%
Other	0.02%	0.22%
Change in valuation allowance	6.34%	(12.87)%
Effective income tax rate	0%	0%

The Company does not have any uncertain tax positions at December 31, 2023 and 2022, that would affect its effective tax rate. The Company does not anticipate a significant change in the amount of unrecognized tax benefits over the next twelve months. Because the Company is in a loss carryforward position, the Company is generally subject to US federal and state income tax examinations by tax authorities for all years for which a loss carryforward is available. If and when applicable, the Company will recognize interest and penalties as part of income tax expense.

NOTE 7 - COMMITMENTS AND CONTINGENCIES

License Agreements

Wonpung

On August 20, 2007, the Company entered into a License Development and Commercialization Agreement with Wonpung Mulsan Co, a shareholder of the Company. Wonpung has exclusive territorial rights in countries it selects in Asia to market up to two drugs the Company is currently developing and a right of first refusal (ROFR) for up to an additional five drugs that the Company may develop in the future as defined in more detail in the license agreement. If the parties cannot agree to terms of a license agreement, then the Company shall be able to engage in discussions with other potential licensors. As of March 19, 2024, no discussions are active between the Company and Wonpung.

The Company 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 it is currently developing. The licensing terms for the ROFR products are subject to future negotiations and binding arbitration. 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.

Third Party Licensor

Based upon a prior acquisition, the Company assumed an obligation to pay a third party (Dr. Charles E. Inturrisi and Dr. Paolo Manfredi – see below): (A) royalty payments up to 2% on net sales of licensed products that are not sold by sublicensee and (B) on each and every sublicense earned royalty payment received by licensee from its sublicensee on sales of license product by sublicensee, the higher of (i) 20% of the royalties received by licensee; or (ii) up to 2% of net sales of sublicensee. The Company will also make milestone payments of up to $4 or $2 million, for the first commercial sale of product in the field that has a single active pharmaceutical ingredient, and for the first commercial sale of product in the field of product that has more than one active pharmaceutical ingredient, respectively. As of December 31, 2023, the Company has not generated any revenue related to this license agreement.

Inturrisi / Manfredi

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 Agreements, Relmada assigned its existing rights, including patents and patent applications, to esmethadone in the context of psychiatric use (the Existing Invention) to Licensor. Licensor then granted Relmada under the License Agreement a perpetual, worldwide, and exclusive license to commercialize the Existing Invention and certain further inventions regarding esmethadone in the context of other indications such as those contemplated above. In consideration of the rights granted to Relmada under the License Agreement, Relmada paid the Licensor an upfront, non-refundable license fee of $180,000. Additionally, Relmada will pay Licensor $45,000 every three months 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. Relmada will also pay Licensor tiered royalties with a maximum rate of 2%, decreasing to 1.75%, and 1.5% in certain circumstances, on net sales of licensed products covered under the License Agreement. Relmada will also pay Licensor tiered payments up to a maximum of 20%, and decreasing to 17.5%, and 15% in certain circumstances, of all consideration received by Relmada for sublicenses granted under the License Agreement. As of December 31, 2023, no events have occurred, and the Company continues to pay Licensor $45,000 every three months.

Arbormentis, LLC

On July 16, 2021, the Company entered into a License Agreement with Arbormentis, LLC, a privately held Delaware limited liability company, by which the Company acquired development and commercial rights to a novel psilocybin and derivate program from Arbormentis, LLC, worldwide excluding the countries of Asia. The Company will collaborate with Arbormentis, LLC on the development of new therapies targeting neurological and psychiatric disorders, leveraging its understanding of neuroplasticity, and focusing on this emerging new class of drugs targeting the neuroplastogen mechanism of action. Under the terms of the License Agreement, the Company paid Arbormentis, LLC an upfront fee of $12.7 million, consisting of a mix of cash and warrants to purchase the Company's common stock, in addition to potential milestone payments totaling up to approximately $160 million related to pre-specified development and commercialization milestones. Arbormentis, LLC is also eligible to receive a low single digit royalty on net sales of any commercialized therapy resulting from this agreement. The license agreement is terminable by the Company but is perpetual and not terminable by the licensor absent material breach of its terms by the Company.

The new licensed program stems from an international collaboration among U.S., European and Swiss scientists that has focused on the discovery and development of compounds that may promote neural plasticity. Dr. Paolo Manfredi, Relmada's Acting Chief Scientific Officer and co-inventor of REL-1017, and Dr. Marco Pappagallo, Relmada' s Safety/Adjudication Officer, are among the scientists affiliated with Arbormentis, LLC.

Leases and Subleases

On August 1, 2021, the Company relocated its corporate headquarters to 2222 Ponce de Leon, Floor 3, Coral Gables, FL 33134, pursuant to a lease agreement with monthly rent of approximately $11,000. The lease period was for five months. The lease agreement expired on December 31, 2021 and was renewed for the calendar year 2022, 2023 and 2024 with monthly rent of approximately $9,000, $7,000 and $7,000, respectively.

Beginning on January 1, 2023, we also leased office space at 880 Third Avenue, 12th Floor, New York, NY 10022 with monthly rent of approximately $14,500 that was terminated on November 30, 2023.

Beginning on December 1, 2023, we leased office space at 12 E 49th Street, New York, NY 10022 for with monthly rent of approximately $12,000 that expires on July 31, 2024.

In accordance with ASC 842, *Leases*, the Company recognizes rent expense evenly over the 12 months.

The Company incurred rent expense of approximately $283,600 and $129,600 for the years ended December 31, 2023 and 2022, respectively.

On June 8, 2017, the Company entered into an Amended and Restated License Agreement with Actinium. Pursuant to the terms of the agreement, Actinium licensed the furniture, fixtures, equipment and tenant improvements located in the office (FFE) for a license fee of $7,529 per month until December 8, 2022. Actinium had at any time during the term of this agreement the right to purchase the FFE for $496,914, less any previously paid license fees. On July 7, 2022, Actinium exercised its right to purchase the FFE for $52,698. The license of FFE qualifies as a sales-type lease. At inception, the Company derecognized the underlying assets of $493,452, recognized discounted lease payments receivable of $397,049 using the discount rate of 8.38% and recognized loss on sales-type lease of fixed assets of $96,403. As of December 31, 2023 and 2022, there was no unearned interest income.

Legal

From time to time, the Company may become involved in lawsuits and other legal proceedings that arise in the course of business. Litigation is subject to inherent uncertainties, and it is not possible to predict the outcome of litigation with total confidence. Except as disclosed below, the Company is currently not aware of any legal proceedings or potential claims against it whose outcome would be likely, individually or in the aggregate, to have a material adverse effect on the Company's business, financial condition, operating results, or cash flows.

NOTE 8 - OTHER POSTRETIREMENT BENEFIT PLAN

Relmada participates in a multiemployer 401(k) plan that permits eligible employees to contribute funds on a pretax basis subject to maximum allowed under federal tax provisions. The Company matches 100% of the first 3% of employee contributions, plus 50% of employee contributions that exceed 3% but do not exceed 5%.

The employees choose an amount from various investment options for both their contributions and the Company's matching contribution. The Company's contribution expense was $140,982 and $105,216 for the years ended December 31, 2023 and 2022, respectively.

NOTE 9 - SUBSEQUENT EVENTS

The Company's management reviewed all material events through the date the financial statements were issued for subsequent event disclosure consideration.

From January 1, 2024 through March 19, 2024, 50,000 options were issued to an advisor with an exercise price of $3.44 and a 10-year term, vesting over a 4-year period. These options awarded are subject to shareholder approval.

On January 31, 2024 Executive officers purchased 171,645 shares of common stock at a weighted average purchase price of $3.86.

Subsequent to December 31, 2023, 74,999 outstanding options were exercised for total cash proceeds of $246,747.

Exhibits

Certain of the agreements filed as exhibits to this Report contain representations and warranties by the parties to the agreements that have been made solely for the benefit of the parties to the agreement. These representations and warranties:

- may have been qualified by disclosures that were made to the other parties in connection with the negotiation of the agreements, which disclosures are not necessarily reflected in the agreements;
- may apply standards of materiality that differ from those of a reasonable investor; and
- were made only as of specified dates contained in the agreements and are subject to subsequent developments and changed circumstances.

Accordingly, these representations and warranties may not describe the actual state of affairs as of the date that these representations and warranties were made or at any other time. Investors should not rely on them as statements of fact.

Exhibit Number	Description
2.1	Share Exchange Agreement, dated May 20, 2014, by and among Camp Nine, Inc., Relmada Therapeutics, Inc., and the stockholders of Relmada Therapeutics, Inc. (incorporated by reference to Exhibit 2.1 of Relmada's Form 8-K filed with the SEC on May 27, 2014).
3.1	(i) Articles of Incorporation of Camp Nine, Inc. (incorporated by reference to Exhibit 3.1 of Relmada's Registration Statement on Form S-1 filed with the SEC on November 13, 2012).
	(ii) Certificate of Designation dated May 13, 2014 (incorporated by reference to Exhibit 4.1 to Relmada's Report on Form 8-K filed with the SEC on May 19, 2014).
	(iii) Nevada Certificate of Amendment to Articles of Incorporation of Camp Nine, Inc., effective May 30, 2014 (incorporated by reference to Exhibit 3.1 of Relmada's Form 8-K filed with the SEC on June 2, 2014).
	(iv) Nevada Certificate of Amendment to Articles of Incorporation of Camp Nine, Inc., effective July 8, 2014 (incorporated by reference to Exhibit 3.1 of Relmada's Form 8-K filed with the SEC on July 14, 2014).
	(v) Certificate of Change of Relmada Therapeutics, Inc. dated September 26, 2019 (incorporated by reference to Exhibit 3.1 of Relmada's Form 8-K filed with the SEC on September 27, 2019).
	(vi) Certificate of Amendment to Articles of Incorporation dated September 22, 2022 (incorporated by reference to Exhibit 3.1 of Relmada's Form 8-K filed with the SEC on September 22, 2022).
3.2	Second Amended and Restated Bylaws of Relmada Therapeutics, Inc. (incorporated by reference to Exhibit 3.2 of Relmada's Form 8-K filed with the SEC on November 25, 2015).

Exhibit Number	Description
4.1	Form of Warrants to Purchase Common Stock issued in 2012 and 2013 in connection with Relmada Therapeutics, Inc. Series A Preferred Stock (incorporated by reference to Exhibit 4.1 of Relmada's Form 8-K filed with the SEC on May 27, 2014).
4.2	Form of Warrants to Purchase Common Stock issued in 2012 and 2013 in connection with Relmada Therapeutics, Inc. 8% Senior Subordinated Promissory Notes (incorporated by reference to Exhibit 4.2 of Relmada's Form 8-K filed with the SEC on May 27, 2014).
4.3	Form of B Warrant dated May__, 2014 issued to investors by Relmada Therapeutics, Inc. (incorporated by reference to Exhibit 4.4 of Relmada's Form 8-K filed with the SEC on May 27, 2014).
4.4	Form of B Warrant dated June 10, 2014 issued to investors by Camp Nine, Inc. (incorporated by reference to Exhibit 4.2 of Relmada's Form 8-K filed with the SEC on June 16, 2014).
4.5	Form of Convertible Promissory Note (incorporated by reference to Exhibit 4.1 of Relmada's Form 10-Q filed with the SEC on February 12, 2018).
4.6	Form of Warrant to Purchase Common Stock (incorporated by reference to Exhibit 4.2 of Relmada's Form 10-Q filed with the SEC on February 12, 2018).
4.7	Form of 2018 Warrant (incorporated by reference to Exhibit 4.1 of Relmada's Form 10-Q filed with the SEC on November 13, 2018).
4.8	Form of 2019 Warrant (incorporated by reference to Exhibit 4.1 of Relmada's Form 10-Q filed with the SEC on May 15, 2019).
4.9	Form of Exchanged Warrant [(incorporated by reference to Exhibit 4.1 of Relmada's Form 8-K filed with the SEC on September 22, 2022).]
4.10	Description of Securities (incorporated by reference to the description of the Company's common stock, par value $0.001 per share, under the heading "Description of Securities We May Offer—Authorized Capital Stock; Issued and Outstanding Capital Stock," "—Common Stock," "—Forum for Adjudication of Disputes, "—Anti-takeover Effects of Our Articles of Incorporation and By-laws, and "—Anti-takeover Effects of Nevada Law" in the Company's Registration Statement on Form S-3 (File No. 333-245054), filed with the Securities and Exchange Commission on August 12, 2020)
10.1	Agreement and Plan of Merger dated as of December 31, 2013 between Relmada Therapeutics, Inc. and Medeor, Inc. (incorporated by reference to Exhibit 10.1 of Relmada's Form 8-K filed with the SEC on May 27, 2014).
10.2	2014 Stock Option and Equity Incentive Plan (incorporated by reference to Exhibit 10.14 of Relmada's Form S-1/A filed with the SEC on December 9, 2014)
10.3	Director Agreement, dated July 14, 2015, by and between Charles J. Casamento and Relmada Therapeutics, Inc. (incorporated by reference to Exhibit 10.1 of Relmada's Form 8-K filed with the SEC on July 16, 2015)
10.4	Director Indemnity Agreement, dated July 14, 2015, by and between Charles J. Casamento and Relmada Therapeutics, Inc. (incorporated by reference to Exhibit 10.2 of Relmada's Form 8-K filed with the SEC on July 16, 2015)
10.5	Amended 2014 Stock Option and Equity Incentive Plan (incorporated by reference to Exhibit 10.1 of Relmada's Form 8-K filed with the SEC on August 7, 2015).
10.6	Form of Indemnification Agreement (incorporated by reference to Exhibit 10.2 of Relmada's Form 8-K filed with the SEC on August 7, 2015).

Exhibit Number	Description
10.7	License Agreement, dated January 16, 2018, between Relmada Therapeutics, Inc. Dr. Charles E. Inturrisi and Dr. Paolo Manfredi (incorporated by reference to Exhibit 10.1 of Relmada's Form 8-K filed with the SEC on January 19, 2018).
10.8	Intellectual Property Assignment Agreement, dated January 16, 2018, between Relmada Therapeutics, Inc. Dr. Charles E. Inturrisi and Dr. Paolo Manfredi (incorporated by reference to Exhibit 10.2 of Relmada's Form 8-K filed with the SEC on January 19, 2018).
10.9	Form of Note and Warrant Purchase Agreement (incorporated by reference to Exhibit 10.1 of Relmada's Form 10-Q filed with the SEC on February 12, 2018).
10.10	Third Amendment to the 2014 Stock Option and Equity Incentive Plan, as amended (incorporated by reference to Exhibit 10.3 of Relmada's Form 10-Q filed with the SEC on May 14, 2018).
10.11	Form of Unit Purchase Agreement among Relmada Therapeutics, Inc. and certain accredited investors (incorporated by reference to Exhibit 10.1 of Relmada's Form 10-Q filed with the SEC on November 13, 2018).
10.12	Amendment No. 4 to the Relmada Therapeutics, Inc. 2014 Stock Option and Equity Incentive Plan, as amended (incorporated by reference to Exhibit 10.1 of Relmada's Form 10-Q filed with the SEC on May 15, 2019).
10.13	Form of Share Purchase Agreement, dated September 23, 2019 and September 26, 2019, among Relmada Therapeutics, Inc. and certain accredited investors named therein (incorporated by reference to Exhibit 10.4 of Relmada's Form 10-Q filed with the SEC on November 13, 2019).
10.14	Form of Registration Rights Agreement, dated September 23, 2019 and September 26, 2019, among Relmada Therapeutics, Inc. and certain accredited investors named therein (incorporated by reference to Exhibit 10.5 of Relmada's Form 10-Q filed with the SEC on November 13, 2019).
10.15	Amended and Restated Unit Purchase Agreement dated November 27, 2019, between Relmada Therapeutics, Inc., and certain accredited investors (incorporated by reference to Exhibit 10.1 of Relmada's Form 8-K filed with the SEC on December 3, 2019).
10.16	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 (incorporated by reference to Exhibit 10.2 of Relmada's Form 8-K filed with the SEC on December 3, 2019).
10.17	Director Agreement, effective December 19, 2019, by and between Eric Schmidt and Relmada Therapeutics, Inc. (incorporated by reference to Exhibit 10.1 of Relmada's Form 8-K filed with the SEC on December 26, 2019).
10.18	Indemnity Agreement, effective December 19, 2019, by and between Eric Schmidt and Relmada Therapeutics, Inc. (incorporated by reference to Exhibit 10.2 of Relmada's Form 8-K filed with the SEC on December 26, 2019).
10.19	Director Agreement, effective December 19, 2019, by and between John Glasspool and Relmada Therapeutics, Inc. (incorporated by reference to Exhibit 10.3 of Relmada's Form 8-K filed with the SEC on December 26, 2019).

Exhibit Number	Description
10.20	Indemnity Agreement, effective December 19, 2019, by and between John Glasspool and Relmada Therapeutics, Inc. (incorporated by reference to Exhibit 10.4 of Relmada's Form 8-K filed with the SEC on December 26, 2019).
10.21	Employment Agreement, dated January 9, 2020, by and between Maged Shenouda and Relmada Therapeutics, Inc. (incorporated by reference to Exhibit 10.1 of Relmada's Form 8-K filed with the SEC on January 10, 2020).
10.22	Employment Agreement, dated January 9, 2020, by and between Charles Ence and Relmada Therapeutics, Inc. (incorporated by reference to Exhibit 10.2 of Relmada's Form 8-K filed with the SEC on January 10, 2020).
10.23	Amended and Restated Employment Agreement, dated January 9, 2020, by and between Sergio Traversa and Relmada Therapeutics, Inc. (incorporated by reference to Exhibit 10.3 of Relmada's Form 8-K filed with the SEC on January 10, 2020).
10.24	Amendment No. 5 to Stock Option and Equity incentive Plan (incorporated by reference to Exhibit 10.1 of Relmada's Form 8-K filed with the SEC on March 9, 2020).
10.25	Open Market Sale Agreement[SM] dated as of May 15, 2020 by and between Relmada Therapeutics, Inc. and Jefferies LLC. (incorporated by reference to Exhibit 10.7 of Relmada's Form 10-Q filed with the SEC on May 15, 2020).
10.26	Relmada Therapeutics, Inc., 2021 Equity Incentive Plan (incorporated by reference to Exhibit 10.61 of Relmada's Form 10-K filed with the SEC on March 24, 2021).
10.27	License Agreement dated as of July 16, 2021, between Arbormentis, LLC and Relmada Therapeutics, Inc. (incorporated by reference to Exhibit 10.2 of Relmada's Form 10-Q filed with the SEC on August 10, 2021).
10.28	Exchange Agreement between Relmada Therapeutics, Inc., and Venrock Healthcare Capital Partners EG, L.P., Venrock Healthcare Capital Partners II, L.P., VHCP Co-Investment Holdings II, LLC, Venrock Healthcare Capital Partners III, L.P., and VHCP Co-Investment Holdings III, LLC, dated September 21, 2022 (incorporated by reference to Exhibit 10.1 of Relmada's Form 8-K filed with the SEC on September 22, 2022).

Exhibit Number	Description
10.29	Amendment No. 2 dated December 27, 2022, to the License Agreement originally dated January 16, 2018, as heretofore amended, between Relmada Therapeutics, Inc., and Dr. Charles E. Inturrisi and Dr. Paolo Manfredi (incorporated by reference to Exhibit 10.1 of Relmada's Form 8-K filed with the SEC on December 28, 2022).
10.30	Advisory Agreement dated as of January 1, 2023, between Relmada Therapeutics, Inc., and Paul Kelly (incorporated by reference to Exhibit 10.1 of Relmada's Form 8-K filed with the SEC on January 5, 2023).
10.31	Director Agreement between Relmada Therapeutics, Inc., and Fabiana Fedeli (incorporated by reference to Exhibit 99.1 of Relmada's Form 8-K filed with the SEC on January 17, 2023).
10.32	Indemnity Agreement between Relmada Therapeutics, Inc., and Fabiana Fedeli (incorporated by reference to Exhibit 99.2 of Relmada's Form 8-K filed with the SEC on January 17, 2023).
21.1	List of Subsidiaries (incorporated by reference to Exhibit 21.1 of Relmada's Form 10-K filed with the SEC on September 9, 2014).
23.1	Consent of Marcum LLP
31.1*	Certification of Principal Executive Officer, pursuant to 18 U.S.C. Section 1350 as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial and Accounting Officer, pursuant to 18 U.S.C. Section 1350 as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1†	Certification of Principal Executive Officer, pursuant to 18 U.S.C. Section 1350 as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2†	Certification of Principal Financial and Accounting Officer, pursuant to 18 U.S.C. Section 1350 as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS*	Inline XBRL Instance Document.
101.SCH*	Inline XBRL Taxonomy Extension Schema Document.
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document.
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document.
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101).

* Filed herewith
† Furnished herewith

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following person on behalf of the Registrant.

Dated: March 19, 2024

RELMADA THERAPEUTICS, INC.

By: /s/ Sergio Traversa
Sergio Traversa
Chief Executive Officer
(Duly Authorized Officer and
Principal Executive Officer)

By: /s/ Maged Shenouda
Maged Shenouda
Chief Financial Officer
(Duly Authorized Officer and
(Principal Financial and Accounting Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following person on behalf of the Registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Sergio Traversa Sergio Traversa	Chief Executive Officer, and Director	March 19, 2024
/s/ Maged Shenouda Maged Shenouda	Chief Financial Officer	March 19, 2024
/s/ Charles J. Casamento Charles J. Casamento	Chairman of the Board	March 19, 2024
/s/ Paul Kelly Paul Kelly	Director	March 19, 2024
/s/ John Glasspool John Glasspool	Director	March 19, 2024
/s/ Fabiana Fedeli Fabiana Fedeli	Director	March 19, 2024

Exhibit 23.1

INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM'S CONSENT

We consent to the incorporation by reference in the Registration Statements of Relmada Therapeutics, Inc. on Form S-3 (File No. 333-264189), on post-effective Amendment No. 1 on Form S-3 to Forms S-1 (File Nos. 333-229258 and 333-233228), on Forms S-8 (File Nos. 333-272811 and 333-257723), and on Post-Effective Amendment No. 1 to Forms S-8 (File Nos. 333-231477, 333-224920 and 333-207253) of our report dated March 19, 2024, with respect to our audits of the consolidated financial statements of Relmada Therapeutics, Inc as of December 31, 2023 and 2022 and for the years ended December 31, 2023 and 2022, which report is included in this Annual Report on Form 10-K of Relmada Therapeutics, Inc**.** for the year ended 2023.

/s/ Marcum LLP

Marcum LLP

Houston, Texas
March 19, 2024

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO
18U.S.C SECTION 1350
AS ADOPTED PURSUANT TO SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002

I, Sergio Traversa, certify that:

1. I have reviewed this Report on Form 10-K of Relmada Therapeutics, Inc. as of December 31, 2023;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods present in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiary, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financing reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involved management or other employees who have a significant role in the registrant's internal control over financial reporting.

Relmada Therapeutics, Inc.

By: /s/ Sergio Traversa
Sergio Traversa
Chief Executive Officer
(Principal Executive Officer)

Date: March 19, 2024

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL AND ACCOUNTING OFFICER
PURSUANT TO
18U.S.C SECTION 1350
AS ADOPTED PURSUANT TO SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002

I, Maged Shenouda, certify that:

1. I have reviewed this Report on Form 10-K of Relmada Therapeutics, Inc. as of December 31, 2023;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods present in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiary, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financing reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involved management or other employees who have a significant role in the registrant's internal control over financial reporting.

Relmada Therapeutics, Inc.

By: /s/ Maged Shenouda
Maged Shenouda
Chief Financial Officer
(Principal Financial and Accounting Officer)

Date: March 19, 2024

Exhibit 32.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Relmada Therapeutics, Inc., a Nevada corporation (the "Company") on Form 10-K for the year ended December 31, 2023 as filed with the Securities and Exchange Commission (the "Report"), I, Sergio Traversa, Chief Executive Officer of the Company, certify, pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. Section 1350, that to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Relmada Therapeutics, Inc.

By: /s/ Sergio Traversa
Sergio Traversa
Chief Executive Officer
(Principal Executive Officer)

Date: March 19, 2024

Exhibit 32.2

CERTIFICATION OF PRINCIPAL FINANCIAL AND ACCOUNTING OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Relmada Therapeutics, Inc., a Nevada corporation (the "Company") on Form 10-K for the year ended December 31, 2023 as filed with the Securities and Exchange Commission (the "Report"), I, Maged Shenouda, Chief Financial Officer of the Company, certify, pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. Section 1350, that to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Relmada Therapeutics, Inc.

By: /s/ Maged Shenouda
Maged Shenouda
Chief Financial Officer
(Principal Financial and Accounting Officer)

Date: March 19, 2024