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

FORM 10-K

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

For the fiscal year ended **December 31, 2020**

or

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

For the transition period from _____ to _____

Commission file number: **01-39834**

Clene Inc.

(Exact name of registrant as specified in its charter)

Delaware	**85-2828339**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
6550 South Millrock Drive, Suite G50 Salt Lake City, Utah	**84121**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(801) 676 9695**

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, $0.0001 par value	CLNN	The Nasdaq Capital Market
Warrants, to acquire one-half of one share of Common Stock for $11.50 per share	CLNNW	The Nasdaq Capital 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 Exchange Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required 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 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 such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a 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. ☐

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

The common stock of the registrant has been traded on the Nasdaq Capital Market under the symbol "CLNN" since December 31, 2020, which is the business day following the consummation of the business combination among the registrant and Tottenham Acquisition I Limited, which traded on the Nasdaq Capital Market under the symbol "TOTA." The aggregate market value of TOTA's common stock held by non-affiliates of TOTA, based on the closing price of TOTA's common stock on the Nasdaq Capital Market as of June 30, 2020, the last business day of TOTA's most recently completed second fiscal quarter, was approximately $23.3 million, based on the closing price of TOTA's common stock on the Nasdaq Capital Market of $10.79 per share.

The number of shares outstanding of the Registrant's shares of common stock as of March 25, 2021 was 59,526,171.

DOCUMENTS INCORPORATED BY REFERENCE

Certain portions of the registrant's definitive proxy statement, in connection with its 2021 annual meeting of stockholders, to be filed within 120 days after the end of fiscal year ended December 31, 2020, are incorporated by reference into Part III of this Annual Report on Form 10-K.

CLENE INC.
Annual Report on Form 10-K for the Year Ended December 31, 2020

PART I

Throughout this Annual Report on Form 10-K (the "Annual Report"), the "Company," and references to "we," "us," or similar such references should be understood to be references to the combined company, Clene Inc. When this Annual Report references "Clene" and describes the business of Clene, it refers to the business of Clene Nanomedicine, Inc. and its subsidiaries, prior to the consummation of the business combination (referred to throughout as the "Reverse Recapitalization"). Following the date of the Reverse Recapitalization, references to "Clene" should be understood to reference Clene Inc. Given that the Reverse Recapitalization is accounted for as a reverse recapitalization, as described in more detail below, and the accounting acquirer is Clene Nanomedicine, Inc., the post-Reverse Recapitalization financial statements included in this Annual Report show the consolidated balances and transactions of the Company and Clene as well as comparative financial information of Clene (the acquirer for accounting purposes).

CAUTIONARY STATEMENT REGARDING FORWARD LOOKING STATEMENTS

This Annual Report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). The statements contained in this Annual Report that are not purely historical are forward-looking statements. Our forward-looking statements include, but are not limited to, statements regarding our or our management team's expectations, hopes, beliefs, intentions or strategies regarding the future. In addition, any statements that refer to projections, forecasts or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking statements. The words "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intends," "may," "might," "plan," "possible," "potential," "predict," "project," "should," "will," "would" and similar expressions may identify forward-looking statements, but the absence of these words does not mean that a statement is not forward-looking. Forward-looking statements in this Annual Report may include, for example, statements about:

- the benefits of the Reverse Recapitalization;
- the future financial performance of the Company;
- the clinical results of our drug candidates;
- the likelihood of commercial success for our drug candidates;
- changes in the market for our services;
- expansion plans and opportunities; and
- other factors detailed under the section entitled "*Risk Factors*."

These forward-looking statements are based on information available as of the date of this Annual Report, the information incorporated herein by reference and our management's current expectations, forecasts and assumptions, and involve a number of judgments, risks and uncertainties. Accordingly, forward-looking statements should not be relied upon as representing our views as of any subsequent date. We undertake no obligation to update forward-looking statements to reflect events or circumstances after the date they were made, whether as a result of new information, future events or otherwise, except as may be required under applicable securities laws.

As a result of a number of known and unknown risks and uncertainties, our actual results or performance may be materially different from those expressed or implied by these forward-looking statements. Some factors that could cause actual results to differ include:

- the outcome of any legal proceedings that may be instituted against us following the consummation of the Reverse Recapitalization;
- the inability to maintain the listing of our Common Stock or warrants on The Nasdaq Stock Market;
- our ability to demonstrate the efficacy and safety of our drug candidates;
- the clinical results for our drug candidates, which may not support further development or marketing approval;
- actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials and marketing approval;

- our ability to achieve commercial success for our marketed products and drug candidates, if approved;
- our ability to obtain and maintain protection of intellectual property for our technology and drugs;
- our reliance on third parties to conduct drug development, manufacturing and other services;
- our limited operating history and our ability to obtain additional funding for operations and to complete the licensing or development and commercialization of our drug candidates;
- the impact of the COVID-19 pandemic on our clinical development, commercial and other operations;
- changes in applicable laws or regulations;
- the possibility that we may be adversely affected by other economic, business, and/or competitive factors; and
- other risks and uncertainties set forth in the section entitled "*Risk Factors*".

ITEM 1. BUSINESS

Overview

We are a clinical-stage pharmaceutical company pioneering the discovery, development, and commercialization of novel clean surfaced nanotechnology (CSN) therapeutics. CSN therapeutics are comprised of atoms of transition elements that when assembled in nanocrystalline form, possess unusually high, unique catalytic activities not present in those same elements in bulk form. These nanocatalytic activities drive, support, and maintain beneficial metabolic and energetic intercellular reactions within diseased, stressed, and damaged cells.

Our patent-protected, proprietary position affords us the potential to develop a broad and deep pipeline of novel CSN therapeutics to address a range of diseases with high impact on human health. We began in 2013 by innovating an electrochemistry drug development platform that draws from advances in nanotechnology, plasma and quantum physics, material science, and biochemistry. Our platform process results in nanocrystals with faceted surfaces that are free of the chemical surface modifications that accompany other production methods. Many traditional methods of nanoparticle synthesis involve the unavoidable deposition of potentially toxic organic residues and stabilizing surfactants on the particle surfaces. Synthesizing stable nanocrystals that are both nontoxic and highly catalytic has overcome this significant hurdle in harnessing transition metal catalytic activity for therapeutic use.

Our clean-surfaced nanocrystals exhibit catalytic activities many-fold higher than other commercially available nanoparticles, produced using various techniques, that we have comparatively evaluated. We have multiple drug assets currently in development for applications in neurology, infectious disease, and oncology. Our efforts are currently focused on addressing the high unmet medical needs in two areas: first, those related to central nervous system disorders including Multiple Sclerosis ("MS"), Parkinson's Disease ("PD") and Amyotrophic Lateral Sclerosis ("ALS"); and second, those related to the pandemic caused by COVID-19, a highly infectious viral respiratory disease with serious and sometimes fatal co-morbidities.

The Clene Approach

The Clene approach to drug development is *innovation focused* and *scientifically driven*.

- *Innovation focused* — There are a significant number of diseases with high impact on human health that have proven exceedingly challenging for traditional small-molecule or biologic drug development approaches. Our approach involves the innovation of highly active therapeutic nanocatalysts with novel mechanisms of action that result from proprietary advances in nanotechnology, plasma and quantum physics, biochemistry, and materials science. This platform affords us the ability to make new drug modalities targeting a wide range of diseases that have eluded intervention using traditional small molecule or monoclonal antibody approaches.

- *Scientifically driven* — Clear scientific rationale and sound experimental design drive our discoveries, from basic science to clinical trials. We believe we have established ourselves as an industry leader in position for the development of therapeutic catalytic nanocrystals. We have deep knowledge of the chemical properties, safety profiles, and catalytic abilities of transitional metal nanocrystals and have proven abilities to produce concentrated, stable, highly active, clean-surfaced nanocrystal suspensions using efficient, "green," scalable processes. In so doing, we are establishing, new classes of nanomedicines with the potential to address some of the most serious diseases affecting human health.

Strategy and Leadership

The management team is key to the successful execution of this strategic plan and fulfillment of our business model. Our exceptional team brings extensive expertise and industry experience to their roles in leading the company skillfully and effectively. The members of the executive team have established track records in scientific innovation, early and late-stage pharmaceutical development, commercialization, marketing, and the generation and protection of intellectual property.

Our innovation of CSN therapeutic candidates places us at the forefront of novel drug development for a host of high impact, high unmet need human diseases. As we lead the development of CSN therapeutics, our business strategy can be encapsulated by the following:

- *First mover advantage* — We believe that our proprietary knowledge of the processes needed to manufacture clean-surfaced, highly faceted, catalytically active nanocrystals, and of the resulting toxicological and physicochemical properties associated with these nanocrystals, places us in a leadership position in the innovation and development of new candidate therapeutics for diseases that have proven to be extremely difficult to target using traditional methods.

- *Wide range of applicability* — Energy metabolism is a fundamental mechanism in all living cells, and CSN therapeutics that improve cellular bioenergetic efficiencies have the potential to be applied to many different disease states and cell types. An advantage of this approach is that a single drug candidate can be developed to hit multiple targets in multiple diseased cell types, presently being investigated across multiple clinical trials with our lead asset, CNM-Au8, through its clinical development program. We continue to explore ways in which the unique mechanisms of action of CSN therapeutics can be applied across different diseases.

- *Flexibility and tunability* — Nanocatalytic activities are determined by the shape, faceting, size, and chemical composition of nanocrystals. Our CSN platform has demonstrated flexibility in its ability to make, for instance, both pure gold and gold-platinum nanocrystals of consistent and reproducible shapes and sizes, in addition to making solutions of ionic zinc and silver. Because of the ease with which new single elemental and composite nanocrystals can be made of varying shapes and sizes using our proprietary techniques, we plan to continue developing a wide range of CSN therapeutics to generate a deep pipeline of drug candidates to treat a host of different diseases.

Intellectual Property, Trade Secrets and Manufacturing

We are the sole inventors of our manufacturing processes, devices, and drugs. These inventions are protected by a comprehensive intellectual property portfolio of over 100 patents issued worldwide, with over 30 additional patents pending. See "— *Intellectual Property*" for more details. The patents relate to (1) the devices that manufacture our CSN therapeutic drug candidates, (2) the processes involved in the use of these devices, (3) the drug candidates manufactured in these devices, and (4) methods of use for the drug candidates. In addition to filings for U.S. and foreign patents, we will continue to protect and maintain our proprietary position by the use of trademarks, trade secrets, copyright protection, and continued technological innovation. For example, years of intensive research and development were invested in fine-tuning our production and delivery processes to the point where we expect to be able to consistently, reliably, and affordably produce our drug candidates, including CNM-Au8, to meet large scale needs. We believe that any attempts to reverse engineer or otherwise replicate our discoveries would be extraordinarily challenging for potential competitors without violating our intellectual property protections.

We are also focused on building out a robust and relevant trade secret portfolio. Our trade secret portfolio largely relates to the liquid handling and processing of our water-based products from start to finish. In the case of our lead asset, CNM-Au8, highly purified water containing at least one processing enhancer enters the production device where it is exposed to a plasma-conditioning step. The exact nature of the plasma conditioning affects additional constituents that can become part of the flowing water thus affecting the subsequent crystal growth processes. Likewise, many details of the electrode design, configuration and operation also affect the electrochemical crystal growth processes that occur at each electrode set. Similarly, many design and operational aspects of each trough device directly affect the electrochemical crystal growth processes that occur at each electrode set. Finally, various aspects of liquid handling subsequent to crystal growth, such as concentration and filling, are critical so as not to introduce any contaminates into the liquid, which could alter the surfaces of the nanocrystals, thus adding toxicity and/or adversely affecting efficacy of the biological catalysis processes. We continue to explore additional ways to expand our trade secret portfolio in various aspects of the design, production, control and manufacture of our products.

Our manufacturing facility meets rigorous international Good Manufacturing Processes ("GMP") standards in producing our CSN therapeutics. Furthermore, we have the space and know-how to expand and scale up production as we continue to meet increased demands for our products.

Products

Our CSN therapeutic candidates aim to address high unmet medical needs in several disease areas including:

(1) disease modification of **central nervous system disorders**, including MS, PD and ALS;

(2) the treatment of **infectious diseases**, including COVID-19;

(3) accelerated **wound healing and scar formation**; and,

(4) the treatment of **selected cancer types**.

In addition to the development of faceted, clean-surfaced nanocrystals, our electro-crystal-chemistry platform can produce ionic solutions of various transition elements including silver, zinc, and others — elements which have proven historical utility in the treatment of disease.

- **CNM-Au8**, our lead asset, is a highly concentrated aqueous suspension of clean-surfaced, highly faceted nanocrystalline gold ("Au"). CNM-Au8's nanocatalytic mechanisms target the bioenergetic deficits, oxidative stress, and accumulation of misfolded proteins that are common to many neurodegenerative diseases. CNM-Au8 is hypothesized to act as a neuroprotective and remyelinating therapy in neurodegenerative disease states in order to: 1) drive, support, and maintain beneficial metabolic and energetic intracellular reactions within diseased, stressed, and/or damaged cells, 2) directly catalyze the reduction of harmful, reactive oxygen species, and 3) promote protein homeostasis via activation of the heat shock factor-1 pathway, recognized to dampen the cytotoxicity caused by misfolded and denatured proteins, which are known to occur ubiquitously in neurodegenerative diseases. We believe that CNM-Au8 is the only drug candidate in development with these unique nanocatalytic mechanisms of action. Nonclinical toxicology studies have demonstrated no adverse effect levels ("NOAELs") even up to maximum feasible dosing levels for oral administration. *In vitro* and in *vivo* pharmacology studies have demonstrated that CNM-Au8 treatment enhances remyelination and neuroprotection in numerous models of MS, PD, and ALS. A Phase 1 First-In-Human study did not reveal safety or tolerability concerns for CNM-Au8 in healthy human volunteers dosed in accordance with the study protocol. There are four Phase 2 clinical studies presently underway evaluating the efficacy and safety of CNM-Au8 for the treatment of MS, PD, and ALS, an Expanded Access Program for ALS, and one Phase 3 registrational clinical trial underway that has the potential to fully support a New Drug Application (NDA) for the treatment of ALS, each of which is discussed in detail below.

- **CNM-ZnAg** is a broad-spectrum antiviral, antibacterial agent comprised of zinc (Zn^{2+}) and silver (Ag^{+}) ions under development to treat disease-causing infections, such as COVID-19, and to provide immune support for symptom resolution. Zn^{2+} and Ag^{+} ions are produced in aqueous solutions using our electrochemistry manufacturing platform; combining Zn^{2+} and Ag^{+} ions made in this manner leads to enhanced bioavailability of the ions and potentially, synergistic immune system effects. One clinical study commenced in February, 2021 in Brazil, to determine ZnAg efficacy for the treatment of symptomatic subjects with COVID-19 to prevent hospitalization.

- **CNM-AgZn-17** is a gel polymer suspension of Ag^{+} and Zn^{2+} under development for treatment of infectious diseases and to support wound healing. We have demonstrated in *in vitro* assays that CNM-AgZn17 has broad-based anti-viral and anti-bacterial activity against common and antibiotic resistant pathogens such as Methicillin-resistant *Staphylococcus aureus*. We have also shown enhanced wound healing benefits in animal models of diabetic wound healing and decreased scar formation following burns. We anticipate filing an Investigational New Drug (IND) application with the FDA and subsequently plan to initiate a Phase 1 dermal First-In-Human safety study with CNM-AgZn17 in 2022.

- **CNM-PtAu7** is a gold-platinum combination nanocrystal with the potential to be an effective treatment for oncology indications. We have demonstrated *in vitro* up-regulation of pro-apoptotic and down-regulation of anti-apoptotic genes in the human breast cancer cell lines EFM-19 and MT-3 using CNM-PtAu7. We have further demonstrated down-regulation of genes associated with the electron transport chain activity which may relate to changes in tumorigenesis activity. We anticipate initiating standard animal toxicology programs in late 2022 with an IND filing planned between 2023 – 2024, subject to evaluation of the safety and efficacy learnings from the preclinical oncology assays and toxicology findings.

Supplements

Our patented electrochemistry manufacturing platform further enables us to develop very low concentration dietary supplements to advance the health and well-being of broad populations. These dietary supplements can vary greatly and include nanocrystals of varying composition, shapes and sizes as well as ionic solutions with diverse metallic constituents.

Dietary supplements are marketed and distributed through our wholly owned subsidiary, dOrbital, Inc. (“dOrbital”), or through an exclusive license with 4Life Research LLC (“4Life”). These include:

- **rMetx**™ (ZnAg Immune Boost) by dOrbital; rMetx™ is an aqueous zinc-silver ion dietary (mineral) supplement made using our electrochemistry manufacturing platform with bioactive immune-supporting properties. rMetx™ is sold through dOrbital, and, a substantially similar product under the tradename, Zinc Factor™, is sold by 4Life Research LLC (“4Life”), an international supplier of health supplements and a related party, under a supply agreement.

- **KHC46 (**Gold Factor™) by 4Life: KHC46 is an aqueous gold dietary (mineral) supplement of very low-concentration Au nanoparticles produced using our electrochemistry manufacturing platform. KHC46 has different production methods and uses different devices resulting in different physiochemical properties from our lead drug candidate, CNM-Au8. KHC46 is licensed exclusively to 4Life for worldwide marketing and distribution.

Clinical Development Pipeline

We have four Phase 2 clinical studies presently underway for the treatment of neurodegenerative disorders including MS, ALS, and PD, one Expanded Access Program for ALS patients, one Phase 3 registrational clinical trial presently underway for disease-modification in ALS, and a Phase 2 clinical study for the treatment of COVID-19, which has received regulatory approval for conduct in Brazil. In addition, we anticipate launching a clinical study for the treatment of PD in late 2021. The chart below reflects the respective stages of our main drug candidates.

Our CSN Therapeutics Platform

We have developed a new pharmaceutical technology, CSN therapeutics. By uniting concepts from electrochemistry, nanotechnology, plasma and quantum physics, material science, and biochemistry, we have created and refined a proprietary electrocrystallization method that results in a single component or multiple components in nanocrystals of the transition elements that are clean-surfaced, highly faceted, and biologically catalytically active. These nanocrystals can be concentrated as aqueous suspensions and orally administered. We are further able to produce ionic solutions of various transitions elements utilizing our electrochemistry manufacturing platform. Once in the gastrointestinal system, nanocrystals pass into the blood stream, and accumulate in organs such as the liver, kidneys, and spleen, with lower amounts crossing the blood brain barrier and reaching the brain, spinal cord, and cerebrospinal fluid. Nanocrystals can remain active within the body for days before they are eliminated via the hepatobiliary-fecal system as well as via the urinary system.

Once inside the body, CSN therapeutics cross cellular membranes and enter cells where they directly donate and receive electrons within biological systems. In this way, each nanocrystal acts as a potent nanocatalyst, that can drive, support, and maintain beneficial metabolic and energetic intercellular reactions within diseased, stressed, and damaged cells. These catalytic, nanocrystal-based therapeutic drugs represent an entirely new approach to drug development, substantially differing from the standard paradigm of small-molecule drugs and large-molecule biologics. Unlike traditional pharmacological approaches, which are limited to single targets or specific signaling pathways, our technology platform has produced metallic nanocrystals that are beneficial through multi-modal activities in multiple cell types across multiple diseases. By utilizing intracellular medicinal catalysts to support bioenergetic reactions within cells, we believe this technology represents a revolutionary advance in the treatment of the underlying pathophysiology of neurodegeneration and related diseases associated with bioenergetic failure.

Figure 1 below shows examples of the kinds of nanocrystals that can be produced using our CSN therapeutic platform.

Figure 1. Representative CSN Therapeutic Nanocrystals

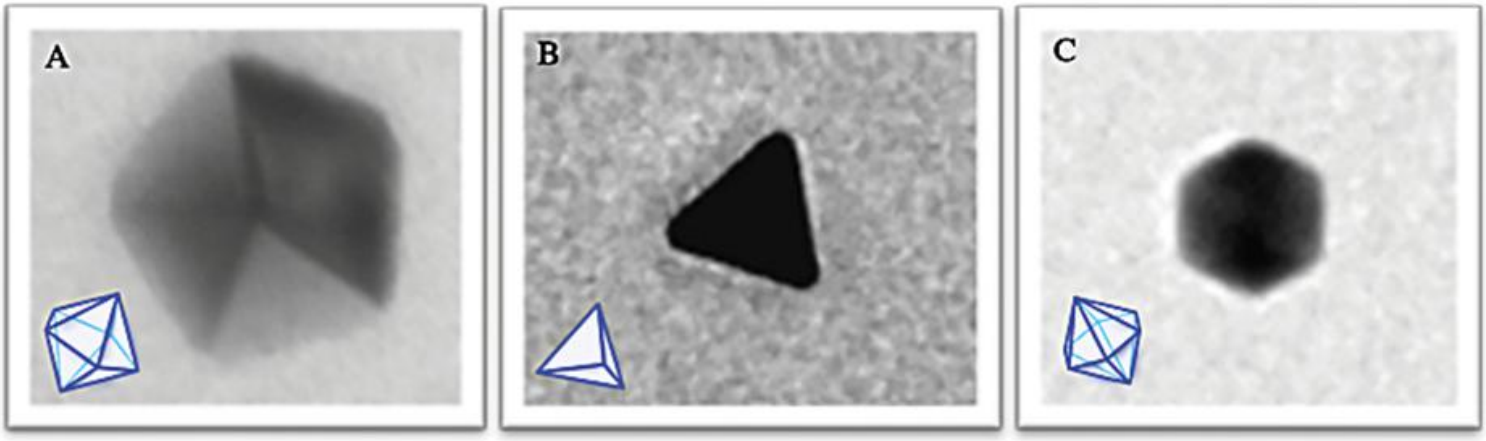


Figure 1. Representative transmission electron micrographs of the commonly observed crystalline shapes of gold nanocrystals (CNM-Au8) resulting from our CSN therapeutic platform. Insets are wireframes illustrating each classic shape: A, pentagonal bipyramid; B, tetrahedron; and C, hexagonal bipyramid. These nanocrystals are 10-13 nm in diameter.

Nanocatalysis

A catalyst lowers the activation energy of a chemical reaction in such a way as to accelerate the rate of the reaction, without being consumed in the reaction. In doing so, it does not change the equilibrium of the substrates and products, and it can catalyze both forward and reverse reactions until homeostasis, or a balance of substrates and products, has been achieved.

Several industrial uses of metal nanocatalysts have been discovered, but to our knowledge, we are the only company currently developing nanocatalysts to directly modulate biological systems as therapeutic drug candidates. Prior to our invention of the CSN therapeutic platform, the methods employed to make stable nanoparticles required the use of organic solvents or capping agents, which would contaminate the surfaces of the nanoparticles and were substantially difficult to remove. There are multiple conflicting reports in the literature regarding the toxicity of these nanoparticles, ranging from reportedly non-toxic to highly toxic to living organisms. We believe this lack of consistency may have been due to the varying degrees to which different nanoparticle preparations were contaminated with organic reagents, leading to observed toxic effects. Because our electrocrystal chemistry method does not involve the use of any organic solvents or reduction chemicals, we have observed that our nanocrystals possess substantially higher catalytic activity in living organisms than those reported for nanoparticles made using other methods. All of the toxicology studies completed with our lead asset, CNM-Au8, have resulted in NOAEL findings.

Transition metal nanocatalysts are surface catalysts. Unlike enzymes, which are protein catalysts that lower activation energies using active site binding pockets, metal nanocatalysts carry out their catalytic activities on their surfaces, where they act as exceptionally efficient electron donors and receivers. For this reason, unmodified, clean surfaces that are free of contaminating chemicals are extremely important for catalytic activity. The facets and vertices of the nanocrystals serve as the surface areas where electron exchange can take place. Metal nanocatalysts have been shown to have a variety of different catalytic activities, including superoxide dismutase, peroxidase, and catalase-like activities for reducing reactive oxygen species, to reactions involving the oxidation of glucose, ascorbic acid, or the energetic metabolite, nicotinamide adenine dinucleotide (“NAD”). Figure 2 is an illustration of nanocatalysis, showing a single gold nanocrystal converting molecules of nicotinamide adenine dinucleotide hydride (“NADH”) in the background into NAD in the foreground. Gold nanocrystals have been described as electron reservoirs because their surfaces can readily accept as well as donate thousands of electrons per second in order to catalyze biochemical reactions, allowing them to accelerate reaction rates to extraordinarily high levels. For example, the conversion of NADH to NAD is usually very slow at room temperature. Upon addition of our gold nanocrystal suspension CNM-Au8, we have observed the very rapid conversion of NADH into NAD. Importantly, the NAD reaction drives adenosine triphosphate (ATP) production in both the mitochondrion as well as in the cytoplasm, via a reaction called glycolysis. ATP is the universal currency of energy in all living things; without the ability to convert NADH to NAD and vice versa, cells would be quickly depleted of ATP energy stores and die. CSN therapeutics capture the natural, extraordinary nanocatalytic activities of clean-surfaced, faceted nanocrystals to produce metabolites of high energetic or protective value to the cell.

Figure 2. Nanocatalysis Mechanism Representation

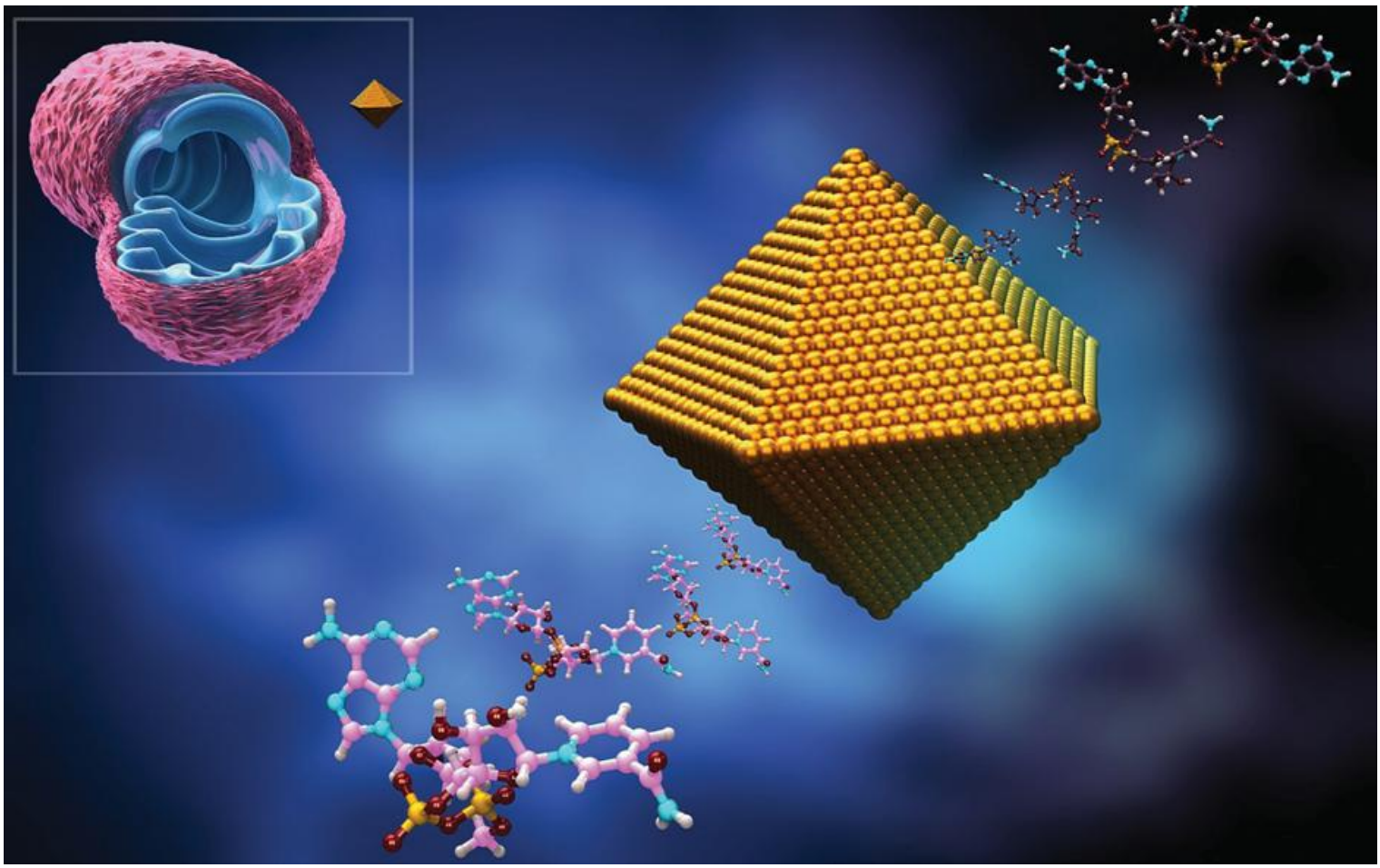


Figure 2. Illustration of nanocatalytic activity (Not to scale). A pentagonal bipyramidal gold nanocrystal is shown with its electron cloud to represent the ability of the nanocrystal to rapidly exchange electrons with substrates interacting with its surface. In the background, NADH molecules drawn as dark chemical ball-and-stick figures are catalytically converted into NAD in the foreground as bright pink ball-and-stick figures. A pink and blue mitochondrion on the left can use available NAD for the generation of ATP (Illustrated by Ella Maru).

Our Focus on Central Nervous System Disorders

Over the past several decades, traditional small molecule and biologic drug development approaches have suffered serious setbacks in the attempts to address nervous system disorders. A likely contributor to these setbacks is the multifactorial mechanisms underlying these diseases themselves, which are sufficiently complex they may not be amenable to "one drug-one target" disease modification. In the face of these failures, we believe our new paradigm of nanocrystal drug development, producing novel drugs with unique nanocatalytic, multi-modal mechanisms of action, is advantageous.

Multiple lines of evidence now point to bioenergetic failure as a key contributor to neurodegenerative disease. Neurons, and their associated support cells, in particular oligodendrocytes, are amongst the highest energy-consuming cells in the body: the brain represents only two percent of human body weight, yet it consumes over twenty-percent of the body's metabolic energy. As humans age, our cell's ability to convert food into energy in the form of ATP becomes less efficient. Eventually, the nervous system's demand for ATP surpasses the cells' ability to supply it, and as a consequence, neurons begin to fail and subsequently die. Genetic and environmental factors determine which neuronal types are most susceptible to bioenergetic failure in any individual. In PD, dopaminergic and other neuronal cell types manifest mitochondrial failure, leading to impaired energy production. In ALS, mitochondrial dysfunction is considered a hallmark of both sporadic and familial ALS, and several genetic causal variants of ALS have been linked to dysregulated neuronal energy metabolism. In MS, the cells capable of remyelinating damaged axons have been shown to be under metabolic stress, rendering them incapable of undergoing the energetically demanding process of repairing damaged myelin.

Preclinical work has shown that CNM-Au8 nanocrystals cross the blood brain barrier to potentially protect multiple central nervous system cell types. In multiple preclinical studies, we have demonstrated these central nervous system cells may benefit from nanocatalysis in several ways: oligodendrocytes receive an energetic boost sufficient to drive myelin production; dopaminergic, hippocampal, and cortical neurons improve energy metabolism sufficient to enhance survival and maintain function in response to multiple disease-relevant stressors. Human astrocytes derived from patients with ALS have the capacity to kill motor neurons when grown in a co-culture, and these motor neurons exhibit markedly reduced toxicity when co-cultures are treated with CNM-Au8. By their very nature, faceted clean-surfaced nanocrystals with nanocatalytic capabilities circumvent many of the challenges that have plagued the central nervous system pharmaceutical drug development field in the past. Importantly, the mechanism by which they act through nanocatalysis produces several useful energetic metabolites while reducing the presence of harmful ones. These mechanisms are well suited to address the complex failures that occur in neurodegenerative diseases on multiple levels and within multiple central nervous system cell types.

The innovation of CSN therapeutics is that we are positioned to address the most significant challenge posed by numerous central nervous system diseases. Unlike the "one drug-one target" model, faceted clean surfaced nanocrystals act by multiple mechanisms to enhance the cellular bioenergetic state, while simultaneously and independently reducing oxidative stress and stimulating protein homeostasis inside central nervous system cells. Each nanocrystal is capable of exchanging thousands of electrons per second, potentially addressing deficits in diseased central nervous system cells in a manner that does not further deplete the cells of their internal energy stores. Our data demonstrate CSN therapeutics thereby support cells and replenish cellular bioenergetic deficiencies. In other words, CSN therapeutics support the cells of the central nervous system with the basic building blocks of energy they require to function normally.

Market Potential of CSN Therapeutics for Neurodegenerative Diseases

Despite the urgent demand for treatments and the tremendous market opportunities for neurodegenerative disease therapeutics, effective treatments are limited. Currently, there are no existing therapies that either promote remyelination or have been demonstrated to improve function in people with non-active, progressive MS. People with non-active, progressive MS account for approximately one-third of all MS cases and they suffer progressive loss of function, severely reduced quality of life and shortened life spans. Further, the current FDA-approved therapeutic agents for ALS have very limited disease-modifying effects. And, there are no currently available disease-modifying therapies for PD. All of the existing PD therapies are limited to symptomatic improvement and none have been shown to prevent or slow the loss of dopaminergic neurons. If the clinical studies presently underway provide evidence of remyelination or demonstrate improved neurological function, CSN therapeutics will have significant commercial sales potential in treating MS, PD, or ALS.

Not a single approved MS drug worldwide has been approved to show an effect on remyelination and neuroprotection. CNM-Au8's effects on remyelination and neuroprotection for central nervous system disorders, together with the urgent market demand for safe and effective treatments, provides us with a global unique first-mover-advantage with significant market potential for the treatment of central nervous system diseases. Our most advanced CSN therapeutic candidate, CNM-Au8, has been developed to address the significant unmet medical needs in the treatment of the central nervous system disorders, MS, PD, and ALS. MS, PD, and ALS each severely impact healthspan and lifespan of those who suffer from these disorders, resulting in significant demand for disease-modifying treatments.

CNM-Au8 and Restoration of Bioenergetic Metabolism in MS, ALS, and PD

Overview

CNM-Au8 is a concentrated, orally-delivered suspension of pure gold nanocrystals in pharmaceutical grade water buffered with sodium bicarbonate. A single 60 milliliter, 30 milligram dose contains over one quadrillion nanocrystals. The median ferret diameter of CNM-Au8 nanocrystals is approximately 13 nanometers with each nanocrystal consisting of an estimated 30,000 to 70,000 gold atoms. CNM-Au8's nanocatalytic mechanism, directly donating and/or receiving electrons, enhances intracellular bioenergetic reaction rates without requiring associated energetic investment from cells, thus increasing cells' net energetic capacity. CNM-Au8 treatment results in improved bioenergetic metabolism within cells of the central nervous system. Through this mechanism, CNM-Au8 may protect multiple neuronal and glial populations including oligodendrocytes and/or neurons from oxidative, inflammatory, hypoxic, and excitotoxic insults, potentially resulting in enhanced myelination and improved neuronal survival while preserving neurite processes and synapse integrity.

Standard ICH M3(R2) toxicology studies were conducted on CNM-Au8 in three animal species, which yielded no toxicity findings resulting in a NOAEL finding up to maximum feasible dosing. A First-in-Humans Phase 1 Clinical Trial of orally administered single and multiple ascending doses of CNM-Au8 was then carried out in 86 healthy human volunteers. All doses (up to 90 mg/day) of CNM-Au8 were well-tolerated.

CNM-Au8 has received regulatory approval to proceed to Phase 2 clinical studies designed to assess the safety and efficacy of CNM-Au8 for brain metabolite target engagement and functional and physiologic improvements indicative of remyelination, and neuroprotection. Details for each clinical trial of CNM-Au8 are given below in the *Clinical Development Plan* section for each indication.

Mechanism of Action

CNM-Au8 acts through nanocatalysis to improve the bioenergetics, reduce harmful reactive oxygen species, and induce protein homeostatsis, via the heat shock protein-1 pathway in nervous system cells. These unique mechanism of actions lead to a cascade of beneficial effects as summarized in Figure 3.

Figure 3. Nanocatalytic Biological Mechanism of Action

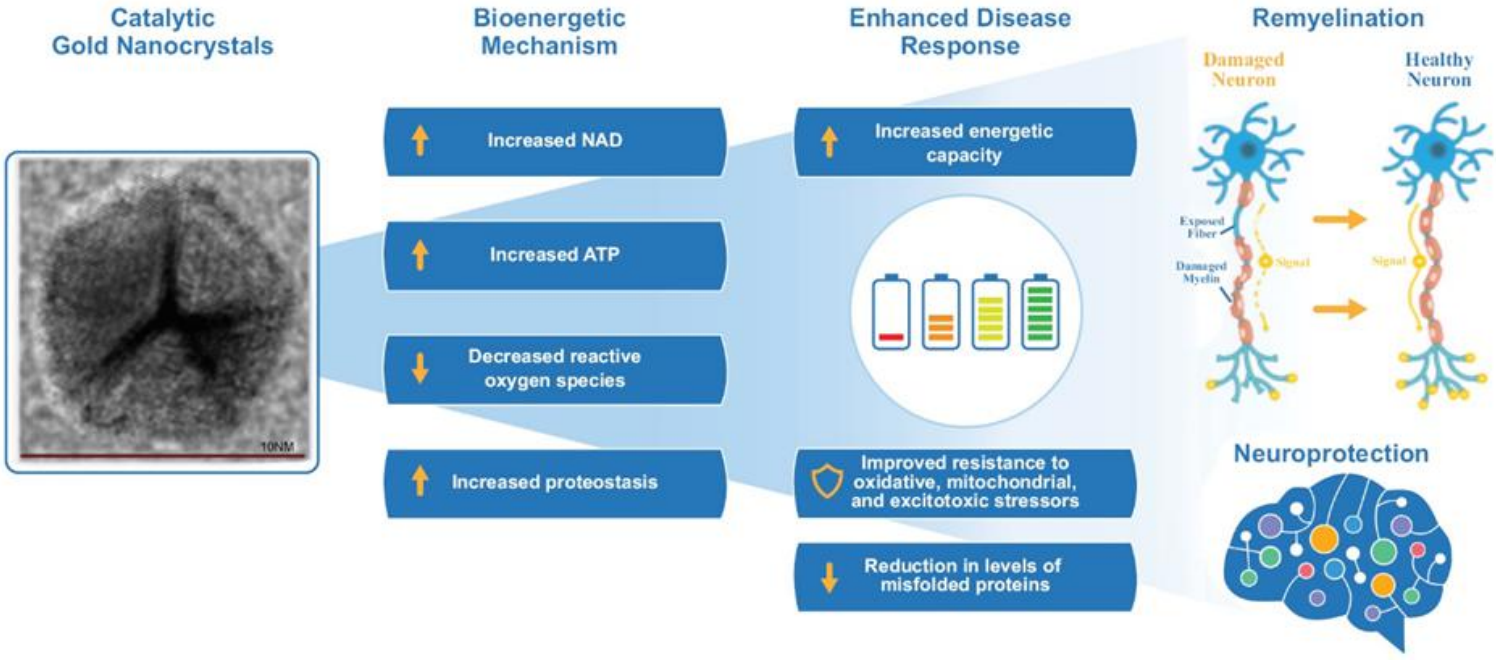


Figure 3. CNM-Au8 mediated nanocatalysis enhances cellular energetic capacity and decreases oxidative stress, resulting in increased NAD and ATP production as well as increased proteostatic activity via the heat shock factor 1 pathway. Together, these activities lead to a cascade of enhanced disease responses in neurons, oligodendrocytes, and astrocytes, cell types that are most vulnerable to energetic deficiencies. CNM-Au8 thereby mediates remyelination and neuroprotective effects in neurodegenerative diseases such as MS, ALS, and PD.

One of the key metabolites catalyzed by CNM-Au8 is nicotinamide adenine dinucleotide ("NAD^+") (Fig. 4). NAD^+ and its reduced partner NADH are vital for driving cellular energy ATP-generating reactions in living cells (Fig. 4A). Brain imaging studies have shown the ratio of NAD^+ to NADH typically decreases with aging. Lowered NAD^+ levels in both the blood and brain have been associated with neurological diseases such as schizophrenia, multiple sclerosis, Parkinson's Disease, and Huntington's Disease. Boosting NAD^+ activity in neurodegenerative disease preclinical models has consistently demonstrated beneficial anti-aging and neuroprotective effects. CNM-Au8 exhibits higher catalytic activity for directly oxidizing NADH into NAD than any other commercially available gold nanoparticle we have tested (Fig. 4C, D). We have shown that treating cultured nervous system cells with CNM-Au8 increases their intracellular pools of NAD^+ and ATP, demonstrating that CNM-Au8 increases the energetic capacity of central nervous system cells (Fig. 4E, F). This optimization of ATP (Fig. 4F) allows oligodendrocytes to increase myelin production, as well as help numerous other types of central nervous system cells resist environmental and disease-related stressors that would otherwise cause them to die.

The statistical analyses shown in Figure 4 were conducted by one-way analysis of variance (ANOVA) to compare means of each treatment group to mean of the vehicle control (corrected for multiple comparisons). The p-value (Fig. 4E, F) represents the probability of obtaining test results at least as extreme as the results observed in the assay, under the general assumption that there is no difference between the groups (the null hypothesis). The lower (smaller) the p-value, the greater the statistical significance of the observation, and the less likely the null hypothesis is true. The scientific community and regulatory authorities, such as the FDA, conventionally regard p-values of 0.05 or less to be significant when replicated in independent clinical studies. Consistently statistically significant preclinical results, such as those described here, are used to support investigative new drug applications to investigate the clinical effects of an investigational product.

One significant stressor shared by many neurodegenerative diseases is the accumulation of harmful reactive oxygen species ("ROS") within neurons as their energetic demands begin to exceed their ability to produce enough ATP to carry out normal functions. Chronic oxidative stress, caused by accumulation of ROS, can overwhelm the mitochondrial systems that normally tightly regulate ROS levels. Accumulation of excess ROS damages cell membranes, allows calcium ion imbalances, and eventually leads to cell death.

Figure 4. NAD Oxidation and Biological Effects on ATP and NAD+

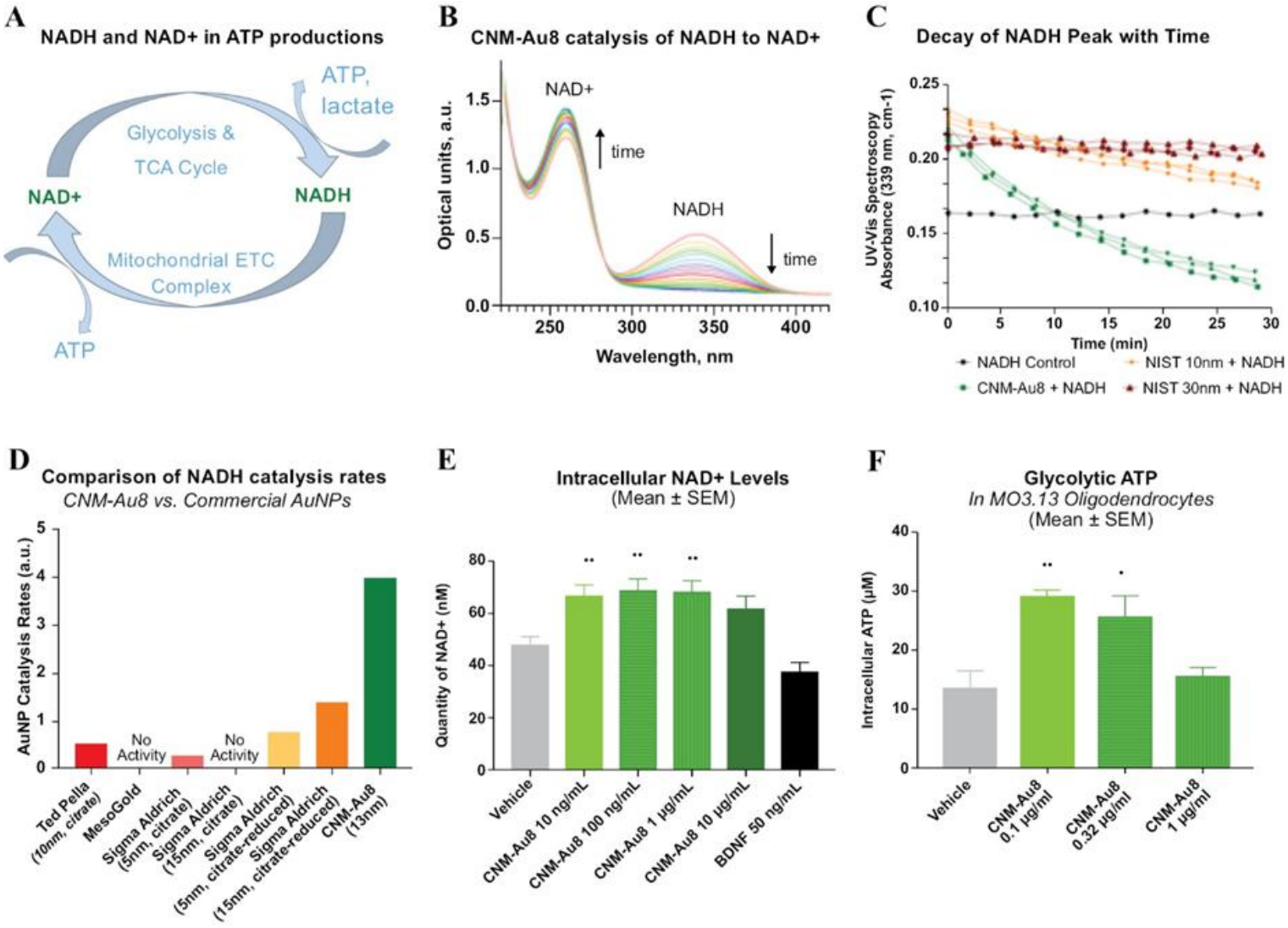
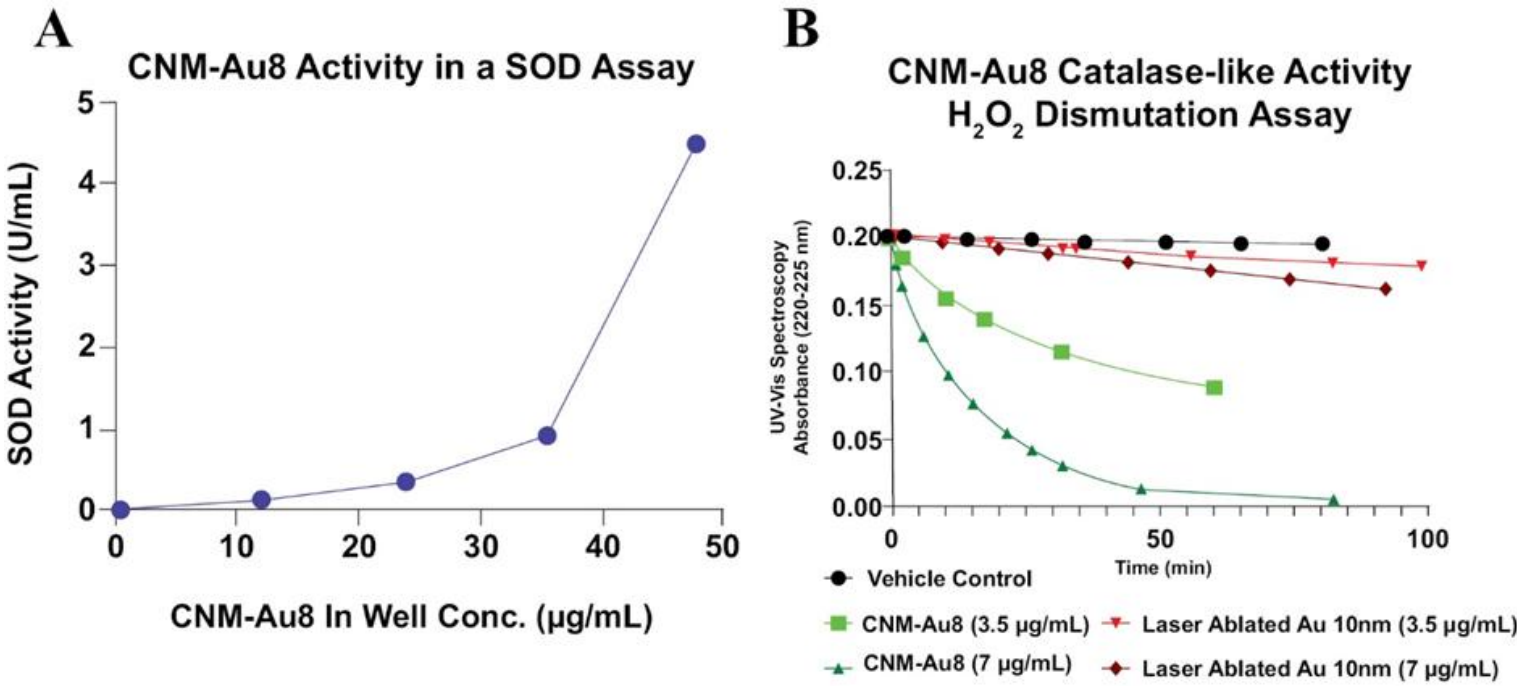


*Figure 4. Bioenergetic nanocatalysis by CNM-Au8. A, The NAD-NADH reduction-oxidation couple plays a key role in both ATP-generating reactions, glycolysis and mitochondrial electron transport chain ("ETC") oxidative phosphorylation. B, Ultraviolet-visible light spectroscopy was used to show the catalytic activity of CNM-Au8 with time. As the reaction progresses, NADH is consumed, as demonstrated by the decrease in the NADH absorbance peak at 340 nm, while NAD+ is generated, as shown by the corresponding increase in the NAD+ absorbance peak at 260 nm. C, the rate of decay of the NADH absorbance peak is greater for CNM-Au8 than it is for citrate-reduced gold, nanoparticles of 10 nm (orange) and 30 nm (red) diameters (purchased from the National Institute of Standards and Technology), indicating that CNM-Au8 has a catalytic rate at least three-fold higher than NIST comparators under the same reaction conditions. D, Catalytic rate of CNM-Au8 is demonstrably superior to several commercially available gold nanoparticles. Sigma Aldrich provides reactant-free, "citrate reduced" gold nanoparticles, in which extra procedures are used to clean the surfaces of reactants. "Citrate" gold nanoparticles may still have residual reactants present in the suspensions. E, Intracellular NAD+ levels increase in response to CNM-Au8 treatment in primary rodent neuron-glial co-cultures. F, Intracellular ATP levels increase in primary rodent oligodendrocyte cultures in response to CNM-Au8 treatment. Panels E-F, quantities shown are group means +/− SEM. One-way ANOVA, corrected for multiple comparisons, was used to compare means of each treatment group to mean of the vehicle control; a statistically significant difference between treatment and vehicle is denoted by asterisks: *p < 0.05; **p < 0.01.*

In addition to boosting NAD+ levels inside nervous system cells, CNM-Au8 directly acts to reduce ROS by directly catalyzing their reduction (Fig. 5). CNM-Au8 possesses anti-oxidative catalytic activity and has been demonstrated to directly reduce oxygen radicals in a superoxide dismutase-like manner, as well as convert hydrogen peroxide into water and oxygen in a catalase-like manner (Fig. 5A, B). Anti-oxidative activity for CNM-Au8 has been demonstrated in primary mouse oligodendrocyte cultures, in which basal levels of ROS were reduced with treatment (Fig. 5C). In a Parkinson's Disease *in vitro* model, ROS generated by treating primary rodent dopaminergic cells with the neurotoxin 1-methyl-4-phenylpyridinium ("MPP") was lowered in response to CNM-Au8 treatment in the presence of MPP (Fig. 5D). The statistical analyses shown in Figure 5 were conducted by one-way analysis of variance (ANOVA) to compare means of each treatment group to mean of the vehicle control (corrected for multiple comparisons). The p-value (Fig. 5C, D) represents the probability of obtaining test results at least as extreme as the results observed in the assay, under the general assumption that there is no difference between the groups (the null hypothesis).

Previous drug development efforts for neurodegenerative diseases have included numerous antioxidants, all of which failed to show disease-modifying effects. We believe CNM-Au8 remains in a different class from standard antioxidants because, to our knowledge, no other antioxidant demonstrates catalytic ability to increase bioenergetic metabolites NAD+ and ATP, while independently catalytically decreasing reactive oxygen species.

Figure 5. Reduction of Reactive Oxygen Species



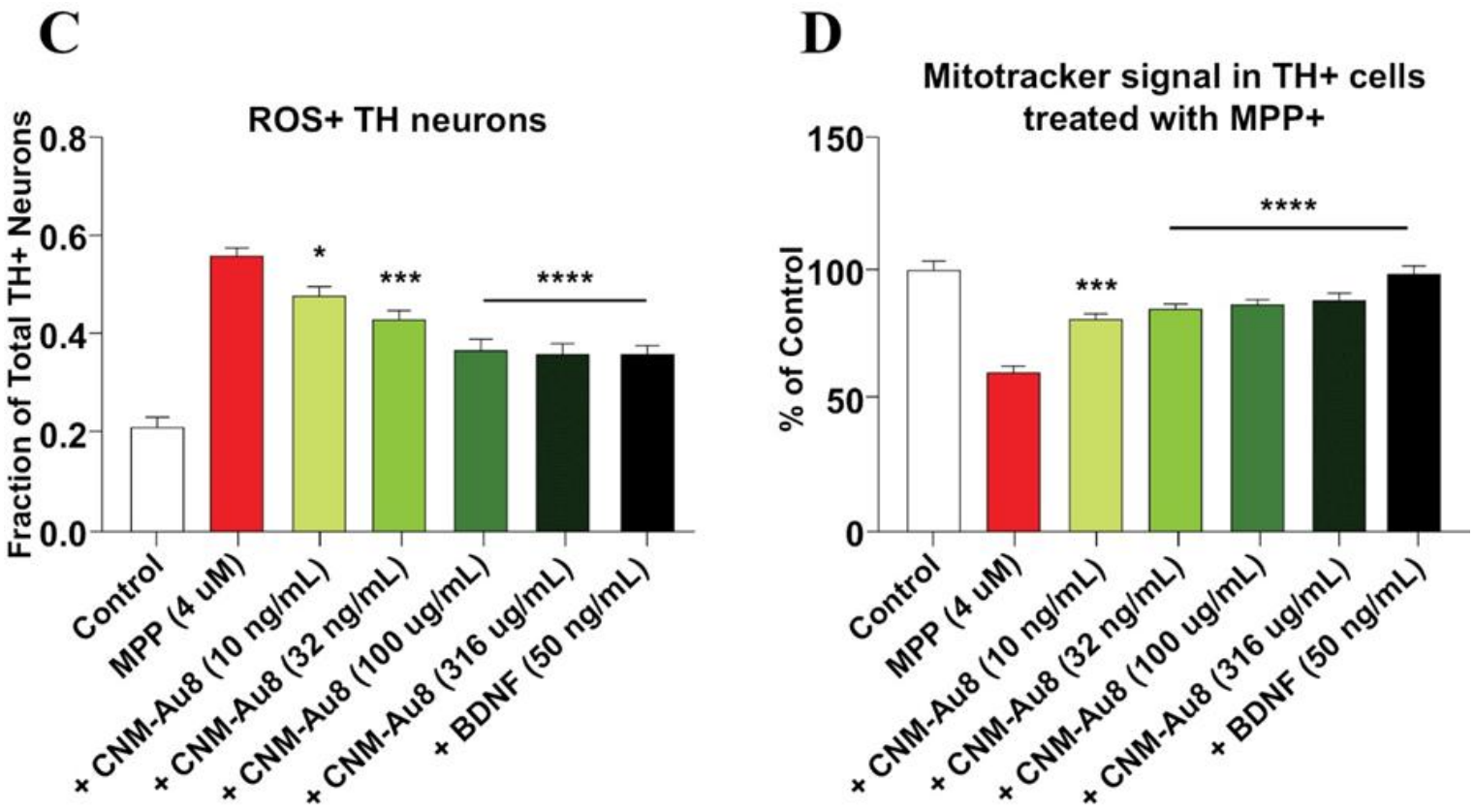


*Figure 5. CNM-Au8 is a catalytically active antioxidant. A, SOD-like activity of CNM-Au8 on superoxide radicals was measured using a colorimetric SOD assay kit (Cayman Chemical). B, Decay of the absorbance peak of hydrogen peroxide (H2O2) as the dismutation of H2O2 takes place in the presence of CNM-Au8 (green) or comparator AuNPs of similar diameter (red) or no gold (black). C,D, Neurotoxin (MPP+) induced mitochondrial stress and death of dopaminergic neurons in primary E15 rat co-cultures is prevented by CNM-Au8 (green), as determined by TH+ cell number (not shown), reduction of ROS as measured as by the fraction of dopaminergic ("TH") cells fluorescing with CELLROX Green signal, a marker of cytosolic oxidizing environment (C), and increased mitochondrial membrane potential (Mitotracker Red CMXRos) (D). Panels C-D, quantities shown are group means +/− SEM. One-way ANOVA, corrected for multiple comparisons was used to compare means of each treatment group of MPP with CNM-Au8 treatment to the mean of the MPP (4μM) alone treatment group; a statistically significant difference between each CNM-Au8 treatment group and MPP alone is denoted by asterisks: *p < 0.05; **p < 0.01, ***p < 0.001; ****p < 0.000. Untreated "Control" group is included to demonstrate the significant effect of MPP treatment to increase levels of ROS in TH neurons in Panel C and reduce mitochondrial membrane potential in Panel D, which was not included in the ANOVA analysis.*

Previous drug development efforts in the neurodegenerative disease space have targeted misfolded protein aggregates as toxic drivers of disease; for example, alpha-synuclein in PD, amyloid beta in Alzheimer's Disease, and TAR DNA binding protein 43 ("TDP-43") in ALS. An important component of the mechanism of action of CNM-Au8 is its ability to dose-dependently reduce aggregated alpha-synuclein and TDP-43 in cellular models of PD and ALS, respectively (Fig. 6). We believe this activity is, at least in part, attributable to the robust induction of twenty gene transcripts of the Heat Shock Factor 1 pathway, which we observed in oligodendrocytes in response to CNM-Au8 treatment (Robinson, et al. Nanocatalytic activity of clean-surfaced, faceted nanocrystalline gold enhances remyelination in animal models of multiple sclerosis. Sci Rep 10, 1936 (2020)) as well as due to an indirect cellular response to NAD upregulation, which has been shown to activate autophagic and proteostatic responses.

In summary, CNM-Au8 exhibits a novel mechanism of action via its nanocatalytic activities, involving:

(1) Enhancement of bioenergetic metabolism via increased production of NAD+ and ATP

(2) Reduction of oxidative stress, and

(3) Enhancement of proteostatic, autophagic responses that reduce accumulation of toxic protein aggregates that are hallmarks of neurodegenerative diseases.

Figure 6. Reduction in Misfolded Protein Aggregates

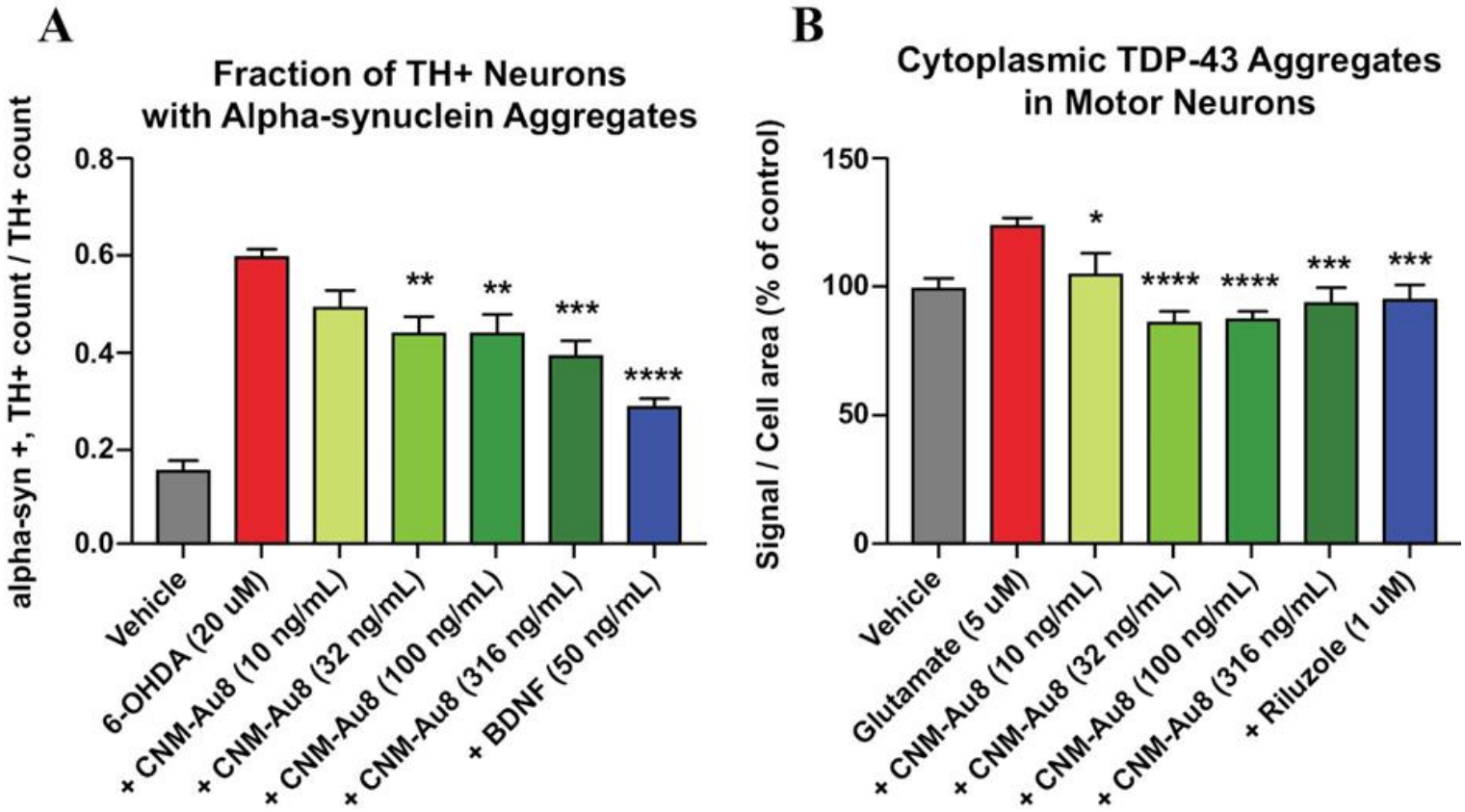


*Figure 6. CNM-Au8 reduces accumulation of protein aggregates in cellular models of PD and ALS. A) Primary culture of E15 rat mesencephalic neurons were pre-treated with vehicle, CNM-Au8, or positive control BDNF for 48h on day 4 of culture. 6-OHDA (20 uM) was added for 48 h then fixed and stained for anti-TH and anti- a-syn. B, Rat spinal motor neurons were cultured and treated with vehicle, glutamate (5 uM) or glutamate (5 uM) and CNM-Au8, then fixed and stained for anti-neurofilament, anti-TDP-43, and Hoechst. Group means plotted +/- SEM. * p <0.05; ** p < 0.01; *** p < 0.001; **** p< 0.0001; treatment vs. vehicle, one-way ANOVA corrected for multiple comparisons.*

Safety and Tolerability of CNM-Au8

We completed a Phase 1 First-In-Human study of CNM-Au8 in 2016 to demonstrate it was safe for further clinical development, and to assess the pharmacokinetic profile at different dosing concentrations.

Trial design. The Phase 1 First-In-Human study of CNM-Au8 was a randomized, placebo-controlled, double-blind, escalating single- and multiple-dose study to evaluate the safety, tolerability, and pharmacokinetics of CNM-Au8 in healthy male and female volunteers. There were two phases to this study: a single-ascending dose ("SAD") phase and a multiple-ascending dose ("MAD") phase. The SAD Phase was conducted first followed by the MAD Phase of the study.

- Single Ascending Dose: 40 subjects were randomized to CNM-Au8 (n=30) or placebo (n=10) at a 3:1 ratio in single dose escalating cohorts who received CNM-Au8 at 15 mg, 30 mg, 60 mg, or 90 mg with follow-up study duration for each subject of 18 days.

- Multiple Ascending Dose: 46 subjects were randomized to CNM-Au8 (n=35) or placebo (n=11) in multiple dose cohorts who received CNM-Au8 at 15mg, 30 mg, 60 mg, and 90 mg with the duration of treatment at 21 days and follow-up of each subject was up to 50 days.

Safety. Safety assessments revealed no significant findings. All doses used in this study were determined to be well-tolerated based on the frequency of reported treatment emergent adverse events ("TEAEs"). TEAEs occurred more frequently on placebo (86%) than in the CNM-Au8 dosing groups in both the SAD and MAD phases combined (75%). No subjects discontinued the study due to TEAEs and no serious adverse events ("SAEs") were reported across any treatment group. The most frequently reported TEAEs were almost entirely of Grade 1 (mild) severity and transient. The most frequently reported TEAEs consisted of headaches, somnolence, fatigue, abdominal pain, diarrhea, nausea, and dizziness.

Pharmacokinetics. PK analyses from the MAD Phase showed that at the end of 21 days, the maximum concentration of gold in blood was determined to be 1.53 ng/mL, 1.98 ng/mL, 2.35 ng/mL, and 3.33 ng/mL for each group dosed with 15, 30, 60, or 90 mg respectively. Pharmacokinetic (PK) analyses demonstrated that CNM-Au8 has a half-life of 14-21 days. The end-of-study drug exposure levels in humans either matched or exceeded the equivalent exposure that demonstrated neuroprotection and remyelination efficacy in animal models.

Conclusion. The First-In-Human safety results demonstrated no safety signals following dosing with CNM-Au8 at or above clinically used doses and drug exposure levels in humans either matched or exceeded the equivalent exposure that demonstrated neuroprotection and remyelination efficacy in animal models.

After successful completion of Phase 1 studies of CNM-Au8, we progressed CNM-Au8 into multiple Phase 2 studies designed to test the efficacy of CNM-Au8 in specific disease indications. Based on the safety findings and the strength of our preclinical remyelination and neuroprotection data, we have initiated four Phase 2 studies in central nervous system disorders including MS, PD, and ALS. We have also partnered with a major academic institution to implement a Phase 3 registrational clinical program with CNM-Au8 for the treatment of ALS. We are accumulating increasing human safety exposure in our ongoing Phase 2 and Phase 3 clinical programs. To date, on a blinded basis we have seen no concerning or dose-limiting safety signals, and two independent data safety monitoring boards overseeing our randomized double-blind placebo controlled trials have recommended continuing the conduct of the trials following unblinded evaluation of the safety data.

Multiple Sclerosis

MS Market Opportunity

Multiple sclerosis is an inflammatory and degenerative disorder of the central nervous system involving immune-mediated destruction of the brain, optic nerves, and spinal cord. MS results from autoimmune attacks on the myelin sheath, the protective covering wrapping the axons of neurons. When myelin is destroyed by autoinflammatory immune attacks, neurons become damaged and can ultimately die, leading to motor symptoms, cognitive disability, visual impairment and other neurological impairments.

MS typically begins between the ages from 20 to 40, and it is the leading cause of non-traumatic disability in young adults. Women are affected approximately three-times as often as men, except in individuals with the less common, primary-progressive form of the disease, where there is no gender preponderance. MS is the most common inflammatory demyelinating disease, with a prevalence that varies considerably, from high levels in North America and Europe to low rates in Eastern Asia and sub-Saharan Africa.

The diagnosis of multiple sclerosis is predominantly a clinical one that is aided by radiological tests (e.g., magnetic resonance imaging). Other diagnostic methods include blood tests, evoked potential tests, lumbar puncture, and optical coherence tomography, which is a new technology for examining the effects of multiple sclerosis on the health of nerve cells and axons in the retina. Utilizing magnetic resonance imaging, a new diagnostic classification for multiple sclerosis — clinically isolated syndrome has been included in the updated 2017 International (McDonald) Criteria. Ongoing improvements in diagnostic technologies may increase the number of patients diagnosed with multiple sclerosis.

MS Current Therapies and Limitations

All of the currently available drugs for treating multiple sclerosis either treat the symptoms caused by MS or act to reduce the degree of autoimmune-mediated inflammation. These drugs are typically referred to as disease-modifying therapies (“DMTs”). Nearly all of the current approved DMTs are approved for the treatment of relapsing forms of MS (“RMS”). They commonly act via immunosuppression or via immunomodulation, and thereby act to minimize autoimmune-associated attacks on myelin. Immunomodulatory DMTs reduce the risk of having an inflammatory attack, referred to as a “relapse”, and can slow the development of disability in those patients having attacks (i.e., “active” patients). As a corollary, DMTs may possibly diminish the risk of conversion of relapsing MS to secondary progressive multiple sclerosis (“SPMS”). The newer DMTs have been shown to substantially reduce autoimmune-mediated attacks and to delay the progression of the disease in active patients. However, there are no drugs available which can reduce the ongoing loss of function (i.e., disease progression) in non-active (those no longer having attacks) MS patients. None of the approved DMTs have been shown to clinically improve remyelination of damaged and demyelinated axons in MS lesions. Currently available DMTs for the treatment of MS include: *Injectable medications*, Avonex (interferon beta-1a), Betaseron (interferon beta-1b), Extavia (interferon beta-1b), Copaxone (glatiramer acetate), Plegridy (peginterferon beta-1a), Rebif (interferon beta-1a), Glatiramer acetate generic equivalent (Glatiramer Acetate Injection, Glatopa (glatiramer acetate); *Oral medications*, Aubagio (teriflunomide), Gilenya (fingolimod), Tecfidera (dimethyl fumarate), Mavenclad (cladribine), Mayzent (siponimod)*; Infusion medications*, Lemtrada (alemtuzumab), Novantrone (mitoxantrone), Ocrevus (ocrelizumab), and Tysabri (natalizumab). Advances in MS treatment with new B-cell depleting therapies, including ocrelizumab, have largely ameliorated inflammatory disease activity as measured by the reduction in risk of having relapses and the lack of occurrence of new gadolinium enhancing (inflammatory) lesions, as detected by MRI. However, despite the stabilization of MS disease activity in active MS patients by these agents for these MS patients, significant improvement in overall function has not been shown. Importantly, for the DMTs that have been approved to date, efficacy and safety are generally inversely correlated.

There is an increasing demand for better treatment strategies. Although current drugs for multiple sclerosis can reduce the risk of an inflammatory attack and slow down the progression of the disease in some MS patients, patients’ responses to drugs can be variable and suboptimal. For non-active MS patients, there is no available DMT that can substantially alter their progressive worsening. Also, the side effects of current MS drugs range from mild to serious, which may lead to reduced patient adherence.

Potential Advantages of CNM-Au8 for MS

We believe that CNM-Au8 has the potential to be a global first-in-class remyelinating and neuroprotective disease-modifying nanotherapeutic drug for MS. CNM-Au8 supports neurologic functions by enhancing bioenergetic activities in neurons and oligodendrocytes that have been attacked by the disease. Unlike the current immunomodulating MS DMTs, CNM-Au8 is thought to act to directly support neuroprotection and remyelination by improving bioenergetics, reducing harmful reactive oxygen species and inducing protective heat shock protein mechanisms. CNM-Au8 is administered orally, penetrates the blood brain barrier, and to date has a favorable safety, tolerability, and toxicology profile. Used alternately or in conjunction with standard immunomodulatory DMTs, CNM-Au8 treatment may improve patients' quality of life and potentially reverse disease progression because of its enhancing bioenergetic activities in neurons and oligodendrocytes that have been attacked by the disease, even in patients whose inflammatory attacks are well-controlled.

Summary of Nonclinical Pharmacology Myelination Studies for MS

Myelination is a complex process resulting in the wrapping of axons by oligodendrocyte ("OL") membranes containing specialized proteins and lipids. The resulting myelin sheath provides metabolic support to the axon and facilitates axonal electrical conduction, which in turn allows for central nervous system processing of motor, sensory, and higher order cognitive functions. During active myelination, OLs synthesize on the order of 100,000 proteins per minute and several thousand new lipid molecules per second, reflecting the significant energetic investment needed for biomass generation, and making this cell type among the most energetically demanding in the body. In MS, myelin is destroyed by autoimmune-mediated inflammatory attacks, and neurons whose axons were once protected and supported by myelin become damaged and can ultimately die. OL precursor cells are known to be present near MS lesions and can play a role in remyelination, but studies have shown that these cells are energetically compromised and remyelination is suboptimal in most central nervous system lesions.

Bioenergetic deficits have been noted in the brains of living patients with MS using ^{31}Phosphorus magnetic resonance spectroscopy ("^{31}P-MRS"). In autopsied brains from MS patients, oligodendrocyte precursor cells near MS lesions displayed impaired mitochondrial complex activity and other energetic deficits. These bioenergetic deficits play key roles in MS disease progression. CNM-Au8 is uniquely designed to directly address these important pathophysiological mechanisms.

We investigated the ability of CNM-Au8 to address OL energetic deficits, to induce remyelination and to restore functional activities and motor behaviors in a comprehensive remyelination preclinical program involving multiple *in vitro* and *in vivo* assays to determine CNM-Au8 efficacy. This work has been published as a peer-reviewed publication in Scientific Reports and is briefly summarized here.

In vitro experiments on primary OL precursor cells demonstrated robust induction of myelin production by CNM-Au8. RNASeq analyses of CNM-Au8 treated OL precursors cells demonstrated that multiple transcripts for known myelination genes are upregulated, and that glycolytic activity and ATP production are also increased. Several *in vivo* experiments were also conducted to demonstrate that orally delivered CNM-Au8 results in increased remyelination in the brains and spinal cords of animals treated with cuprizone or lysolecithin, two agents that are known to strip neurons of myelin via different mechanisms (Robinson et al. *Sci Rep*. 2020 Feb 11;10(1):1936). As fully described in the peer-reviewed publication by Robinson et al. both orally delivered cuprizone, or stereotactically injected lysolecithin are commonly used techniques to cause demyelination of the corpus callosum or spinal cord, respectively. Cuprizone, which is administered to rodents by including this agent in their chow, is a copper chelating agent that specifically causes mature oligodendrocyte death within multiple brain regions, including the corpus callosum. Maximal demyelination due to cuprizone feeding typically occurs within five weeks, which can be visually monitored and quantified using transmission electron microscopy. Lysolecithin injection results in the rapid degradation of myelin within a localized area of the spinal cord, observable using Luxol Fast Blue or toluidine staining for myelin with light microscopy, or also with transmission electron microscopy of the lesion, within a day of injury, allowing for the observation of remyelination within the induced lesion within the following weeks. Remyelination of the corpus callosum or spinal cord using either technique requires the migration of surviving oligodendrocyte precursor cells to the sites of demyelination, differentiation of these cells into mature myelinating oligodendrocytes, and rapid generation of specialized proteins and lipids for formation of new myelin membrane wraps around axons in this energetically demanding process. Multiple independent *in vivo* remyelination assays, using either cuprizone or lysolecithin as demyelination agents, were performed to demonstrate the remyelinating ability of CNM-Au8. For example, CNM-Au8 was provided either prophylactically, at the same time as the start of cuprizone feeding, or only after two weeks of cuprizone feeding, therapeutically, in order to allow demyelination to start to take place prior to administration of CNM-Au8. In both contexts, CNM-Au8 demonstrated greater recovery of myelin in affected brain areas than vehicle-treated controls. Furthermore, animals that were provided with CNM-Au8 only after full demyelination (five complete weeks of cuprizone treatment) had taken place displayed evidence of higher levels of mature myelin marker expression in their brains than vehicle controls, indicating that CNM-Au8 was not blocking the action of cuprizone but rather inducing recovery by stimulating the differentiation of oligodendrocytes. Similar results were confirmed by the lysolecithin experiments, which indicated that myelin destroyed by a completely different mechanism could be recovered with the daily oral administration of CNM-Au8 for one or two weeks after focal demyelination by lysolecithin. Treatment with CNM-Au8 significantly improved not only the quantifiable detection of myelinated axons in the brains of experimental animals, but also mouse behaviors and functional movements in the open field test and kinematic assays. For example, quantitation of the number of myelinated versus unmyelinated axons in 587 transmission electron microscope images, averaging 84 images per treatment group (with 15 mice per treatment group, seven treatment groups total), demonstrated a statistically significant ($p < 0.0001$ using one-way ANOVA corrected for multiple comparisons) recovery of remyelinated axons in therapeutically treated animals who were dosed with CNM-Au8 by gavage compared to vehicle treated, cuprizone-fed controls. In independent demyelination model studies using lysolecithin, lesioned animals treated with CNM-Au8 exhibited a 43% mean increase in myelinated axons within lesions post-LPC injection compared to vehicle controls ($p = 0.15$, unpaired t-test comparing CNM-Au8 treated rats to vehicle treated controls). Finally, in a cuprizone-mediated demyelination model study of both gross and fine motor behaviors, the group of animals receiving therapeutically delivered CNM-Au8 displayed detectable improvements in behaviors in both open field and fine motor kinetics assessments. Principal component analysis of gait metrics showed no statistical difference ($p = 0.47$) between CNM-Au8 treated, cuprizone-fed animals compared to the sham treated group, whereas there was a detectable difference in vehicle-treated, cuprizone-fed animals and sham controls ($p = 0.032$; 2-way ANOVA) by the end of study at week 6. Figure 7 shows examples of the observed induction of myelination by CNM-Au8 from selected in *vitro* and in vivo experiments reported in Robinson et al. These studies were fully funded by Clene and were the result of collaborations among academic researchers from Northwestern University, George Washington University, and various other academic consultants and employees of Clene.

Figure 7. Remyelination Summary

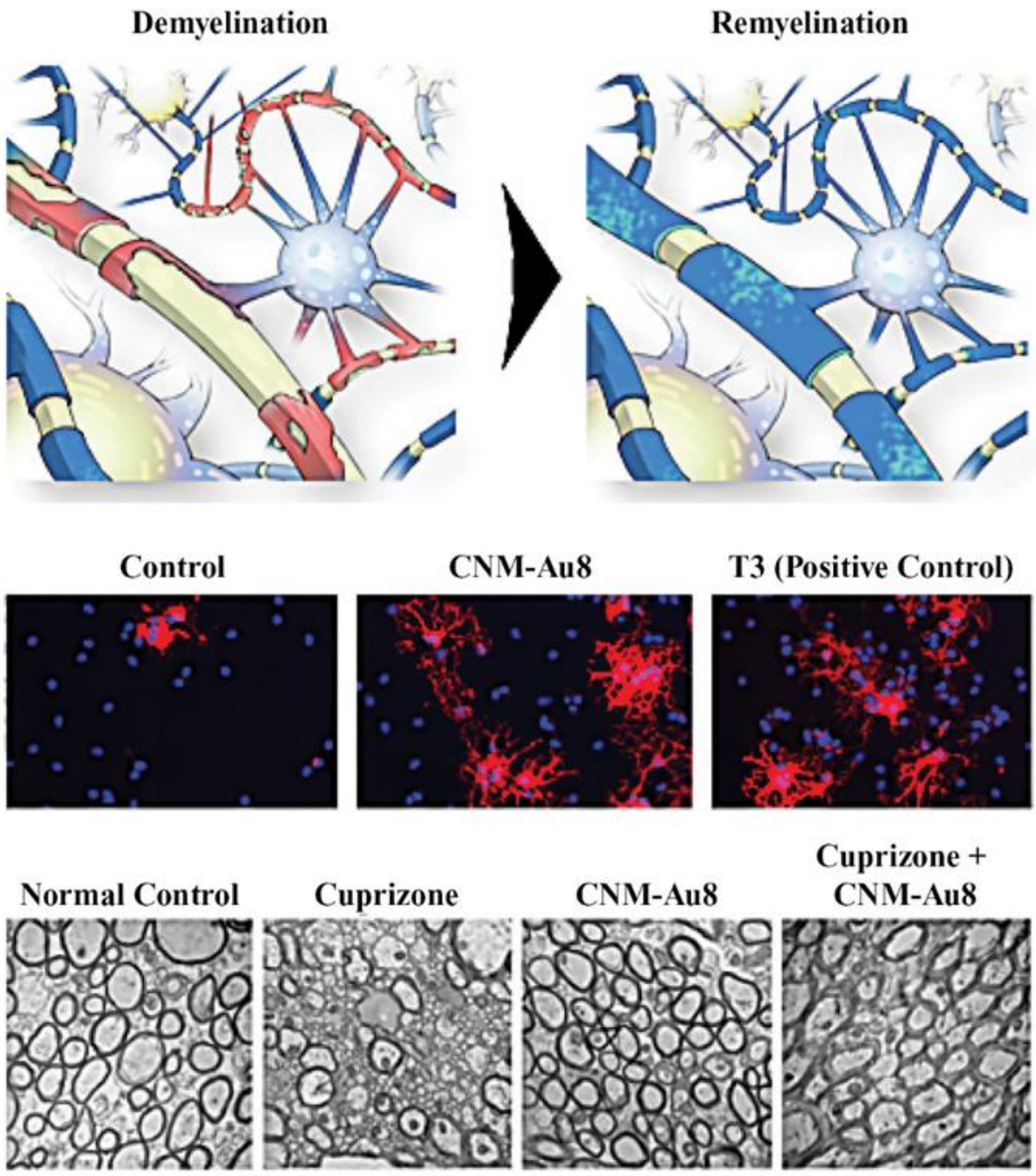


Figure 7. A summary of myelinating activities of CNM-Au8. Top row, Left: illustration of the demyelination (red) of a neuron's axon (yellow) that occurs in MS. Right: Illustration of restored myelination along the axon (blue) provided by the OL (blue cell). Middle row: isolated primary mouse OL precursors treated with vehicle control (left), 3 μg/mL CNM-Au8, or positive control and myelin-inducing agent tri-iodothyronine ("T3"). Cells are fixed and stained for Myelin Basic Protein ("MBP"), a marker of mature myelin in red, and the nuclear stain DAPI in blue, to reveal the presence of all OL precursor cells in the field of view. Many more cells expressing MBP are seen in the CNM-Au8 treated cells compared to vehicle-treated cells. Bottom row: transmission electron images of slices of corpus callosum of mice treated with, left to right: no cuprizone, cuprizone for five weeks, CNM-Au8 for five weeks, or cuprizone for five weeks and CNM-Au8 for the last three of the five weeks. Myelin can be seen as dark rings in each micrograph. Cuprizone treatment destroys myelin, while CNM-Au8 treatment alone does not change myelin. CNM-Au8 treatment of cuprizone-treated animals results in the recovery of myelin in the brains of these animals.

Clinical Development of CNM-Au8 as a Disease-Modifying Drug for MS

Based on safety findings in our Phase 1 clinical study of CNM-Au8 and our robust preclinical remyelination data, we have launched two Phase 2 clinical studies to investigate the effects of CNM-Au8 in MS patients.

VISIONARY-MS

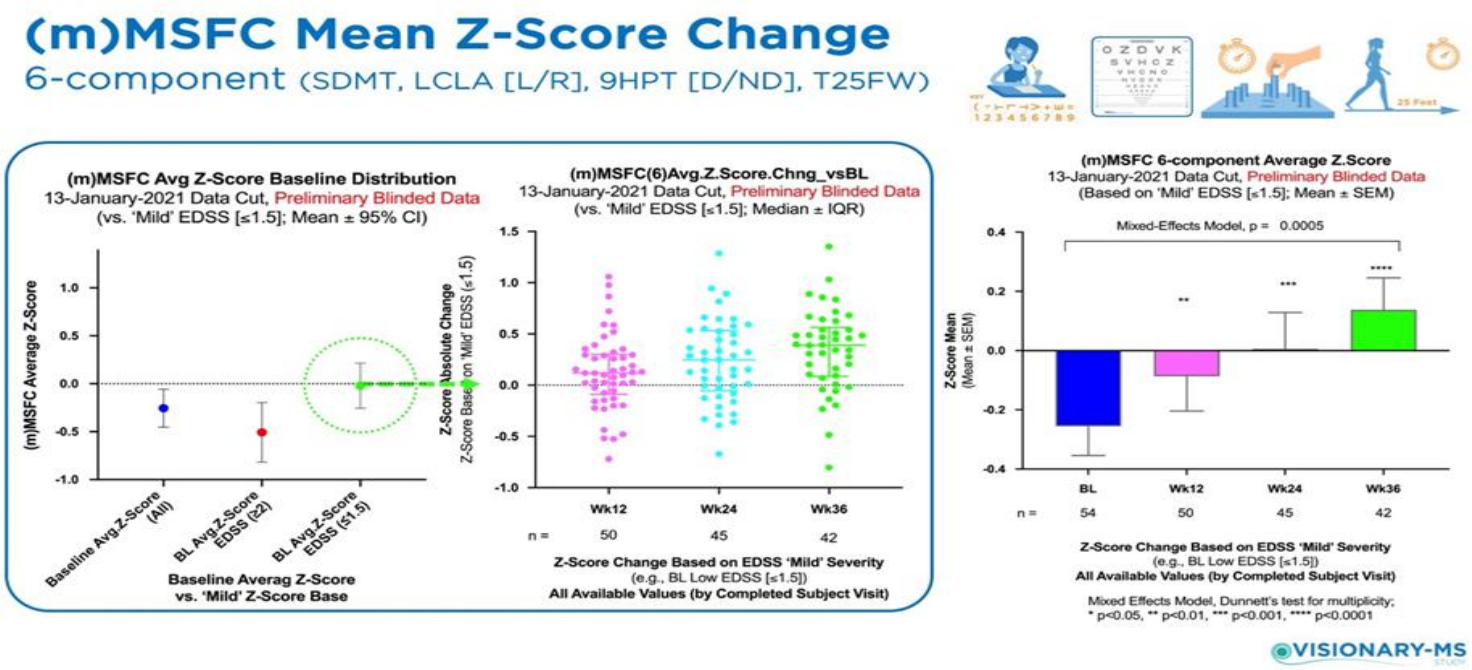
The VISIONARY-MS study, launched in December 2018, is an ongoing double-blind, randomized, placebo-controlled Phase 2 trial evaluating the efficacy and safety of two doses of CNM-Au8 as a remyelinating and neuroprotective treatment in people who have stable relapsing MS with chronic visual impairment. Enrolled participants must have chronic optic neuropathy, defined as visual impairment with no episodes of acute optic neuritis within the six months prior to enrollment, and stable (non-active) disease, defined as no MS relapses within the three months prior to entry. Concomitant immunomodulatory MS DMTs are allowed. Participants are randomized to low-dose CNM-Au8 (15 mg/day), high-dose CNM-Au8 (30 mg/day), or matching placebo. The primary endpoint is improvement in low contrast letter acuity ("LCLA") from baseline to week 24.

Contrast is the quantity of lightness or darkness contained by an object in comparison to its background. The smallest difference in contrast distinguished by the eye is known as the contrast threshold, usually reported as its reciprocal value, which is also known as contrast sensitivity (1/contrast threshold). Therefore, if a large amount of contrast is necessary for a patient to identify an object, they have poor contrast sensitivity and will have a low numerical value for this measurement. Contrast sensitivity can be thought of as a spectrum, in that black letters on a white background will be easier for any individual to discern than lower-contrast grey on white letter chart, regardless of whether or not visual abnormalities are present. The contrast threshold is the minimum amount of contrast necessary for an individual to discern an object from its background, and for people with MS the contrast threshold has been found to be higher than that of healthy individuals, even when visual acuity is equal between the two groups. contrast sensitivity is on a spectrum and may elicit more subtle changes in the contrast threshold that will be missed by high contrast visual acuity. LCLA tests low-contrast vision at various spatial frequencies that may be particularly affected by damage to specific inter-neural connections in the complex visual pathway.

In the VISIONARY-MS study, all participants remain in the double-blind, placebo-controlled treatment period through week 48, until the last participant completes week 24. In this way, double-blind, placebo-controlled data will be generated for most patients in the study through week 48, improving the study's ability to assess the long-term effects of CNM-Au8 on clinical endpoints. The study is presently being conducted across eight clinical sites in Australia, and site expansion into North America is presently underway. Health Canada and the U.S. Food and Drug Administration ("FDA") have both approved conduct of the trial within Canada and the United States, respectively. Incremental clinical research site initiation is subject to ongoing COVID-19 related research restrictions. As of February 26, 2021, 56 participants were enrolled in the VISIONARY-MS study with exposure to the investigational product up to 48-weeks.

Preliminary, interim, blinded efficacy results from VISIONARY-MS were reported as an invited oral presentation at the Joint NAIMS-IMSVISUAL Symposium at the Americas Committee for Treatment and Research in Multiple Sclerosis ("ACTRIMS") Forum 2020 held February 27-29 in West Palm Beach, Florida. Results from the first 34 enrolled participants up to week 36 demonstrate clinically-relevant median improvements in LCLA and the three remaining modified Multiple Sclerosis Functional Composite sub-scales ("(m)MSFC"), including Symbol Digit Modalities Test (SDMT, cognition), 9-Hole Peg Test (9HPT, upper extremity function), and Timed 25-foot Walk (T25FWT, gait) in the population, as a whole. Updated preliminary, interim, blinded efficacy results were presented at the 8th Joint ACTRIMS-ECTRIMS meeting, called MS Virtual, on September 11th, 2020, and at the ACTRIMS Forum 2021 on February 26, 2021. These updated blinded interim analyses compared changes in Multiple Sclerosis Functional Composite (MSFC) scores over the study treatment period to the baseline values of study participants with mild disease, as defined by Baseline Expanded Disability Status Scale (EDSS) scores of 1.5 or less. Notably, baseline scores for these participants demonstrate less neurological impairment than those of the overall study population, providing a valid comparator group. Changes in the four MSFC sub-scales (LCLA, SDMT, 9HPT, and T25FW) were compared to baseline scores of the comparator group with mild disease. These comparisons were performed at each study time-point (Weeks 12, 24, and 36). At each visit, the overall study population (randomized 2:1 active CNM-Au8 to placebo) showed notable increasing mean improvements in overall MSFC scores and key MSFC sub-scales compared to the comparator group (mixed-effects model; $p<0.0001$ vs. baseline). We believe these data support CNM-Au8's potential to drive meaningful neurological improvements in MS patients. Further, we believe these observations are notable given the expected long-term decline in LCLA, SDMT, 9HPT, and T25FW amongst MS patients reported from data sets including from the MS Outcome Assessments Consortium ("MSOAC") (Goldman et al. Neurology. 2019 Nov 19;93(21):e1921-e1931). MSOAC includes prospectively acquired RMS patient-level data from fourteen separate MS clinical trials including over 12,776 participants combined into a single database and followed for up to 24-months. When LCLA, SDMT, 9HPT, and T25FW were analyzed as a multidimensional measure rather than individually, progression on any one of these performance measures was more sensitive than the commonly used MS Expanded Disability Status Scale (EDSS), and demonstrated long-term declines in RMS patients. The increasing mean improvements observed across the entire study population (CNM-Au8 and placebo) may suggest a clinical effect CNM-Au8 when contrasted with the anticipated decline reported in publications from the MSOAC data. Figure 8 represents a summary of the observed average change in an integrated MSFC average 6-component Z-score of the change from Baseline by each 12-week study interval across all study participants in VISIONARY-MS (e.g., low dose, high dose, placebo) for all visits recorded as of 13-January-2021 and indicate continuing improvement over the course of the study.

Figure 8. VISIONARY-MS Mean (m)MSFC Z-Score Change vs. Baseline



Glanzman, R., H. Beadnall, M. T. Hotchkin, A. Klistorner, M. Barnett, R. Sergott, A. Rynders, K. S. Ho, and Mark G. Mortenson. "Update to a Phase 2 clinical trial of catalytic gold nanocrystals, CNM-Au8, for the treatment of chronic optic neuropathy." Presented at the ACTRIMS Forum 2021, February 26, 2021.

Available blinded safety data from VISIONARY-MS indicate that CNM-Au8 is well-tolerated with most adverse events characterized as mild in severity. No serious adverse events related to the investigational product (e.g., placebo, CNM-Au8) have been reported to date. The most frequently reported adverse events include headache, upper respiratory infection, and sore throat. The full unblinded results from the study are anticipated in the first half of 2022, subject to ongoing COVID-19 related research restrictions.

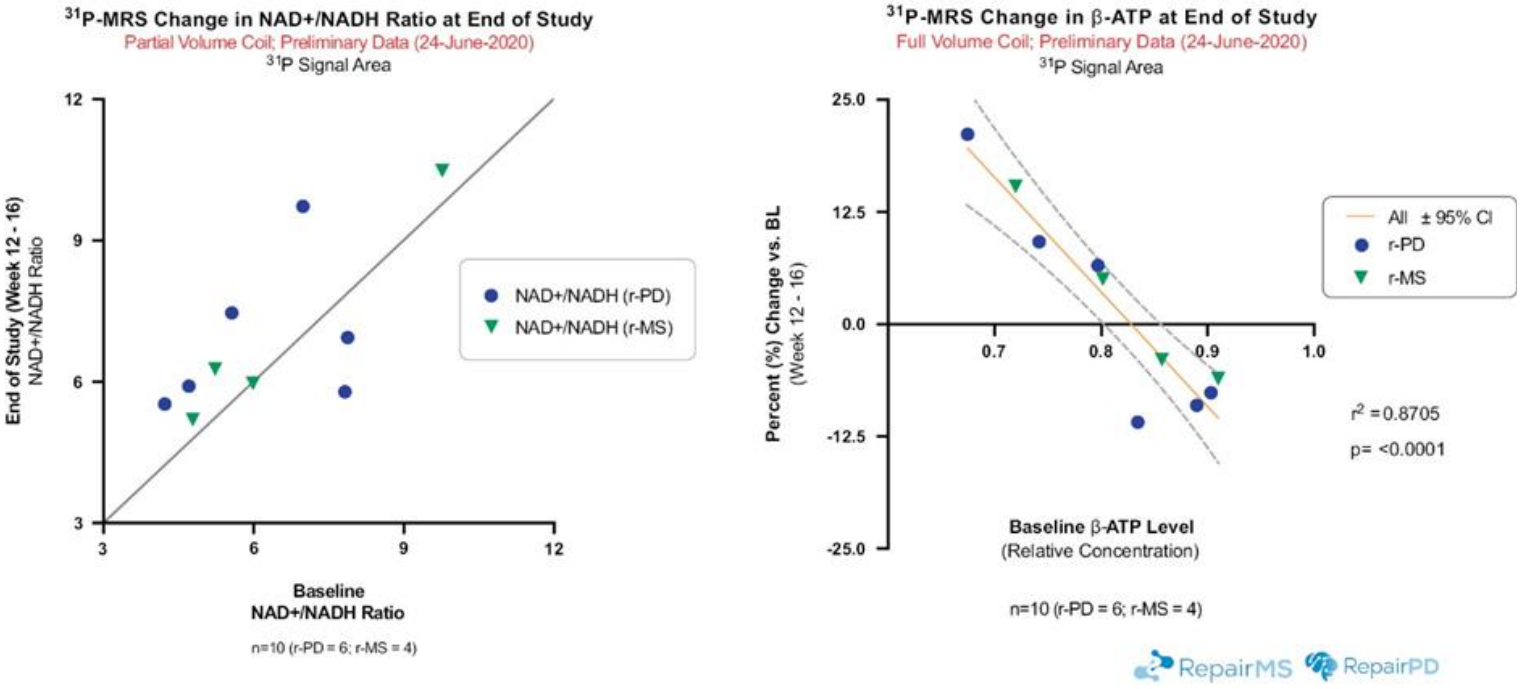
REPAIR-MS and REPAIR-PD

Two Phase 2, central nervous system imaging trials, REPAIR-MS and REPAIR-PD, were initiated to demonstrate central nervous system target engagement by measuring the effects of orally delivered CNM-Au8 on brain energy metabolites in patients with MS and PD *in vivo.* These bioenergetic metabolites are measured non-invasively and semi-quantitatively by utilizing ^{31}P-MRS imaging with a 7 Tesla (7T) MRI scanner. The REPAIR studies are being conducted at the University of Texas Southwestern, a center with specialized capabilities for conducting and analyzing 7T ^{31}P-MRS imaging studies. Both REPAIR studies were approved for clinical conduct by the FDA and commenced in December 2019 (REPAIR-PD)/January 2020 (REPAIR-MS) with full data availability anticipated in the second half of 2021 for both REPAIR-PD and REPAIR-MS, subject to ongoing COVID-19 related research restrictions. As of February 25, 2021, twelve participants were enrolled in REPAIR-PD study with exposure to CNM-Au8 up to 21-weeks, and ten participants were enrolled in the REPAIR-MS study with exposure to CNM-Au8 up to 18-weeks.

An interim analysis of data from study completers as of mid-July 2020 from these ongoing trials was conducted and reported at the 8th Joint ACTRIMS-ECTRIMS (MS Virtual 2020) meeting held September 11th, 2020. A full volume head coil was used to collect whole brain spectral waveforms in ~600 voxels with a spatial resolution of 2 cm^3 for the following metabolites: NAD pool (both NAD+ and NADH together), ATP, phosphocreatine, extracellular and intracellular inorganic phosphate, uridine diphosphate glucose, phosphocholine, phosphoethanolamine, glycerophosphocholine, and glycerophosphoethanolamine. A partial volume head coil was used in the same patient cohort to measure occipito-parietal levels of individual NAD+ and NADH phosphorous metabolites to determine the ratio of NAD+/NADH. Results for 4 MS and 6 PD completers (all competed subjects prior to a COVID-19 related research pause) were analyzed. Percent change from baseline ("BL") at the end-of-study ("EOS") visit was highly correlated to BL levels for key bioenergetic markers. Overall, the data indicate that CNM-Au8 normalized the levels of multiple bioenergetic metabolites measured. Patients with whole-brain NAD levels less than the BL mean significantly increased NAD levels at the EOS visit, while patients with whole-brain BL NAD levels greater than the mean normalized levels to the BL mean. Importantly, this relationship was observed for total NAD levels (r^2 = 0.6585; p = 0.0044), ß-ATP (r^2 = 0.8705; p < 0.0001), and several other ^{31}P metabolites, indicating a homeostatic effect of CNM-Au8 on brain bioenergetics. In the 4 MS patients, there were marked correlations for NAD (r^2 = 0.9241; p = 0.039), ß-ATP (r^2 = 0.968; p=0.016), and several other phosphorous metabolites. These preliminary results reflect target engagement in the brains of PD and MS patients, and provide the first clinical evidence to support the catalytic effects of CNM-Au8 on brain bioenergetic metabolites. Figure 9 below illustrates the changes in NAD/NADH ratio via the partial volume coil assay and correlations in mean ß-ATP levels versus baseline values for the full volume coil.

Figure 9. Interim Data from All Completers in REPAIR-MS and REPAIR-PD

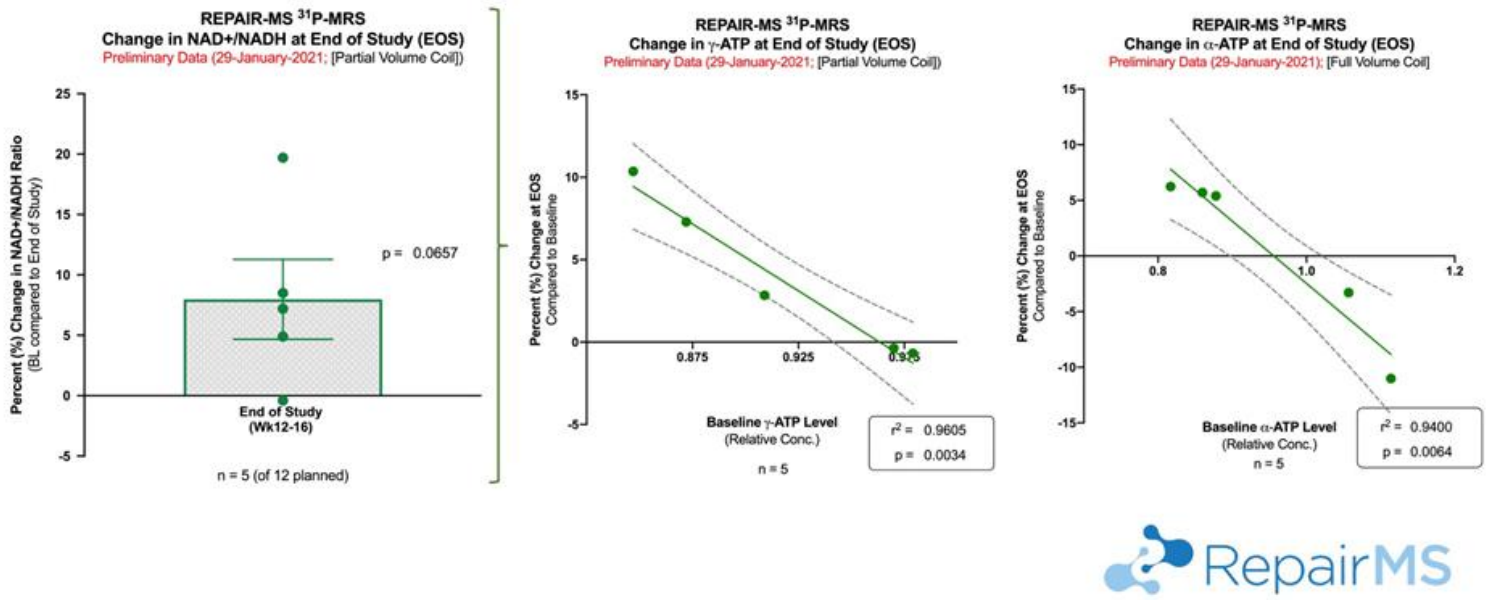
Left, Change in NAD+/NADH Ratio by Subject. Right, Normalization of Brain ß-ATP by Subject



A subsequent updated interim analysis of MS participants was presented at the ACTRIMS Forum 2021 on February 26, 2021, specific to the 5 MS participants who have completed the ^{31}P-MRS imaging. Among those who completed the study, the data indicate that CNM-Au8 increased the ratio of NAD+/NADH in the brains of MS subjects, resulting in normalized levels of multiple bioenergetic metabolites measured including ATP. Patients with whole-brain α-ATP and γ-ATP levels less than the BL mean significantly increased these levels at the EOS visit, while patients with whole-brain BL α-ATP and γ-ATP levels greater than the mean normalized levels to the BL mean, indicating a homeostatic effect of CNM-Au8 on brain bioenergetics (r^2 = 0.94 [α-ATP] and 0.96 [γ-ATP]; p < 0.01) (Figure 10).

Figure 10. Updated Interim Data from All Completers in REPAIR-MS

Left, Change in NAD+/NADH Ratio by Subject. Center and Right, Normalization of Brain ATP by Subject



Parkinson's Disease

PD Market Opportunities

Parkinson's disease (PD) is a chronic, progressive neurodegenerative disorder involving the progressive loss of dopaminergic neurons in the *substantia nigra* area of the midbrain. The degeneration of dopaminergic neurons leads to resting tremor, bradykinesia, limb rigidity, and gait and balance problems as well as increasingly recognized cognitive loss and behavioral changes due to more generalized neuronal loss. Both genetic and environmental factors are thought to contribute to the development of PD in addition to ageing, which is the most significant risk factor for developing the disease. Approximately one in one hundred individuals over the age of 60 is affected by PD.

PD Current Therapies and Limitations

While there are a number of approved Parkinson's therapies, such as dopamine agonists, COMT and MAO-B inhibitors, and deep brain stimulation, these treatments are limited to symptomatic improvement. No treatment is currently available to prevent the destruction of dopaminergic neurons. The inexorable progression of loss of dopaminergic innervation leads to progressively worsening symptoms with "on" (dyskinesias) and "off" (rigidity) symptoms that become increasingly difficult to manage. In addition, long-term use of levodopa, a commonly-prescribed dopamine precursor used to treat Parkinsonian symptoms, often results in dyskinesia that in itself becomes disabling. Despite an enormous effort over the past several decades, no disease-modifying or neuroprotective therapeutic for PD is available. A therapeutic that alters or slows the clinical progression, and thus improves PD healthspan and lifespan, would address a very significant unmet need.

Neuronal bioenergetic failure underlies PD, as evidenced by the observed impaired mitochondrial and lysosomal functioning, neuronal sensitivity to glutamate toxicity, accumulation of oxidative stress, autophagic failure in clearing misfolded proteins, and loss of synapse integrity associated with this disease. As such, improvement of cellular bioenergetic efficiency, as is possible with CNM-Au8, represents an important and previously unaddressed therapeutic target for this disease.

Potential Advantages of CNM-Au8 for PD

We believe that CNM-Au8 has the potential to be a global first-in-class disease modifying nanotherapeutic drug for PD. While current therapies for PD are designed to stimulate surviving dopaminergic neurons in order to elicit partial functional effects, none of them prevent the inexorable degeneration of dopaminergic neurons to change the course of disease progression. Our nonclinical studies demonstrate that CNM-Au8 is robustly neuroprotective of dopaminergic neurons across a variety of disease-relevant insults created using a variety of toxins and stressors. In addition, CNM-Au8 may have a tolerability profile superior to existing approved products like commonly used drugs for PD, such as levodopa/carbidopa that result in risk of dyskinesias after long-term use.

Summary of Nonclinical Pharmacology and General Neuroprotection Studies for PD

Excitotoxic injury, oxidative stress, and the accumulation of misfolded alpha-synuclein are hallmarks of the failing bioenergetic pathways associated with PD. In order to determine whether CNM-Au8 could act as a neuroprotective agent for PD, we conducted a series of *in vitro* and *in vivo* studies designed to test efficacy of CNM-Au8 in protecting various neuronal cell types from a variety of PD relevant disease-related stressors.

The potential of CNM-Au8 to confer neuroprotection in PD disease-specific cellular models was first demonstrated *in vitro*. Primary rat dopaminergic cells were challenged with 1-methyl-4-phenyl-1,2,3,6-tatrahydropyridine, (MPTP, which is metabolized to its active form MPP+) or alternatively with 6-hydroxydopamine (6-OHDA), which are both toxins specific to dopaminergic neurons. Treatment of primary neuronal-glial cocultures with CNM-Au8 increased the numbers of surviving dopaminergic neurons in response to either toxin in a dose-dependent manner, as well as affected overall improvement in neuronal health by a variety of metrics, including preservation of neurite network, reduction in oxidative stress, increase in mitochondrial staining, and reduction in alpha-synuclein aggregates. The activity of CNM-Au8 was then tested in the standard 6-OHDA-unilateral lesion model of PD. Lesioned rats, and a sham control group, were orally administered vehicle or CNM-Au8 for 4-weeks (2-weeks post-lesion) or 6-weeks (one-day post lesion) following the establishment of a lesion in the striatum. Significant functional improvements due to CNM-Au8 treatment was demonstrated in both the behavioral apomorphine-induced rotation and cylinder paw placement tests. In addition, larger numbers of surviving dopaminergic neurons were detected in the striatum of CNM-Au8-treated lesioned animals compared to vehicle controls. These studies independently demonstrated that CNM-Au8 treatment has robust neuroprotective properties in preclinical models of PD.

Clinical Development of CNM-Au8 as a Disease-Modifying Drug for PD

REPAIR-PD

We initiated the Phase 2 REPAIR-PD study to determine CNS target engagement by measuring the effects of orally delivered CNM-Au8 on brain energy metabolites in patients with PD as discussed previously. The REPAIR-PD study is being conducted at the University of Texas Southwestern. The REPAIR-PD study was approved for clinical conduct by the U.S. Food and Drug Administration (FDA) and commenced in December 2019. The REPAIR-PD study is anticipated to conclude in the second half of 2021 subject to COVID-19 related research restrictions. As of February 25, 2021, twelve participants were enrolled in the REPAIR-PD study with exposure up to 21-weeks.

In July 2020, an interim analysis of data from completers of these ongoing trials was conducted. A full volume coil was used to collect whole brain spectral waveforms in ~600 voxels with a spatial resolution of 2 cm^3 for the following metabolites: NAD pool (both NAD+ and NADH together), ATP, phosphocreatine, extracellular and intracellular inorganic phosphate, uridine diphosphate glucose, phosphocholine, phosphoethanolamine, glycerophosphocholine, and glycerophosphoethanolamine. A partial volume coil was used on the same patient cohort to measure combined occipital and parietal levels of NAD+ and NADH phosphorous metabolites to determine the ratio of NAD+/NADH. Results for 4 MS and 6 PD completers (all competed subjects prior to a COVID-19 related research pause) were analyzed. These data suggest that CNM-Au8 was able to normalize the levels of all bioenergetic metabolites measured. Percent change from BL at the EOS visit was highly correlated to BL levels for key bioenergetic markers. Patients with NAD levels less than the BL mean significantly increased whole-brain NAD levels at the EOS visit, while patients with BL NAD levels greater than the mean normalized levels to the BL mean. Importantly, this relationship was observed for total NAD levels ($r^2 = 0.6585$; $p = 0.0044$), ß-ATP ($r^2 = 0.8705$; $p < 0.0001$), and several other ^{31}P metabolites, indicating a homeostatic effect of CNM-Au8 on brain bioenergetics. These preliminary results robustly demonstrate target engagement in the brains of PD patients, and provide the first clinical evidence demonstrating the catalytic effects of CNM-Au8 on brain bioenergetic metabolites. For details, please see the "— REPAIR-MS and REPAIR-PD" section and Figure 9 above.

RESCUE-PD

A second Phase 2 clinical study is planned to investigate the effects of CNM-Au8 on slowing or preventing disease progression in PD patients. This study, the RESCUE-PD study, will follow patients with PD to determine the effects of CNM-Au8 on stabilizing disease activity as a neuroprotective therapeutic. The RESCUE-PD study is planned to commence in late 2022, with results anticipated within 24-36 months following study initiation.

Amyotrophic Lateral Sclerosis

ALS Market Opportunities

Amyotrophic lateral sclerosis is an adult-onset, progressive, and fatal neurodegenerative disorder of the neuromuscular system resulting in muscle weakness and paralysis leading to death as early as three to five years after initial diagnosis. ALS involves the progressive degeneration of motor neurons in the spinal cord and brain, which are responsible for controlling voluntary muscle movement. In ALS, this progressive loss of motor neurons leads to muscle weakness, loss of muscle mass, and inability to control movement. Although there are two FDA approved drugs for ALS, riluzole and edaravone, neither treatment substantially halts or reverses the progressive nature of this disease. The onset of disease for the majority of individuals with ALS occurs between 40 and 60 years old and is more common in men. After the age of 65, the difference in incidence between males and females decreases.

ALS Current Therapies and Limitations

Current ALS treatment therapies are largely palliative, aiming only to provide temporary relief from symptoms without addressing the underlying disease progression. For example, one approach to the loss of respiratory function, which is the most common cause of ALS-related death, is non-invasive ventilation. Despite the great need for an effective disease-modifying treatment, and significant research efforts by the pharmaceutical industry to meet this need, there have been limited clinical successes and no curative therapies approved to date. There are two FDA-approved therapeutic agents for the treatment of ALS: riluzole, an anti-glutamatergic agent, and edaravone, a free-radical scavenger. However, both of these treatments are acknowledged to have limited disease-modifying effects, as riluzole extends participant lifespans by an average of only two to three months, while edaravone slows the decline of the ALSFRS-R score, a clinical measure of functional decline, in only a small subset of participants who are at an early stage of disease. There is clearly an urgent unmet need for the development of safe and effective disease-modifying therapeutics for ALS.

Potential Advantages of CNM-Au8 for ALS

We believe that CNM-Au8 has the potential to be a first-in-class disease modifying nanotherapeutic drug for ALS. In a human induced pluripotent stem cell (“iPSC”) model of ALS, CNM-Au8 demonstrated clearly superior human motor neuron protection compared to riluzole. Furthermore, oral delivery of CNM-Au8 to ALS model mice extended the median lifespan of these animals by over three times the lifespan extension attributed to edaravone or riluzole treatment reported in the literature. While the mechanism of action of edaravone shares one similar component with CNM-Au8, namely, reduction of oxidative stress, we believe the important difference in activity lies in CNM-Au8’s demonstrated potential to enhance bioenergetic activity in diseased neurons as well as to significantly reduce oxidative stress. Furthermore, we believe the complex nature of many of the neurodegenerative diseases, including ALS, calls for a therapeutic drug with multimodal activity that can act to enhance the bioenergetic profile of multiple central nervous system cell types; for this, CNM-Au8 may be uniquely suited to address the therapeutic challenges posed by such complicated and devastating diseases.

Summary of Nonclinical Pharmacology Neuroprotection Studies for ALS

Motor neurons progressively degenerate during the course of ALS. To demonstrate neuroprotection of motor neurons by CNM-Au8, *in vitro* neuroprotection assays were first used. Rat motor neurons were challenged with glutamate to induce excitotoxicity, or with amyloid beta 1-42 peptide (“A-beta”), which is toxic to motor neurons. In Alzheimer’s Disease, A-beta aggregates participate in the formation of amyloid plaques. CNM-Au8 treatment of motor neurons challenged with glutamate or with A-beta increased numbers of surviving motor neurons and preserved neurite networks in a dose-dependent manner.

Aggregation of misfolded proteins that display neurotoxic properties is a hallmark of many neurodegenerative diseases, including ALS. Accumulation of mis-localized, cytoplasmic TAR DNA-binding protein 43 (“TDP-43”) in motor neurons is associated with over 90% of ALS cases, and TDP-43 aggregates have been shown to disrupt cellular functions in motor neurons. In neuron-glial co-culture assays, application of glutamate or A-beta to rat motor neurons causes TDP-43 aggregates to accumulate in the cytoplasm of motor neurons. Treatment of the glutamate- or A-beta-challenged motor neurons with CNM-Au8 significantly reduced the accumulation of TDP-43 aggregates in a dose-dependent manner.

In addition to animal models, iPSCs have emerged as a new technique for neurodegenerative disease modeling using human-derived cells. iPSCs can be generated from a human skin or blood samples, and then differentiated *in vitro* into astrocytes and motor neurons. Using this technique, ALS patient-derived astrocytes were shown to be toxic to normal healthy human motor neurons. Introduction of CNM-Au8 to these toxic ALS patient astrocyte-motor neuron co-cultures resulted in a significant, dose-dependent rescue of human motor neurons and preservation of motor neuron neurite networks. Collectively, these results indicated that CNM-Au8 exerts motor neuron protection effects in several different models, including in response to excitotoxic stress, A-beta toxicity, and toxic astrocytes.

To investigate the efficacy of CNM-Au8 in an *in vivo* model of ALS, two studies were conducted in separate transgenic ($SOD1^{G93A}$) mouse model strains that model the human SOD1 familial form of ALS. In a study using rapidly progressing $SOD1^{G93A}$ animals, CNM-Au8 treated animals showed significant reduction of brainstem atrophy and brainstem vacuolization normally seen in untreated $SOD1^{G93A}$ mice. In the study using slower-progressing $SOD1^{G93A}$ animals, CNM-Au8 treated animals showed significant treatment effects in a number of behavioral and functional tests, including overall clinical score, weights hold, static rod orientation time, and average wheel-running velocity. Median survival of CNM-Au8 treated animals significantly exceeded vehicle-treated controls by 23 days (approximately 20% of the animal's expected life-span).

Clinical Development of CNM-Au8 as a Disease-Modifying Drug for ALS

Orphan Drug Status for ALS

The U.S. FDA granted orphan drug development status to CNM-Au8 for the treatment of ALS in May 2019. Following FDA orphan drug designation, sponsors may qualify for seven-year FDA-administered Orphan Drug Exclusivity, partial tax credits for research and development expenses, potential research and development grants, waived FDA fees, and protocol assistance from the FDA.

RESCUE-ALS

RESCUE-ALS is a Phase 2, randomized, double-blind, placebo-controlled study of the efficacy, safety, pharmacokinetics, and pharmacodynamics of CNM-Au8 in ALS patients. As of September 7th, 2020, the study was fully enrolled with 42 participants. In the study, patients will be randomized 1:1 to either receive 30 mg of CNM-Au8 once daily or matching placebo over a 36-week double-blind treatment period. Efficacy will be assessed as the change in motor neuron loss as measured by electromyography (e.g., MUNIX, the primary endpoint; and secondary endpoints, including MScanFit, MUSIX, Split Hand Index, and the Neurophysiology Index). Exploratory endpoints include standard clinical, safety, and quality of life assessments. The study is being conducted at two sites in Australia and led by ALS clinicians who are experts in electrophysiology techniques. As of February 25, 2021, the study had over-enrolled with 45 of 42 planned participants in the RESCUE-ALS study with exposure to the investigational product up to 36-weeks. Twelve participants had enrolled in the long-term open-label extension following completion of the week 36 end-of-study visit.

RESCUE-ALS is being substantially funded by FightMND who provided Clene with a grant of AUD$1.37 million. In general, the grant terms from Fight MND include repayment of funds received in the event of commercialization of CNM-Au8 for the treatment of ALS in Australia from future net sales proceeds up to a mid single-digit multiplier of the original grant amount of AUD $1.37M. Funding is disbursed based on the achievement of performance milestones related to patient enrollment targets. All intellectual property rights from the study activities will be owned by the company. Results of this study are anticipated in the second half of 2021.

Healey-ALS Platform Trial

In September of 2019, the Sean M. Healey & AMG Center ("Healey Center") for ALS at Massachusetts General Hospital selected CNM-Au8 as one of the first three drugs for inclusion in the first Platform Trial for the treatment of ALS. The Healey Center Platform Trial for ALS will test promising experimental therapeutics with a design that allows for the testing of multiple drugs simultaneously in order to rapidly identify and accelerate the development of novel therapies for ALS, while offering the advantages of reduced trial time, reduced costs and increased patient participation. The trial includes substantial financial support from philanthropic donors and the Healey Center, and provides access to 54 expert ALS clinical trial sites across the United States from the Northeast Amyotrophic Lateral Sclerosis ("NEALS") consortium.

The trial is a Phase 3, multicenter, double-blind, placebo controlled registrational clinical trial to assess the safety, efficacy, pharmacokinetics, and pharmacodynamics of CNM-Au8 in treating ALS. Participants will be randomized 3:1 between active treatment and placebo with active treatment equally distributed between low dose (30 mg) CNM-Au8 and high dose (60 mg) CNM-Au8. The primary endpoint is rate of change in ALSFRS-R score from baseline to week 24, with secondary endpoints of changes in slow vital capacity and hand-held dynamometry measurements. Exploratory endpoints include a combined joint-rank score based on survival and change in ALSFRS-R score from baseline to week 24, voice pathology measurements, and biofluid-based pharmacodynamic and metabolic markers.

Clene will contribute a direct fee to the Healey ALS Center toward the clinical conduct of this trial; there will be no additional licensing fees or milestone requirements. Clene will own all CNM-Au8 data while placebo data will be shared across the different treatment regimens within the platform trial. Study enrollment commenced in August 2020. Results for CNM-Au8 are anticipated in the first half of 2022 subject to the achievement of enrollment targets.

CNM-Au8 Expanded Access Program

Based on interest in the potential of CNM-Au8 to delay disease progression in ALS patients, clinical experts at Massachusetts General Hospital requested early access to use CNM-Au8 in an Expanded Access Program ("EAP"). An EAP is a potential pathway for a patient with an immediately life-threatening condition or serious disease or condition to gain access to an investigational medical product (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available. To qualify an EAP within the United States the following should apply, (i) a patient has a serious disease or condition, or whose life is immediately threatened by their disease or condition, (ii) there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition, (iii) patient enrollment in a clinical trial is not possible, (iv) potential patient benefit justifies the potential risks of treatment, and (iv) providing the investigational medical product will not interfere with investigational trials that could support a medical product's development or marketing approval for the treatment indication. The EAP is conducted under a study protocol filed with the FDA and commenced in August 2019. The EAP will collect safety and pharmacokinetic data in ALS patients not otherwise eligible for clinical studies due to standard inclusion and exclusion criteria. As of February 25, 2021, 37 participants had been enrolled in the EAP with exposure up to 69-weeks. An EAP provides additional safety data for FDA review and will be considered as part of the safety data package for CNM-Au8, and may provide supportive long-term safety data with respect to an NDA submission should the Healey ALS platform trial result in a statistically significant treatment benefit.

REPAIR-ALS

The REPAIR-ALS Phase 2 study is modeled after the REPAIR-MS and REPAIR-PD studies, discussed previously, and will investigate the effects of CNM-Au8 on improvement of bioenergetics and brain cellular membrane markers by non-invasively measuring brain levels of these markers utilizing ^{31}P-MRS. The REPAIR-ALS study has been approved for clinical conduct by the U.S. Food and Drug Administration (FDA) and is planned to commence following completion of the REPAIR-MS and REPAIR-PD programs.

Additional CSN Therapeutics in the Pipeline

Three other drug candidates are at various IND-enabling stages of research. Utilizing our CSN therapeutic drug development platform, we have developed additional drug candidates based on the transition elements silver and zinc (CNM-ZnAg) for anti-viral/anti-bacterial and wound healing applications (CNM-AgZn17), and gold and platinum (CNM-PtAu7) for oncology applications.

CNM-ZnAg, a Broad Spectrum Anti-viral and Anti-Bacterial agent in Development for Treatment of COVID-19

CNM-ZnAg was developed for use as an orally deliverable, broad-spectrum antiviral and antibacterial agent. It is formulated as an ionic solution of zinc (Zn^{+2}) and silver (Ag^{+}) with a limited presence (<1%) of silver Ag^{0} nanoparticles, all generated using the CSN platform in a manner that does not involve traditional inorganic synthesis methods utilized to generate zinc and silver compounds. The rationale for integrating a zinc-silver ionic solution was premised on the recognized historical activity of both Zn and Ag (as independent entities) for antimicrobial and antiviral disease treatment. Initial development studies both internally as well as externally from other labs revealed that when Zn^{2+} and Ag^{+} are administered together, they exhibit synergistic antiviral and antibacterial properties that are not observed when Zn^{2+} or Ag^{+}, or Ag^{0} nanoparticles are administered singly.

In the human body, zinc is an essential structural component of <750 zinc finger transcription factors, and is a catalytic component of approximately 2000 enzymes, encompassing all known enzyme classes. Most significantly, zinc is essential for the proper function of the immune system, and is specifically involved in multiple steps in the antiviral response. Zinc has demonstrated direct antiviral properties; in addition, zinc stimulates both innate and acquired antiviral responses. Thus, zinc-based treatments are hypothesized to support systemic immunity, while also acting to specifically inhibit viral replication, viral protein processing, and/or viral-infection-related symptoms. Silver has long been studied for its anti-infective activity. Silver's microbial-treatment properties have been documented for centuries, and silver has been the most extensively studied metal for the purpose of fighting infections and preventing food spoilage. Prophylaxis of silver nitrate against gonococcal ophthalmia neonatorum with silver ions was considered the standard of care in many countries until the end of the 20th century, prior to the advent of antibiotics. Independent research had demonstrated silver nanoparticles have been shown to be active against several types of viruses including human immunodeficiency virus, hepatitis B virus, herpes simplex virus, respiratory syncytial virus, and monkey pox virus. Silver nanoparticles and silver ions reduce viral infectivity when added concomitantly with the virus inocula, possibly by blocking interaction of the virus with the host cell.

A standard toxicology program based on ICH M3(R2) guidelines has been completed for CNM-ZnAg. The toxicity of CNM-ZnAg was evaluated at high concentrations up to the maximum feasible dose administered via oral gavage up to four times daily for 28 days in rats and 7 days in canines. Across all studies, there were no deaths, no test-article-related clinical observations, and no effects on: body weight, food consumption, hematology endpoints, clinical pathology findings, blood coagulation times, urinalysis, or urine chemistry. Standard i*n vivo* genotoxicity studies in rodents, including a 2-day COMET assay and a 28-day evaluation of micronucleated reticulocytes, revealed no test-article effects on genotoxicity.

A seven-day human tolerability study of the dietary supplement was previously conducted by an antecedent company to determine the safety and tolerability in forty (40) healthy human volunteers. There were no self-reported adverse events and laboratory assessments indicated no significant changes from baseline in body weight, blood pressure, heart rate, liver enzymes (AST/ALT), blood glucose, or blood lipids (total cholesterol, LDL/HDL, triglycerides). There were no safety findings associated with administration of the dietary supplement over the 7-day dosing period.

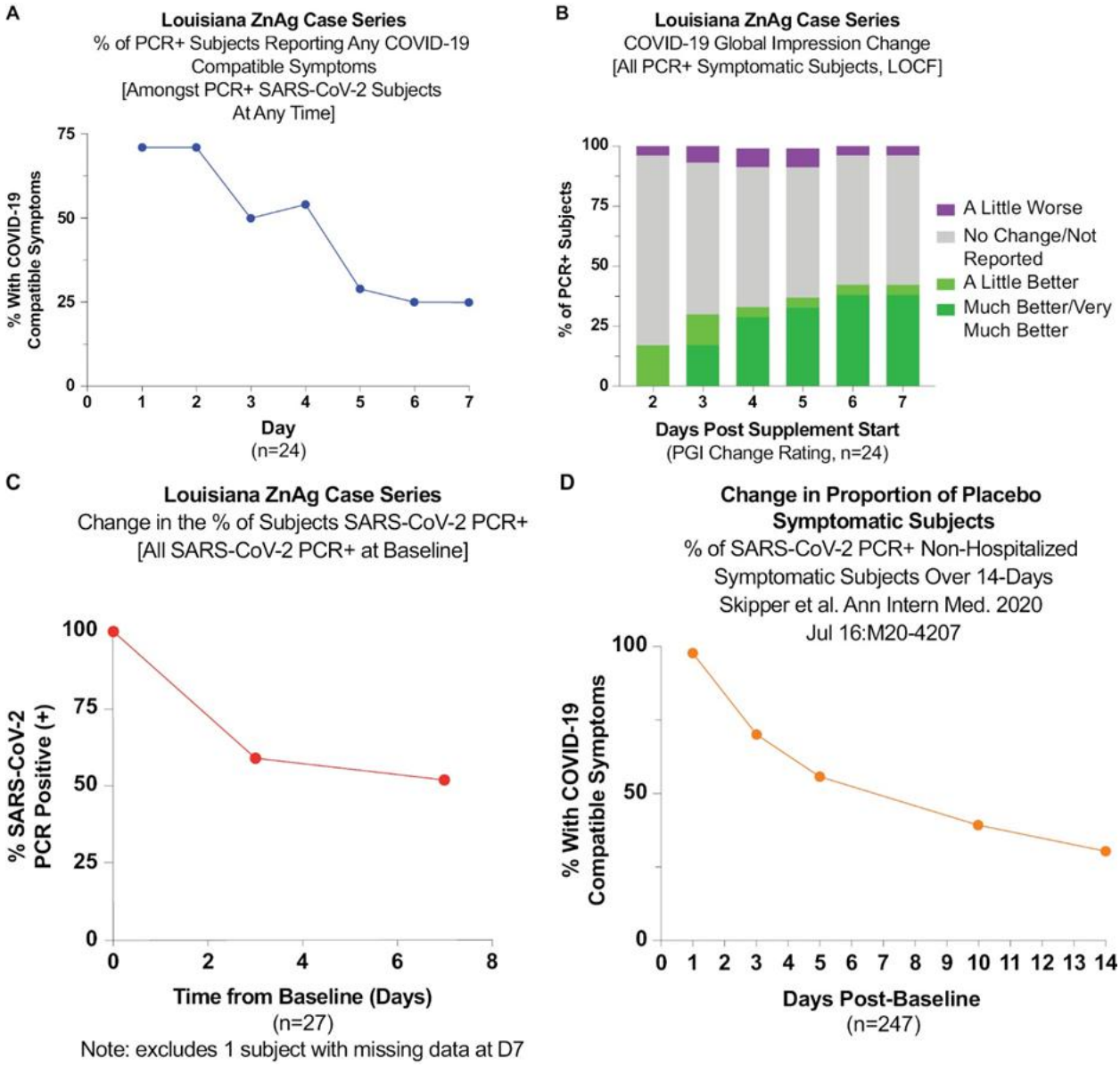
Clinical Development of CNM-ZnAg as a Therapeutic Treatment for COVID-19

COVID-19 is a rapidly emerging respiratory disease, resulting in substantial morbidity and mortality. Symptoms of COVID-19 are highly variable, with most infected individuals presenting with varying degrees of respiratory distress, fever, cough, sore throat, malaise, myalgias, nausea, diarrhea, anosmia, and ageusia. The median incubation period, from exposure to symptom onset, is approximately 4 to 5 days, and 97.5% of patients who are symptomatic will have symptoms within 11.5 days after infection. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the viral infection which causes COVID-19. Due to the international infection rates and potentially serious nature of this disease, COVID-19 was characterized as a pandemic by the World Health Organization on March 11, 2020. A CDC summary of PCR-positive COVID-19 cases in the U.S. as of May 30^{t}, 2020 showed approximately 28% were known to be symptomatic, 14% had been hospitalized, 2% were admitted to an intensive care unit, and 5% died.

To reduce disease impact on public health, a strategy of identifying, isolating, and quarantining infected or exposed individuals has been put in place to slow or stop transmission; however, these preventative activities, while necessary, do not alleviate the disease burden of individuals who have already become infected. The anti-viral therapy remdesivir is approved by the FDA for emergency use within the U.S. for treatment of hospitalized patients with COVID-19, however, the therapeutic benefit demonstrated in clinical trials was modest, and access has been limited regionally. Outside of the hospital setting, there are no therapies proven to reduce the severity or duration of COVID-19 infection. Further, the timeline and efficacy for vaccine development remains uncertain. Therefore, there is a significant unmet medical need to urgently decrease the morbidity and improve time to recovery in COVID-19 infected individuals.

Because of exigent worldwide need, Clene determined to rapidly develop CNM-ZnAg as a candidate treatment for COVID-19 based on the hypothesis that CNM-ZnAg may provide immune support benefits. On a limited basis, a dietary supplement version of ZnAg has been provided under 21 CFR 111 to support immune health. Preliminary uncontrolled observational case series with the dietary supplement yielded results suggesting oral administration of ZnAg to individuals with PCR-confirmed, COVID-19 infections may improve subject well-being and limit the duration of the disease. Results from a large case-series study of a COVID-19 outbreak in a US-based industrial food processing facility and its associated congregate housing are described below. Sixty-two (62) company employees and managers voluntarily received the ZnAg dietary supplement orally daily (while in quarantine and in congregate housing), completed a standardized daily symptom survey, and underwent repeated SARS-CoV-2 PCR testing prior to ZnAg treatment initiation and again following 7 days of ZnAg supplement intake. The study population was of predominantly Hispanic ethnicity (74%). The mean age was 33.6 (10.8) years, with 84% male. Twenty-seven (27) subjects were identified prior to supplement intake as SARS-CoV-2 positive by PCR testing. Amongst subjects with PCR+ confirmed SARS-CoV-2 at treatment start, 44% transitioned to PCR negative following 7-days of supplement administration (Fig. 11A). Amongst the 35 SARS-CoV-2 PCR negative subjects prior to treatment initiation, 88% remained SARS-CoV-2 negative by repeat PCR testing after 7-days of treatment. Amongst the 27 SARS-CoV-2 positive individuals, 24 reported symptoms consistent with COVID-19, generally self-reported as mild-to-moderate intensity. Symptom resolution (Fig. 10A), and PCR detected viral clearance (Fig. 11C) decreased rapidly following ZnAg treatment initiation consistent with a marked improvement in participants' global impression of change (Fig. 11B). The rate of symptomatic resolution (~75%) by Day 7 appears qualitatively greater than the placebo improvement rate (~50%) from a study completed in a comparable COVID-19 non-hospitalized symptomatic patient population (Fig. 11D, Skipper et al. Ann Intern Me. 2020 Jul 16;M20-4207).

Figure 11. PCR Status and Symptomatic Changes in Food Processing Facility Workers Infected with, or Exposed to, COVID-19



Given the potential for a clinical effect together with no identified safety signals from animal toxicology or initial human tolerability studies, we are planning to investigate CNM-ZnAg in a randomized, placebo-controlled clinical trial to determine the efficacy and safety of CNM-ZnAg for symptomatic improvement of COVID-19. This clinical study intended for 276 patients launched in Brazil in February 2021. Brazil represents a geography with a significant number of COVID-19 cases, robust clinical infrastructure and clinical trial experience, reasonable economic costs, and limited competition for participants for the enrollment of COVID-19 clinical research. The study is a randomized double-blind placebo-controlled study of CNM-ZnAg to decrease the incidence of hospitalization (primary endpoint) at Day 28 and improve the time to symptom resolution (secondary endpoint) in PCR confirmed SARS-CoV-19 subjects aged 40 and over. The study will evaluate two different doses of CNM-ZnAg, for which will be combined for analyses versus placebo.

CNM-AgZn17 for Wound-Healing and Burn Treatment

CNM-AgZn17 consists of an ionic solution of silver and zinc in a polymer gel formulation for topical application to the skin. We have demonstrated in *in vitro* assays that CNM-AgZn17 has broad-based anti-viral and anti-bacterial activity against common and antibiotic resistant pathogens such as Methicillin-resistant *Staphylococcus aureus*. We have also shown enhanced wound healing benefits in animal models of diabetic wound healing and less scar formation from during burn healing.

We are presently completing a standard toxicology program in animals to demonstrate safety in order to advance to first-in-human dosing studies. We have progressed to GLP dermal toxicity studies for topical applications expected to complete in 2022. Subject to regulatory filings of these toxicology findings and other results, we anticipate initiating a standard Phase 1 dermal First-In-Human safety study with CNM-AgZn17 with single-ascending dose and multiple-ascending dose cohorts by late 2022. The goal of this study will be to demonstrate safety sufficient to advance to Phase 2 clinical programs with CNM-AgZn17. Given the multiple preclinical benefits demonstrated to date with CNM-AgZn17, we envision a clinical program focused on healing burn and/or surgical wounds, which is anticipated to initiate in 2023.

CNM-PtAu7 — Our Oncology Targeted Nanotherapeutic

CNM-PtAu7 is a suspension of novel nanocrystals comprised of alloyed gold and platinum. We have demonstrated that treatment of human breast cancer cell lines EFM-19 and MT-3 with CNM-PtAu7 induces the expression of pro-apoptotic genes and represses the expression of anti-apoptotic genes, consistent with an anti-oncogenic effect. We have further demonstrated down-regulation of genes associated with the electron transport chain activity, which may also suppress tumorigenic activity. Further investigations related to the anti-tumor effects of CNM-PtAu7 are planned in additional malignant cell lines. CNM-PtAu7 has been patented in all major markets worldwide including the United States, Europe, China, Singapore, and Japan.

Research and Development

Overview

We are deeply invested in our research and development ("R&D") program. Our R&D activities are essential to attaining and sustaining the position as a recognized global leader in the development of CSN therapeutics. Our R&D plan is to continue the innovation of novel nanocatalysts and ionic suspensions of metallic transition elements with recognized medicinal value and underexplored, or as yet undiscovered, physicochemical and catalytic properties.

We have developed in-house all of the technologies that are critical to our R&D processes, and guard those technologies with appropriate intellectual property protections, and will continue to do so. We conduct our research activities through an in-house R&D team at our facility in Maryland, and engage in external clinical research collaborations to support our R&D activities as well.

Internal R&D

Our internal or in-house R&D activities are executed by a group of experienced research scientists, materials scientists, engineers, molecular biologists, medical doctors, clinical trial operational specialists, and a management team with deep expertise in the biopharmaceutical industry. Our in-house R&D team has a full range of capabilities ranging from drug discovery to preclinical development to and the design and implementation of clinical trials. We believe our R&D team is experienced, qualified, and will enable us to achieve our long-term goal of developing and commercializing innovative CSN therapeutics for patients worldwide. Our in-house R&D operates functionally through four sub-teams: (1) our research engineering team, (2) biological science discovery team, (3) nonclinical development team, and (4) clinical development team which work collaboratively to ensure the success of our R&D efforts.

Our research engineering team is responsible for the development and optimization of new CSN therapeutic candidates along with developing the technical processes and infrastructure to ensure reproducible CMC batch production of our CSN therapeutic candidates. Members of our research engineering team have PhDs and/or master's degrees in chemistry, material science and engineering, electrical engineering, and solid-state physics. Our research engineering team leader has a degree in electrical engineering and has been instrumental in the design of our electro-crystal-chemistry platform including the various continuous flows through apparatuses we use to produce our CSN therapeutics.

Our biological science discovery team is responsible for the initial characterization of CSN therapeutics, conducting biological assays, and assessing the activity and toxicity of drug candidates through *in vitro* and *in vivo* assays. Our biological discovery team assesses the CSN therapeutic candidates once initial development has been completed by our research engineering team. This team is led by an experienced research scientist who is a medical doctor and has a PhD in molecular science. Our biological discovery team collaborates closely with our research engineering team to refine our CSN candidate selection, for instance based on structural characteristics, in order to optimize the biological effects of our CSN candidate therapeutics.

Our nonclinical development team is responsible for developing a complete dataset of nonclinical animal pharmacology, toxicology, and safety studies, which is sufficient to support regulatory filings with human research ethics committees and government regulatory authorities in order to obtain approval for use in human studies. Our nonclinical development team works collaboratively with our biological science discovery team and clinical development team to translate our findings into animals and prepare for eventual studies in patients. This team also leads our external collaboration research activities with universities and academic experts. Our nonclinical development team is led by a research scientist with a PhD in Developmental Biology from Stanford University and a Master of Science degree in Genetics from the University of Cambridge where she was a Marshall Scholar. She is also an adjunct faculty member of the University of Utah School of Medicine.

Our clinical development team is led by our chief medical officer, who is a board-certified neurologist and Fellow of the American Academy of Neurology. Once our CSN therapeutic candidates have demonstrated sufficient safety and toxicology results to advance to human studies, the clinical development team designs, implements, and oversees the operational conduct of our clinical trials. The clinical trials are designed to prove our CSN therapeutics are safe and effective in the treatment of diseases.

Outsourced R&D Activities

In line with industry practice, we also outsource certain R&D activities to key academic partners, nonclinical research organizations, and to third-party clinical research organizations ("**CROs**"). We have collaborated with experts at key academic universities which have myelination and neuroprotection expertise. These university collaborators have conducted animal experiments to demonstrate the effects of CNM-Au8 treatment on remyelination and neuroprotection in animals and in cell-based *in vitro* assays. To support our research efforts, we have partnered with academic experts at The Johns Hopkins University in ALS, Cambridge University for myelination-related experiments, Northwestern University for myelination-related experiments, the George Washington University for myelination-related experiments, and the University of Edinburgh for myelination-related research. In general, we outsource the majority of toxicology, pharmacology, and toxicokinetic studies to expert nonclinical CROs.

To provide maximum flexibility and efficiency to operations, we engage industry-leading CROs to manage, conduct and support our clinical studies and to supplement our internal R&D teams' capabilities. We apply a rigorous process to selecting CROs to conduct research studies for us; selection is based on the quality, reputation, and research experience in the field of central nervous system disorders. In addition to the scope, depth and quality of the service and product offerings of the CROs, for clinical trial management, we place emphasis on the ability of the CROs to facilitate optimal site selection, to recruit patients in a timely manner, and to conduct complex clinical trials efficiently. Our CROs are widely recognized within their functional areas of research.

We enter into separate agreements with CROs and our external partners for each clinical trial or nonclinical research project. All CROs and other external research collaborators were all independent third parties. Principal terms of the service agreements with our key CROs and external partners are summarized as follows:

- *Services. The CRO, nonclinical research organization, or academic site implements and manages the study in accordance with the protocol designed by us as specified in the service agreement.*
- *Term*. The CRO, nonclinical research organization, or academic site is required to support the clinical trial or nonclinical studies within the prescribed time limit until the end of the clinical trial.
- *Payments.* We are required to make payments to our partners in accordance with the payment schedule agreed by the parties.
- *Intellectual property rights. We own intellectual property rights arising from the research activities related to our background intellectual property.*
- *Risk allocation.* Each party indemnifies the other party for losses caused by its fault or gross negligence. We indemnify the CRO and external partners for theoretical risks related to CNM-Au8.

We monitor and evaluate our CROs and external research partners with various activities including site visits, ongoing project team reviews, and/or assessments by third party assessors. We strive to achieve clinical trial excellence by maintaining strong quality control measures. We perform core functions such as clinical development strategy formulation and protocol design in house, and exercise control and oversight over key functions of clinical trial management. We conduct regular site visits to oversee site initiation, patient recruitment, and data quality monitoring, except when precluded by COVID-19 related research restrictions. We also engage third party consultants to perform clinical trial audits. Data quality is further assessed by in-house data review, including medical review, document review, and monitoring report review. We will not work with a vendor who does not have processes established surrounding data privacy and safeguards to ensure compliance through the clinical trial. We have maintained a stable relationship with our CROs and other external research partners.

Clinical Trial Management

To support our clinical trials, our internal clinical trials team designs, implements, collects and analyzes data for our clinical trials. When additional services are required to support a clinical trial, we conduct a feasibility and qualification assessment for potential vendors and CROs. These vendors are vetted through review of their current operational structure and established procedures, knowledge, and experience about the study, indication, or population, and past feedback from participating clinical sites. Our internal clinical development team supervises CROs on key clinical activities, such as patient eligibility review, medical data review, and SAE review, to ensure that the performance of these CROs complies with our protocols and applicable laws, which in turn protects the integrity and authenticity of the data from our clinical trials. Our internal clinical development team holds meetings with CROs to evaluate the CRO’s performance by following up on clinical progress and resolving potential issues and risks.

Financial Grants

We have been awarded grants from various organizations, including the U.S. Congressionally Directed Medical Research Program administered by the Department of Defense, the National Multiple Sclerosis Society, and FightMND, a not-for-profit registered charity in Australia, who together have issued us grants totaling approximately $2.6 million. We also receive indirect financial support for one of the clinical studies in which we participate, the Healey ALS Platform Trial, administered by the Massachusetts General Hospital, which is conducting a study of our CNM-Au8 drug candidate along with other drugs in a platform trial, at significantly lower costs to us than we would otherwise incur if we were to conduct a comparably designed study on our own at reasonable market rates.

These grants include the following terms:

- The Congressionally Directed Medical Research Program administered by the Department of Defense is an award for $1.25M for additional preclinical work in specific ALS models, which was awarded to us in December 2019. At the time of this Annual Report we had not yet finalized contracting with the Department of Defense.

- The NMSS grant is for a total of $339,000 for biomarker analyses of the VISIONARY-MS study. The grant was awarded to us in September 2019 and includes terms related to repayment of funds received in the event of commercialization of CNM-Au8 for the treatment of MS based on achievement of sales milestones up to a mid single-digit multiplier of the original grant amount. Funding is milestone based on the achievement of analytical validation and reporting to the NMSS. All intellectual property rights from grant related activities vest in the company.

- The FightMND grant is for AUD $1.37M and was awarded to us in August 2019. The grant includes terms related to repayment of funds received in the event of commercialization of CNM-Au8 for the treatment of ALS in Australia from future net sales proceeds up to a mid single-digit multiplier of the original grant amount. Funding is milestone based on the achievement of performance milestones related to patient enrollment targets. All intellectual property rights from grant related activities will be owned by the company.

- The Michael J. Fox Foundation grant was awarded to us in January 2021. The grant provides for preclinical research funding for an in vivo rodent model with CNM-Au8 treatment in well characterized alpha-synuclein over-expression, and additional research in human induced pluripotent stem cell derived neurons with commonly recognized Parkinson’s genetic defects. Funding is milestone based and all intellectual property rights from grant related activities will be owned by the company.

Manufacturing

We manufacture CSN therapeutics at our own production facility based in Maryland, USA based on novel manufacturing processes and devices that were entirely invented by us. Our Maryland manufacturing facility is compliant with GMP where we operate an ISO8 level clean room that contains the specialized electro-crystal-chemistry devices, or continuous flow trough apparatuses, that we have invented and patented to produce our CSN therapeutics from highly pure raw materials. At our present operating scale, we produce in-process gold nanocrystal suspension, the active pharmaceutical ingredient (API) for our lead asset, CNM-Au8, on an ongoing basis. Our current API production capabilities are fully sufficient to meet our needs for both research and development and supply for our ongoing Phase 2 and Phase 3 clinical trials, and we believe our processes can be scaled to achieve commercially viable quantities.

Through years of intensive research and development we have fine-tuned our production and delivery processes to the point where we can consistently, reliably, and affordably produce our core drug candidates, including CNM-Au8. We have also invested considerable time and substantial resources in perfecting the handling and storage systems in a manner that maintains stability and efficacy of our nanocrystal suspensions. In general, the manufacturing process for CSN therapeutics involves the following steps:

- Sufficient quantities of processing enhancers (e.g., sodium bicarbonate, others) are dissolved in highly purified water. The resulting mixture is referred to as “process water.”

- The process water is transferred to the conditioning portion of the trough apparatus at a constant nominal rate, where the process water is exposed to an atmospheric plasma in each trough apparatus, creating “conditioned water.”

- The conditioned water then flows into the electrochemical crystal growth portion of the trough apparatus, at a constant rate, where the conditioned water is exposed to a series of pairs of wire electrodes. The flow of the conditioned water is controlled, and the electrodes are continuously monitored and controlled by computerized, automated controllers.

- The electrodes are slowly advanced at a nominal rate to ensure that the conditioned water is exposed to the same electrochemical processing conditions to ensure batch-to-batch reproducibility, thus maintaining consistent size and shapes of the nanocrystals in each nanocrystal suspension.

- In-process bulk product, API, containing elemental nanocrystals, is continuously produced. The in-process bulk product is collected into large containers.

- The nominal concentration of active drug ingredients is achieved by executing a concentration step where in-process API is treated by a proprietary concentration procedure.

- The concentrated product is verified to adhere to physiochemical release specifications.

- The concentrated bulk suspension is subsequently filtered during filling to remove any microbiological contaminants and volumetrically filled into single unit containers. The final drug candidate is assayed to ensure it meets release specifications.

We have developed plans to expand our production capacity at our Maryland facility in order to supply additional planned Phase 3 clinical studies following evaluation of the Phase 2 clinical trial results. We have the technical expertise and capabilities to expand capacity to support eventual commercialization. During Part 1 of this planned expansion, we will more than triple the number of continuous flow trough apparatus and increase our storage capacity within our existing clean room environment. During Part 2 of our planned expansion, we will scale our production capacity by more than doubling our clean-room area along with the addition of more continuous flow trough apparatus and storage reservoirs. At the completion of this planned expansion we believe we will have sufficient capacity to support multiple Phase 3 studies in addition to enabling initial commercial supply of CNM-Au8. We also have initiated design studies to significantly scale our production processes as demand for our products increases to supply commercial marketing needs. We believe our current production environment has established Clene as the leading world-class manufacturer of clean surfaced nanocrystal therapeutics, and following the completion of our planned expansion, our facilities, equipment, and processes will comply with international practices and support our long term strategic plans, taking into consideration quality, costs, manageability, expandability and controls.

License Arrangements

In 2018, we established a license agreement and an exclusive supply agreement with 4Life, an international supplier of health supplements and one of our shareholders.

Under this license agreement, we granted to 4Life an exclusive and royalty-bearing license in relation to products that are very low concentration silver, gold, and other similar very low-concentration non-pharmaceutical supplement products produced by our electro-crystal-chemistry technology platform. This exclusive grant does not include ZnAg, for which 4Life has a non-exclusive right. 4Life is allowed to develop, make, manufacture, use, sell and commercialize the licensed products worldwide within the field of dietary supplements and certain non-pharmaceutical products for human use, internally or externally, which contain metallic-based constituents that are formed by our electrochemistry manufacturing techniques. 4Life will use its reasonably diligent commercial efforts to introduce the products to certain commercial markets following regulatory approval for their sale as nutritional mineral supplements. The initial term of this license agreement commenced on August 31, 2018 and will continue until five years after 4Life's introduction of the first nutritional supplement licensed product into the marketplace, which occurred on July 1, 2020. The license agreement may be renewed for additional five year periods by mutual agreement. Upon expiration of the license agreement the exclusive provisions in the agreement will convert to non-exclusive. The license agreement may only terminate by mutual agreement between the parties, or upon breach by either party that results in termination of the agreement under applicable law.

Under an exclusive supply agreement, 4Life will purchase the licensed products exclusively from us and we will sell the licensed products exclusively through 4Life, except for ZnAg which is not exclusively sold through 4Life. Upon the occurrence of certain future events, 4Life can achieve the right to exclusively manufacture the licensed products under the license agreement, other than ZnAg for which this right does not apply. The initial term of the exclusive supply agreement commenced on August 31, 2018 and will continue until five years after the minimum sales commencement date, which both parties anticipate will be in April 2021. The exclusive supply agreement may be renewed for additional five year periods by mutual agreement. 4Life may terminate the exclusive supply agreement for cause, which is stated to include repudiation, uncured material breach, insolvency, bankruptcy, general assignment for benefit of creditors, failure to provide reasonable assurances of financial and operational capacity, prolonged unremedied force majeure, and failure to proper notify of change in control. Clene may terminate the exclusive supply agreement in the event of a repudiation, uncured material breach, insolvency, bankruptcy or general assignment for benefit of creditors by 4Life.

At the time of commercial sales, single-digit royalty payments are owed to us by 4Life based on the size of 4Life's basket of total product sales. Royalties are payable quarterly under the license agreement until termination of the license agreement. In addition, 4Life will pay us our fully encumbered manufacturing expenses plus a guaranteed double-digit margin. We began supplying KHC46 (Gold Factor™) and a low dose zinc-silver solution (Zinc Factor™) during the first half of 2020 under this license agreement.

To date, we have not licensed our electrochemistry platform, any CSN therapeutics or any drug candidates to any other parties.

Competition

While the industry of the treatment for central nervous system diseases is quite competitive and subject to frequent changes, there are currently no existing therapies that claim effects on remyelination and neurodegeneration in patients. CNM-Au8's core effects of remyelination and neuroprotection provide us a globally unique first-mover-advantage for the treatment of central nervous system diseases. Together with our expanded intellectual property portfolio, we believe that it would be challenging for any potential competitors entering into the market of remyelination and neuroprotection focused therapeutics to replicate our efforts without violating our intellectual property protections.

Intellectual Property

Our intellectual property is protected through extensive global patents, institutional expertise and experience, and specialized technical know-how, which enable us to maintain our leading position in the development of CSN therapeutics for high-medical need diseases.

To date, we have over 100 issued patents worldwide and over 30 patents pending worldwide. We have world-wide rights to protect and thus commercialize our CSN therapeutics and believe that our issued, and pending patents, provide sufficient protection to secure the future commercial potential of our CSN therapeutics.

We have filed and obtained patents in the United States (US); Australia (AU); Brazil (BR); Canada (CA); China (CN); European Patent Office (EP), including Switzerland (CH), Germany (DE), Denmark (DK), Finland (FI), France (FR), Great Britain (CB), Ireland (IE), Italy (IT), Netherlands (NL), Norway (NO), Spain (ES), and Sweden (SE); Egypt (EG); India (IN); Indonesia (ID); Israel (IL); Japan (JP); Korea (KR); Mexico (MX); New Zealand (NZ); Philippines (PH); Russia (RU); Singapore (SG); and the United Arab Emirates (AE); with multiple fundamental patent families protecting our CSN therapeutics. The following table lists the material granted patent families in connection with our CSN therapeutics.

Description	Jurisdiction	Application Date (US)	Grant Date (US)
Continuous methods for treating liquids and manufacturing certain constituents (e.g., nanoparticles) in liquids, apparatuses and nanoparticles and nanoparticle/liquid solution(s) resulting therefrom (these patents relate to CNM-Au8 and ZnAg)	*Issued:* US (3), CA, AU, CN, ID, IL, IN, JP, KR, MX, PH. *Granted:* EPO *Pending:* US	January 7, 2010 November 15, 2013 August 11, 2017 January 13, 2010 August 27, 2013	December 31, 2013 August 29, 2017 October 9, 2018 September 24, 2013 July 12, 2016 Expiration dates for these patents will occur in 2028 in the applicable foreign jurisdictions and in 2030 in the US*
Continuous, semi-continuous and batch methods for treating liquids and manufacturing certain constituents (e.g., nanoparticles) in liquids, apparatuses and nanoparticles and nanoparticle/liquid solution(s) and colloids resulting therefrom (these patents relate to CNM-Au8 and ZnAg)	*Issued:* US (2), AU, CA, CN, EP, IN, IS, JP, KR, SG, RU; CH, DE, DK, FI, FR, IE, NL, NO, SE, GB. *Allowed: US* *Pending: IN, EP*	July 12, 2011 August 25, 2014	June 30, 2015 July 31, 2018 Expiration dates for these patents will occur in 2030 in the US and the applicable foreign jurisdictions*
Novel gold-based nanocrystals for medical treatments and electrochemical manufacturing processes therefor (these patents relate to CNM-Au8)	*Issued:* US (2), AE, AU (3), CA, CN, ID, IN, IL, JP (3), KR (3), MX, RU, SG; CH, DE, DK, ES, FI, FR, GB, IE, IT, NL, NO, SE. *Allowed: US, AU* *Pending:* BR, JP, MX, PH (2)	December 28, 2012	March 28, 2017 Expiration dates for these patents will occur in 2030 in the US and the applicable foreign jurisdictions*
Novel gold-platinum based bi-metallic nanocrystal suspensions, electrochemical manufacturing processes therefor and uses for the same (these patents do not relate to any specifically named product candidates herein)	*Issued:* US, AE, AU, CA, CN, ID, IL, IN, JP, KR, MX, NZ, RU, SG; CH, DE, DK, ES, FI, FR, GB, IE, IT, NL, NO, SE. *Pending:* BR, EG, PH	December 16, 2013	July 12, 2016 Expiration dates for these patents will occur in 2030 in the US and in 2032 in the applicable foreign jurisdictions*
Methods and treatment for certain demyelination and dysmyelination-based disorders and/or promoting remyelination (these patents relate to CNM-Au8)	*Issued:* AU, PH, RU, SG. *Granted:* EPO *Allowed:* ID, KR, MX, NZ (2) *Pending:* CA, CN, IN, IL, JP, SG	NA	NA Expiration dates for these patents will occur in 2033 in the US and the applicable foreign jurisdictions*

* expiration dates do not include possible patent extensions for certain countries

To date, we have not been involved in any proceedings in respect of, and we had not received notice of any claims of infringement of, any intellectual property rights that may be threatened or pending, in which we may be a claimant or a respondent.

Government Regulation

The FDA and other regulatory authorities at federal, state, and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring, and post-approval reporting of drugs such as those Clene is developing. Clene, along with third-party contractors, are required to comply with the various preclinical, clinical, and commercial approval requirements of the governing regulatory agencies of the countries in which Clene wishes to conduct studies or seek approval or licensure of CNM-Au8 or any future drug candidate.

FDA Drug Approval Process

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act ("FDCA") and implementing regulations. The process required by the FDA before drug candidates may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's current Good Laboratory Practices regulations;
- submission to the FDA of an investigational new drug ("IND") application, which must become effective before clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an independent review board whose role is to review the research before the trial is commenced and continuously throughout the trial to assure the protection of the rights and welfare of the human subjects. These boards are often called "institutional review boards" ("IRB");
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug candidate for its intended purpose;
- preparation of and submission to the FDA of a new drug application ("NDA") after completion of all pivotal clinical trials that includes substantial evidence of safety and efficacy from results of nonclinical testing and clinical trials;
- a determination by the FDA within 60 days of its receipt of a NDA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with GMP and to assure that the facilities, methods, and controls are adequate to preserve the drug candidate's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with Good Clinical Practices ("GCP");
- satisfactory completion of an FDA Advisory Committee review, if applicable; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States.

Preclinical and Clinical Development

Prior to beginning the first clinical trial with a drug candidate in the United States, Clene must submit an IND application to the FDA. An IND application is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics ("PK"), pharmacology, and pharmacodynamic ("PD") characteristics of the drug candidate; chemistry, manufacturing, and controls ("CMC") information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or other questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold until the IND sponsor and the FDA resolve the outstanding concerns or questions. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with Good Clinical Practice (GCP) and regulations governing the protection of human research subjects, including the requirement that all research subjects provide voluntary informed consent for their participation in any clinical study. Clinical trials are conducted under clinical study protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. For new indications, a separate new IND may be required. An Institutional Review Board (IRB) must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins. and must monitor the study until completed. Often each institution or clinical site has its own IRB. The IRB is responsible for ensuring that human subject's rights and privacy are maintained. Regulatory authorities, the IRB, or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board (DSMB), which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study. The DSMB may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries. For purposes of NDA approval, human clinical trials are typically conducted in three sequential phases (which may overlap or be combined).

- Phase 1 — The investigational product is initially introduced into a small number of healthy human subjects or patients with the target disease or condition. These studies are generally designed to test the safety, dosage tolerance, absorption, metabolism, distribution, and elimination of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.

- Phase 2 — The investigational product is administered to a larger, but still limited patient population with a specified disease or condition to evaluate the preliminary efficacy (usually based on a biomarker of disease), optimal dosages, and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger, confirmatory Phase 3 clinical trials.

- Phase 3 — The investigational product is administered to an expanded patient population to provide statistically significant evidence of relevant clinical efficacy and to further test for safety, and potentially further evaluate different dosages, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval by health authorities.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These studies, termed Phase 4 studies, may be implemented as a condition of approval of the NDA. Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the drug candidate, and must finalize a process for manufacturing the product in commercial quantities in accordance with current GMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Drug companies such as Clene are subject to legal requirements restricting, or imposing penalties for, the employment or use of individuals who have been debarred or excluded under various laws, including the provisions of 21 U.S.C. §§ 335a, 335b, or 335c, 42 U.S.C. § 1320a-7, in connection with making materially false or fraudulent statements to FDA, the offering or making of any prohibited payment, gratuity or other thing of value to personnel of the FDA or any other Governmental Entity, or other acts, statements, or omissions subject to FDA's policy titled "Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities" set forth in 56 Fed. Reg. 46191 (September 10, 1991), Employment of such individuals, or the occurrence of such violations in the development and regulatory application process may prevent or delay any approval of a company's new drug application.

NDA Submission, Review and Approval

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of nonclinical studies and clinical trials are submitted to the FDA as part of a New Drug Application (NDA) requesting approval to market the product for one or more indications. The NDA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's CMC, and proposed labeling, among other things. The submission of a NDA requires payment of a substantial application user fee to FDA (unless a waiver or exemption applies).

Once an NDA has been submitted, the FDA's goal is to review standard applications within ten months after it accepts the application for filing (a 60-day process), or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. In both standard and priority reviews, the review process can be significantly extended by FDA requests for additional information or clarification. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective and the facility in which it is manufactured, processed, packed, or held meets standards designed to assure the product's continued safety and efficacy. The FDA may convene an advisory committee to provide clinical insight on application review questions. Before approving an NDA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with GMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs. If the FDA determines that the application, manufacturing processes, or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates a NDA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response Letter will describe all of the deficiencies that the FDA has identified in the NDA, except that, where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response Letter without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the Complete Response Letter, the FDA may recommend actions that the applicant might undertake to resolve any findings and place the NDA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a NDA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the NDA with a Risk Evaluation and Mitigation Strategy ("REMS"), to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Expedited Development and Review Programs

A marketing application for a drug candidate submitted to the FDA for approval may be eligible for FDA programs intended to expedite the FDA review and approval process, such as priority review, fast track designation, breakthrough therapy, and accelerated approval.

A product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or to provide a significant improvement in the treatment, diagnosis or prevention of a serious disease or condition compared to marketed products. For products containing new molecular entities, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (compared with ten months under standard review).

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need by providing a therapy where none exists or a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast track designation provides opportunities for more-frequent interactions with the FDA review team to expedite development and review of the product. The FDA may also review sections of the NDA for a fast track product on a rolling basis before the complete application is submitted, if the sponsor and FDA agree on a schedule for the submission of the application sections, and the sponsor pays any required user fees upon submission of the first section of the NDA. The review clock does not begin until the final section of the NDA is submitted.

In addition, under the provisions of the Food and Drug Administration Safety and Innovation Act ("FDASIA") enacted in July 2012, a sponsor can request designation of a drug candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

Additionally, products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review and approval will not be shortened. Furthermore, priority review, fast track designation, breakthrough therapy designation, and accelerated approval do not change the standards for approval but may expedite the development or approval process.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. Orphan designation must be requested before submitting an NDA. After the FDA grants orphan designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. The orphan drug designation in and of itself does not convey any advantage in, or automatically shorten the duration of, the regulatory review or approval process. However, a drug granted orphan status allows the sponsor to receive tax credits and a user fee waiver.

If a product that has orphan designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a full NDA, to market the same product for the same indication for seven years, 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. A designated orphan product may not receive orphan exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Post-Approval Requirements

Any products manufactured or distributed by Clene pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to quality control and quality assurance, record-keeping, reporting of adverse events, periodic reporting, product sampling, and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to FDA review and approval. There also are continuing user fee requirements, under which FDA assesses an annual program fee for each product identified in an approved NDA. Manufacturers and their subcontractors are required to register their establishments and list the drugs they manufacture with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with GMPs, which impose certain procedural and documentation requirements upon Clene. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from GMPs and impose reporting requirements upon Clene and any third-party manufacturers or packagers that it may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain compliance with GMP and other aspects of regulatory compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of a product, mandated modification of promotional materials or issuance of corrective information, issuance by FDA or other regulatory authorities of safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product, or complete withdrawal of the product from the market or product recalls;

- fines, warning or untitled letters or holds on post-approval clinical studies;

- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of existing product approvals;

- product seizure or detention, or refusal of the FDA to permit the import or export of products; or

- injunctions, consent decrees or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety, efficacy, and conditions of use of the drug that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising, and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product’s labeling and that differ from those tested by Clene and approved by the FDA. Such off-label uses are common across medical specialties.

Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer’s communications on the subject of off-label use of their products.

Other U.S. Healthcare Laws and Compliance Requirements

In the United States, Clene's current and future operations 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 and Medicaid Services ("CMS"), which is part of the U.S. Department of Health and Human Services ("HHS"), as well as other divisions of HHS (such as the Office of Inspector General, Office for Civil Rights and the Health Resources and Service Administration), the U.S. Department of Justice ("DOJ") and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, Clene's clinical research, sales, marketing and scientific/educational grant programs have to comply with the anti-fraud and abuse provisions of the Social Security Act (such as the Anti-Kickback Statute), the false claims laws, the anti-fraud provisions of and the privacy and security provisions of regulations implementing the Health Insurance Portability and Accountability Act ("HIPAA"), the Drug Supply Chain Security Act, and similar state laws, each as amended, as applicable. Clene's business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patients, and customers may be subject to healthcare laws, regulations and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which Clene conducts its business. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, patient brokering, false claims, privacy and security, price reporting, drug distribution, and physician sunshine laws. Some of Clene's pre-commercial activities are subject to some of these laws.

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

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

The federal false claims and civil monetary penalty laws, including the FCA, which imposes significant penalties and can be enforced by private citizens through civil qui tam actions, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false or fraudulent claim for payment to, or approval by, the federal government, including federal healthcare programs, such as Medicare and Medicaid, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. For instance, historically, pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, off-label, and thus generally non-reimbursable, uses. Penalties for federal civil False Claims Act violations may include up to three times the actual damages sustained by the government, plus significant mandatory civil penalties, and exclusion from participation in federal healthcare programs.

HIPAA created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the Anti-Kickback Statute, the Affordable Care Act amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Clene may be subject to data privacy and security regulations by both the federal government and the states in which Clene conducts its business. 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. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates, which are independent contractors or agents of covered entities that create, receive, maintain, or transmit protected health information in connection with providing a service on behalf of, to or for 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 HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, many state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways, are often not pre-empted by HIPAA, and may have a more prohibitive effect than HIPAA, thus complicating compliance efforts.

Additionally, the federal Physician Payments Sunshine Act (the "Sunshine Act"), and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to CMS information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members. Failure to report accurately could result in penalties. In addition, many states have similar statutes or regulations to the above federal laws that may be broader in scope and may apply regardless of payor. Clene may also be subject to state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, and/or state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, drug pricing or marketing expenditures. These laws may differ from each other in significant ways further complicating compliance efforts. Additionally, to the extent that Clene has business operations in foreign countries or sell any of Clene's products in foreign countries and jurisdictions, including Canada or the E.U., Clene may be subject to additional regulation.

Clene may someday develop products that, once approved, may be administered by a physician. Under currently applicable U.S. law, certain products not usually self-administered (including injectable drugs) may be eligible for coverage under Medicare through Medicare Part B. Medicare Part B is part of original Medicare, the federal health care program that provides health care benefits to the aged and disabled, and covers outpatient services and supplies, including certain biopharmaceutical products, that are medically necessary to treat a beneficiary's health condition. As a condition of receiving Medicare Part B reimbursement for a manufacturer's eligible drugs, the manufacturer is required to participate in other government healthcare programs, including the Medicaid Drug Rebate Program and the 340B Drug Pricing Program. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of HHS as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Under the 340B Drug Pricing Program, the manufacturer must extend discounts to entities that participate in the program.

In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price ("ASP") and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. It is difficult to predict how Medicare coverage and reimbursement policies will be applied to Clene's products in the future and coverage and reimbursement under different federal healthcare programs are not always consistent. Medicare reimbursement rates may also reflect budgetary constraints placed on the Medicare program.

In order to distribute products commercially, Clene must comply with state laws that require the registration of manufacturers and wholesale distributors of drug products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. The federal government as well as some states also impose requirements on manufacturers and distributors to maintain records regarding the history of products in the chain of distribution. Federal law requires manufacturers to provide product tracing information to subsequent supply chain partners. The federal Drug Supply Chain Security Act ("DSCSA") governs the system of tracing certain prescription drugs as they are distributed in the U.S. A goal of the DSCSA is to protect consumers from drugs that may be counterfeit, contaminated, stolen, or adulterated. The law requires manufacturers to, prior to or at the time of each transfer of ownership of a drug, provide the subsequent owner with transaction history, transaction information, and a transaction statement. In the event of a recall or an inquiry regarding a potentially illegitimate product, manufacturers must be able to provide information regarding the transaction history and transaction information of their products. Violations of the DSCSA may result in fines or imprisonment. In addition, many states regulate manufacturers and enforce recordkeeping and licensure requirements.

Several states have enacted legislation requiring pharmaceutical and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of Clene's activities are potentially subject to federal and state consumer protection and unfair competition laws.

Ensuring business arrangements with third parties comply with applicable healthcare laws and regulations is a costly endeavor. If Clene's operations are found to be in violation of any of the federal and state healthcare laws described above or any other current or future governmental regulations that apply to Clene, it may be subject to penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, or refusal to allow Clene to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting obligations and oversight if Clene becomes subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of Clene's operations, any of which could adversely affect its ability to operate its business and results of operations.

Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug candidates for which Clene may obtain regulatory approval. In the United States and in foreign markets, sales of any products for which Clene receives regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage and establish adequate reimbursement levels for such products. In the United States, third-party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid in the United States, and commercial payors are critical to new product acceptance.

Clene's ability to commercialize any products successfully also will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from third-party payors, which decide which therapeutics they will pay for and establish reimbursement levels. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a therapeutic is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Clene cannot be sure that coverage or reimbursement will be available for any product that Clene commercializes and, if coverage and reimbursement are available, what the level of reimbursement will be. Coverage may also be more limited than the purposes for which the product is approved by the FDA or comparable foreign regulatory authorities. Reimbursement may impact the demand for, or the price of, any product for which Clene obtains regulatory approval.

Third-party payors are increasingly challenging the price, examining the medical necessity, and reviewing the cost-effectiveness, of medical products, therapies and services, in addition to questioning their safety and efficacy. Obtaining reimbursement for Clene's products may be particularly difficult because of the higher prices often associated with branded drugs and drugs administered under the supervision of a physician. Clene may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of its products, in addition to the costs required to obtain FDA approvals. Clene's drug candidates may not be considered medically necessary or cost-effective by payors. Obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require Clene to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of Clene's product on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Adequate third-party reimbursement may not be available to enable Clene to maintain price levels sufficient to realize an appropriate return on its investment in product development. If reimbursement is not available or is available only at limited levels, Clene may not be able to successfully commercialize any drug candidate that it successfully develops.

Different pricing and reimbursement schemes exist in other countries. In the E.U., governments influence the price of biopharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular drug candidate to currently available therapies. Other member states allow companies to establish their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any drug candidates for which Clene receives regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, political and economic pressures as well as legislative changes in the United States has increased, and Clene expects will continue to increase, the pressure on drug pricing. The downward pressure on the rise in healthcare costs in general, particularly prescription medicines, medical devices and surgical procedures and other treatments, has become very intense. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which Clene receives regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of drug candidates, restrict or regulate post-approval activities, and affect the ability to profitably sell drug candidates for which marketing approval is obtained. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

For example, the Affordable Care Act has substantially changed healthcare financing and delivery by both governmental and private insurers. Among the Affordable Care Act provisions of importance to the pharmaceutical and biotechnology industries, in addition to those otherwise described above, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively, and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price ("AMP");

- changes to the Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts, which through subsequent legislative amendments, has been increased to 70%, starting in 2019, off negotiated prices of applicable branded drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;

- extension of manufacturers' Medicaid rebate liability to covered outpatient drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;

- expansion of the entities eligible for discounts under the 340B Drug Discount Program;

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;

- expansion of healthcare fraud and abuse laws, including the FCA and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;

- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected;

- requirements to report certain financial arrangements with physicians and teaching hospitals;

- a requirement to annually report certain information regarding drug samples that manufacturers and distributors provide to physicians;

- establishment of a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending; and

- a licensure framework for follow on biologic products.

Some of the provisions of the Affordable Care Act have yet to be implemented, and there have been legal and political challenges to certain aspects of the Affordable Care Act. Clene anticipates that the Affordable Care Act, if substantially maintained in its current form, will continue to result in additional downward pressure on coverage and the price that it receives for any approved product, and could seriously harm its business. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent Clene from being able to generate revenue, attain profitability, or commercialize its products. Such reforms could have an adverse effect on anticipated revenue from drug candidates that Clene may successfully develop and for which it may obtain regulatory approval and may affect its overall financial condition and ability to develop drug candidates.

Further legislation or regulation could be passed that could harm Clene's business, financial condition and results of operations. Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. For example, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect beginning on April 1, 2013 and will stay in effect through 2027 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control biopharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

The Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act ("FCPA"), prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring Clene to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect Clene's business. These and other laws govern Clene's use, handling and disposal of various biological, and chemical substances used in, and wastes generated by, Clene's operations. If Clene's operations result in contamination of the environment or expose individuals to hazardous substances, Clene could be liable for damages and governmental fines. Clene believes that it is in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on its business. Clene cannot predict, however, how changes in these laws may affect its future operations.

Other Regulations

Clene is also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances. Clene may incur significant costs to comply with such laws and regulations now or in the future.

Human Capital

As of March 1, 2021, we had a total of 74 employees, 63 of which were full-time, located in Utah and Maryland. The table below sets forth our employees by role:

Department	Count of Employees	% of Total
Manufacturing	20	27%
Microbiology Lab	8	11%
Quality Control & Bioanalytics	8	11%
Research and Development	7	9%
Senior Management	7	9%
Clinical	11	16%
Quality Assurance	4	5%
Finance	5	7%
Human Resources	3	4%
Information Technology	1	1%
Total	**74**	**100%**

None of our employees are represented by a labor union or are covered by a collective bargaining agreement, and we believe that we have good relations with our employees.

Corporate Information

The mailing address for our principal executive office is 6550 South Millrock Drive, Suite G50, Salt Lake City, Utah 84121, and our telephone number is (801) 676-9695. Our website address is http:// https://clene.com. The information contained in or accessible from our website is not incorporated into this Annual Report, and you should not consider it part of this Annual Report. We have included our website address in this Annual Report solely as an inactive textual reference.

Executive Officers

Name	Age	Position
Robert Etherington	54	President, Chief Executive Officer and Director
Mark Mortenson	62	Chief Science Officer
Robert Glanzman	64	Chief Medical Officer
Ted (Tae Heum) Jeong	50	Chief Financial Officer

Robert Etherington. Mr. Etherington has been Clene's president, chief executive officer and director since April 2013 and is in charge of overall management, business, and strategy of Clene. Mr. Etherington has over 28 years of experience in commercialization of pharmaceuticals and biotech products. Mr. Etherington began his pharmaceutical career with a number of sales and marketing roles at Parke-Davis, a division of Pfizer, culminating in a Team Leader position over the drug Lipitor. He left Pfizer in 2000 to be the founding Director of Marketing during the IPO year of Swiss-based, Actelion Pharmaceuticals, focused in cardiopulmonary disease. Mr. Etherington has served on the board of BioUtah, an independent trade association serving the life science industry in the State of Utah, including a term as vice-chair, chairman and executive chair, since June 2016. Mr. Etherington has also been a director of Corsair LLC, a privately held biotechnology company, since March 2018. Mr. Etherington obtained a bachelor's degree of art from Brigham Young University in August 1990. He received his master's degree of business administration from Brigham Young University in April 1992, majored in business with a pharmaceutical healthcare emphasis. Mr. Etherington also completed the alumnus-granting General Management Program in Harvard University in June 2011. Mr. Etherington was selected to serve on the board of directors because, as CEO of Clene, he provides valuable operational and strategic insights to the board's decision-making process. The board also values and benefits from Mr. Etherington's experience in the pharmaceutical industry.

Mark Mortenson. Mr. Mortenson is Clene's co-founder and chief science officer of Clene. Mr. Mortenson is the co-inventor of the technology platform developed to produce clean-surface nanocrystal (CSN™) therapeutics, as well as the inventor/co-inventor on 30 other US patents and hundreds of corresponding foreign patents. Mr. Mortenson is a former chief patent counsel responsible for approximately 5,500 patents and patent applications in the United States and 44 foreign countries, and is the former chief operating officer of research, development, and manufacturing for an advanced materials-based company of over 300 employees. Mr. Mortenson received his bachelor's degrees in physics and in ceramic engineering from Alfred University in 1980, his master's degree in material science from Pennsylvania State University in 1982, and his Juris Doctor from George Washington University in 1986.

Robert Glanzman. Dr. Glanzman has been Clene's Chief Medical Officer since July 2019. Dr. Glanzman is board certified in neurology, and a Fellow of the American Academy of Neurology. Dr. Glanzman spent seven years as Assistant Clinical Professor at Michigan State University, where he maintained clinical practice, taught residents and acted as principal investigator for numerous clinical trials. Dr. Glanzman spent eight years at Pfizer as Senior Medical Director and Team Leader of the medical affairs team for interferon beta-1a (Rebif). In 2007, he moved to Novartis where he oversaw the successful Phase III development of fingolimod (Gilenya) and the commercial launch of interferon beta-1b (Extavia), in the US. In 2009, he was recruited by the Roche Group as Global Development Team Leader for the ocrelizumab (Ocrevus) program from the end of Phase II through the initiation of Phase III, in 2012. Following this, he held positions of increasing responsibilities at Purdue Pharmaceuticals, Nektar Therapeutics and, from December 2015 to June 2019, was Chief Medical Officer of GeNeuro S.A. Dr. Glanzman has co-authored numerous peer-reviewed publications. Dr. Glanzman received a bachelor's degree of science in biology from the University of North Carolina at Charlotte in 1982. He obtained a doctorate in medicine from the Wake Forest University School of Medicine in 1987. Dr. Glanzman's clinical training includes an internship in internal medicine at the NY Medical College, completed in 1988, a residency in neurology at the University of Michigan, completed in 1991, and a fellowship in diagnostic nuclear medicine at Duke University, completed in June 1992.

Dr. Ted (Tae Heum) Jeong. Dr. Jeong has been Clene's chief financial officer since December 2020. Dr. Jeong has more than 20 years of experience as a venture capitalist and a financial executive. He is a managing partner at KSV Global Innovations, a growth-stage investment firm which he co-founded in 2018. Before becoming CFO of Clene, Dr. Jeong was CFO of Rexahn Pharmaceuticals, Inc. (Nasdaq: REXN), an oncology and CNS-focused biopharmaceutical company, from 2002 to 2018, where he completed equity financings totaling more than $170 million and was also responsible for forming strategic alliances and executing license deals in the U.S., Europe, and Asia. From 1997 to 2002, he served as the Senior Investment Manager at Hyundai Venture Investment Corporation, a subsidiary of the Hyundai Motors conglomerate and one of the largest venture capital firms in South Korea, where he operated two of the first healthcare venture capital funds in Korea. From 2019 to 2021, he also served on the board of directors of Neurobo Pharmaceuticals (Nasdaq: NRBO), where he was chair of the audit committee. Dr. Jeong received his bachelor's and master's degrees of science in chemistry from Pohang University of Science & Technology. He also holds a master of science in finance degree from Johns Hopkins University, and a doctorate of management from the University of Maryland.

ITEM 1A. RISK FACTORS

An investment in our securities carries a significant degree of risk. You should carefully consider the following risks, as well as the other information contained in this Annual Report, including our historical financial statements and related notes included elsewhere in this Annual Report, before you decide to purchase our securities. Any one of these risks and uncertainties has the potential to cause material adverse effects on our business, prospects, financial condition and operating results which could cause actual results to differ materially from any forward-looking statements expressed by us and a significant decrease in the value of our Common Shares and Warrants. Refer to "Cautionary Statement Regarding Forward-Looking Statements."

Risks Relating to Our Business and Industry

We depend substantially on the successful commercialization of our drug candidates in the future, which may fail to materialize or experience significant delays.

As a new biopharmaceutical business, we currently do not have any drugs available for commercial sales nor do we have any drugs that have been approved for sale by the regulatory authorities. We have invested a significant portion of our efforts and financial resources in research and development of our leading drug candidate, CNM-Au8, which in early-stage studies has shown potential for the treatment of patients with multiple sclerosis ("MS"), amyotrophic lateral sclerosis ("ALS") and Parkinson's disease ("PD"). Our ability to generate significant revenue and become profitable in the future depends substantially on the future sales generated by CNM-Au8 and our drug candidates, which in turn depends on the successful research and development ("R&D"), regulatory approval, commercialization and sale of our drug candidates presently under clinical development for the treatment of patients with neurological disorders. We are also developing new drugs based on our technology that have not yet entered into human studies. The ultimate success of our drug candidates is subject to us achieving certain milestones, including without limitation:

- identifying, assessing, acquiring and obtaining evidence of biological activity of new drug candidates to treat certain diseases;
- obtaining satisfactory evidence of safety of these drug candidates in animal toxicology studies;
- obtaining regulatory approval for the conduct of, successful enrollment in, and completion of, clinical trials of our drug candidates;
- obtaining satisfactory proof of the clinical efficacy and safety of our drug candidates from these clinical trials;
- obtaining approvals and marketing authorizations from regulatory authorities for our drug candidates;
- developing sustainable and scalable manufacturing processes to produce these drug candidates;
- successfully expanding manufacturing processes to support global commercialization capacity of our drug candidates; and
- launching and commercializing drug candidates for which we have obtained regulatory approvals and marketing authorizations, either directly or with a collaborator or distributor.

If we do not achieve one or more of these milestones in a timely manner, or at all, we could experience significant delays in our ability to obtain approval for and/or to successfully commercialize our drug candidates, which would materially harm our business and we may not be able to generate sufficient revenues and cash flows to continue our operations.

Even if we are able to generate revenues from the future sales of our drug candidates, we may not become profitable and may need to obtain additional funding to continue operations. Any required funding may not be available on favorable terms or at all. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease our value significantly and could impair our ability to raise capital, expand our business or continue our operations, which in turn may adversely affect our business, financial condition, and results of operations.

We currently do not generate revenue from the commercial sales of drug candidates and we may not become profitable when expected, or at all.

Our main business is the research and development, and if successful, sales of drug candidates. As all of our drug candidates are still in the R&D stage, we currently do not generate revenue from the sale of drug candidates, and have recorded continued losses. We generate a small amount of revenue related to supply agreements for dietary (mineral) supplements and from sales of another product, however, such revenue is not expected to be a major contributor to revenue in the future. If we fail to commercialize our drug candidates as planned due to failures to complete clinical trials, obtain regulatory approval, conduct commercial scale manufacturing or for any other reason, we may experience significant delays or failure in generating revenue and realizing profit from the commercial sale of our drug candidates.

Further, we expect to incur significant costs in the future, in particular for the R&D and commercialization of our drug candidates. Our R&D expenses amounted to $15.2 million, $9.6 million and $6.6 million, respectively, in 2020, 2019 and 2018, respectively. As drug candidates presently undergoing preclinical research enter into the clinical trial stage, costs associated with such drug candidates may increase significantly. In the future, as we move more drug candidates into the clinical trial stage, conduct more clinical trials for commercialized products to broaden their use, and carries out commercial production of our drug candidates, the costs associated with such operations may increase significantly.

As we operate in the highly competitive pharmaceutical market, we compete to commercialize our drug candidates ahead of our competitors, putting us under pressure to incur R&D and other expenses with a potential negative impact on our short-term profitability. On the other hand, our commercialized drug candidates may fail to realize their sales potential as expected due to competition, insufficient market demand, product defects, or any other reason. Therefore, even after we start to generate revenue from the sales of our commercialized drug candidates in the future, we may still not be profitable for an extended period of time or at all.

We have incurred significant net losses and net operating cash outflows since our inception.

Investment in biopharmaceutical drug development is highly speculative. It entails substantial upfront capital expenditures and significant risk that a drug candidate might fail to gain regulatory approval or become commercially viable. We continue to incur significant expenses related to our ongoing operations. We have incurred substantial losses since our inception. During 2020, 2019 and 2018, we recorded a loss for the year of $19.3 million, $16.2 million and $11.7 million, respectively. As of December 31, 2020, we had an accumulated deficit of $153.6 million. For details, see *Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.* Substantially all of our operating losses have resulted from costs incurred in connection with our R&D programs and administrative expenses associated with our operations, and we expect that our R&D expenses will continue to increase in the future.

We expect to continue to incur losses for the foreseeable future, and we expect these losses to increase as we continue to expand our development of, and seeks regulatory approvals for, our drug candidates, and we continue to build up our commercialization and sales workforce in anticipation of the future roll-out of our late-stage drug candidates. Typically, it takes many years to develop one new drug from the drug discovery stage to the time it is available for treating patients. In addition, we will continue to incur costs associated with operating as a public company and in support of our growth as a development-stage or commercial-stage pharmaceutical company. The size of our future net losses will depend, in part, on the number and scope of our drug development programs and the associated costs of those programs, the cost of commercializing any approved products, our ability to generate revenues and the timing and amount of milestones and other payments we make or receive through arrangements with third parties. If any of our drug candidates fails in clinical trials or does not gain regulatory approval, or if approved, fails to achieve market acceptance, we may never become profitable. Our failure to become and remain profitable would decrease our value significantly and impair our ability to raise capital, maintain our R&D efforts, expand our business or continue our operations.

Our ability to continue as a going concern requires that we obtain sufficient funding to finance our operations, which may not be available on acceptable terms, or at all. A failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our drug development or commercialization efforts.

As of December 31, 2020, we had cash totaling $59.3 million and an accumulated deficit of $153.6 million. During 2020, we incurred a net loss totaling $19.3 million, and used cash in operating activities totaling $18.9 million. We expect to continue to incur losses and use cash in operating activities in 2021 and for the foreseeable future. We expect that the cash on hand as of December 31, 2020 will be sufficient to fund our operations for a period extending beyond twelve months from the date the consolidated financial statements are issued. For details, please see *Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations — Liquidity and Capital Resources*. Our ability to continue as a going concern requires that we obtain sufficient funding to finance our operations until our drug candidates begin generating sufficient revenue. As part of our ongoing business plans, we will continue seeking funding through equity financing and may seek debt financing or other capital sources. We may not be able to obtain financing on acceptable terms, or at all. The terms of any financing may adversely affect the holdings or the rights of our shareholders. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce or eliminate research and development programs and commercialization efforts. These factors, among others, may raise substantial doubt about our ability to continue as a going concern.

We have a limited operating history, which may make it difficult to evaluate our current business and predict our future performance.

We are a biopharmaceutical company formed in December 2012 focusing on the discovery and development of innovative drugs for the treatment of neurological diseases and other disorders. Our limited operating history, particularly in light of the rapidly evolving nanocrystal therapies field, may make it difficult to evaluate our current business and predict our future performance.

As a relatively new business, we have not yet demonstrated an ability to manufacture drugs at a commercial scale, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. We have not had any product approved for commercial sale and have not generated any revenue from product sales. Consequently, any assessment you make about our current business or future success or viability may not be as accurate as it could be if we had a longer operating history and had been able to reduce some of the uncertainties as set out above. Further, our limited financial track record, without any revenue yet from our expected future principal business, may be of limited reference value for your assessment of our business.

We may encounter difficulties in managing our growth and expanding our operations successfully.

As we seek to advance our drug candidates through clinical trials, we will need to expand our development, regulatory, compliance, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management. Our future financial performance and our ability to commercialize our drug candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train and integrate additional management, administrative, and sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successful growth and could harm our future business, financial condition and operating results.

Changes in government regulation or in practices relating to the pharmaceutical and biotechnology industries, including potential healthcare reform, could decrease the need for our drug candidates, or make it more difficult to obtain regulatory approvals for our drug candidates and commercialize them.

In recent years, the U.S. Congress, the President, executive branch agencies, and state legislatures have considered various types of healthcare reform to control growing healthcare costs. Similar reform movements have occurred in parts of Europe and Asia. Healthcare reform legislation could also increase the costs of drug development and commercialization that could limit the profits to be made from the development of new drugs. This could adversely affect R&D expenditures by pharmaceutical and biotechnology companies, which could in turn decrease the business opportunities available to us in the U.S. and other countries. We are unable to predict what reform proposals will be adopted in the future, if any.

If we, or any CRO we may engage, fails to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We and certain of the third parties we contract with, such as our contract research organizations, or CROs, are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment, and disposal of hazardous materials and wastes. In addition, our planned construction projects can only be put into operation after certain regulatory procedures have been completed with the relevant administrative authorities in charge of environmental protection, health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also may produce hazardous waste products at some future time. We generally contract with third parties for the disposal of these materials and wastes. We cannot entirely eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources.

Although we maintain workers' compensation insurance to cover the costs and expenses we may incur due to injuries to our employees resulting from the use of or exposure to hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage, use or disposal of biological or hazardous materials.

In addition, the environmental, health and safety laws and regulations applicable to us and our third-party contractors may change and impose stricter requirements in the future. As a result, we may be required to incur substantial costs to comply with future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our internal computer systems, or those used by any CRO or other contractors or consultants we may engage, may fail or suffer security breaches.

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses and unauthorized access. Although, to our knowledge, we have not experienced any material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and business operations.

In the ordinary course of our business, we collect and store sensitive data, including, among other things, legally protected patient health information, personally identifiable information about our employees, intellectual property, and proprietary business information. We manage and maintains our applications and data utilizing on-site systems and outsourced vendors. These applications and data encompass a wide variety of business-critical information including research and development information, commercial information, and business and financial information. Because information systems, networks and other technologies are critical to many of our operating activities, shutdowns or service disruptions of our systems or those of the vendors that provide information systems, networks or other services to us pose increasing risks. Such disruptions may be caused by events such as computer hacking, phishing attacks, ransomware, dissemination of computer viruses, worms and other destructive or disruptive software, denial of service attacks and other malicious activity, as well as power outages, natural disasters (including extreme weather), terrorist attacks or other similar events. Such events could have an adverse impact on us and our business, including loss of data and damage to equipment and data. In addition, system redundancy may be ineffective or inadequate, and our disaster recovery planning may not be sufficient to cover all eventualities. Significant events could result in a disruption of our operations, damage to our reputation or a loss of revenues. In addition, we may not have adequate insurance coverage to compensate for any losses associated with such events.

We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in our information systems and networks and those of our vendors, including personal information of our employees and patients, and company and vendor confidential data. In addition, outside parties may attempt to penetrate our systems or those of our vendors or fraudulently induce our personnel or the personnel of our vendors to disclose sensitive information in order to gain access to our data and/or systems. Like other companies, we have on occasion experienced, and will continue to experience, threats to our data and systems, including malicious codes and viruses, phishing and other cyber-attacks. The number and complexity of these threats continue to increase over time. If a material breach of our information technology systems or those of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks.

In addition, we could be subject to regulatory actions and/or claims made by individuals and/or groups in private litigation involving privacy issues related to data collection and use practices and other data privacy laws and regulations, including claims for misuse or inappropriate disclosure of data, as well as unfair or deceptive practices. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become increasingly sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely. As we outsource more of our information systems to vendors, engages in more electronic transactions with payers and patients and relies more on cloud-based information systems, the related security risks will increase and we will need to expend additional resources to protect our technology and information systems.

We manufacture all of our drug candidates ourselves, and intend to manufacture most, if not all, of any approved drugs ourselves as well.

We currently have manufacturing facilities in the U.S. and may build additional manufacturing facilities in other markets to expand our manufacturing capacity. These facilities may encounter unanticipated delays and expenses due to a number of factors, including regulatory requirements. If construction, regulatory evaluation, and/or approval of our new facilities is delayed, we may not be able to manufacture sufficient quantities of our drug candidates, if approved, which would limit our development and commercialization activities and our opportunities for growth. Cost overruns associated with constructing or maintaining our facilities could require us to raise additional funds from other sources, which may not be available on favorable terms or at all.

Much of the equipment used in our manufacturing process was developed and built by us, and it would be difficult or even impossible to purchase or create suitable replacements in a short period of time. Further, for much of this equipment we have an insufficient amount of or no spare parts available. Were certain equipment, some of which is critical to the production of our drug candidates, to become damaged, lost, or otherwise unusable, we would have to construct new parts, which could take a considerable time, causing a temporary halt to at least a portion of our production operations in the meantime. Further, we are constantly seeking to further fine-tune and develop our advanced manufacturing techniques and process controls to fully utilize our facilities. Advances in manufacturing techniques may render our facilities and equipment inadequate, in which case we may lose competitive advantage.

To produce our drug candidates in the quantities that we believe will be required to meet anticipated market demand, if approved, we will need to increase or "scale up" the production process by a significant factor over current levels of production. A significant part of the scaling up process will include seeking for ways to increase the automation and semi-automation of our production process, which will require additional research and development, investment, potential new regulatory approvals, and cooperation with third parties, some of which may not be successful. If we are unable or delayed in scaling up, or if the cost of doing so is not economically feasible for us, we may not be able to produce our approved drug candidates in a sufficient quantity to meet future demand.

Delays in completing and receiving regulatory approvals for our manufacturing facilities could delay our development plans or commercialization efforts.

Our manufacturing facilities will be subject to ongoing, periodic inspection by various regulatory authorities, including the U.S. Food and Drug Administration ("**FDA**"), European Medicines Agency ("**EMA**"), China's National Medical Products Administration ("**NMPA**"), Health Canada, and the Australian Therapeutics Goods Administration ("**TGA**") or other comparable regulatory agencies to ensure compliance with good manufacturing practices ("**GMP**"). Our failure to follow and document our adherence to such GMP or other regulatory requirements may lead to significant delays in the availability of products for clinical or, in the future, commercial use, and may result in the termination of or a hold on a clinical trial, or may delay or prevent filing or approval of marketing applications for our drug candidates or the commercialization of our drugs, if approved. We also may encounter problems with the following:

- achieving adequate or clinical-grade materials that meet FDA, EMA, NMPA, Health Canada, TGA or other comparable regulatory agency standards or specifications with consistent and acceptable production yield and costs;
- shortages of qualified personnel, raw materials or key contractors; and
- ongoing compliance with GMP and other requirements of the FDA, EMA, NMPA, TGA or other comparable regulatory agencies.

Failure to comply with applicable regulations could also result in sanctions being imposed on us, including fines, injunctions, civil penalties, a requirement to suspend or put on hold one or more of our clinical trials, failure of regulatory authorities to grant marketing approval of our drug candidates, delays, suspension or withdrawal of approvals, supply disruptions, license revocation, seizures, or recalls of our drug candidates, operating restrictions and civil or criminal prosecutions, any of which could harm our business.

Damage to, destruction of or interruption of production at our manufacturing facilities would negatively affect our business and prospects.

If our manufacturing facilities or the equipment in them is damaged or destroyed, we may not be able to quickly or inexpensively replace our manufacturing capacity or replace it at all. In the event of a temporary or protracted loss of the facilities or equipment, we might not be able to transfer manufacturing to a third party. Even if we could transfer manufacturing to a third party, the shift would likely be expensive and time-consuming, particularly since the new facility would need to comply with the necessary regulatory requirements and we would need regulatory agency approval before selling any of our future approved drugs manufactured at that new facility. Such an event could delay our clinical trials or reduce our product sales if and when we are able to commercialize one or more of our drug candidates. Any interruption in manufacturing operations at our manufacturing facilities could result in our inability to satisfy the demands of our clinical trials or commercialization. Any disruption that impedes our ability to manufacture our drugs in a timely manner could materially harm our business, financial condition and operating results.

Currently, we maintain insurance coverage against damage to our property and equipment in amounts we believe are reasonable. However, our insurance coverage may not reimburse us, or may not be sufficient to reimburse us, for any expenses or losses we may suffer. We may be unable to meet the requirements for our drugs if there were a catastrophic event or failure of our manufacturing facilities or processes.

Our future success depends on our ability to retain key executives and to attract, train, retain and motivate qualified and highly skilled personnel.

We are highly dependent on Mark Mortenson, our co-founder and chief science officer, Rob Etherington, CEO, President and a Director, and the other principal members of our management and scientific teams. Although we have formal employment agreements with select executive officers, these agreements do not prevent our executives from terminating their employment with us at any time. Further, Mr. Etherington and Mr. Mortenson have not entered into formal employment agreements with us. We do not maintain “key person” insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, technical, clinical, and manufacturing and sales and marketing personnel in the future will also be critical to our success. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our discovery, clinical development, operations, and commercialization strategy. The loss of the services of our executive officers or other key employees and consultants could impede the achievement of our research, development, and commercialization objectives and seriously harm our ability to successfully implement our business strategy.

We benefit from certain tax and financial incentives, the expiration of or changes to which could adversely affect our profitability.

We benefit from certain tax treatments, as well as tax concessions in relation to our research and development costs. We receive refundable tax credits through the R&D tax credits in the United States, Australia, and the state of Maryland. In the United States, the R&D credit is used to offset federal employment taxes on our United States payroll. In Australia, we receive a refundable tax offset of 43.5% of R&D deductions. In Maryland, we receive the Basic Research and Development Tax credit of 3% of the lesser of eligible R&D expenses and the Maryland Base Amount, which is used to offset state income taxes and may be applied against following years’ taxes until the credit is used or the credit may be carried forward for seven years. We also receive a tax exemption in Maryland for state personal property and sales tax, as well as the Maryland enterprise zone hiring and job creation tax credits.

In addition, current or future tax treatments, tax concessions, tax allowances and financial incentives applicable to us may be changed, terminated, or otherwise become unavailable due to many factors, including changes in government policy or administrative decisions by the relevant government authorities. Due to potential changes in government policies, we cannot be certain of the level of government grants we will receive in the future. Our post-tax profitability and cash flows may be adversely affected as a result of one or more of these or other factors.

Our financial position and operations may be adversely affected by the COVID-19 outbreak.

An outbreak of the respiratory illness COVID-19 caused by a strain of novel coronavirus, SARS-Cov-2, has spread worldwide, causing many governments to implement measures to slow the spread of the outbreak through quarantines, strict travel restrictions, heightened border scrutiny, and other measures. The outbreak and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce. The future progression of the outbreak and its effects on our business and operations are uncertain.

We and our CROs and clinical sites may experience disruptions in supply of drug candidates and/or procuring items that are essential for our research and development activities, including raw materials used in the manufacturing of our drug candidates, medical and laboratory supplies used in our clinical trials or preclinical studies or animals that are used for preclinical testing, in each case, for which there may be shortages because of ongoing efforts to address the outbreak. Any disruption in the supply chain from the recent COVID-19 outbreak, or any potential future outbreak could have a material adverse effect on our clinical trial plans and business operations.

Additionally, we have enrolled, and will seek to enroll, patients in our clinical trials at sites located in many areas affected by COVID-19 and, as a result, our trials may be impacted. In addition, even if sites are actively recruiting, we may face difficulties recruiting or retaining patients in our ongoing and planned clinical trials if patients are affected by the virus or are fearful of visiting or traveling to clinical trial sites because of the outbreak. Prolonged delays or closure to enrollment in our trials or patient discontinuations could have a material adverse impact on our clinical trial plans and timelines.

The response to the COVID-19 pandemic may redirect resources with respect to regulatory and intellectual property matters in a way that would adversely affect our ability to obtain regulatory approvals and protect our intellectual property. In addition, we may face impediments to regulatory meetings and approvals due to measures intended to limit in-person interactions.

Any negative impact that the COVID-19 outbreak has on the ability of our suppliers to provide materials for our drug candidates or on recruiting or retaining patients in our clinical trials or our ability to collect patient data could cause costly delays to clinical trial activities, which could adversely affect our ability to obtain regulatory approval for and to commercialize our drug candidates, increase our operating expenses, and have a material adverse effect on our financial results.

The COVID-19 pandemic has significantly impacted economies worldwide, which could result in adverse effects on our business and operations. We cannot be certain what the overall impact of the COVID-19 pandemic will be on our business. It has the potential to adversely affect our business, financial condition, results of operations, and prospects.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the SEC and the Nasdaq Global Market have imposed various requirements on public companies, including establishing and maintaining effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance.

We have identified material weaknesses in our internal control over financial reporting. If we fail to remediate the material weakness, or if we experience additional material weaknesses in the future or otherwise fails to maintain an effective system of internal controls in the future, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect investor confidence in us and, as a result, the value of our Common Stock.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. In addition, any testing by us, as and when required, conducted in connection with Section 404 of the Sarbanes-Oxley Act or any subsequent testing by our independent registered public accounting firm, as and when required, may reveal deficiencies in our internal control over financial reporting that are deemed to be significant deficiencies or material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our Common Stock.

In connection with the audit of our financial statements for the year ended December 31, 2020, 2019 and 2018, our management identified material weaknesses in our internal control over financial reporting. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. The material weaknesses identified relate to the fact that we did not design or maintain an effective control environment commensurate with our financial reporting requirements, including (a) lack of a sufficient number of trained professionals with an appropriate level of accounting knowledge, training and experience to appropriately analyze, record and disclose accounting matters timely and accurately, and (b) lack of structures, reporting lines and appropriate authorities and responsibilities to achieve financial reporting objectives. This deficiency in our control environment contributed to the following additional deficiencies (each of which individually represents a material weakness) in our internal control over financial reporting.

- we did not design and maintain formal accounting policies, procedures and controls to achieve complete, accurate and timely financial accounting, reporting and disclosures, including controls over the preparation and review of account reconciliations and journal entries;

- we did not design and maintain effective controls over segregation of duties related to manual journal entries. Specifically, certain personnel have the ability to both prepare and post manual journal entries without an independent review by someone without the ability to prepare and post manual journal entries;

- we did not design and maintain formal accounting policies, processes and controls to analyze, account for and disclose complex transactions. Specifically, we did not design and maintain controls to analyze, account for and disclose warrants to purchase preferred stock and convertible promissory notes with embedded derivatives, including ensuring complete and accurate data was used in the valuations; and

- we did not design and maintain effective controls over certain information technology general controls for IT systems that are relevant to the preparation of the financial statements. Specifically, we did not design and maintain: (a) user access controls to ensure appropriate segregation of duties and that adequately restrict user and privileged access to financial applications, programs, and data to appropriate personnel, (b) program change management controls to ensure that IT program and data changes affecting financial IT applications and underlying accounting records are identified, tested, authorized and implemented appropriately, (c) computer operations controls to ensure that data backups are authorized and monitored, and (d) testing and approval controls for program development to ensure that new software development is aligned with business and IT requirements.

The control deficiencies identified resulted in the misstatement of our redeemable convertible preferred stock warrant liability, accrued liabilities, general and administrative expenses, Australian research and development credit, and amounts and classification within our statement of cash flows and related financial disclosures, which led to a restatement of our 2017 financial statements. Additionally, each of the control deficiencies described above could result in a misstatement of one or more account balances or disclosures that would result in a material misstatement to the annual or interim consolidated financial statements that would not be prevented or detected. Accordingly, our management has determined that each of the control deficiencies described above constitute a material weakness.

To remedy the identified material weaknesses, we have implemented and continue to implement, several measures, including, among others:

- hiring additional competent and qualified accounting and reporting personnel with appropriate knowledge and experience of U.S. GAAP and SEC financial reporting requirements;

- establishing and designing internal financial reporting structures and authorizing certain departments or capable and responsible persons to be in charge of the overall financial management and financial objectives;

- establishing an ongoing program to provide sufficient additional training to our accounting staff, especially training related to U.S. GAAP and SEC financial reporting requirements;

- designing and preparing accounting policies in accordance with relevant rules, especially in relation to complex and major transactions;

- updating our internal staff manual and ensuring effective segregation of duties for our accounting staff in relation to manual journal entries; and

- upgrading our internal IT systems to facilitate financial management and reporting procedures.

Although we have begun to implement measures to address the material weaknesses, the implementation of these measures may not fully address the material weaknesses and deficiencies in our internal control over financial reporting, and we cannot conclude that these matters have been fully remedied. Further, in the future we may determine that we have additional material weaknesses. Our failure to remediate the material weaknesses or failure to identify and address any other material weaknesses or control deficiencies could result in inaccuracies in our financial statements and could also impair our ability to comply with applicable financial reporting requirements and related regulatory filings on a timely basis, which could cause investors to lose confidence in our reported financial information, which may result in volatility in and a decline in the market price of our securities.

Pursuant to Section 404, after the Reverse Recapitalization, we, as the surviving entity, are required to furnish a report by our management on the effectiveness of our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

There is significant uncertainty associated with our drug candidates and their viability as a commercial product.

Metallic nanocrystal therapeutic candidates, such as our lead product, CNM-Au8, are considered emerging and novel investigational products for the potential treatment of neurological diseases and other disorders. We are developing CNM-Au8 for the treatment of neurological disorders such as MS, ALS, and PD through remyelination and/or neuroprotection mechanisms related to catalysis of certain biological reactions. There are currently no approved remyelination therapies and the evidence for an effect of neuroprotection treatments on these indications is thus far limited. Since there is limited clinical trial data and precedent for the development of nanocrystal therapies that promote remyelination and neuroprotection to treat these indications, there is a substantial risk that the design or outcomes of our clinical trials will not be satisfactory to support regulatory approval. In addition, there are generally limited or no regulatory precedents concerning metallic nanocrystal drug marketing authorization, or a regulatory framework to appropriately differentiate approved nanocrystal product labeling. Our lead metallic nanocrystal drug candidate, CNM-Au8, contains nanocrystals made entirely of high purity gold alone. It is unclear how regulatory authorities will identify or classify the active moiety of CNM-Au8, including whether it is classified as a new chemical entity or comparable designation. The inability to obtain sufficiently differentiated active moiety classification from gold generically could potential limit CNM-Au8 and our drug candidates from ever achieving profitability.

Moreover, the mechanisms of action for nanocrystal therapies are not thoroughly understood, and adverse events or side effects may be observed in clinical studies and reported by medical practitioners in connection with patient usage in the future. If those adverse events or side effects prove significant, they may hamper the ability of our drug candidates to pass through clinical trials or they may outweigh the benefits that patients derive from using our drug candidates, both of which could potentially prevent our drug candidates from ever achieving profitability.

Our drug candidates are not metabolized and may accumulate in the body following long-term usage, making the long-term effects of taking our drug candidates for substantial periods of time uncertain. While all of the current toxicology studies of our drug candidates have resulted in no-adverse-effect levels as the date of this Annual Report, we have not completed reproductive or carcinogenicity studies, which we are required to complete in the future. Any negative results from these studies could materially and adversely affect our business, results of operations, financial condition and prospects.

Moreover, the results of clinical trials for nanocrystal therapies could reveal a high and unacceptable severity and prevalence of undesirable side effects. Any such side effects could adversely impact our ability to obtain regulatory approvals. For example, the FDA, NMPA, TGA, EMA or other comparable authorities could order us to suspend or terminate our studies or to cease further clinical development of or deny approval of our drug candidates. In addition, any adverse drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete trials or may result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

We have not previously obtained any regulatory approval for a drug candidate and we may be unable to obtain, or may be delayed in obtaining regulatory approval for any of our drug candidates.

Our business is substantially dependent on our ability to complete the development of, obtain regulatory approval for and successfully commercialize drug candidates in a timely manner. We cannot commercialize drug candidates without obtaining regulatory approval to market each drug from the FDA, NMPA, Health Canada, TGA, EMA and other comparable regulatory authorities. The time required to obtain approval from regulatory authorities is unpredictable but typically takes years following the commencement of pre-clinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a drug candidate's clinical development and may vary among jurisdictions.

Our drug candidates could fail to receive regulatory approval for many reasons, including:

- failure to begin or complete clinical trials due to disagreements with regulatory authorities;
- failure to begin or complete clinical trials due to inability to recruit sufficient numbers of study participants;
- failure to demonstrate that a drug candidate is safe and effective or is safe, pure and potent for our proposed indication;
- failure of clinical trial results to meet the level of statistical significance required for approval;
- data integrity issues related to our clinical trials;
- disagreement with our interpretation of data from preclinical studies or clinical trials;
- changes in approval policies or regulations that render our preclinical and clinical data insufficient for approval or require us to amend our clinical trial protocols;
- regulatory requests for additional analysis, reports, data, nonclinical studies and clinical trials, or questions regarding interpretations of data and results and the emergence of new information regarding our drug candidates;
- insufficient data from the clinical trials of our drug candidates to obtain regulatory approval;
- failure by us or our investigators to conduct a clinical trial in accordance with regulatory requirements or our clinical trial protocols; and
- clinical sites, investigators or other participants in our clinical trials deviating from a trial protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial.

The FDA, NMPA, TGA, EMA or a comparable regulatory authority may require more information, including additional preclinical or clinical data, to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program.

New or unexpected adverse events, or changes in regulatory requirements and guidance may also occur, and we may need to amend clinical trial protocols submitted to applicable regulatory authorities to reflect these changes. Amendments may require us to resubmit clinical trial protocols to institutional review boards ("**IRBs**") or human research ethics committees ("**HREC**") for re-examination, which may impact the costs, timing or successful completion of a clinical trial.

If we experience delays in the completion of, or the termination of, a clinical trial of any of our drug candidates, the commercial prospects of that drug candidate will be harmed, and our ability to generate product sales revenues from any of those drug candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our drug candidate development and approval process, and jeopardize our ability to commence product sales and generate related revenues for that product. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our drug candidates.

We may not be able to successfully identify, discover, develop or in-license new drug candidates.

We cannot guarantee that we will be successful in identifying potential drug candidates for clinical development for a number of reasons. For example, our research methodology may be unsuccessful in identifying potential drug candidates or those we identify may be shown to have harmful side effects or other characteristics that make them unmarketable or unlikely to receive regulatory approval. we have devoted significant resources to discovery efforts through our proprietary electro-crystal-chemistry drug development platform, and we cannot guarantee that we will be successful in identifying additional potential drug candidates, or that we will be able to successfully identify and in-license new drug candidates with high potential from other parties.

Research programs to pursue the development of our drug candidates for additional indications and to identify new drug candidates and drug targets require substantial technical, financial, and human resources. our research programs may initially show promise in identifying potential indications and/or drug candidates, yet fail to yield results for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential indications, and/or drug candidates;
- potential drug candidates may, after further study, be shown to have harmful adverse effects or other characteristics that indicate they are unlikely to be effective drugs; or
- it may take greater human and financial resources to identify additional therapeutic opportunities for our drug candidates or to develop suitable potential drug candidates through internal research programs than we will possess, thereby limiting our ability to diversify and expand our drug portfolio.

Accordingly, there is no assurance that we will ever be able to identify additional therapeutic opportunities for our drug candidates or to develop suitable potential drug candidates through internal research programs, which could materially and adversely affect our future growth and prospects. we may focus our efforts and resources on potential drug candidates or other potential programs that ultimately prove to be unsuccessful.

Pre-clinical and clinical development of drug candidates involves a lengthy and expensive process with an uncertain outcome, and we are unable to predict if or when we will successfully develop or commercialize any of our drug candidates.

There is a risk of failure for each of our drug candidates. It is difficult to predict when or if any of our drug candidates will prove effective and safe in humans or will receive regulatory approval. Before obtaining regulatory approval from regulatory authorities for the sale of any of our drug candidates, we must complete pre-clinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. our internal discovery programs for some of our drug candidates are at an early stage of development and will require significant investment and regulatory approvals prior to commercialization. We are not permitted to market or promote any of our drug candidates until we receive regulatory approval from the FDA, NMPA, TGA, EMA or comparable regulatory authorities, and we may never receive such regulatory approval for any of our drug candidates.

We could encounter regulatory delays if a clinical trial is suspended or terminated by us or, as applicable, by the institutional review boards or the ethics committees of the institutions in which such trials are being conducted, by the data safety monitoring board, which is an independent group of experts that is formed to monitor clinical trials while ongoing, or by the FDA, NMPA, TGA, EMA or other regulatory authorities. Such authorities may impose a suspension or termination due to a number of factors, including: a failure to conduct the clinical trial in accordance with regulatory requirements or the applicable clinical protocols, inspection of the clinical trial operations or trial site by the FDA, NMPA, TGA, EMA or other regulatory authorities that results in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions, or lack of adequate funding to continue the clinical trial. Many of the factors that cause a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our drug candidates. Further, the FDA, NMPA, TGA, EMA or other regulatory authorities may disagree with our clinical trial design or our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials.

Pre-clinical studies and clinical trials are expensive, difficult to design and implement, and can take many years to complete. Moreover, pre-clinical and clinical data are often susceptible to varying interpretations and analysis, and many companies that have believed their drug candidates performed satisfactorily in pre-clinical studies and clinical trials have nonetheless failed to obtain regulatory approval of their drug candidates. Future clinical trials of our drug candidates may not be successful.

Commencement of clinical trials is subject to finalizing the trial design based on ongoing discussions with the FDA, NMPA, TGA, EMA and/or other regulatory authorities. The FDA, NMPA, TGA, EMA and other regulatory authorities could change their position on the acceptability of trial designs or clinical endpoints, which could require us to complete additional clinical trials or impose approval conditions that we do not currently expect. Successful completion of our clinical trials is a prerequisite to submitting an NDA (or analogous filing) to the FDA, NMPA, TGA, EMA and/or other regulatory authorities for each drug candidate and, consequently, the ultimate approval and commercial marketing of our drug candidates. We do not know whether the clinical trials for our drug candidates will be completed on schedule, if at all.

Results of earlier clinical trials may not be predictive of results of later-stage clinical trials.

The results of pre-clinical studies and early clinical trials of our drug candidates may not be predictive of the results of later-stage clinical trials. Drug candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through pre-clinical studies and initial clinical trials. Future clinical trial results may not be favorable for these and other reasons.

In some cases, there can be significant variability in the safety and/or efficacy results between different trials of the same drug candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, including genetic differences, patient adherence to the dosing regimen, and the rate of dropout among clinical trial participants. As drug candidates are developed through pre-clinical to early- to late-stage clinical trials towards approval and commercialization, it is customary that various aspects of the development program, such as manufacturing and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. In the case of any trials we conduct, results may differ from earlier trials due to the larger number of clinical trial sites and additional countries and languages involved in such trials. Any of these changes could make the results of planned clinical trials or other future clinical trials we may initiate less predictable and could cause our drug candidates to perform differently, which could delay completion of clinical trials, delay approval of our drug candidates, and/or jeopardize our ability to commence commercialization of our drug candidates.

Clinical trials of our drug candidates may fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities, or may not otherwise produce positive results, which may cause us to incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our drug candidates.

Before obtaining regulatory approval for the sale of our drug candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. We may experience numerous unexpected events during, or as a result of, clinical trials that could delay or prevent us from receiving regulatory approval or commercializing our drug candidates, including:

- regulators, IRBs, or HRECs may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

- our inability to reach agreements on acceptable terms with prospective CROs, clinical trial vendors, and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

- manufacturing issues, including problems with manufacturing, supply quality, compliance with GMP, or obtaining from third parties sufficient quantities of a drug candidate for use in a clinical trial;

- clinical trials of our drug candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon drug development programs;

- the number of patients required for clinical trials of our drug candidates may be larger than we anticipate;

- our third-party contractors, including clinical investigators, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

- we may not investigate, may not be able to license, or may be unable to properly conduct companion diagnostic tests to identify patients who are likely to benefit from treatment with our drug candidates;

- we might have to suspend or terminate clinical trials of our drug candidates for various reasons, including a finding of a lack of clinical response or other unexpected characteristics or a finding that participants are being exposed to unacceptable health risks;

- regulators, IRBs or HRECs may require that we or our investigators suspend or terminate clinical research or not rely on the results of clinical research for various reasons, including non-compliance with regulatory requirements;

- the cost of clinical trials of our drug candidates may be greater than we anticipate;

- the supply or quality of our drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be insufficient or inadequate; and

- our drug candidates may have undesirable side effects or unexpected characteristics, causing us or our investigators, regulators, institutional review boards or ethics committees to suspend or terminate the clinical trials, or reports may arise from pre-clinical studies or clinical trials of other therapies that raise safety or efficacy concerns about our drug candidates.

If we are required to conduct additional clinical trials or other testing of our drug candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our drug candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if they raise safety concerns, we may (i) be delayed in obtaining regulatory approval for our drug candidates; (ii) not obtain regulatory approval at all; (iii) obtain approval for indications that are not as broad as intended; (iv) have the drug removed from the market after obtaining regulatory approval; (v) be subject to additional post-marketing testing requirements; (vi) be subject to restrictions on how the drug is distributed or used; or (vii) be unable to obtain reimbursement for use of the drug.

Significant clinical trial delays may also increase our development costs and could shorten any periods during which we have the exclusive right to commercialize our drug candidates or allow our competitors to bring drugs to market before we do. This could impair our ability to commercialize our drug candidates and may harm our business and results of operations.

If we encounter difficulties enrolling patients in clinical trials, clinical trials of our drug candidates may be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until our conclusion. we may experience difficulties in patient enrollment in our clinical trials for a variety of reasons, including:

- the size and nature of the patient population;

- the design of the trial, including the patient eligibility criteria defined in the protocol;

- the size of the study population required for analysis of the trial’s primary endpoints;

- the proximity of patients to trial sites;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- competing clinical trials for similar therapies or other new therapeutics;
- clinicians' and patients' perceptions as to the potential advantages and side effects of the drug candidate being studied in relation to other available therapies, including any new drugs or treatments that may be approved for the indications we are investigating;
- our ability to obtain and maintain patient consents;
- the risk that patients enrolled in clinical trials will not complete a clinical trial; and
- the availability of approved therapies that are similar in mechanism to our drug candidates.

Failure of our timely completion of clinical trials would delay the approval and commercialization of our drug candidates, impair the commercial performance of our drug candidates, and consequently harm our business and results of operations.

If we are not able to obtain, or experiences delays in obtaining, required regulatory approvals, we will not be able to commercialize our drug candidates, and our ability to generate revenue will be materially impaired.

Before obtaining regulatory approvals for the commercial sale of any drug candidate for a target indication, we must demonstrate in preclinical studies and well-controlled clinical trials, and, with respect to approval in the U.S., to the satisfaction of the FDA, that the drug candidate is safe and effective for use for that target indication and that the manufacturing facilities, processes and controls are adequate. In addition to preclinical and clinical data, the New Drug Application ("**NDA**") must include significant information regarding the chemistry, manufacturing, and controls for the drug candidate. Obtaining approval of an NDA is a lengthy, expensive and uncertain process, and approval may not be obtained. After we submits an NDA to the FDA, the FDA decides whether to accept or reject the submission for filing. We cannot be certain that any submissions will be accepted for filing and review by the FDA.

We have not yet demonstrated an ability to file for or receive regulatory approval for our drug candidates. For example, we do not have experience in preparing the required materials for regulatory submission or navigating the regulatory approval process. As a result, our ability to successfully submit an NDA and obtain regulatory approval for our drug candidates may involve more inherent risk, take longer, and cost more than it would if we were a company with experience in obtaining regulatory approvals.

Regulatory authorities outside of the U.S., such as the NMPA and EMA, also have requirements for approval of drugs for commercial sale with which we must comply prior to marketing in those areas. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our drug candidates. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and obtaining regulatory approval in one country does not mean that regulatory approval will be obtained in any other country.

Approval processes vary among countries and can involve additional product testing and validation, and additional administrative review periods. Seeking non-U.S. regulatory approval could require additional nonclinical studies or clinical trials, which could be costly and time consuming. The non-U.S. regulatory approval process may include all of the risks associated with obtaining FDA approval. For all of these reasons, we may not obtain non-U.S. regulatory approvals on a timely basis, if at all.

The process to develop, obtain regulatory approval for and commercialize drug candidates is long, complex and costly both inside and outside the United States, and approval is never guaranteed. Even if our drug candidates were to successfully obtain approval from the regulatory authorities, any approval might significantly limit the approved indications for use, or require that precautions, contraindications or warnings be included on the product labeling, or require expensive and time-consuming post-approval clinical trials or surveillance as conditions of approval. Following any approval for commercial sale of our drug candidates, certain changes to the drug, such as changes in manufacturing processes and additional labeling claims, may be subject to additional review and approval by the FDA, NMPA, TGA, EMA and comparable regulatory authorities. Also, regulatory approval for any of our drug candidates may be withdrawn. If we are unable to obtain regulatory approval for our drug candidates in one or more jurisdictions, or any approval contains significant limitations, our target market will be reduced and our ability to realize the full market potential of our drug candidates will be harmed. Furthermore, we may not be able to obtain sufficient funding or generate sufficient revenue and cash flows to continue the development of any other drug candidate in the future.

Favorable designations may not be granted, or if granted, be withdrawn later, for any of our drug candidates, and may not lead to faster development or regulatory review or approval.

We do not currently have Fast Track Designation or, Breakthrough Therapy Designation, but may seek one or more of such designations in the future.

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 need for that condition, the drug sponsor may apply for FDA Fast Track Designation. The FDA has broad discretion whether or not to grant this designation. Even if we believe a particular drug candidate is eligible for this designation, we cannot assure that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a development, review or approval process faster than conventional FDA procedures. The FDA may withdraw a Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Many drugs that have received Fast Track Designation have failed to obtain approval from the FDA.

A Breakthrough Therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor can help to identify the most efficient path for development.

Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe, after completing early clinical trials, that one of our drug candidates meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead decide not to grant that designation. In any event, the receipt of a Breakthrough Therapy Designation for a drug candidate may not result in a faster development, review or approval process compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our drug candidates qualify as Breakthrough Therapies, the FDA may later decide that such drug candidates no longer meet the conditions for qualification.

The U.S. FDA granted orphan drug development status to our lead drug candidate, CNM-Au8, for the treatment of ALS in May 2019. Regulatory authorities in some jurisdictions, including the U.S. and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a disease with a patient population of fewer than 200,000 individuals in the U.S., or that affects more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that costs of research and development of the product for the indication can be recovered by sales of the product in the U.S. Generally, if a drug with an orphan drug designation subsequently receives the first regulatory approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the FDA or EMA, from approving another marketing application for the same drug for the same indication during the period of exclusivity. The applicable period is seven years in the United States and 10 years in the European Union. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or the EMA 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.

Although we have obtained orphan drug exclusivity for CNM-Au8 for the treatment of ALS in the U.S., and may obtain the same exclusivity for other drug candidates or indication, that exclusivity may not effectively protect the drug candidate from competition because different drugs can be approved for the same condition and the same drugs can be approved for a different condition but used off-label for any orphan indication we may obtain. Even after an orphan drug is approved, the FDA can subsequently approve a drug that is otherwise the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective, or makes a major contribution to patient care.

Any of our future approved drug candidates will be subject to ongoing or additional regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experiences unanticipated problems with our drug candidates.

Any of our future approved drug candidates will be subject to ongoing or additional regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the U.S. and requirements of comparable regulatory authorities in European Union, China, Australia and other markets.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA, NMPA, TGA, EMA and other comparable regulatory authority requirements ensuring that quality control and manufacturing procedures conform to GMP. As such, we will be subject to continual review and inspections to assess compliance with GMP and adherence to commitments made in any NDA, other marketing application, and previous responses to any inspection observations if we were to build manufacturing facilities in the future. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

Any approvals that we receive for our drug candidates may be subject to limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, which could adversely affect the drug's commercial potential or contain requirements for potentially costly post-marketing testing and surveillance to monitor the safety and efficacy of the drug candidate. The FDA, NMPA, TGA, EMA or a comparable regulatory authority may also require a risk evaluation mitigation strategy program as a condition of approval of our drug candidates or following approval. In addition, if the FDA, NMPA, TGA, EMA or a comparable regulatory authority approves our drug candidates, we will have to comply with requirements, including, for example, submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with GMP and good clinical practice GCP, for any clinical trials that we conduct post-approval.

The FDA and other regulatory authorities strictly regulate the marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for their approved indications and for use in accordance with the provisions of the approved label. The FDA, NMPA, TGA, EMA and other regulatory authorities 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.

Even if we are able to commercialize any approved drug candidates, the drugs may become subject to national or other third-party reimbursement practices or unfavorable pricing regulations, which could harm our business.

The regulations that govern regulatory approvals, pricing and reimbursement for new therapeutic products vary widely from country to country. In Europe, Canada, Australia, China, and some markets outside China, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a drug in a particular country, but then be subject to price regulations that delay our commercial launch of the drug and negatively impact our revenues.

Our ability to commercialize any approved drug candidates successfully also will depend in part on the extent to which reimbursement for these drugs and related treatments will be available from government health administration authorities, private health insurers, and other organizations.

A primary trend in the global healthcare industry is cost containment. Government authorities and these third-party payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications.

In the U.S., no uniform policy of coverage and reimbursement for drugs exists among third-party payers. As a result, obtaining coverage and reimbursement approval of a drug from a government or other third-party payer is a time-consuming and costly process that could require us to provide to each payer supporting scientific, clinical, and cost-effectiveness data for the use of our future approved drugs on a payer-by-payer basis, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given drug, the resulting reimbursement rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Additionally, third-party payers may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of our future approved drug candidates. Patients are unlikely to use any of our future approved drugs unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of the drug. Because some of our drug candidates may have a higher cost of goods than conventional small molecule therapies, and may require long-term follow-up evaluations, the risk that coverage and reimbursement rates may be inadequate for us to achieve profitability may be greater.

Increasingly, third-party payers are requiring that companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot assure that reimbursement will be available for any approved drug candidate that we commercializes and, if reimbursement is available, what the level of reimbursement will be. Reimbursement may impact the demand for, or the price of, any approved drug candidate that we commercialize. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any drug candidate that it successfully develops.

There may be significant delays in obtaining reimbursement for approved drug candidates, and coverage may be more limited than the purposes for which the drug candidates are approved by the FDA, NMPA, TGA, EMA or other comparable regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Payment rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on payments allowed for lower cost drugs that are already reimbursed, and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payers and by any future weakening of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payers for any future approved drug candidates and any new drugs that we develop could have a material adverse effect on our business, operating results and overall financial condition.

We intend to seek approval alone or in conjunction with partners to market our drug candidates in the U.S., China, European Union, Australia, Canada, and other jurisdictions. In China, Australia, Canada, and the European Union, the pricing of drugs is subject to governmental control, and it can take considerable time after obtaining marketing regulatory approval to get the future approved drugs reimbursed. Market acceptance and sales of any of our future approved drug candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payers for drugs and may be affected by existing and future healthcare reform measures.

Our drug candidates approved in the future may fail to achieve the degree of market acceptance by physicians, patients, third-party payers and others in the medical community necessary for commercial success and the market opportunity for the drug candidate may be smaller than we estimate.

Our future approved drug candidates may fail to gain sufficient market acceptance by physicians, patients, third-party payers and others in the medical community. For example, current multiple sclerosis treatments are well established in the medical community, and physicians may continue to rely on these treatments to the exclusion of our drug candidates that are in clinical trials for the same or similar indications. In addition, physicians, patients, and third-party payers may prefer other novel products to ours. If our drug candidates do not achieve an adequate level of acceptance, we may not generate significant product sales revenues and we may not become profitable. The degree of market acceptance of our drug candidates, if approved for commercial sale, will depend on a number of factors, including:

- the clinical indications for which our drug candidates are approved;
- whether physicians, hospitals, treatment centers and patients consider our drug candidates as a safe and effective treatment;
- the potential and perceived advantages of our drug candidates over alternative treatments;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of regulatory authorities;
- limitations or warnings contained in the labeling approved by regulatory authorities;
- the timing of market introduction of our drug candidates as well as competitive drugs;
- the cost of treatment in relation to alternative treatments;
- the availability of adequate coverage, reimbursement and pricing by third-party payers and government authorities;

- the willingness of patients to pay out-of-pocket in the absence of coverage and reimbursement by third-party payers and government authorities; and

- the effectiveness of our sales and marketing efforts.

If any approved drug candidates that we commercialize fail to achieve market acceptance among physicians, patients, hospitals, treatment centers or others in the medical community, we will not be able to generate significant revenue. Even if our future approved drug candidates achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our drug candidates, are more cost-effective or render our drug candidates obsolete.

If our drug candidates cause, or are perceived to cause, undesirable side effects, it can result in delays or failure to receive regulatory approval or limitations on the commercial profile of an approved label.

Undesirable side effects caused by our drug candidates could cause either us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, NMPA, TGA, EMA or other regulatory authorities. If the results of the ongoing clinical trials of our drug candidates reveal a high and unacceptable severity and prevalence of undesirable side effects, the clinical trials of our drug candidates could be suspended or terminated and the FDA, NMPA, TGA, EMA or comparable regulatory authorities could order us to cease further development of or deny approval of our drug candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the clinical trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Clinical trials assess a sample of the potential patient population. With a limited number of patients and a limited duration of exposure, rare and severe side effects of our drug candidates may only be uncovered with a significantly larger number of patients exposed to the drug candidates. If our drug candidates receive regulatory approval and we or others discover undesirable side effects caused by such drugs (or any other similar drugs) or that such drug candidates are less effective than previously believed, a number of potentially significant negative consequences could result, including:

- the FDA, NMPA, TGA, EMA or other comparable regulatory authorities may withdraw or limit their approval of such drug candidates;

- the FDA, NMPA, TGA, EMA or other comparable regulatory authorities may require the addition of labeling statements, such as a “boxed” warning or a contra-indication;

- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;

- we may be required to change the way such drug candidates are distributed or administered, conduct additional clinical trials or change the labeling of our drug candidates;

- the FDA, NMPA, TGA, EMA or other comparable regulatory authorities may require the development of risk evaluation and mitigation strategies and plans to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;

- we may be subject to regulatory investigations and government enforcement actions;

- we may decide to remove such drug candidates from the marketplace;

- we could be sued and held liable for injury caused to individuals exposed to or taking our drugs; and

- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected drug candidates and could substantially increase the costs of commercializing our drugs, if approved, and significantly impact our ability to successfully commercialize our drugs and generate revenue.

Adverse drug reactions and negative results from off-label use of our products could materially harm our business reputation, product brand name, financial condition and expose us to liability.

Products distributed or sold in the pharmaceutical market may be subject to off-label drug use. Off-label drug use is prescribing a product for an indication, patient population, dosage strength or frequency, or other condition of use that is not in accordance with regulatory approved usage and labeling. Even though the FDA, NMPA, TGA, EMA and other comparable regulatory authorities actively enforce the laws and regulations prohibiting the promotion of off-label use, there remains the risk that our products are subject to off-label drug use and is prescribed in a patient population or dosage that has not been approved by competent authorities. Off-label use of our products may be less effective or entirely ineffective and may cause adverse drug reactions. Any of these occurrences can create negative publicity and significantly harm our business reputation, product brand name, commercial operations, and financial condition, including our share price. These occurrences may also expose us to liability and cause, or lead to, a delay in the progress of our clinical trials and may also ultimately result in failure to obtain regulatory approval for our drug candidates.

As a company, we have no experience in launching and marketing drugs. If we are unable to develop sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements or arrangements with third parties, we may not be successful in commercializing any drugs and generate drug candidate sales revenue.

We have not yet demonstrated an ability to launch and commercialize any of our drug candidates. As a result, our ability to successfully commercialize any approved drugs may involve more inherent risk, take longer, and cost more than it would if we were a company with prior experience launching and marketing drugs.

We will have to compete with other pharmaceutical and biopharmaceutical companies to recruit, hire, train and retain marketing and sales personnel. We must either develop internal sales, marketing, and commercial distribution capabilities for any or all of our approved drugs or pursue collaborative arrangements regarding the sales and marketing of our approved drugs. However, there can be no assurance that we will be able to develop such distribution capabilities or establish or maintain such collaborative arrangements, or if we are able to do so, that they will have effective sales forces. Any revenue we receive will depend upon the efforts of such third parties. we would have little or no control over the marketing and sales efforts of such third parties, and our revenue from product sales may be lower than if we had commercialized our approved drugs by ourselves. We also face competition in our search for third parties to assist it with the sales and marketing efforts for our approved drugs.

As a result, we may not be able to generate product sales revenue.

We face substantial competition from other pharmaceutical and biotechnology companies, and our operating results may suffer if we fail to compete effectively.

The development and commercialization of new drugs is highly competitive. We face competition from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell drugs or are pursuing the development of drugs for the treatment of neurological diseases and other disorders for which we are commercializing our drugs or developing our drug candidates. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing, and commercialization.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any drugs that we commercialize or may develop. Our competitors may also obtain approval from the FDA, NMPA, TGA, EMA or other comparable regulatory authorities for their drugs more rapidly than we may obtain approval for our drugs, which could result in our competitors establishing a strong market position before we are able to enter the market and/or could slow our regulatory approval.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

We may be subject, directly or indirectly, to applicable anti-kickback, false claims laws, physician payment transparency laws, fraud and abuse laws or similar healthcare and security laws and regulations in the U.S. and other jurisdictions, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and others play a primary role in the recommendation and prescription of any products for which we obtain regulatory approval. If we obtain FDA approval for any of our drug candidates and begin commercializing those drugs in the U.S., our operations may be subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician payment sunshine laws and regulations. These laws may impact, among other things, our proposed sales, marketing, and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business.

Additionally, we are subject to state and non-U.S. equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope and may apply to healthcare services reimbursed by any source, not just governmental payers, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or other voluntary industry codes of conduct. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. There are ambiguities as to what is required to comply with these state requirements, and if we fail to comply with applicable state law requirements, we could be subject to penalties.

Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including penalties, fines and/or exclusion or suspension from federal and state healthcare programs such as Medicare and Medicaid and debarment from contracting with the U.S. government. In addition, private individuals have the ability to bring actions on behalf of the U.S. government under the federal False Claims Act as well as under the false claims laws of several states.

Neither the U.S. government nor the U.S. courts have provided definitive guidance on limitations to potential liability under the fraud and abuse laws as they may apply to our business. Law enforcement authorities are increasingly focused on enforcing these laws, often using new and creative legal theories, and it is possible that some of our practices may be challenged under these laws. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Regardless of the compliance efforts, 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 any such actions are instituted against us, defending against such actions, even if successful, would distract the company and key personnel from our core mission and impose potentially significant costs. If we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid, and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our approved drugs outside the U.S. will also likely subject us to non-U.S. equivalents of the healthcare laws mentioned above, among other non-U.S. laws, as well as the U.S. Foreign Corrupt Practices Act (FCPA).

If any of the physicians or other providers or entities with whom we expect to do business are 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, which may also adversely affect our business.

Any failure to perform proper quality control and quality assurance would have a material adverse effect on our business and financial results.

The manufacturing of our drug candidates and future approved drugs is subject to applicable laws, regulations, and GMP. These regulations govern manufacturing processes and procedures, including record keeping and the implementation and operation of quality management systems to control and assure the quality of investigational products and products approved for sale. We apply stringent quality controls at each stage of our production process to comply with these requirements. We perform extensive tests throughout the manufacturing processes to ensure the safety and effectiveness of our drug candidates. We may, however, detect instances in which an unreleased product was produced without adherence to our manufacturing procedures or the raw material used in our production process was not collected to store in accordance with the GMP or other regulations, resulting in a determination that the implicated products should be destroyed.

In addition, if we fail to comply with relevant quality control requirements under laws and GMP, we could experience a disruption in the supply of our products, which could delay or prevent further sales of such products, which could have a material adverse effect on our business and financial results.

In addition, quality issues may arise during scale-up activities. If we are unable to successfully ensure consistent and high quality of our products during large-volume production, the sales of our products may not be able to be promoted, which could have a material adverse effect on our business and financial results.

We may explore the licensing of commercialization rights or other forms of collaboration worldwide, which will expose us to additional risks.

Non-U.S. markets are an important component of our growth strategy. we initially intend to focus on opportunities in the U.S., European Union, Canada, Australia, Japan, and China, in particular. If we fail to obtain licenses or enter into collaboration arrangements with third parties in these or other markets, or if these parties are not successful, our revenue-generating growth potential will be adversely affected. Moreover, international business relationships subject us to additional risks that may materially adversely affect our ability to attain or sustain profitable operations, including:

- efforts to enter into collaboration or licensing arrangements with third parties in connection with our international sales, marketing, and distribution efforts may increase our expenses or divert our management's attention from the acquisition or development of our drug candidates;
- difficulty of effective enforcement of contractual provisions in local jurisdictions;
- differing regulatory requirements for drug approvals and marketing internationally;
- changes in a specific market's political and cultural climate or economic condition;
- potential third-party patent rights or potentially reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers, and regulatory requirements;
- economic weakness, including inflation;
- compliance with tax, employment, immigration, and labor laws for employees traveling abroad;
- the effects of applicable non-U.S. tax structures and potentially adverse tax consequences;
- currency fluctuations, which could result in increased operating expenses and reduced revenue;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- workforce uncertainty and labor unrest;
- failure of our employees and contracted third parties to comply with Office of Foreign Asset Control rules and regulations and the Foreign Corrupt Practices Act; and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters, including earthquakes, volcanoes, typhoons, floods, hurricanes, and fires.

These and other risks may materially and adversely affect our ability to attain or sustain revenue from international markets.

Illegal and/or parallel imports and counterfeit pharmaceutical products may reduce demand for our future approved drug candidates and could have a negative impact on our reputation and business.

The importation, whether authorized by governmental policy or illegally, of competing products from countries where government price controls or other market dynamics result in lower prices may adversely affect the demand for our future approved drugs and, in turn, may adversely affect our sales and profitability where we commercialize our products. Unapproved foreign imports of prescription drugs are illegal under the current laws of the U.S., China, European Union, Australia and other jurisdictions. However, illegal imports may continue to occur or even increase as the ability of patients to obtain these lower priced imports continues to grow. Furthermore, cross-border imports from lower-priced markets (parallel imports) into higher-priced markets could harm sales of our future approved drugs and exert commercial pressure on pricing within one or more markets. In addition, competent government authorities may expand consumers' ability to import lower priced versions of our future approved products or competing products from outside the countries where we operate. Any future legislation or regulations that increase consumer access to lower priced medicines from outside the countries where we operate could have a material adverse effect on our business.

Certain products distributed or sold in the pharmaceutical market may be manufactured without proper licenses or approvals, or are fraudulently mislabeled with respect to their content or manufacturers. These products are generally referred to as counterfeit pharmaceutical products. The counterfeit pharmaceutical product control and enforcement system, particularly in developing markets such as China, may be inadequate to discourage or eliminate the manufacturing and sale of counterfeit pharmaceutical products imitating our products. Since counterfeit pharmaceutical products in many cases have very similar appearances compared with the authentic pharmaceutical products but are generally sold at lower prices, counterfeits of our products can quickly erode the demand for our future approved drugs. Our reputation and business could suffer harm as a result of counterfeit pharmaceutical products sold under our or our collaborators' brand name(s). In addition, theft of inventory at warehouses, plants or while in-transit, which are not properly stored and which are sold through unauthorized channels, could adversely impact patient safety, as well as our reputation and business.

We rely on third parties to conduct our preclinical studies and clinical trials and we must work effectively with collaborators to develop our drug candidates. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our drug candidates and our business could be substantially harmed.

We rely upon and plan to continue to rely upon third-party CROs and third-party vendors to monitor, collect samples, analyze samples, report data, and manage data for our ongoing preclinical and clinical programs.

We rely on these parties for execution of our preclinical studies and clinical trials, and controls only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal and regulatory requirements, and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We, our CROs and third-party vendors supporting our clinical programs, and our clinical investigators, are required to comply with GCPs, which are regulations and guidelines enforced by the FDA, NMPA, TGA, EMA, and other comparable regulatory authorities for all of our drugs in clinical development. If we or any of our CROs or clinical investigators fails to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, NMPA, TGA, EMA or comparable regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our pivotal clinical trials must be conducted with product produced under GMP. our failure to comply with these regulations may require it to repeat clinical trials, which would delay the regulatory approval process.

If any of our relationships with these third-parties terminates, we may not be able to enter into arrangements with alternative CROs or vendors, or to do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and nonclinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they or our clinical investigators obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements, or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our drug candidates. As a result, our results of operations and the commercial prospects for our approved drugs would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding additional CROs involves additional cost and delays, which can materially influence our ability to meet our desired clinical development timelines. There can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse effect on our business, financial condition and prospects.

Our future revenues are dependent on our ability to work effectively with collaborators to develop our drug candidates, including to obtain regulatory approval. Our arrangements with collaborators will be critical to successfully bringing products to market and commercializing them. We relies on collaborators in various respects, including to undertake research and development programs, conduct clinical trials, manage or assist with the regulatory filings and approval process, and to assist with our commercialization efforts. We do not control our collaborators; therefore, we cannot ensure that these third parties will adequately and timely perform all of their obligations to us. If they fail to complete the remaining studies successfully, or at all, it could delay, adversely affect or prevent regulatory approval. We cannot guarantee the satisfactory performance of any of our collaborators and if any of our collaborators breach or terminate their agreements with us, we may not be able to successfully commercialize the licensed product which could materially and adversely affect our business, financial condition, cash flows and results of operations.

Our third-party CROs and third-party vendors may also be impacted by the COVID-19 outbreak. See "— *Our financial position and operations may be adversely affected by the COVID-19 outbreak*."

We have entered into research collaborations and may form or seek collaborations or strategic alliances or enter into licensing arrangements in the future, and we may not realize the benefits of such collaborations, alliances, or licensing arrangements.

We may form or seek strategic alliances, create joint ventures or collaborations, or enter into licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our drug candidates and any future drug candidates that we may develop. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing shareholders, or disrupt our management and business.

We have entered into collaborative research arrangements with some of the world's leading academic institutions and research centers and are working with key scientists in the field of central nervous system disorders. We face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our drug candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our drug candidates as having the requisite potential to demonstrate safety and efficacy or commercial viability. If and when we collaborate with a third party for development and commercialization of a drug candidate, we can expect to relinquish some or all of the control over the future success of that drug candidate to the third party. For any drug candidates that we may seek to in-license from third parties, we may face significant competition from other pharmaceutical or biotechnology companies with greater resources or capabilities than we have, and any agreement that we do enter may not result in the anticipated benefits.

Further, collaborations involving our drugs are subject to numerous risks, which may include the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration;
- collaborators may not pursue development and commercialization of our drug candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus due to the acquisition of competitive drugs, availability of funding, or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial, abandon a drug candidate, repeat or conduct new clinical trials, or require a new formulation of a drug candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, drugs that compete directly or indirectly with our drugs;
- a collaborator with marketing and distribution rights to one or more drugs may not commit sufficient resources to their marketing and distribution;
- collaborators may not properly develop, maintain, or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;

- disputes may arise between us and a collaborator that cause the delay or termination of the research, development, or commercialization of our drug candidates, or that result in costly litigation or arbitration that diverts management attention and resources;

- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable drug candidates; and

- collaborators may own or co-own intellectual property covering our drugs that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property.

As a result, we may not be able to realize the benefit of current or future research collaborations, strategic partnerships, or the potential licensing of third-party drugs if we are unable to successfully integrate such products with our existing operations and company culture, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a drug candidate, reduce or delay our development program or one or more of our other development programs, delay our potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our drug candidates or bring them to market and generate product sales revenue, which would harm our business prospects, financial condition and results of operations.

Our business depends on the use of raw materials, and a decrease in the supply, or an increase in the cost of these raw materials could materially and adversely affect our business, financial condition and results of operations.

In order to manufacture our products, we must obtain sufficient quantities of high-quality raw materials at commercially acceptable prices and in a timely manner. Certain critical raw materials, such as wires made of high-purity gold and other transition elements, are available from a limited number of suppliers in the market. As a result, any disruption in production or inability of our suppliers to produce adequate quantities to meet our needs could impair our ability to operate our business on a day-to-day basis and to continue our research and development of future drug candidates. Moreover, we expect our demand for such materials to increase as we expand our business scale and commercialize our products, and we cannot guarantee that current suppliers have the capacity to meet our demand. We are also exposed to the risk of increased material costs, which we may not be able to pass on to customers and as a result, we could have lower profitability. In addition, although we have implemented quality inspection procedures on such materials before they are used in our manufacturing processes and also require our suppliers to maintain high quality standards, we cannot guarantee that we will be able to secure sufficient quantities of raw materials at high quality standards, nor detect all quality issues in the supplies we use. For example, should the highly purified water that we utilize be compromised in any way, it could render entire batches unusable or, depending on the nature of the impurity, potentially dangerous to patients. We cannot assure you that third parties will be able to maintain and renew all licenses, permits, and approvals necessary for their operations or comply with all applicable laws and regulations. Failure to do so by them may lead to interruption in their business operations, which in turn may result in shortages of the raw materials utilized by us. If we are unable to obtain adequate raw materials and the quality of our products suffer as a result, we may have to delay clinical trials and regulatory filings, recall our products, be subject to product liability claims, fail to comply with continuing regulatory requirements, and incur significant costs to rectify such issues, which may have a material and adverse effect on our business, financial condition and results of operations.

If we are unable to obtain and maintain sufficient patent protection for our drug candidates through intellectual property rights, or if the scope of such intellectual property rights obtained is not sufficiently broad, third parties could develop and commercialize products similar or identical to our products, and our ability to commercialize our approved drugs successfully may be adversely affected.

Our success depends in large part on our ability to protect our proprietary technology, drug candidates in clinical studies, and approved drugs on market (if approved) from competition by obtaining, maintaining and enforcing our intellectual property rights, including patent rights. We seek to protect the drug candidates and technology that it considers commercially important by filing patent applications in most important commercial markets, including the U.S., the People's Republic of China ("**PRC**"), Europe, Canada, Japan, Korea, and other countries, relying on trade secrets or pharmaceutical regulatory protection or employing a combination of these methods. However, the patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. As a result, we may not be able to prevent competitors from developing and commercializing competitive drugs in all such fields and territories.

Patents may be invalidated and patent applications may not be granted for a number of reasons, including known or unknown prior art, deficiencies in the patent application or the lack of novelty of the underlying invention or technology. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and any other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases, not at all. Therefore, we cannot be certain that it was the first to make the inventions claimed in our patents or pending patent applications or that it was the first to file for patent protection of such inventions. Furthermore, the PRC, EPO, and the U.S. have adopted the "first-to-file" system under which whoever first files a patent application will be awarded the patent if all other patentability requirements are met. Under the first-to-file system, third parties may be granted a patent relating to a technology which we invented.

The coverage sought by the claims in a patent application can be significantly reduced before the patent is issued, and the scope of the claims can be reinterpreted after issuance. Even if patent applications we license or own currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. In addition, the patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain.

The issuance of a patent is not conclusive as to our inventorship, scope, validity, or enforceability, and our patents may be challenged in the courts or patent offices in any country. We may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, revocation, re-examination, post-grant and *inter partes* review, or interference proceedings or similar proceedings in foreign jurisdictions challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or approved drugs and compete directly with us without payment, or result in our inability to manufacture or commercialize drug candidates and approved drugs without infringing, misappropriating or otherwise violating third-party patent rights. Moreover, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge the priority of our invention or other features of patentability of our patents and patent applications. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and drug candidates. Such proceedings also may result in substantial costs and require significant time from our scientists and management, even if the eventual outcome is favorable to us. Consequently, we do not know whether any of our technology or drug candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

Furthermore, although various extensions may be available, the life of a patent and the protection it affords, is limited. For example, approved therapies may face competition from generic medications after the related patents have expired, or if they are challenged and invalidated even before their expiry. Manufacturers of generic drugs may challenge the scope, validity or enforceability of our patents in court, and we may not be successful in enforcing or defending those intellectual property rights and, as a result, may not be able to develop or market the relevant product exclusively, which would have a material adverse effect on any potential sales of that product. The issued patents and pending patent applications, if issued, for our drug candidates are expected to expire on various dates as described in "Business — Intellectual Property" of this Annual Report. Upon the expiration of our issued patents or patents that may issue from our pending patent applications, we will not be able to assert such patent rights against potential competitors and our business and results of operations may be adversely affected.

Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such drug candidates might expire before or shortly after such drugs are commercialized. As a result, our patents and patent applications may not provide it with sufficient rights to exclude others from commercializing products similar or identical to our products. Moreover, some of our patents and patent applications may in the future be co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

We may not be able to protect our intellectual property rights throughout the world or prevent unfair competition by third parties.

Filing, prosecuting, maintaining, and defending patents on drug candidates in all countries throughout the world could be prohibitively expensive for us, and our intellectual property rights in some non-U.S. countries can have a different scope and strength than do those in the U.S. In addition, the laws of certain non-U.S. countries do not protect intellectual property rights to the same extent as the laws of the U.S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing drugs made using our inventions in and into the U.S. or non-U.S. jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own drugs and further, may export otherwise infringing drugs to non-U.S. jurisdictions where we have patent protection, but where enforcement rights are not as strong as those in the U.S. These drugs may compete with our future approved drugs and our patent rights or other intellectual property rights may not be effective or adequate to prevent them from competing.

We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time consuming and unsuccessful. our patent rights relating to our drugs could be found invalid or unenforceable if challenged in court or before the U.S. Patent and Trademark Office or comparable non-U.S. authority.

Competitors may infringe our patent rights or misappropriate or otherwise violate our intellectual property rights. To counter infringement or unauthorized use, litigation may be necessary in the future to enforce or defend our intellectual property rights, protect our trade secrets or determine the validity and scope of our own intellectual property rights or the proprietary rights of others. Enforcement or defense of intellectual property rights can be expensive and time consuming. Any claims that we assert against perceived infringers could also provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property rights. Many of our current and potential competitors have the ability to dedicate substantially greater resources to enforce and/or defend their intellectual property rights than we can. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating our intellectual property. An adverse result in any litigation proceeding could put our patents, as well as any patents that may issue in the future from our pending patent applications, at risk of being invalidated, held unenforceable or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

In patent litigation in the U.S., defendant counterclaims in district courts or in the patent trademark and appeal board (PTAB) alleging invalidity or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the U.S. or abroad, even outside the context of litigation. Such mechanisms include ex parte re-examination, inter partes review, post-grant review, derivation and equivalent proceedings in non-U.S. jurisdictions, such as opposition proceedings. Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover and protect our drug candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we, our patent counsel, and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our drug candidates. Such a loss of patent protection could have a material adverse impact on our business.

We may not be able to prevent misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the U.S. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

If we are sued for infringing the intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our drug candidates.

Our commercial success depends in part on our avoiding infringement of the patents and other intellectual property rights of third parties. We are aware of other issued patents belonging to third parties that exist in fields in which we are developing our drug candidates. There may also be third-party patents or patent applications of which we are currently unaware, and given the dynamic area in which we operate, additional patents are likely to be issued that relate to some aspects of our business. There is a substantial amount of litigation and other claims and proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries generally. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our drug candidates may give rise to claims of infringement of the patent rights of others.

Third parties may assert that we are using technology in violation of their patent or other proprietary rights. Defense of these claims, regardless of their merit, could involve substantial litigation expense and divert our technical personnel, management personnel, or both from their normal responsibilities. If third parties bring successful claims against us for infringement of their intellectual property rights, we may be subject to injunctive or other equitable relief, which could prevent us from developing and commercializing one or more of our drug candidates. We may also have to pay substantial damages, including treble damages and attorneys' fees in the case of willful infringement, or redesign our infringing drug candidates, which may be impossible or require substantial time and cost. In the event of an adverse result in any such litigation, or even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our drug candidates. Any such license might not be available on reasonable terms or at all. In the event that we are unable to obtain such a license, we would be unable to further develop and commercialize one or more of our drug candidates, which could harm our business significantly. We may also elect to enter into license agreements in order to settle patent infringement claims or to resolve disputes prior to litigation, and any such license agreements may require us to pay royalties and other fees that could significantly harm our business.

Intellectual property litigation may lead to unfavorable publicity that harms our reputation and increases our operating losses, causing the market price of our Common Stock to decline.

During the course of any intellectual property litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the market price of the ordinary shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and most foreign jurisdictions either annually or in several stages over the lifetime of the patent. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. Although an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees, and failure to properly legalize and submit formal documents. In any such event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

If we do not obtain patent term extension and data exclusivity for any drug candidates it may develop, our business may be materially harmed.

Depending upon the timing, duration, and specifics of any FDA marketing approval of any drug candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or Hatch Waxman Amendments. The Hatch Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during clinical trials and the FDA regulatory review process. A comparable extension right may exist in other foreign jurisdictions as well. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of drug approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. In addition, no patent term extension system has been established in the PRC beyond the new pilot program, and implementation of the pilot program may not occur quickly. As a result, the patents we have in the PRC are not yet eligible to be extended for patent term lost during clinical trials and the regulatory review process. If we are unable to obtain patent term extension or term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our drug candidates.

The U.S. has recently enacted and is currently implementing wide-ranging patent reform legislation. Recent U.S. Supreme court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained, if any. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. There could be similar changes in the laws of foreign jurisdictions that may impact the value of our patent rights or other intellectual property rights.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to our issued patents and pending patent applications, we rely on trade secrets, including unpatented know-how, technology, and other proprietary information, to maintain our competitive position and to protect our drug candidates. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties that have access to them, such as our employees, corporate collaborators, outside scientific collaborators, sponsored researchers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. However, any of these parties may breach such agreements and disclose our proprietary information, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive, time-consuming, and the outcome is unpredictable. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us and our competitive position would be harmed.

We may be subject to claims that our employees have wrongfully used or disclosed the alleged trade secrets of their former employers.

Many of our employees, including our senior management, were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees, including each member of our senior management, executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. we are not aware of any threatened or pending claims related to these matters or concerning the agreements with our senior management, but in the future litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property rights do not necessarily protect us from all potential threats to our competitive advantages.

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 compounds that are similar to our drug candidates but that are not covered by the claims of the patents that we own or may in the future exclusively license;
- we might not have been the first to make the inventions covered by the issued patents or pending patent applications that it owns or may in the future exclusively license, which could result in the patent applications not issuing or being invalidated after issuing;
- we might not have been the first to file patent applications covering certain of our inventions, which could prevent the issuance of the patent applications or cause them to be invalidated after issuance;
- 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 pending patent applications will not lead to issued patents;

- issued patents that we own or have exclusively licensed may not provide it with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;

- we may obtain patents for certain drug candidates many years before it receives NDA approval for these drugs, and because patents have a limited life, which may begin to run prior to the commercial sale of the related drugs, limiting the commercial value of our patents;

- our competitors might conduct research and development activities in countries where we does not have patent rights and then use the information learned from such activities to develop competitive drugs for commercialization in our major markets;

- we may fail to develop additional proprietary technologies that are patentable;

- we may fail to apply for or obtain adequate intellectual property protection in all the jurisdictions in which it operates; and

- the patents of others may have an adverse effect on our business, for example by preventing we from commercializing one or more of our drug candidates for one or more indications.

- any of the aforementioned threats to our competitive advantage could have a material adverse effect on our business.

Risks Related to the Reverse Recapitalization and Integration of Businesses

We will incur significant increased expenses and administrative burdens as a public company, which could have an adverse effect on our business, financial condition and results of operations.

As a newly public company, we will face increased legal, accounting, administrative and other costs and expenses as a public company that we did not incur as a private company. The Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act"), including the requirements of Section 404, as well as rules and regulations subsequently implemented by the SEC, the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010 and the rules and regulations promulgated and to be promulgated thereunder, the PCAOB and the securities exchanges, impose additional reporting and other obligations on public companies. Compliance with public company requirements will increase costs and make certain activities more time-consuming. A number of those requirements will require us to carry out activities we have not done previously. In addition, additional expenses associated with SEC reporting requirements will be incurred. Furthermore, if any issues in complying with those requirements are identified (for example, if the auditors identify a material weakness or significant deficiency in the internal control over financial reporting), we could incur additional costs rectifying those issues, and the existence of those issues could adversely affect our reputation or investor perceptions of it. It may also be more expensive to obtain director and officer liability insurance. Risks associated with our status as a public company may make it more difficult to attract and retain qualified persons to serve on the board of directors or as executive officers. The additional reporting and other obligations imposed by these rules and regulations will increase legal and financial compliance costs and the costs of related legal, accounting and administrative activities. These increased costs will require us to divert a significant amount of money that could otherwise be used to expand the business and achieve strategic objectives. Advocacy efforts by shareholders and third parties may also prompt additional changes in governance and reporting requirements, which could further increase costs.

We qualify as an emerging growth company within the meaning of the Securities Act, and if we take advantage of certain exemptions from disclosure requirements available to emerging growth companies, it could make our securities less attractive to investors and may make it more difficult to compare our performance to the performance of other public companies.

We qualify as an "emerging growth company" as defined in Section 2(a)(19) of the Securities Act, as modified by the JOBS Act. As such, we are eligible for and intend to take advantage of certain exemptions from various reporting requirements applicable to other public companies that are not emerging growth companies for as long as we continue to be an emerging growth company, including (i) the exemption from the auditor attestation requirements with respect to internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act, (ii) the exemptions from say-on-pay, say-on-frequency and say-on-golden parachute voting requirements and (iii) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We will remain an emerging growth company until the earliest of (i) the last day of the fiscal year in which the market value of the shares of our Common Stock that are held by non-affiliates exceeds $700 million as of June 30 of that fiscal year, (ii) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more during such fiscal year, (iii) the date on which we have issued more than $1 billion in non-convertible debt in the prior three-year period or (iv) the last day of the fiscal year following the fifth anniversary of the date of the first sale of common stocks in TOTA's IPO.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, we will not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies and our financial statements may not be comparable to other public companies that comply with new or revised accounting pronouncements as of public company effective dates. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies.

Further, even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. In addition, if we are a smaller reporting company with less than $100 million in annual revenue, we would not be required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act.

We cannot predict if investors will find our common shares less attractive because we may rely on these exemptions. If some investors find our common shares less attractive as a result, there may be a less of an active trading market for our common shares and our share price may be more volatile.

Risks Related to Our Common Stock

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws that went into effect upon the consummation of the Reverse Recapitalization could make a merger, tender offer or proxy contest difficult, thereby depressing the trading price of our Common Stock.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control that shareholders may consider favorable, including transactions in which shareholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our Common Stock, thereby depressing the market price of our Common Stock. Such provisions including the following:

- a classified board of directors with three-year staggered terms, which could delay the ability of shareholders to change the membership of a majority of our board of directors;

- the ability of our board of directors to issue shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without shareholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;

- the requirement for the affirmative vote of holders of at least 66⅔% of the voting power of all of the then-outstanding shares of the voting stock, voting together as a single class, to amend the provisions of our amended and restated certificate of incorporation or our amended and restated bylaws, which may inhibit the ability of an acquiror to effect such amendments to facilitate an unsolicited takeover attempt;

- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of our board of directors or the resignation, death or removal of a director, which prevents shareholders from being able to fill vacancies on our board of directors for a period of time; and

- the requirement that a special meeting of shareholders may be called only by the board of directors, the chairman of our board of directors or our Chief Executive Officer, which could delay the ability of our shareholders to force consideration of a proposal or to take action, including the removal of directors.

These and other provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for shareholders or potential acquirors to obtain control of our board of directors or initiate actions that are opposed by our then-current board of directors, including the ability to delay or impede a merger, tender offer or proxy contest. The existence of these provisions could negatively affect the price of our Common Stock and limit opportunities for shareholders to realize value in a corporate transaction.

There can be no assurance that we will be able to comply with the continued listing standards of Nasdaq.

If Nasdaq delists our shares of Common Stock or warrants from trading on its exchange for failure to meet Nasdaq's listing standards, we and our shareholders could face significant material adverse consequences including:

- a limited availability of market quotations for our securities;
- reduced liquidity for our securities;
- a determination that our Common Stock is a "penny stock" which will require brokers trading in our Common Stock to adhere to more stringent rules and possibly result in a reduced level of trading activity in the secondary trading market for our securities;
- a limited amount of news and analyst coverage; and
- a decreased ability to issue additional securities or obtain additional financing in the future.

The price of our Common Stock and warrants may be volatile.

The stock markets in general and the markets for biotechnology stocks have experienced extreme volatility. The market for the common stock of smaller companies such as ours is characterized by significant price volatility when compared to the shares of larger, more established companies that trade on a national securities exchange and have large public floats, and our share price is more volatile than the shares of such larger, more established companies for the indefinite future.

The price of our Common Stock and warrants may fluctuate due to a variety of factors, including:

- changes in the industries in which we operate;
- variations in our operating performance and the performance of our competitors in general;
- material and adverse impact of the COVID-19 pandemic on the markets and the broader global economy;
- actual or anticipated fluctuations in our quarterly or annual operating results;
- publication of research reports by securities analysts about us or our competitors or our industry, such as occurred in February 2021;
- the public's reaction to our press releases, our other public announcements and our filings with the SEC;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;
- additions and departures of key personnel;
- changes in laws and regulations affecting our business;
- commencement of, or involvement in, litigation involving us;
- changes in our capital structure, such as future issuances of securities or the incurrence of additional debt;
- the volume of shares of our Common Stock available for public sale; and
- general economic and political conditions such as recessions, interest rates, fuel prices, foreign currency fluctuations, international tariffs, social, political and economic risks, pandemics and acts of war or terrorism.

These market and industry factors may materially reduce the market price of our Common Stock and our warrants regardless of our operating performance.

Future offerings of debt or equity securities by us may adversely affect the market price of our Common Stock.

In the future, we may attempt to obtain financing or to further increase our capital resources by issuing additional shares of our Common Stock or offering debt or other equity securities, including commercial paper, medium-term notes, senior or subordinated notes, debt securities convertible into equity or shares of preferred stock. Future acquisitions could require substantial additional capital in excess of cash from operations. We would expect to obtain the capital required for acquisitions through a combination of additional issuances of equity, corporate indebtedness and/or cash from operations.

Issuing additional shares of our Common Stock or other equity securities or securities convertible into equity may dilute the economic and voting rights of our existing shareholders or reduce the market price of our Common Stock or both. Upon liquidation, holders of such debt securities and preferred shares, if issued, and lenders with respect to other borrowings would receive a distribution of our available assets prior to the holders of our Common Stock. Debt securities convertible into equity could be subject to adjustments in the conversion ratio pursuant to which certain events may increase the number of equity securities issuable upon conversion. Preferred shares, if issued, could have a preference with respect to liquidating distributions or a preference with respect to dividend payments that could limit our ability to pay dividends to the holders of our Common Stock. Our decision to issue securities in any future offering will depend on market conditions and other factors beyond our control, which may adversely affect the amount, timing and nature of our future offerings.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 2. PROPERTIES

To date, we do not have any owned properties. We have leased a number of properties from independent third parties in the United States. We utilize our Salt Lake City location for our headquarters functions including finance, clinical development, clinical operations, translational medicine, and business operations. We lease property in North East, Maryland, the United States for our manufacturing and R&D activities.

The following summary sets forth the details of our leased properties:

- EOS at Millrock Park, LLC (leased Salt Lake City, Utah offices) for approximately 5200 square feet, expiring April 2027 with an option to extend thereafter.

- Upper Chesapeake Flex One, LLC (leased North East, Maryland facility) for approximately 21,000 square feet, expiring October 2026 with an option to extend thereafter.

ITEM 3. LEGAL PROCEEDINGS

We may be subject to legal proceedings, investigations and claims incidental to the conduct of our business from time to time. We are not currently a party to any material litigation or other legal proceedings brought against us. We are also not aware of any legal proceeding, investigation or claim, or other legal exposure that has a more than remote possibility of having a material adverse effect on our business, financial condition or results of operations.

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

Shares of our Common Stock and warrants began trading on Nasdaq under the symbol "CLNN," and "CLNNW," respectively, on December 31, 2020. We have not paid any cash dividends on our shares of Common Stock to date. Historical market price information regarding our Common Stock is not provided because, as of the date of this Annual Report, there has been no established public market for either our Common Stock or warrants for a full quarterly period or any interim period for which financial statements are included, or required to be included, in this Annual Report.

It is the present intention of our board of directors to retain all earnings, if any, for use in our business operations and, accordingly, our board does not anticipate declaring any dividends in the foreseeable future. The payment of cash dividends in the future will be dependent upon our revenues and earnings, if any, capital requirements and general financial condition.

Holders of Record

As of March 25, 2021, there were 59,526,171 issued and outstanding shares of our Common Stock held by 189 stockholders of record. The number of record holders was determined from the records of our transfer agent and does not include beneficial owners of shares of Common Stock whose shares are held in the names of various security brokers, dealers, and registered clearing agencies.

Recent Sales of Unregistered Securities

PIPE Investment

The Company entered into subscription agreements with various investors for the private placement of Common Stock (the "Private Placement"), all of which closed shortly before the closing of the Reverse Recapitalization. Under the Private Placement, 2,239,500 shares of Common Stock (the "PIPE Shares") were sold, resulting in net proceeds of $22.2 million. Pursuant to the subscription agreements, investors in the Private Placement also received warrants to purchase a number of shares equal to one-half (1/2) of the number of PIPE Shares, totaling 1,119,750 shares of PubCo Common Stock, at an exercise price of $0.01 per share for each of the PIPE Shares (the "PIPE Warrants"), subject to a 180-day holding period. On February 16, 2021, the Company filed a registration statement on Form S-1 to register the PIPE Shares and the Common Stock underlying the PIPE Warrants.

Plan-Related Issuances

Since January 1, 2018, we granted to our employees, consultants, and other service providers options to purchase an aggregate of 2,259,788 shares of our common stock under our 2014 Stock Plan ("2014 Plan"), at exercise prices ranging from $0.7918 to $7.99 per share.

Warrants

Between August 23, 2018 and August 31, 2018, we issued and sold to an investor warrants to purchase an aggregate of 399,690 shares of our Series C preferred stock, for an exercise price of $0.0007 per share. We received aggregate consideration of $288.

Preferred Stock

Between August 23, 2018 and July 31, 2019, we issued and sold to investors an aggregate of 7,264,519 shares of our Series C preferred stock for prices ranging from $0.0007 to $4.1699 per share. We received aggregate consideration of $28,175,545.

Between August 10, 2020 and November 18, 2020, we issued and sold to investors an aggregate of 9,394,057 shares of our Series D preferred stock for prices ranging from $4.1418 to $4.6018 per share. We received aggregate consideration of $42,540,558.

Use of Proceeds

None.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

ITEM 6. SELECTED FINANCIAL DATA

Not applicable.

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion and other parts of this Annual Report on Form 10-K contain forward-looking statements reflecting our current expectations, estimates and assumptions concerning events and financial trends that may affect our future operating results or financial position. Actual results and the timing of events may differ materially from those contained in these forward-looking statements due to a number of factors, including those discussed in the sections titled "Risk Factors" and "Cautionary Note Regarding Forward-Looking Statements" appearing elsewhere in this Annual Report on Form 10-K. Unless the context otherwise requires, for purposes of this section, the terms "we," "us," "the Company" or "our" are intended to mean the business and operations of Clene Inc. and its consolidated subsidiaries.

Business Overview

We are a clinical-stage pharmaceutical company pioneering the discovery, development, and commercialization of novel, clean-surfaced nano (CSN) therapeutics. CSN therapeutics are comprised of atoms of transition elements that, when assembled in nanocrystalline form, possess unusually high, unique catalytic activities not present in those same elements in bulk form. These nanocatalytic activities drive, support, and maintain beneficial metabolic and energetic intercellular reactions within diseased, stressed, and damaged cells.

Our patent-protected, proprietary position affords us the potential to develop a broad and deep pipeline of novel CSN therapeutics to address a range of diseases with high impact on human health. We began in 2013 by innovating an electrochemistry drug development platform that draws from advances in nanotechnology, plasma and quantum physics, material science, and biochemistry. Our platform process results in nanocrystals with faceted structures and surfaces that are free of the chemical surface modifications that accompany other production methods. Many traditional methods of nanoparticle synthesis involve the unavoidable deposition of potentially toxic organic residues and stabilizing surfactants on the particle surfaces. Synthesizing stable nanocrystals that are both nontoxic and highly catalytic has overcome this significant hurdle in harnessing transition metal catalytic activity for human therapeutic use.

Our clean-surfaced nanocrystals exhibit catalytic activities many fold higher than multiple other commercially available nanoparticles, produced using various techniques, that we have comparatively evaluated. We now have multiple drug assets currently in development and/or clinical trials for applications in neurology, infectious disease, and oncology. Our development and clinical efforts are currently focused on addressing the high unmet medical needs in two areas: first, those related to central nervous system disorders including Multiple Sclerosis ("**MS**"), Parkinson's Disease ("**PD**") and Amyotrophic Lateral Sclerosis ("**ALS**"); and second, those related to the pandemic caused by COVID-19, a highly infectious viral respiratory disease with serious and sometimes fatal co-morbidities.

On December 30, 2020, Chelsea Worldwide, Inc., our predecessor company, consummated the previously announced business combination (referred to as the "**Reverse Recapitalization**") pursuant to a merger agreement, dated as of September 1, 2020 (the "**Merger Agreement**"), by and among Clene Nanomedicine, Inc. ("**Clene Nanomedicine**"), Tottenham Acquisition I Limited ("**Tottenham**" or "**TOTA**"), the public entity prior to the Reverse Recapitalization, Chelsea Worldwide Inc., a Delaware corporation and wholly owned subsidiary of Tottenham ("**PubCo**"), Creative Worldwide Inc., a Delaware corporation and wholly owned subsidiary of PubCo ("**Merger Sub**"), and Fortis Advisors LLC, a Delaware limited liability company as the representative of our shareholders ("**Shareholders' Representative**"). Prior to the Reincorporation Merger discussed below, Tottenham was incorporated in the British Virgin Islands as a blank check company for the purpose of entering into a merger, share exchange, asset acquisition, stock purchase, recapitalization, reorganization or other similar business combination with one or more businesses or entities.

The Reverse Recapitalization was effected in two steps: (i) Tottenham was reincorporated to the state of Delaware by merging with and into PubCo (the "**Reincorporation Merger**"); (ii) promptly following the Reincorporation Merger, Merger Sub was merged with and into Clene Nanomedicine, resulting in Clene Nanomedicine being a wholly owned subsidiary of PubCo (the "**Acquisition Merger**"). On the Closing Date, PubCo changed its name from Chelsea Worldwide Inc. to Clene Inc. and listed its shares of common stock, par value $0.0001 per share ("Common Stock") on Nasdaq under the symbol "CLNN." As a result of the Reverse Recapitalization, Clene Nanomedicine became a wholly owned direct subsidiary of Clene Inc. For periods prior to the closing of the Reverse Recapitalization on December 30, 2020, the disclosure in Management's Discussion and Analysis of Financial Condition and Results of Operations has been updated to give effect to the Reverse Recapitalization.

On February 16, 2021, we filed a registration statement on Form S-1 to register 4,541,481 shares of Common Stock underlying outstanding warrants that we had previously issued. The SEC has not yet declared this registration statement to be effective. We will receive an aggregate gross proceed of $30.7 million if all of these warrants are exercised. In addition, the registration statement on Form S-1 will register the sale by certain selling stockholders of 23,251,553 shares of our Common Stock. We will not receive any proceeds from the sales by the selling shareholders. In conjunction with the preparation of the registration statement on Form S-1, we incurred offering costs of $27,000, which will be recognized as an expense within general and administrative expenses on consolidated statement of operations in the first quarter of 2021.

We currently have no drugs approved by the US Food and Drug Administration (FDA) for commercial sale and have not generated any revenue from drug sales. We have never been profitable and have incurred operating losses in each year since inception. We began supplying low dose dietary supplements to 4Life, LLC, one of our shareholders, and had minimal direct sales of our rMetx™ ZnAg Immune Boost dietary supplement product. Our total operating losses were $20.2 million and $16.3 million for the years ended December 31, 2020 and 2019, respectively. Substantially all of our operating losses resulted from research and development expenses and administrative expenses. As of December 31, 2020 we had an accumulated deficit of $153.6 million.

We expect to continue investing in product development, sales and marketing and customer support for our products and expect to incur additional losses in the future to fund our operations and conduct product research and development. We also recognize the need to raise additional capital to fully implement our business plan. The long-term continuation of our business plan is dependent upon the generation of sufficient revenues from our products to offset expenses and capital expenditures. In the event that we do not generate sufficient revenues and are unable to obtain funding, we will be forced to delay, reduce, or eliminate some or all of our research and development programs, product portfolio expansion, commercialization efforts or capital expenditures, which could adversely affect our business prospects, ability to meet long-term liquidity needs or we may be unable to continue operations.

Impact of the COVID-19 Coronavirus Pandemic

The COVID-19 pandemic, which began in December 2019 and has spread worldwide, has caused many governments to implement measures to slow the spread of the outbreak. The outbreak and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred, supply chains have been disrupted, and facilities and production have been suspended. The future progression of the pandemic and its effects on our business and operations remain uncertain. The COVID-19 pandemic may affect our ability to initiate and complete preclinical studies, delay the initiation of future clinical trials, disrupt regulatory activities, or have other adverse effects on our business and operations. In particular, we and our clinical research organizations (“CROs”) may face disruptions that may affect our ability to initiate and complete preclinical studies, cause manufacturing disruptions, or create delays at clinical trial sites. The pandemic has already caused significant disruptions in the financial markets, and may continue to cause such disruptions, which could impact our ability to raise additional funds to support our operations. Moreover, the pandemic has significantly impacted economies worldwide and could result in adverse effects on our business and operations.

We are monitoring the potential impact of the COVID-19 pandemic on our business and financial statements. While the COVID-19 pandemic has led to various research restrictions and paused certain of our clinical trials, these impacts have been temporary and to date we have not experienced material business disruptions or incurred impairment losses in the carrying values of our assets as a result of the pandemic. We are not aware of any specific related event or circumstance that would require us to revise the estimates reflected in our financial statements. The extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition, including planned and future clinical trials and research and development costs, will depend on future developments that are highly uncertain, including as a result of new information that may emerge concerning COVID-19, the actions taken to contain or treat it, and the duration and intensity of the related effects.

Reverse Recapitalization with Tottenham and Clene Nanomedicine

On December 30, 2020, we completed the previously announced Reverse Recapitalization, pursuant to which Tottenham was reincorporated and merged with and into PubCo with PubCo surviving the merger in connection with the Reincorporation Merger and the Merger Sub was merged with and into Clene Nanomedicine, resulting in Clene Nanomedicine being a wholly owned subsidiary of PubCo. On the closing of the Reverse Recapitalization, PubCo changed its name from Chelsea Worldwide Inc. to Clene Inc.

At the closing of the Reverse Recapitalization, Clene Inc. acquired 100% of the issued and outstanding Clene Nanomedicine common stock, in exchange for 54,339,012 shares of Clene Inc. Common Stock issued to the Clene Nanomedicine common shareholders, among which 2,716,958 shares of the Clene Inc. Common Stock are to be issued and held in escrow to satisfy any indemnification obligations incurred under the Merger Agreement.

At the closing of the Reverse Recapitalization, each stock option of Clene Nanomedicine common stock was cancelled and the holders thereof in exchange received 0.1320 newly issued stock options of our Common Stock, which is 95% of the exchange ratio determined in the Merger Agreement. Pursuant to the Merger Agreement, we issued 370,101 of restricted stock units ("RSUs") to the option holders which complements the 5% closing payment shares held in escrow for Clene Nanomedicine common shareholders discussed above. In addition, we issued 1,136,961 RSUs to option holders to complement the earn-out payments that would contingently be issued to certain current Clene Nanomedicine's shareholders upon the achievement of milestones. See "Earn-out Share" for the milestones detail.

Immediately after giving effect to the Reverse Recapitalization and the PIPE offering discussed in below, there were 59,526,171 shares of Common Stock issued and outstanding, and warrants to purchase 5,566,363 shares of Common Stock issued and outstanding.

The transaction was accounted for as a "reverse recapitalization" and Tottenham was treated as the "acquired" company for accounting purposes. Accordingly, for accounting purposes, the Reverse Recapitalization was treated as the equivalent of Clene Nanomedicine issuing shares for the net assets of Tottenham, accompanied by a recapitalization. The net assets of Tottenham were recorded at historical costs, with no goodwill or other intangible assets recorded. Reported amounts from operations included herein prior to the Reverse Recapitalization are those of Clene Nanomedicine.

The PIPE Offering

Prior to the completion of the Reverse Recapitalization on December 30, 2020, we entered into subscription agreements on December 28, 2020, with various investors (the "**PIPE**"). Pursuant to the subscription agreements, we issued 2,239,500 shares of our Common Stock (the "**PIPE Shares**") at a price of $10.00 per share with net proceeds of $22.2 million. The purpose of the PIPE is to fund general corporate expenses. In addition, investors in the PIPE offering will also receive warrants to purchase a number of shares equal to one-half (1/2) of the number of PIPE Shares, for an aggregate total of 1,119,750 shares of our Common Stock, at an exercise price of $0.01 per share (the "**PIPE Warrants**"), subject to a 180-day holding period.

Basis of Presentation and Consolidation

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("**GAAP**") and include the accounts of the Company and its wholly owned subsidiaries, Clene Nanomedicine, a subsidiary incorporated in Delaware, Clene Australia Pty Ltd ("**Clene Australia**"), a subsidiary incorporated in Australia, and dOrbital, Inc., a subsidiary incorporated in Delaware, after elimination of all significant intercompany accounts and transactions.

Key Factors Affecting Our Results of Operations

Our results of operations, financial condition and the period-to-period comparability of our financial results are principally affected by the following factors:

Earn-out Shares

In connection with the Reverse Recapitalization, certain of Clene Nanomedicine's current shareholders and Tottenham's former officers and directors and the Sponsor (collectively, the "**Initial Shareholders**") are entitled to receive earn-out payments (collectively, referred to as "**Earn-out Shares**") based on achieving milestones discussed below. The earn-out payments (the "**Contingent Earn-out**") have been classified as liabilities in the consolidated balance sheets as of December 31, 2020 and will be initially measured at fair value and remeasured subsequently in each reporting period. The change in fair value of the contingent earn-out will be recorded in the consolidated statements of operations and comprehensive loss.

The Clene Nanomedicine contingent earn-out provision includes (i) Milestone 1 that is based on achieving a certain volume-weighted average price of the shares of the Company Common Stock within three years after the closing of the Reverse Recapitalization or the change of control price equaling or exceeding a certain price if a change of control transaction occurs within the three years following the closing of the Reverse Recapitalization, (ii) Milestone 2 that is based on achieving a certain volume-weighted average price of the shares of the Company Common Stock within five years after the closing of the Reverse Recapitalization or the change of control price equaling or exceeding a certain price if a change of control transaction occurs within the five years following the closing of the Reverse Recapitalization, and (iii) Milestone 3 that is based on completing by December 30, 2021 a randomized placebo-controlled study for treatment of COVID-19 coronavirus.

The Initial Shareholders contingent earn-out provision includes Milestone 1 and Milestone 2 listed above. Upon the consummation of the Reverse Recapitalization, Clene Nanomedicine and the Initial Shareholders are entitled to receive up to 8,346,185 and 750,000 shares of the Company's Common Stock, respectively.

The estimated fair value of the contingent consideration was determined using a Monte Carlo simulation that simulated the future path of the Company's stock price over the earn-out period. The assumptions utilized in the calculation are based on the achievement of certain stock price milestones including projected stock price, volatility, and risk-free rate. For potential payments related to a product development milestone, the fair value was determined based on the Company's expectations of achieving such a milestone and the simulated estimated stock price on the expected date of achievement.

Contingent earn-out payments involve certain assumptions requiring significant judgment and actual results may differ from assumed and estimated amounts.

Research and Development Expenses

The discovery and development of novel drug candidates require a significant investment of resources over a prolonged period of time, and a core part of our strategy is to continue making sustained investments in this area. As a result of this commitment, our pipeline of drug candidates has been advancing and expanding, with two clinical-stage drug candidates currently being investigated.

We anticipate that our research and development expenses will increase significantly due to the increase in clinical trial expenses incurred to develop our drug candidates, expenses incurred for payments to CROs, principal investigators and clinical trial sites, costs of materials to support our clinical trials and preclinical studies, costs associated with preclinical activities, share awards granted to our research and development personnel and salaries for our expanding research and development personnel headcount. Our research and development expenses are affected by the timing and advancement of our existing product pipeline as well as the timing and quantity of new drug programs commenced.

Since inception, we have dedicated significant resources to our research and development activities. Our research and development expenses were $15.2 million and $9.6 million, representing 74.8%, and 58.6% of our total operating expenses in 2020 and 2019, respectively. As we continue to advance our clinical programs for our drug products, we expect our research and development expenses to increase in absolute amounts and to continue to represent a significant percentage of our total operating expenses.

Funding for Our Operations

Since our inception, we have dedicated substantially all of our resources to the development of our drug candidates. We have financed our operations principally through proceeds from the issuance of preferred stock, issuance of common stock upon exercise of common stock options, convertible promissory notes, issuances of notes payable, and the consummation of the Reverse Recapitalization.

Since our inception and through the date of this Annual Report, we have funded our operations primarily with proceeds from the following sources:

- gross proceeds of $87.2 million from sales of our preferred stock and other equity financing;
- gross proceeds of $28.1 million from borrowings under convertible promissory notes;
- gross proceeds of $0.6 million through external lenders; and
- gross cash proceeds of $31.7 million through the Reverse Recapitalization and the PIPE offering.

In February 2021, we filed a registration statement on Form S-1 to register 4,541,481 shares of Common Stock underlying outstanding warrants. We will receive aggregate gross proceeds of $30.7 million if all of these are exercised. In addition, we received $0.5 million from a Michael J. Fox Foundation grant in January 2021 which provides for our preclinical research funding.

We have also been awarded grants from various other organizations, including the U.S. Congressionally Directed Medical Research Program administered by the Department of Defense, the National Multiple Sclerosis Society, and FightMND, a not-for-profit registered charity in Australia, who together have issued us grants totaling approximately $2.6 million. We also receive indirect financial support for one of the clinical studies in which we participate, the Healey ALS Platform Trial, administered by the Massachusetts General Hospital, which is conducting a study of our CNM-Au8 drug candidate along with other drugs in a platform trial, at significantly lower costs to us than we would otherwise incur if we were to conduct a comparably designed study on our own at reasonable market rates.

The net cash used in our operating activities was $18.9 million and $13.2 million for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had cash of $59.3 million. We expect that the cash on hand as of December 31, 2020 will be sufficient to fund our operations for a period extending beyond twelve months from the date the consolidated financial statements are issued. We have based this estimate on assumptions that may prove to be wrong, and we may exhaust our available capital resources sooner than we anticipate. See "*— Liquidity and Capital Resources*." We expect our expenses to increase significantly in connection with our ongoing activities, particularly as we advance the clinical development of our clinical-stage drug products and continue research and development of our preclinical drug products and initiate additional clinical trials of, and seek regulatory approval for, these and other future drug products. As we continue to grow and expand, we will incur more expenses relating to regulatory compliance and sales and marketing personnel as we prepare to commence commercialization once we obtain regulatory approval of our drug products.

General and Administrative Expenses

Our administrative expenses consist primarily of staff costs, agency and consulting fees, utilities, rent and general office expenses, and share grants. We recorded administrative expenses of $5.2 million and $6.8 million for the years ended December 31, 2020 and 2019, respectively. We anticipate that our administrative expenses will further increase in future periods to support increases in our research and development activities and as we continue to rapidly advance the clinical programs of our drug products and expect to commercialize our products once we receive regulatory approval. These increases will likely include increased headcount, increased share compensation charges, expanded infrastructure and increased insurance expenses. We also anticipate increasing legal, compliance, accounting and investor and public relations expenses associated with being a public company.

Grants and Government Tax Incentives

We received grants issued by non-government entities related to income which have future related costs expected to be incurred and require us to comply with conditions attached to the grants. These non-government grants related to income are recognized in profit or loss as an offset to research and development expenses when funding has been received and related costs have been incurred. We received tax incentives from the Australian government in the form of cash subsidies for research and development activities related to clinical trial activities conducted by our Australian subsidiary, which are recognized as other income upon compliance with certain conditions. We recognized $0.8 million and $0.1 million of grant funding against research and development expenses for the years ended December 31, 2020 and 2019, respectively. We recognized $3.2 million and $0.6 million of other income for the years ended December 31, 2020 and 2019, respectively, that we classified as Australia research and development credit.

Commercialization of Our Drug Candidates

Our business and results of operations depend on our ability to commercialize our drug candidates, if approved for marketing. Our pipeline is comprised of four drug candidates ranging from pre-clinical to late-stage clinical programs, including two drug candidates at the clinical stage or IND stage. Although we currently do not have any drug candidates approved for commercial sale and have not generated any revenue from drug product sales, we expect to commercialize one or more of our drug products in the coming years as they move toward the final stages of development. While we began selling our ZnAg Immune Boost product online in May 2020, we anticipate revenue generated from sales of this dietary supplement will be small compared to our operating expenses as well as the revenue we expect to generate from future sales of our drug candidates for which we are currently conducting clinical trials.

Components of Results of Operations

Revenue

Because all our drug candidates are still at clinical stage, we did not generate any revenue for the year ended December 31, 2019. We generated an immaterial amount of revenue for the year ended December 31, 2020, which we separate as product revenue and royalty revenue. Product revenue is generated under our dietary supplement segment from 4Life, LLC, a related party, related to supply agreements for the low dose mineral supplement KHC46 and a low dose zinc-silver solution, two dietary (mineral) supplements that we began supplying during this period. We also generated minimal product revenue from sales of rMetx™ ZnAg Immune Boost during this period.

Royalty revenue is paid to us by 4Life, LLC, under an exclusive and royalty-bearing license agreement relating to sales of KHC46 only. For more details on this agreement, see *Item 1. Business — License Arrangements.*

Operating Expenses

Research and Development Expenses

Research and development costs are charged to operations as incurred. We account for nonrefundable advance payments for goods and services that will be used in future research and development activities initially as an asset and then as expenses when the goods have been received or when the service has been performed rather than when the payment is made.

We had research and development expenses for the years ended December 31, 2020 and 2019 of $15.2 million and $9.6 million, respectively. Research and development expenses consist of costs incurred by us for the discovery and development of our drug candidates. Research and development costs include payroll and personnel expenses, including salaries and related benefits and stock-based compensation for employees engaged in research and development functions, clinical trial supplies, fees for clinical trial services, consulting costs, and allocated overhead, including rent, equipment, utilities, depreciation, insurance, and facilities maintenance costs. We expect our research and development expenses to increase as more of our drug candidates progress through their clinical trials.

Historically, substantially all of our research and development expenses relate to CNM-Au8, our lead asset. Drug candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to per patient clinical trial site fees for larger studies, the costs of opening and monitoring clinical sites, CRO activity, and manufacturing expenses. We expect that our research and development expenses will increase in connection with our clinical development activities in the near term and in the future.

Clinical trial costs, including clinical trial supplies and fees for clinical trial services, are charged to research and development expense as incurred. Our clinical trial accrual process seeks to account for expenses resulting from obligations under contracts with CROs, consultants, and under clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to us under such contracts. We reflect the appropriate trial expenses in the consolidated financial statements by matching the appropriate expenses with the period in which services and efforts are expended. In the event advance payments are made to a CRO, the payments will be recorded as a prepaid asset, which will be expensed over the period of time the contracted services are performed.

General and Administrative Expenses

General and administrative expenses consist of employee salary and benefits, share-based compensation expenses, professional fees for legal, consulting and audit services and business development activities, facility, travel expenses, rental fees and other administrative expenses. We expect our general and administrative expenses to increase as we continue to grow and expand.

Other Income (Expenses)

Other income (expenses) consists of interest expenses, interest income, gains from the termination of a lease arrangement, changes in fair value of preferred stock warrant liability, changes in fair value of derivative liability, change in fair value of contingent earn-out, a research and development credit received from the Australian government, foreign exchange gain, loss on disposal of assets, and loss on extinguishment of convertible notes.

Comparison of the Years Ended December 31, 2020 and 2019

The following table summarizes our results of operations for the years ended December 31, 2020 and 2019:

	December 31,	
	2020	**2019**
	(in thousands)	
Product revenue	$ 176	$ -
Royalty revenue	30	-
Total revenue	206	-
Operating expenses:		
Cost of revenue	65	-
Research and development	15,204	9,563
General and administrative	5,151	6,769
Total operating expenses	20,420	16,332
Loss from operations	(20,214)	(16,332)
Other income (expenses):		
Interest expense	(950)	(88)
Gain on termination of lease	51	-
Change in fair value of preferred stock warrant liability	(14,615)	(361)
Change in fair value of derivative liability	29	-
Change in fair value of Clene Nanomedicine contingent earn-out	12,659	-
Change in fair value of Initial Shareholder contingent earn-out	1,465	-
Australia research and development credit	3,210	599
Loss on extinguishment of convertibles notes	(540)	-
Other income, net	34	27
Total other income (expense), net	1,343	177
Net loss before income taxes	(18,871)	(16,155)
Income tax expense	(406)	-
Net loss	(19,277)	(16,155)
Other comprehensive income (loss):		
Foreign currency translation adjustments	284	(3)
Total other comprehensive income (loss)	284	(3)
Comprehensive loss	$ (18,993)	$ (16,158)

Revenue

We generated revenue of $0.2 million for the year ended December 31, 2020 while no revenue was generated for 2019. $0.2 million of our revenue for the year ended December 31, 2020 was product revenue from supply agreements with a related party for KHC46 and a low dose zinc-silver solution, two dietary supplements that we began supplying during this period. We also generated minimal product revenue from sales of rMetx™ ZnAg Immune Boost during this period. In addition, $30 thousand of our revenue during the same period was royalty revenue from a license agreement with the same related party.

Operating Expenses

Cost of Sales

We incurred cost of sales of $0.1 million for the year ended December 31, 2020 relating to production and distribution costs for the sales of our KHC46 and low dose zinc-silver solution dietary supplement products through supply agreements we have entered into with a related party while no cost of sales was incurred for 2019.

Research and Development Expenses

Research and development expenses were $15.2 million for the year ended December 31, 2020 compared to $9.6 million for 2019. During these periods, substantially all of our research and development expenses were related to the development and clinical trials of CNM-Au8. This increase of $5.6 million, or 59.0%, was primarily due to the progression of our drug candidates through the clinical development process, including increased enrollment into the REPAIR-PD and the REPAIR-MS studies, and calendar payments due for our participation in the Healey-ALS Platform Trial. These efforts resulted in greater associated costs and manufacturing expenses in support of these trials.

General and Administrative Expenses

General and administrative expenses were $5.2 million for the year ended December 31, 2020 compared to $6.8 million for 2019. This decrease of $1.6 million, or 23.9% was primarily due to decreased expenses relating to efforts to list our shares on an international public exchange during 2019, which were subsequently abandoned. For the year ended December 31, 2020, we had a small increase in employee salary and benefits, shares based-compensation expenses due to the growth of our business and professional expenses related to fund raising activities.

Other Income (Expenses)

Other income (expenses), net for the years ended December 31, 2020 and 2019 included the following:

(i) recognized interest expense of $1.0 million and $0.1 million, respectively, due to an increase in the fair value of the Company's notes payable. As of December 31, 2020, the fair value of the Company's notes payable is determined based on the closing price of CLNN shares listed on the Nasdaq.

(ii) recognized expense of $14.6 million and $0.4 million relating to the changes in fair value of preferred stock warrant liability, respectively. The increase of $14.2 million in association with the changes in fair value of preferred stock warrant liability was primarily a result of the increase in the value of outstanding warrants as the estimated value of our company and the likelihood of a liquidation event increased due to consideration of the Reverse Recapitalization. Upon the consummation of the Reverse Recapitalization, we determined that the warrants qualify for classification as permanent equity and we reclassified the resulting warrant liability to additional paid-in capital. No change in fair value of preferred stock warrant liability will be recorded going forward.

(iii) recognized Clene Nanomedicine contingent earn-out liability of $64.7 million upon the closing of the Reverse Recapitalization and subsequently remeasured the contingent earn-out liability to the fair value of $52.1 million at the reporting date. The change in fair value of our Clene Nanomedicine contingent earn-out of $12.6 million was primarily a result of the decrease of the closing price of CLNN shares listed on the Nasdaq for $9.01 per share on December 31, 2020 from $10.82 per share on December 30, 2020 when we recognized the Clene Nanomedicine contingent earn-out liability at inception.

(iv) recognized Initial Shareholders contingent earn-out liability of $7.4 million upon the closing of the Reverse Recapitalization and subsequently remeasured the contingent earn-out liability to the fair value of $5.9 million at the reporting date. The change in fair value of our Initial Shareholders contingent earn-out of $1.5 million was primarily a result of the decrease of the closing price of CLNN shares listed on the Nasdaq for $9.01 per share on December 31, 2020 from $10.82 per share on December 30, 2020 when we recognized the Initial Shareholders contingent earn-out liability at inception.

(v) recognized income of $3.2 million and $0.6 million relating to a research and development credit received from the Australian government, respectively. We recognized Australian research and development credit in an amount equal to the qualifying expenses incurred in each period multiplied by the applicable reimbursement percentage. The increase in research and development credit is the result of increased research and development activities during the year ended December 31, 2020.

(vi) recognized expense of $0.5 million due to loss of extinguishment of convertible notes, while not recording any similar expenses in 2019.

Comprehensive Loss

As a result of the foregoing, we incurred a comprehensive loss of $19.0 million for the year ended December 31, 2020 compared to a comprehensive loss of $16.2 million for 2019.

Taxation

United States

We are incorporated in Delaware in the U.S. and subject to statutory U.S. federal corporate income tax at a rate of 21% for the years ended December 31, 2020 and 2019. We are also subject to state income tax in Utah and Maryland, at a rate of 4.95% and 8.25%, respectively, for the years ended December 31, 2020 and 2019. We recorded a full valuation allowance against our net deferred tax assets due to the uncertainty as to whether such assets will be realized resulting from our three-year cumulative loss position and the uncertainty surrounding our ability to generate pre-tax income in the foreseeable future. This valuation allowance was $22.1 million and $16.8 million as of December 31, 2020 and 2019, respectively.

Australia

Our wholly owned subsidiary, Clene Australia Pty Ltd, was established in Australia on March 5, 2018 and is subject to corporate income tax at a rate of 27.5%. Clene Australia total income tax expense was $0.4 million for the year ended December 31, 2020. In 2019, Clene Australia had no taxable income and therefore, no provision for income taxes was required. We recorded $3.2 million as other income in 2020 for a refund of research and development credits pertaining to Clene Australia Pty Ltd for the 2020 and 2019 tax year. We recorded $0.6 million as other income in 2019 for a refund of research and development credits pertaining to Clene Australia Pty Ltd for the 2018 tax year.

JOBS Act

The JOBS Act permits an emerging growth company ("**EGC**") such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We have elected to use the extended transition period under the JOBS Act until the earlier of the date we (1) are no longer an emerging growth company or (2) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our consolidated financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We will remain an emerging growth company until the earliest to occur of: (1) the last day of the fiscal year in which we have more than $1.07 billion in annual revenue; (2) the date on which we are deemed to be a "large accelerated filer," which would occur if the market value of our equity securities held by non-affiliates exceeds US$700 million as of the last business day of our most recently completed second fiscal quarter; (3) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period; and (4) the last day of the fiscal year ending after the fifth anniversary of Tottenham's initial public offering, or August 6, 2023.

We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for public companies.

Smaller Reporting Company Status

We are a Smaller Reporting Company ("**SRC**") as defined in Item 10(f)(1) of Regulation S-K. Smaller reporting companies may take advantage of certain reduced disclosure obligations, including, among other things, providing only two years of audited financial statements. We will remain a smaller reporting company until (1) the market value of our Common Stock held by non-affiliates exceeds $250 million as of the end of the second fiscal quarter and our annual revenues exceed $100 million during the previous fiscal year, or (2) the market value of our Common Stock held by non-affiliates exceeds $700 million as of the end of the second fiscal quarter.

Liquidity and Capital Resources

Since inception, we have incurred annual net losses from our operations. Substantially all of our losses have resulted from the funding of our research and development programs and general and administrative expenses associated with our operations. We incurred net losses of $19.3 million and $16.2 million for the years ended December 31, 2020 and 2019, respectively. Our loss from operations was $20.2 million and $16.3 million for the years ended December 31, 2020 and 2019, respectively. We have financed our operations principally through proceeds from the sale of preferred stock, the sale of preferred stock warrants and the sale of convertible notes that have converted into shares of preferred stock, and through the funds we raised from the consummation of the Reverse Recapitalization and the PIPE offering. During the years ended December 31, 2020 and 2019, we raised an aggregate of $69.5 million and $5.5 million, respectively, consisting of net proceeds from issuances of preferred stock, common stock upon exercise of common stock options, convertible promissory notes, notes payable, the Reverse Recapitalization and the PIPE offering. In February 2021, we filed a registration statement on Form S-1 to register 4,541,481 shares of Common Stock underlying outstanding warrants. We will receive aggregate gross proceeds of $30.7 million if all of these are exercised.

The net cash used in our operating activities was $18.9 million and $13.2 million for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had cash of $59.3 million. We expect that the cash on hand as of December 31, 2020 will be sufficient to fund our operations for a period extending beyond twelve months from the date the consolidated financial statements are issued. We have based this estimate on assumptions that may prove to be wrong, and we may exhaust our available capital resources sooner than we anticipate. We expect our expenses to increase significantly in connection with our ongoing activities, particularly as we advance the clinical development of our clinical-stage drug products and continue research and development of our preclinical drug products and initiate additional clinical trials of, and seek regulatory approval for, these and other future drug products. As we continue to grow and expand, we will incur more expenses relating to regulatory compliance and sales and marketing personnel as we prepare to commence commercialization once we obtain regulatory approval of our drug products.

Our ability to continue as a going concern may require obtaining additional funding to finance operations. As part of our ongoing business plans, we will continue seeking funding through equity financing and may seek debt financing or other capital sources. We may not be able to obtain financing on acceptable terms, or at all. The terms of any financing may adversely affect the holdings or the rights of our shareholders. If we are unable to raise capital when needed or on acceptable terms, we would be forced to delay, reduce or eliminate research and development programs and commercialization efforts.

The following table provides information regarding our cash flows for relevant periods:

	December 31,	
	2020	2019
	(in thousands)	
Net cash used in operating activities	$ (18,929)	$ (13,197)
Net cash used in investing activities	(387)	(294)
Net cash provided by financing activities	69,534	5,503
Net effect of foreign exchange rate changes	269	(1)
Net increase (decrease) in cash	$ 50,487	$ (7,989)

Use of Funds

Our primary use of cash in all periods presented was to fund our research and development, regulatory and other clinical trial costs, and related supporting administration. Our prepaid expenses and other current assets, accounts payable and accrued expense balances in all periods presented were affected by the timing of vendor invoicing and payments, and impacted the cash provided by, or used in, operations. We have no commitments for capital expenditures as of the end of the latest fiscal period.

Operating Activities

Net cash used in operating activities was $18.9 million of cash for the year ended December 31, 2020, which resulted from a net loss of $19.3 million, adjusted for (i) non-cash items of $3.7 million, which primarily consisted of depreciation expense of $1.0 million, stock-based compensation expenses of $0.8 million, changes in the fair value of preferred stock warrant liability of $14.6 million, changes in fair value of the Clene Nanomedicine contingent earn-out of $12.6 million, changes in fair value of the Initial Shareholders contingent earn-out of $1.5 million, loss on extinguishment of convertible notes of $0.5 million and increase in interest accrued on notes payable and accretion of debt discount of $0.9 million, and (ii) a net decrease in operating assets and liabilities of $3.3 million. The net decrease in operating assets and liabilities was primarily attributable to an increase in inventory of $0.2 million, an increase in prepaid expenses and other current assets of $2.9 million due to the increase in Australia research and development credit receivable and prepayments to CROs and other vendors, $0.3 million decrease in accounts payable, $0.2 million increase in income tax payable related to the Australian entity, $0.3 million decrease in accrued liabilities due to the timing of vendor invoicing and payments, $0.1 million decrease in payable to related parties, $0.3 million increase in deferred income tax, $0.1 million increase in deferred revenue from related parties, and $0.1 million decrease in operating lease obligations.

Net cash used in operating activities was $13.2 million of cash for the year ended December 31, 2019, which resulted from a net loss of $16.2 million, adjusted for (i) non-cash items of $1.8 million, which primarily consisted of depreciation of $0.8 million, stock-based compensation expenses of $0.4 million and changes in fair value of preferred stock warrant liability of $0.4 million, and (ii) a net increase in operating assets and liabilities of $1.2 million. The net increase in operating assets and liabilities was primarily attributable to (1) an increase in accrued liabilities of $1.9 million relating to accrued professional fees, (2) a decrease in prepaid expenses and other current assets of $0.4 million relating to prepayments for clinical studies, and (3) a decrease in payment of operating lease obligations of $0.2 million relating to our leased office space.

Investing Activities

Net cash used in investing activities was $0.4 million and $0.3 million for the years ended December 31, 2020 and 2019, respectively, which in each instance was related to purchases of property and equipment.

Financing Activities

Net cash provided by financing activities was $69.5 million for the year ended December 31, 2020, which primarily resulted from (i) funds raised in connection with the Reverse Recapitalization, net of transaction costs, of $5.6 million, (ii) net proceeds from the PIPE transaction of $22.2 million, (iii) proceeds from the issuance of Series D preferred Stock, net of issuance costs, of $35.1 million, (iv) proceeds from the issuance of convertible notes payable of $6.1 million, (v) proceeds from the issuance of notes payable of $0.6 million and (vi) proceeds from issuance of common stock upon exercise of common stock options of $0.1 million partially offset by payments on our finance lease obligations of $0.2 million.

Net cash provided by financing activities was $5.5 million for the year ended December 31, 2019, which primarily resulted from (i) proceeds from issuance of Series C Preferred Stock, net of issuance costs, of $8.1 million and (ii) proceeds from the issuance of notes payable of $0.6 million and was partially offset by (a) payments of notes payable of $3.0 million and (b) payments of finance lease obligations of $0.2 million.

Debt Obligations

In February 2019, we entered into a loan agreement with the Department of Housing and Community Development, a principal department of the State of Maryland, pursuant to which Maryland agreed to provide a $0.5 million term loan. Amounts outstanding under the loan bear simple interest at an annual rate of 8.00%. Repayment of the full balance outstanding is due on February 22, 2034. This loan establishes “Phantom Shares,” based on 119,906 shares of our common stock (based on 863,110 Series C Preferred Shares prior to the Reverse Recapitalization), determined at issuance. The Loan Agreement states the repayment amount is to be the greater of the balance of principal and accrued interest or the Phantom Shares value. We determined that the note should be accounted for at fair value. We record the fair value of the debt at the end of each reporting period. In order to value the note, we consider the amount of the simple interest expense that would be due and consider the value of Phantom Shares. Upon the closing of the Reverse Recapitalization and as of December 31, 2020, the fair value of the Maryland note payable is now determined based on the closing price of CLNN shares listed on the Nasdaq. Expenses of $0.5 million and $34 thousand were recognized during the years ended December 31, 2020 and 2019, respectively. The fair value of $1.1 million and $0.5 million of principal and accrued interest is included in long-term notes payable as of December 31, 2020 and December 31, 2019, respectively.

In April 2019, the Company entered into a loan agreement (the “2019 Cecil Loan”) with Cecil County, Maryland (“Cecil”). Pursuant to the 2019 Cecil Loan, Cecil agreed to provide a $0.1 million term loan. Amounts outstanding under the 2019 Cecil Loan bear simple interest at an annual rate of 8.00%. Under the 2019 Cecil Loan, the Company has agreed to affirmative and negative covenants to which it will remain subject until maturity. These covenants include providing information about the Company and its operations; limitations on the Company’s ability to retire, repurchase, or redeem the Company’s common or preferred stock, options, and warrants other than per the terms of the securities; and limitations on the Company’s ability to pay dividends of cash or property. There are no financial covenants associated with the Loan Agreement. Events of default under the Loan Agreement include failure to make payments when due, insolvency events, failure to comply with covenants, and material adverse effects with respect to the Company. The Company is not in violation of any affirmative or negative covenants. Repayment of the full balance outstanding is due on April 30, 2034. The 2019 Cecil Loan establishes “Phantom Shares,” based on 23,981 shares of the Company’s common stock (based on 172,622 Series C Preferred Shares prior to the Reverse Recapitalization), determined at issuance. The 2019 Cecil Loan states the repayment amount is to be the greater of the balance of principal and accrued interest or the Phantom Share value. The Company determined that the note should be accounted for at fair value. The Company records the fair value of the debt at the end of each reporting period. Upon the closing of the Reverse Recapitalization and as of December 31, 2020, the fair value of the 2019 Cecil Loan is now determined based on the closing price of CLNN shares listed on the Nasdaq. In order to value the note, the Company considers the amount of the simple interest expense that would be due and considers the value of Phantom Shares. Expense of $0.1 million and $6 thousand was recognized during the years ended December 31, 2020 and 2019, respectively. The fair value of $0.2 million and $0.1 million of principal and accrued interest is included in long-term notes payable as of December 31, 2020 and December 31, 2019, respectively.

In February through July 2020, we issued convertible promissory notes (the "2020 Convertible Notes") in an aggregate principal amount of $6.1 million, bearing interest at an annual rate of 5%. The 2020 Convertible Notes were convertible at the earlier of (i) one year, at which point the notes would be convertible into Series C preferred shares at the Series C preferred share issuance price, and (ii) next equity financing of no less than $10.0 million, at which point the notes would be convertible into shares issued in the next equity financing at 90% of the per share issuance price of the next equity financing. The redemption feature at the next equity financing met the requirements of an embedded derivative to be bifurcated and recorded at fair value. We bifurcated the embedded feature at issuance and recorded a derivative liability of $0.7 million at inception in conjunction with a discount on debt to be amortized over the life of the note. We recognized interest expense of $0.2 million, including amortization of debt discount of $0.2 million during the year ended December 31, 2020, in connection with the 2020 Convertible Notes. We also identified two other embedded features in these convertible promissory notes that were not bifurcated, which were the conversion into Series C preferred shares upon maturity and the redemption upon a liquidation event. On August 11, 2020, in connection with our issuance and sale of Series D Preferred Stock prior to the Reverse Recapitalization, all of the outstanding principal and accrued interest under the 2020 Convertible Notes, totaling $6.9 million, was automatically converted into 1,497,135 shares of Series D Preferred Stock at a price equal to 90% of $4.60 per share, the per share price paid in cash by investors in the Series D preferred stock financing. We accounted for the conversion of the 2020 Convertible Notes as a debt extinguishment and recognized a loss on extinguishment of debt of $0.5 million within other income (expense), net in the consolidated statement of operations and comprehensive loss. As of the date of conversion, the unamortized discount on the 2020 Convertible Notes was $0.5 million. The loss on extinguishment was calculated as the difference between (i) the fair value of the 1,497,135 shares of Series D Preferred Stock issued to settle the 2020 Convertible Notes of $6.9 million and (ii) the carrying value of the 2020 Convertible Notes, including the principal balance of the 2020 Convertible Notes of $6.1 million and accrued but unpaid interest of $76 thousand, net of the unamortized debt discount of $5.7 million, plus the then-current fair value of derivative liability associated with the 2020 Convertible Notes at the time of the extinguishment of $0.7 million.

In May 2020, the Company entered into a note payable in the amount of $0.6 million (the "PPP Note") under the Paycheck Protection Program of the CARES Act (the "PPP"). As amended, the PPP permits forgiveness of amounts loaned for payments of payroll and other qualifying expenses within 24 weeks of receipt of loaned funds, given that at least 60% of the total loan is used for payroll. Amounts not forgiven by the PPP have a repayment period of five years. The Company expects the full $0.6 million balance of the PPP Note to be forgiven. The Company will record any forgiveness after approval by the issuer. Until then, the PPP balance is included in long-term notes payable as of December 31, 2020. On January 11, 2021, the U.S. Small Business Administration notified the Company that the Company's PPP loan of $0.6 million had been forgiven. As a result, we will record a gain of $0.6 million in our consolidated statements of operations and comprehensive loss in our first quarter of 2021.

Contractual Obligations and Commitments

The following table sets forth our contractual obligations as of December 31, 2020:

	Payment Due by Period			
	Total	**1 - 3 years**	**3 - 5 years**	**More than 5 years**
	($ in thousands)			
Long-term debt obligations	$ 1,949	$ -	$ -	$ 1,949
Finance lease liabilities	395	369	26	-
Operating lease obligations	1,979	755	1,161	63
Total	$ 4,323	$ 1,124	$ 1,187	$ 2,012

We have made an accounting policy election not to recognize leases with an initial term of 12 months or less within our consolidated balance sheet and to recognize those lease payments on a straight-line basis in our consolidated statements of operations and comprehensive loss over the lease term.

We enter into agreements in the normal course of business with CROs for clinical trials and with vendors for preclinical studies and other services and products for operating purposes, which are cancelable at any time by us, subject to payment of our remaining obligations under binding purchase orders and, in certain cases, nominal early termination fees. These commitments are not deemed significant.

Off-Balance Sheet Arrangements

During the period presented, we did not have, and we currently do not have, any off-balance sheet arrangements, such as relationships with unconsolidated entities or financial partnerships, which are often referred to as structured finance or special purpose entities, established for the purpose of facilitating financing transactions that are not required to be reflected on our balance sheets.

Critical Accounting Policies

Our discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with GAAP. The preparation of these financial statements requires us to make estimates, assumptions and judgments that affect the reported amounts of assets, liabilities, revenues, costs and expenses. We evaluate our estimates and judgments on an ongoing basis, and our actual results may differ from these estimates. We base our estimates on historical experience, known trends and events, contractual milestones and other various factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources.

Our most critical accounting policies are summarized below. See Note 2 to the Accountant's Report included elsewhere in this Annual Report for a description of our other significant accounting policies.

Contingent Earn-out

In connection with the Reverse Recapitalization and pursuant to the Merger Agreement, we agreed to issue additional shares to Clene Nanomedicine's common shareholders immediately prior to the Reverse Recapitalization and to the initial shareholders of Tottenham a certain amount of our Common Stock upon our achieving certain milestones. In accordance with ASC 815 – *Derivatives and hedging*, the Earn-out Shares are not indexed to our Common Stock and therefore are accounted for as a liability with the changes in fair value recorded as a component of other income (expense), net in our consolidated statements of operations and comprehensive loss. The contingent earn-out liabilities were initially measured at fair value upon the closing of the Reverse Recapitalization and are subsequently remeasured to fair value at each reporting date.

Our contingent earn-out liabilities contain unobservable inputs that reflect our own assumptions. We used a Monte Carlo analysis to simulate the future path of our stock price over the earn-out period. The assumptions utilized in the calculation are based on the achievement of certain stock price milestones such as projected stock price, volatility and risk-free rate. For potential payments related to the product development milestone, the fair value was determined based on our expectations of achieving such milestone and the simulated estimated stock price on the expected date of achievement. Our significant unobservable inputs upon the closing of the Reverse Recapitalization and as of December 31, 2020 were as follows: (i) 85% of expected stock price volatility, (ii) risk-free interest rate of 0.4%, and (iii) expected term of 5 years.

We believe our assumptions are reasonable based on available information, our experience, knowledge, and judgments. These estimates can be affected by factors that are difficult to predict including future (i) CLNN closing price per share on the Nasdaq, (ii) estimated stock price volatility over the earn-out period, and (iii) risk free rates. Changes in assumptions and estimates used in our analysis, or future results that vary from assumptions used in the analysis, could affect the fair value of the contingent earn-out and could result in material changes in future periods.

Valuation of Warrants to Purchase Preferred Stock

Prior to the Reverse Recapitalization with Tottenham, we accounted for freestanding warrants to purchase shares of preferred stock as liabilities on the consolidated balance sheet at their estimated fair value as the underlying redeemable convertible preferred stock was considered contingently redeemable and may obligate us to transfer assets to the holders at a future date upon the occurrence of a deemed liquidation event. At the end of each reporting period, changes in the estimated fair value of the warrants to purchase shares of preferred stock were recorded in change in fair value of preferred stock warrant liability in the consolidated statements of operations and comprehensive loss. Immediately prior to the close of the Reverse Recapitalization, all of the outstanding Clene Nanomedicine preferred stock was converted to our Common Stock and the Clene Nanomedicine preferred stock warrants to purchase Clene Nanomedicine preferred stock were converted to warrants to purchase our Common Stock. Upon conversion, we assessed the features of the warrants and determined that they qualify for classification as permanent equity upon the closing of the Reverse Recapitalization. We remeasured the warrants to fair value one final time upon the close of the Reverse Recapitalization and recognized a loss of $14.6 million for the year ended December 31, 2020, within other income, (expense), net on the consolidated statements of operations and comprehensive loss. Upon the closing of the Reverse Recapitalization, the preferred stock warrant liability was reclassified to additional paid-in capital.

For the year ended December 31, 2019, change in the estimated fair value of the preferred stock warrant liability was $0.4 million.

Our preferred stock warrant liabilities contain unobservable inputs that reflect our own assumptions. We used a Black-Scholes valuation model to value the preferred stock warrant liability during 2020 and we used an option pricing model to value the preferred stock warrant liability during 2019. The following table summarizes our significant unobservable inputs as at the dates indicated:

	Prior to the Closing of the Business Combination on December 30, 2020	As of December 31, 2019
Series D Preferred Stock		
Fair value	$10.82	N/A
Expected term	2.3 years	N/A
Expect volatility	101%	N/A
Series C Preferred Stock		
Fair value	N/A	$4.1699
Expected term	N/A	1 year
Expect volatility	N/A	49%
Series A Preferred Stock		
Fair value	$10.82	$3.1046
Expected term	2.3 years	1 year
Expect volatility	101%	71%

Our board of directors determines the fair value of the preferred stock by considering a number of objective and subjective factors, including third-party valuations, valuations of comparable companies, sales of redeemable convertible preferred stock, sales of Common Stock to unrelated third parties, operating and financial performance, the lack of liquidity of our capital stock, and general and industry-specific economic outlook. We estimated the volatility of our preferred stock based on comparable peer companies' historical volatility. The risk-free interest rate for periods within the contractual life of the warrants is based on the U.S. Treasury yield curve in effect at the valuation date. We have no plans to declare any future dividends. The determination of the fair value of the preferred stock warrant liability could change in future periods based upon changes in the value of our preferred stock and other assumptions, as presented above.

Stock-based Compensation

We account for stock-based compensation arrangements with employees in accordance with Accounting Standards Codification (ASC) Topic 718-10, Compensation — Stock Compensation. ASC 718 requires the recognition of compensation expense, using a fair value-based method, for costs related to all share-based payments including stock options. We grant equity awards under our stock-based compensation plan, which may include stock options and restricted common stock.

Prior to the consummation of the Reverse Recapitalization, our determination of the fair value of stock options on the date of grant utilized the Black-Scholes option-pricing model and was impacted by Clene Nanomedicine's common stock price as well as changes in assumptions regarding a number of subjective variables. These variables include, but are not limited to, the expected term that options will remain outstanding, the expected common stock price volatility over the term of the option awards, risk-free interest rates, and expected dividends.

After the closing of the Reverse Recapitalization, our board of directors determined the fair value of each share of Common Stock underlying stock-based awards based on the closing price of our Common Stock as reported by Nasdaq on the date of grant. RSUs that have a market condition are associated with the achievement of certain stock price milestones. The fair value of the RSUs with market conditions are determined using a Monte Carlo valuation model. The assumptions utilized in the Monte Carlo valuation model include projected stock price, volatility and risk-free rate based on the achievement of certain stock price milestones.

The fair value is recognized over the period during which an optionee is required to provide services in exchange for the option award and service-based RSUs, known as the requisite service period (usually the vesting period), on a straight-line basis. For the RSUs with market conditions, the fair value is recognized over the period based on the expected milestone achievement dates as the derived service period (usually the vesting period), on a straight-line basis. For the RSUs with performance conditions, the grant date fair value of these awards is the market price on the applicable grant date, and compensation expense will be recognized when the conditions become probable of being satisfied. The Company will recognize a cumulative true-up adjustment once the conditions become probable of being satisfied as the related service period had been completed in a prior period.

We recognize stock-based compensation expense for the portion of awards that have vested. Stock compensation expense is recorded in research and development and general and administrative expenses based on the classification of the work performed by the grantees. Stock-based compensation expense recognized at fair value includes the impact of estimated forfeitures. In 2017, we adopted new accounting guidance from the Financial Accounting Standards Board ("FASB") on stock compensation, or Accounting Standards Update ("ASU") 2016-09, as described in "Recently Adopted Accounting Standards" below and have elected to account for forfeitures as they occur, rather than estimating expected forfeitures.

The following table sets forth stock-based compensation for the periods presented:

	Year ended December 31,	
	2020	2019
	(in thousands)	
General and administrative	$ 281	$ 161
Research and development	480	238
Total stock-based compensation	$ 761	$ 399

As of December 31, 2020, we had approximately $2.4 million of unrecognized stock-based compensation costs related to non-vested awards which is expected to be recognized over a weighted-average period of 2.04 years.

Stock Options

The following sets forth the outstanding common stock options and related activity for the years ended December 31, 2020 and 2019:

Equity	Number of Options	Weighted Average Exercise Price Per Share	Weighted Average Remaining Term (Years)	Instrinsic Value
Outstanding - December 31, 2018	5,698,090	$ 0.38	6.62	$ 11,089
Granted	1,440,717	2.42	9.66	-
Exercised	(11,878)	0.83	-	31
Forfeited	(248,757)	1.44	-	-
Outstanding - December 31, 2019	6,878,172	0.83	6.36	18,105
Granted	270,555	5.48	5.32	-
Exercised	(83,232)	0.94	-	740
Forfeited	(32,904)	1.65	-	-
Outstanding - December 31, 2020	7,032,591	$ 0.97	5.34	$ 62,462
Options vested and exercisable - December 31, 2020	5,896,034	$ 0.55	4.86	$ 52,694
Options vested and exercisable - Stock options vested and expected to vest December 31, 2020	7,032,591	$ 0.97	5.34	$ 62,462

Prior to the consummation of the Reverse Recapitalization, the exercise price of the stock options granted was based on the fair market value of the common shares of the Company as of the grant date as determined by the Board of Directors, with input from the Company's management. The Board of Directors determined the fair value of the common stock at the time of grant of the options by considering a number of objective and subjective factors, including third-party valuation reports, valuations of comparable companies, sales of redeemable convertible Preferred Stock, sales of common stock to unrelated third parties, operating and financial performance, the lack of liquidity of the Company's capital stock, and general and industry-specific economic outlook.

Stock options are valued using the Black-Scholes option pricing model. Since the Company has limited trading history of its Common Stock, the expected volatility is derived from the average historical stock volatilities of several unrelated public companies within the Company's industry that the Company considers to be comparable to its own business over a period equivalent to the expected term of the stock option grants. The risk-free interest rate for periods within the contractual life of the stock options is based on the U.S. Treasury yield curve in effect at the time of the grant. The expected dividend is assumed to be zero as the Company has never paid dividends and has no current plans to do so. The expected term represents the period that stock-based awards are expected to be outstanding. For option grants that are considered to be "plain vanilla," the Company determines the expected term using the simplified method. The simplified method deems the term to be the average of the time-to-vesting and the contractual life of the options. For other option grants, the Company estimates the expected term using historical data on employee exercises and post-vesting employment termination behavior taking into account the contractual life of the award.

The assumptions used to calculate the value of the stock option awards granted in 2020 and 2019 are presented as follows:

	2020	2019
Expected stock price volatility	75.00% - 119.30%	75.00%
Risk-free interest rate	0.39% - 0.53%	1.46%
Expected dividend yield	0%	0%
Expected term of options	6 years	6 years

The weighted average grant-date fair values of options granted for the years ended December 31, 2020 and 2019 were $2.3923 and $1.5806, respectively.

Restricted Stock Units

On December 30, 2020, we granted the following shares of restricted common stock under the 2020 Stock Plan:

- 370,101 shares to various employees and non-employee directors, which vest on June 30, 2021, subject to the employee's continuous employment through such vesting date. The award represents 5% of the converted stock options under 2014 Stock Plan as a result of the Reverse Recapitalization and complements the 5% closing payment shares held in escrow for Clene Nanomedicine common shareholders. The grant-date fair value of these awards was $4.0 million.

- 454,781 shares to various employees and non-employee directors, which were eligible to vest based on certain market conditions, subject to the employee's continuous employment through such vesting date. The award complements the Milestone 1 earn-out share entitlement of Clene Nanomedicine shareholders and vests based on the same market condition. The grant-date fair value of these awards, using a Monte Carlo simulation, was $4.3 million. Based on the outcome of the market condition as of the December 31, 2020 measurement date, no shares were vested.

- 341,090 shares to various employees and non-employee directors, which were eligible to vest based on certain market conditions, subject to the employee's continuous employment through such vesting date. The award complements the Milestone 2 earn-out share entitlement of Clene Nanomedicine shareholders and vests based on the same market condition. The grant-date fair value of these awards, using a Monte Carlo simulation, was $3.5 million. Based on the outcome of the market condition as of the December 31, 2020 measurement date, no shares were vested.

- 341,090 shares to various employees and non-employee directors, which were eligible vest based on certain performance conditions tied to the completion of the COVID-19 coronavirus treatment study, subject to the employee's continuous employment through such vesting date. The award complements the Milestone 3 earn-out share entitlement of Clene Nanomedicine shareholders and vests based on the same performance condition. The grant-date fair value of these awards was $3.7 million based on a weighted average grant date fair value of $10.82 per share. The Company did not recognize compensation expense because the occurrence of achieving this milestone was not probable. As of the December 31, 2020, no shares were vested.

The following table summarizes the restricted common stock activity during the year ended December 31, 2020:

	Number of RSUs	Weighted Average Grant Date Fair Value
Unvested balance as of December 31, 2019	-	$ -
Granted	1,507,062	10.30
Vested	-	-
Unvested balance as of December 31, 2020	1,507,062	$ 10.30

The assumptions used to calculate the value of the restricted stock units granted in 2020 in the Monte Carlo valuation model include projected stock price, volatility and risk-free rate based on the achievement of certain stock price milestones. Our significant unobservable inputs as of December 31, 2020 were as follows: (i) 85% of expected stock price volatility, (ii) risk-free interest rate of 0.4%, and (iii) expected term of 5 years.

Income Taxes

We account for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in our tax returns. Deferred tax assets and liabilities are determined on the basis of the differences between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. We assess the likelihood that our deferred tax assets will be recovered from future taxable income and, to the extent we believe, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

We account for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that is more-likely-than-not to be realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Recent Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and result of operations is disclosed in Note 2 to our consolidated financial statements included elsewhere in this Annual Report.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Information required by this Item is not applicable as we are electing scaled disclosure requirements available to Smaller Reporting Companies with respect to this Item.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Index to Consolidated Financial Statements

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Clene Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Clene Inc. and its subsidiaries (the "Company") as of December 31, 2020 and 2019, and the related consolidated statements of operations and comprehensive loss, of redeemable convertible preferred stock and stockholders' equity (deficit) and of cash flows for the years then ended, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated 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 of these consolidated financial statements 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 consolidated financial statements are free of material misstatement, whether due to error or fraud.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

Emphasis of Matter

As discussed in Note 1 to the consolidated financial statements, the Company will require additional financing or a collaboration agreement to fund future operations. Management's evaluation of the events and conditions and management's plans to mitigate this matter are also described in Note 1.

/s/ PricewaterhouseCoopers LLP

Salt Lake City, Utah
March 26, 2021

We have served as the Company's auditor since 2019.

CLENE INC.
CONSOLIDATED BALANCE SHEETS
(Amounts in thousands, except share and per share amounts)

	December 31, 2020	December 31, 2019
ASSETS		
Current assets:		
Cash	$ 59,275	$ 8,788
Inventory	191	28
Prepaid expenses and other current assets	3,523	661
Total current assets	62,989	9,477
Right-of-use assets	1,029	1,081
Property and equipment, net	4,225	4,319
TOTAL ASSETS	$ 68,243	$ 14,877
LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK, AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,124	$ 889
Accrued liabilities	3,960	2,878
Income tax payable	164	-
Payable to related parties	-	131
Deferred revenue from related parties	112	-
Operating lease obligations, current portion	194	216
Finance lease obligations, current portion	190	200
Clene Nanomedicine contingent earn-out, current portion	5,924	-
Total current liabilities	11,668	4,314
Operating lease obligations, net of current portion	1,785	1,434
Finance lease obligations, net of current portion	205	389
Notes payable, net of current portion	1,949	640
Deferred income tax	260	-
Redeemable convertible preferred stock warrant liability	-	3,213
Clene Nanomedicine contingent earn-out, net of current portion	46,129	-
Initial Shareholders contingent earn-out	5,906	-
TOTAL LIABILITIES	67,902	9,990
Commitments and contingencies (Note 13)		
Redeemable convertible preferred stock[(1)] (Series A, B, C and D), $0.0001 par value; 0 and 31,036,008 shares authorized as of December 31, 2020 and 2019, respectively; 0 and 27,499,837 shares issued and outstanding as of December 31, 2020 and 2019, respectively; liquidation preference of $0 and $78,875 as of December 31, 2020 and 2019, respectively	-	72,661
Stockholders' equity (deficit): [(1)]		
Common stock, $0.0001 par value: 100,000,000 shares authorized; 59,526,171 and 17,357,505 shares issued and outstanding at December 31, 2020 and December 31, 2019, respectively	6	2
Additional paid-in capital	153,571	1,754
Accumulated deficit	(153,561)	(69,571)
Accumulated other comprehensive income	325	41
TOTAL STOCKHOLDERS' EQUITY (DEFICIT)	341	(67,774)
TOTAL LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK, AND STOCKHOLDERS' EQUITY	$ 68,243	$ 14,877

(1) Retroactively restated for the reverse recapitalization as described in Note 1

See accompanying notes to the consolidated financial statements.

CLENE INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(Amounts in thousands, except share and per share amounts)

	Year Ended December 31,	
	2020	**2019**
Revenue:		
Product revenue	$ 176	$ -
Royalty revenue	30	-
Total revenue	206	-
Operating expenses:		
Cost of revenue	65	-
Research and development	15,204	9,563
General and administrative	5,151	6,769
Total operating expenses	20,420	16,332
Loss from operations	(20,214)	(16,332)
Other income (expense), net:		
Interest expense	(950)	(88)
Gain on termination of lease	51	-
Change in fair value of preferred stock warrant liability	(14,615)	(361)
Change in fair value of derivative liability	29	-
Change in fair value of Clene Nanomedicine contingent earn-out	12,659	-
Change in fair value of Initial Shareholders contingent earn-out	1,465	-
Australia research and development credit	3,210	599
Loss on extinguishment of convertibles notes	(540)	-
Other income, net	34	27
Total other income (expense), net	1,343	177
Net loss before income taxes	(18,871)	(16,155)
Income tax expense	(406)	-
Net loss	(19,277)	(16,155)
Other comprehensive income (loss):		
Foreign currency translation adjustments	284	(3)
Total other comprehensive income (loss)	284	(3)
Comprehensive loss	$ (18,993)	$ (16,158)
Net loss per share-- basic and diluted (Note 19) [1]	$ (1.10)	$ (0.93)
Weighted average common shares used to compute basic and diluted net loss per share [1]	17,503,992	17,357,505

(1) Retroactively restated for the reverse recapitalization as described in Note 1

See accompanying notes to the consolidated financial statements.

CLENE INC.
CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT) (1)
(Amounts in thousands, except share and per share amounts)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balances at December 31, 2018	25,165,036	$ 62,926	17,345,002	$ 2	$ 1,345	$ (53,430)	$ 44	$ (52,039)
Application of ASC 842	-	-	-	-	-	14	-	14
Issuance of Series C preferred stock, net of issuance costs	1,935,111	8,069	-	-	-	-	-	-
Exercise of Series C preferred stock warrants	399,690	1,666	-	-	-	-	-	-
Exercise of stock options	-	-	12,503	-	10	-	-	10
Stock-based compensation expense	-	-	-	-	399	-	-	399
Foreign currency translation adjustment	-	-	-	-	-	-	(3)	(3)
Net loss	-	-	-	-	-	(16,155)	-	(16,155)
Balances at December 31, 2019	27,499,837	$ 72,661	17,357,505	$ 2	$ 1,754	$ (69,571)	$ 41	$ (67,774)
Issuance of Series D Preferred Stock, net of issuance costs of $1.3 million	7,896,922	35,051	-	-	-	-	-	-
Issuance of Series D Preferred Stock in connection with the extinguishment of convertible promissory notes	1,497,135	6,891	-	-	-	-	-	-
Exercise of stock options	-	-	87,613	-	78	-	-	78
Conversion of redeemable convertible preferred stock into common stock in connection with the Reverse Recapitalization	(36,893,894)	(114,603)	36,893,894	4	114,599	-	-	114,603
Extinguishment of preferred stock warrant liability in connection with the conversion of redeemable convertible preferred stock	-	-	-	-	17,828	-	-	17,828
Issuance of common stock upon the Reverse Recapitalization and the private offering	-	-	4,542,995	-	31,833	-	-	31,833
Offering costs in connection with the Reverse Recapitalization	-	-	-	-	(5,911)	-	-	(5,911)
Issuance of common stock as payment of related offering costs	-	-	644,164	-	-	-	-	-
Clene Nanomedicine contingent earn-out recognized in connection with the Reverse Recapitalization (see Note 12)	-	-	-	-	-	(64,713)	-	(64,713)
Initial Shareholders contingent earn-out recognized in connection with the Reverse Recapitalization (see Note 12)	-	-	-	-	(7,371)	-	-	(7,371)
Stock-based compensation expense	-	-	-	-	761	-	-	761
Foreign currency translation adjustment	-	-	-	-	-	-	284	284
Net loss	-	-	-	-	-	(19,277)	-	(19,277)
Balances at December 31, 2020	-	$ -	59,526,171	$ 6	$ 153,571	$ (153,561)	$ 325	$ 341

(1) Retroactively restated for the reverse recapitalization as described in Note 1

See accompanying notes to the consolidated financial statements.

CLENE INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(Amounts in thousands)

	Year Ended December 31,	
	2020	**2019**
Cash flows from operating activities:		
Net loss	$ (19,277)	$ (16,155)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	963	848
Non-cash lease expense	108	153
Change in fair value of preferred stock warrant liability	14,615	361
Change in fair value of Clene Nanomedicine contingent earn-out	(12,659)	-
Change in fair value of Initial Shareholders contingent earn-out	(1,465)	-
Stock-based compensation expense	761	399
Change in fair value of derivative	(29)	-
Loss on extinguishment of convertible notes	540	-
Gain on termination of lease	(51)	-
Accretion of debt discount	179	-
Increase in interest accrued on notes payable	732	40
Changes in operating assets and liabilities:		
Inventory	(163)	(28)
Prepaid expenses and other current assets	(2,862)	(354)
Accounts payable	(312)	(76)
Accrued liabilities	(272)	1,820
Income tax payable	164	-
Payable to related parties	(131)	32
Deferred revenue from related parties	112	-
Deferred income tax	260	-
Operating lease obligations	(142)	(237)
Net cash used in operating activities	(18,929)	(13,197)
Cash flows from investing activities:		
Purchases of property and equipment	(387)	(294)
Net cash used in investing activities	(387)	(294)
Cash flows from financing activities:		
Proceeds from issuance of Series C Preferred Stock, net of issuance costs	-	8,069
Proceeds from exercise of stock options	78	10
Payments of finance lease obligations	(194)	(176)
Proceeds from the issuance of note payable	652	600
Payments of notes payable	-	(3,000)
Payment of offering costs	(4,011)	-
Proceeds from the Reverse Recapitalization and from the private placement	31,833	-
Proceeds from issuance of Series D Preferred Stock, net of issuance costs	35,051	-
Proceeds from the issuance of convertible notes payable	6,125	-
Net cash provided by financing activities	69,534	5,503
Effect of foreign exchange rate changes on cash	269	(1)
Net increase (decrease) in cash	50,487	(7,989)
Cash – beginning of year	8,788	16,777
Cash – end of year	$ 59,275	$ 8,788
Supplemental disclosure of non-cash investing and financing activities:		
Acquisition of property and equipment through finance lease	$ -	$ 403
Acquisition of right-of-use assets and leasehold improvements through operating lease	$ 820	$ 11
Warrant liability settled on exercise	$ -	$ 1,666
Lease liability settled through termination of lease	$ 348	$ -
Issuance of derivative instrument related to convertible notes	$ 705	$ -
Issuance of Series D Preferred Stock upon extinguishment of convertible promissory notes	$ 5,675	$ -
Extinguishment of derivative liability in connection with extinguishment of convertible promissory notes	$ 676	$ -
Deferred transaction costs in accounts payable	$ 546	$ -
Deferred transaction costs in accrued liabilities	$ 1,354	$ -
Conversion of redeemable convertible preferred stock into common stock	$ 114,603	$ -
Extinguishment of preferred stock warrant liability in connection with the conversion of redeemable convertible preferred stock	$ 17,828	$ -
Issuance of common stock as payment of related offering costs	$ 6,442	
Clene Nanomedicine contingent earn-out recognized in connection with the Reverse Recapitalization	$ 64,713	$ -
Initial Shareholders contingent earn-out recognized in connection with the Reverse Recapitalization	$ 7,371	$ -
Supplemental disclosures:		

Cash paid for interest expense	$ 39	$ 48

See accompanying notes to the consolidated financial statements.

CLENE INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of the Business and Basis of Presentation

Clene Inc. (formerly Chelsea Worldwide, Inc.) (the "Company") is a biopharmaceutical company focused on the development of clean-surfaced nanocrystal drugs. The Company has developed an electrocrystal chemistry drug development platform, in which nanocrystals within a suspension are the therapeutic drug. Utilizing technology to create nanocrystal drug suspensions, the Company's platform has produced multiple drug assets, of which its lead assets are currently in development for use in neurological and infectious diseases, among others, such as a study for treatment of COVID-19 coronavirus pandemic. Secondary to the Company's drug development, as part of the Company's identification of potential drug assets, the Company has also identified certain mineral solutions as dietary supplements. The Company's dietary supplements may also be commercialized by a related party, as discussed in Note 20.

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP") and include the accounts of the Company and its wholly owned subsidiaries, Clene Nanomedicine, Inc. ("Clene Nanomedicine"), a subsidiary incorporated in Delaware, Clene Australia Pty Ltd, a subsidiary incorporated in Australia, and dOrbital, Inc., a subsidiary incorporated in Delaware, after elimination of all intercompany accounts and transactions. Certain prior period balances have been reclassified to conform to the current year presentation.

Reverse Recapitalization with Tottenham Acquisition 1 Limited

On December 30, 2020 (the "Closing Date"), Chelsea Worldwide, Inc., our predecessor company, consummated the previously announced business combination (referred to as the "Reverse Recapitalization") pursuant to a merger agreement, dated as of September 1, 2020 (the "Merger Agreement"), by and among Clene Nanomedicine, Tottenham Acquisition I Limited ("Tottenham" or "TOTA"), Chelsea Worldwide Inc., a Delaware corporation and wholly owned subsidiary of Tottenham ("PubCo"), Creative Worldwide Inc., a Delaware corporation and wholly owned subsidiary of PubCo ("Merger Sub"), and Fortis Advisors LLC, a Delaware limited liability company as the representative of the Company's stockholders ("Stockholders' Representative"). Prior to the Reincorporation Merger discussed below, Tottenham was incorporated in the British Virgin Islands as a blank check company for the purpose of entering into a merger, share exchange, asset acquisition, stock purchase, recapitalization, reorganization or other similar business combination with one or more businesses or entities.

The Reverse Recapitalization was effected in two steps: (i) Tottenham was reincorporated to the state of Delaware by merging with and into PubCo (the "Reincorporation Merger"); (ii) promptly following the Reincorporation Merger, Merger Sub was merged with and into Clene Nanomedicine, resulting in Clene Nanomedicine becoming a wholly owned subsidiary of PubCo (the "Acquisition Merger"). On the Closing Date, PubCo changed its name from Chelsea Worldwide Inc. to Clene Inc. and listed its shares of common stock, par value $0.0001 per share ("Common Stock") on the Nasdaq under the symbol "CLNN."

Upon the consummation of the Reverse Recapitalization, each Tottenham ordinary share issued and outstanding immediately prior to the effective time of the Reincorporation Merger (excluding certain shares to be canceled pursuant to the Merger Agreement, any redeemed shares and any dissenting), was automatically cancelled and cease to exist and (i) for each Tottenham ordinary share, the Company issued to each shareholder one validly issued share of the Company's Common Stock; (ii) each warrant to purchase one half (1/2) of one Tottenham Ordinary Share converted into a warrant to purchase one-half of one share of the Company's Common Stock; (iii) each right exchangeable into one-tenth (1/10) of one Tottenham ordinary share converted into a right exchangeable for one-tenth (1/10) of one share of the Company's Common Stock; provided, however, that no fractional shares were issued and all fractional shares were rounded down to the nearest whole share.

On the Closing Date, each share of Clene Nanomedicine common stock was cancelled and the holders thereof in exchange received 0.1389 newly issued shares of Clene Inc. Common Stock, which is the exchange ratio (the "Exchange Ratio"). Pursuant to the Merger Agreement, 5% of the aggregate amount of the closing payment shares, or 2,716,958 shares will be held in escrow to satisfy any indemnification obligation incurred and will be released six months after the closing of the Reverse Recapitalization. In addition, each share of Clene Nanomedicine's preferred stock outstanding immediately prior to the closing of the Reverse Recapitalization was converted into the right to receive the Company's Common Stock based on the same Exchange Ratio. In addition, all outstanding warrants exercisable for common stock in Clene Nanomedicine (other than warrants that expired, were exercised or were deemed automatically net exercised immediately prior to the Acquisition Merger) were exchanged for warrants exercisable for the Company Common Stock with the same terms and conditions except adjusted by the aforementioned Exchange Ratio. At the closing of the Reverse Recapitalization, each stock option of Clene Nanomedicine common stock was cancelled and the holders thereof in exchange received 0.1320 newly issued stock options of the Company's Common Stock, which is 95% of the Exchange Ratio. Pursuant to the Merger Agreement, the Company issued 370,101 of restricted stock units ("RSUs") to the option holders which complements the 5% closing payment shares held in escrow for Clene Nanomedicine common shareholders. The modification of the stock options did not result in a material incremental compensation expense upon closing of the Reverse Recapitalization.

In addition, the Company issued 1,136,961 RSUs to option holders to complement the earn-out payments that would contingently be issued to certain current Clene Nanomedicine's shareholders upon the achievement of milestones. See Note 3 for the milestones detail.

The proceeds received from the Reverse Recapitalization is $3.7 million, net of offering costs of $5.9 million which excludes the fair value of common shares issued as a payment of related offering costs.

In connection with Tottenham's initial public offering in August 2018, Tottenham issued to Chardan Capital Markets, LLC ("Chardan"), options to purchase 220,000 units at $10.00 per unit. Each of the units consists of one and one-tenth shares of Tottenham's ordinary shares for $10.00 per share and one warrant to purchase one-half of one of Tottenham's ordinary shares at an exercise price of $11.50 per share (the "Chardan Unit Purchase Option"). In connection with the Reverse Recapitalization, the Chardan Unit Purchase Option was converted into one Company unit purchase option. The warrants included in the Chardan Unit Purchase Option (the "Chardan Unit Purchase Option Warrants") are exercisable upon the completion of the Reverse Recapitalization and will expire five years after the consummation of the Reverse Recapitalization (i.e., December 30, 2025) (see Note 10).

Also, in connection with the Reverse Recapitalization, 644,164 shares of the Company's Common stock were issued to LifeSci Capital LLC ("LifeSci"), as payment for advisory services rendered in connection with the Reverse Recapitalization (see Notes 3 and 18).

The transaction was accounted for as a "reverse recapitalization" in accordance with accounting principles generally accepted in the United States ("GAAP"). Under this method of accounting, Tottenham was treated as the "acquired" company for financial reporting purposes. This determination is primarily based on the fact that subsequent to the Reverse Recapitalization, Clene Nanomedicine's stockholders have a majority of the voting power of the combined company, Clene Nanomedicine comprises all of the ongoing operations of the combined entity, Clene Nanomedicine comprises a majority of the governing body of the combined company, and Clene Nanomedicine's senior management comprises all of the senior management of the combined company. Accordingly, for accounting purposes, this transaction was treated as the equivalent of Clene Nanomedicine issuing shares for the net assets of Tottenham, accompanied by a recapitalization. The shares and net loss per common share, prior to the Reverse Recapitalization, have been retroactively restated as shares reflecting the Exchange Ratio established in the Reverse Recapitalization (0.1389 Clene Inc. shares for 1 Clene Nanomedicine share). The net assets of Tottenham were recorded at historical costs, with no goodwill or other intangible assets recorded. Operations prior to the Reverse Recapitalization are those of Clene Nanomedicine.

The PIPE Offering

Prior to the completion of the Reverse Recapitalization on December 30, 2020, the Company entered into a subscription agreement on December 28, 2020, with various investors. Pursuant to the subscription agreements, the Company issued 2,239,500 shares of the Company's Common Stock (the "PIPE Shares") at a price of $10.00 per share with net proceeds of $22.2 million. The purpose of the PIPE is to fund general corporate expenses. In addition, investors in the PIPE offering also received warrants to purchase a number of shares equal to one-half (1/2) of the number of PIPE Shares, totaling 1,119,750 shares of the Company's Common Stock, at an exercise price of $0.01 per share for each of the PIPE Shares (the "PIPE Warrants"), subject to a 180-day holding period.

See Note 3 – Reverse Recapitalization with Tottenham and Clene Nanomedicine for additional details on Reverse Recapitalization.

Liquidity

The Company has incurred significant losses and negative cash flows from operations since its inception. The Company incurred net losses of $19.3 million and $16.2 million for the years ended December 31, 2020 and 2019. As of December 31, 2020, the Company's cash totaled $59.3 million, its accumulated deficit was $153.6 million, and the Company had net cash used in operating activities of $18.9 million.

Prior to the Reverse Recapitalization, Clene Nanomedicine's operations were financed through the issuance of equity instruments and the issuance of convertible promissory notes. The Company has not generated significant revenues to date and does not anticipate generating any significant revenues unless it successfully completes development and obtains regulatory approval for its drugs or for its COVID-19 study. The Company expects to incur additional losses in the future to fund its operations and conduct product research and development and recognizes the need to raise additional capital to fully implement its business plan. Additionally, we may attempt to negotiate a collaboration agreement with a third party for development and commercialization of a drug candidate, which may provide upfront and milestone payments to reduce our spending going forward.

The Company expects to continue investing in product development, sales and marketing and customer support for its products. The long-term continuation of the Company's business plan is dependent upon the generation of sufficient revenues from its products to offset expenses and capital expenditures. In the event that the Company does not generate sufficient revenues and is unable to obtain funding, the Company will be forced to delay, reduce, or eliminate some or all of its research and development programs, product portfolio expansion, commercialization efforts or capital expenditures, which could adversely affect the Company's business prospects, ability to meet long-term liquidity needs or the Company may be unable to continue operations.

The Company expects that the cash on hand as of December 31, 2020 will be sufficient to fund its operations for a period extending beyond twelve months from the date the consolidated financial statements are issued.

Impact of the COVID-19 Coronavirus Pandemic

The COVID-19 pandemic, which began in December 2019 and has spread worldwide, has caused many governments to implement measures to slow the spread of the outbreak. The outbreak and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred, supply chains have been disrupted, and facilities and production have been suspended. The future progression of the pandemic and its effects on the Company's business and operations remain uncertain. The COVID-19 pandemic may affect the Company's ability to initiate and complete preclinical studies, delay the initiation of future clinical trials, disrupt regulatory activities, or have other adverse effects on its business and operations. In particular, the Company and its clinical research organizations ("CROs") may face disruptions that may affect the Company's ability to initiate and complete preclinical studies, manufacturing disruptions, and delays at clinical trial sites. The pandemic has already caused significant disruptions in the financial markets, and may continue to cause such disruptions, which could impact the Company's ability to raise additional funds to support its operations. Moreover, the pandemic has significantly impacted economies worldwide and could result in adverse effects on the Company's business and operations.

The Company is monitoring the potential impact of the COVID-19 pandemic on the Company's business and financial statements. While the COVID-19 pandemic has led to various research restrictions and paused certain of Clene Nanomedicine's clinical trials, these impacts have been temporary and to date, the Company has not experienced material business disruptions or incurred impairment losses in the carrying values of its assets as a result of the pandemic and the Company is not aware of any specific related event or circumstance that would require the Company to revise the estimates reflected in these financial statements. The extent to which the COVID-19 pandemic will directly or indirectly impact the Company's business, results of operations, cash flows and financial condition, including planned and future clinical trials and research and development costs, will depend on future developments that are highly uncertain, including as a result of new information that may emerge concerning COVID-19, the actions taken to contain or treat it, and the duration and intensity of the related effects.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the reported amounts of expenses during the reporting period. Significant estimates and assumptions made in the accompanying consolidated financial statements include, but are not limited to the valuation of common stock, stock options, contingent earn-out liability, and Preferred Stock warrants.

The Company bases its estimates on historical experience and on various other assumptions that are believed to be reasonable. Actual results may differ from those estimates or assumptions. Estimates are periodically reviewed in light of changes in circumstances, facts, and experience. Changes in estimates are recorded in the period in which they become known.

Risks and Uncertainties

The product candidates developed by the Company require approvals from the U.S. Food and Drug Administration ("FDA") or foreign regulatory agencies prior to commercial sales. There can be no assurance that the Company's current and future product candidates will receive the necessary approvals or be commercially successful. If the Company is denied approval or approval is delayed, it will have a material adverse impact on the Company's business and its consolidated financial statements.

The Company is subject to risks common to companies in the development stage including, but not limited to, dependency on the need for substantial additional financing to achieve its goals, uncertainty of broad adoption of its approved products, if any, by physicians and patients, significant competition, and untested manufacturing capabilities.

The Company is subject to certain risks and uncertainties and believes that changes in any of the following areas could have a material adverse effect on future financial position or results of operations: ability to obtain future financing; regulatory approval and market acceptance of, and reimbursement for, product candidates; performance of third-party clinical research organizations and manufacturers upon which the Company relies; protection of the Company's intellectual property; litigation or claims against the Company based on intellectual property, patent, product, regulatory or other factors; and the Company's ability to attract and retain employees necessary to support its growth.

Concentrations of Credit Risk

Financial instruments which potentially subject the Company to significant concentrations of credit risk consist primarily of cash. The Company's cash is mainly held in financial institutions. Amounts on deposit may at times exceed federally insured limits. The Company has not experienced any losses on its deposits of cash and does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

Cash and Cash Equivalents

The Company considers all short-term investments with an original maturity of three months or less when purchased to be cash equivalents. As of December 31, 2020 and 2019, the Company has no cash equivalents and no restricted cash balances.

Inventory

Inventory is stated at historic cost on a first -in first-out basis. The Company's inventory consisted of $71,000 in raw materials and $0.1 million in finished goods as of December 31, 2020. The Company's inventory consisted of $28,000 in finished goods as of December 31, 2019.

Deferred Offering Costs

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings, including the Reverse Recapitalization and the PIPE offering, as deferred costs until such financings are consummated. After consummation of the equity financing, these costs are recorded in stockholders' equity (deficit) as a reduction of proceeds generated as a result of the offering. Should an in-process equity financing be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the consolidated statement of operations.

During the year ended December 31, 2020, the Company incurred $5.9 million of offering costs, which excludes the fair value of common shares issued as a payment of related offering costs, to additional paid in capital in connection with the Reverse Recapitalization.

During 2019, the Company had offering costs that were directly related to its proposed initial public offering of $1.0 million. In September 2019, the Company terminated its initial public offering registration process. Accordingly, the Company has written off deferred offering costs previously capitalized to general and administrative expense within the accompanying consolidated statements of operations and comprehensive loss as of December 31, 2019.

Leases

At inception of a contract, the Company determines if a contract meets the definition of a lease. A lease is a contract, or part of a contract, that conveys the right to control the use of identified property, plant, or equipment (an identified asset) for a period of time in exchange for consideration. The Company determines if the contract conveys the right to control the use of an identified asset for a period of time. The Company assesses throughout the period of use whether the Company has both of the following: (1) the right to obtain substantially all of the economic benefits from use of the identified asset, and (2) the right to direct the use of the identified asset. This determination is reassessed if the terms of the contract are changed. Leases are classified as operating or finance leases based on the terms of the lease agreement and certain characteristics of the identified asset. Right-of-use assets and lease liabilities are recognized at the lease commencement date based on the present value of the future lease payments.

The Company leases laboratory and office space (real estate), and certain equipment under non-cancellable operating and finance leases. The carrying value of the Company's right-of-use lease assets is substantially concentrated in its real estate leases, while the volume of lease agreements is primarily concentrated in equipment leases. The Company's policy is to not record leases with an original term of twelve months or less on the consolidated balance sheets. The Company recognizes lease expense for these short-term leases on a straight-line basis over the lease term.

Certain lease agreements may require the Company to pay additional amounts for taxes, insurance, maintenance and other expenses, which are generally referred to as non-lease components. Such variable non-lease components are treated as variable lease payments and recognized in the period in which the obligation for these payments was incurred. Variable lease components and variable non-lease components are not measured as part of the right-of-use asset and liability. Only when lease components and their associated non-lease components are fixed are they accounted for as a single lease component and are recognized as part of a right-of-use asset and liability. Total contract consideration is allocated to the combined fixed lease and non-lease component. This policy election applies consistently to all asset classes under lease agreements.

Leases may contain clauses for renewal at the Company's option. Payments to be made in option periods are recognized as part of the right-of-use lease assets and lease liabilities when it is reasonably certain that the option to extend the lease will be exercised, or is not at the Company's option. The Company determines whether the reasonably certain threshold is met by considering contract-, asset-, market-, and entity-based factors. In the consolidated statements of earnings, operating lease expense, which is recognized on a straight-line basis over the lease term, and the amortization of finance lease ROU assets, which are included in plant, property, and equipment and depreciated, are included in research and development or general and administrative expenses consistent with the leased assets' primary use. Accretion on the liabilities for finance leases is included in interest expense.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Property and equipment consist of lab and office equipment and leasehold improvements. Depreciation is calculated using the straight-line method over the estimated economic useful lives of the assets, which are 3-5 years for lab equipment and 3-7 years for furniture and fixtures. Leasehold improvements are amortized over the lesser of the estimated lease term or the estimated useful life of the assets. Costs for capital assets not yet placed into service are capitalized as construction in progress and depreciated or amortized in accordance with the above useful lives once placed into service. Upon retirement or sale, the related cost and accumulated depreciation and amortization are removed from the accounts and any resulting gain or loss is included in the consolidated statements of operations and comprehensive loss. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred.

Impairment of Long-Lived Assets

Long-lived assets are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate an asset group for recoverability, the Company compares the forecasted undiscounted cash flows expected to result from the use and eventual disposition of the asset group to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use and eventual disposition of an asset group are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset group over its fair value, determined based on discounted cash flows using market participant assumptions. The Company did not record any impairment losses on long-lived assets during the years ended December 31, 2020 or December 31, 2019.

Derivative Instruments

The convertible promissory notes issued in February through July 2020 ("2020 Convertible Notes") contained embedded features that provide the lenders with multiple settlement alternatives. Certain of these settlement features provided the lenders a right to a fixed number of the Company's shares upon conversion of the notes. Other settlement features provided the lenders the right or the obligation to receive cash or a variable number of shares upon the completion of a capital raising transaction, change of control or default of the Company (the "Redemption Features").

The Redemption Features of the 2020 Convertible Notes met the requirements for separate accounting and were accounted for as a single derivative instrument (the "2020 Derivative Instrument"). The 2020 Derivative Instrument was recorded at fair value at inception and was subject to re-measurement to fair value at each balance sheet date and immediately prior to the extinguishment of derivative liability, with any changes in fair value recognized in the consolidated statements of operations and comprehensive loss. In August 2020, in connection with the Company's issuance and sale of Series D Preferred Stock, all of the outstanding principal and accrued interest under the convertible promissory notes was automatically converted into shares of Series D Preferred Stock and the derivative liability was extinguished (see Notes 11 and 12).

Redeemable Convertible Preferred Stock

Prior to the Reverse Recapitalization with Tottenham, the Company recorded all shares of redeemable convertible Preferred Stock at their respective fair values on the dates of issuance, net of issuance costs. The redeemable convertible Preferred Stock was recorded outside of permanent equity because while it was not mandatorily redeemable, upon certain events considered not solely within the Company's control, such as a merger, acquisition, or sale of all or substantially all of the Company's assets (each, a "Deemed Liquidation Event"), the redeemable convertible Preferred Stock would become redeemable at the option of the holders of at least a majority of the then-outstanding shares. The Company did not adjust the carrying values of the redeemable convertible Preferred Stock to the liquidation preferences of such shares because it was uncertain whether or when a Deemed Liquidation Event would occur that would obligate the Company to pay the liquidation preferences to holders of shares of redeemable convertible Preferred Stock. Subsequent adjustments to the carrying values of the liquidation preferences would be made only when it becomes probable that such a Deemed Liquidation Event will occur.

In connection with the Reverse Recapitalization, all shares of redeemable convertible Preferred Stock were converted into shares of the Company's Common Stock. Accordingly, there was no redeemable convertible Preferred Stock outstanding as of December 31, 2020. As of December 31, 2019, the carrying value of the redeemable convertible Preferred Stock was $72.7 million (see Note 17).

Contingent Earn-out

In connection with the Reverse Recapitalization and pursuant to the Merger Agreement, Clene Nanomedicine's common shareholders and Initial Shareholders of Tottenham are entitled to receive additional shares of the Company's Common Stock upon the Company achieving certain milestones described in Note 12. In accordance with ASC 815 – *Derivatives and hedging*, the earn-out shares are not indexed to the Company's own stock and therefore are accounted for as a liability at the reverse recapitalization date and subsequently remeasured at each reporting date with changes in fair value recorded as a component of other income (expense), net in the consolidated statements of operations and comprehensive loss.

The estimated fair value of the contingent consideration was determined using a Monte Carlo simulation that simulated the future path of the Company's stock price over the earn-out period. The assumptions utilized in the calculation are based on the achievement of certain stock price milestones including projected stock price, volatility, and risk-free rate. For potential payments related to a product development milestone, the fair value was determined based on the Company's expectations of achieving such a milestone and the simulated estimated stock price on the expected date of achievement.

The contingent earn-out is categorized as a Level 3 fair value measurement (see Fair Value of Financial Instruments accounting policy) because the Company estimates projections during the earn-out period utilizing unobservable inputs, including various potential pay-out scenarios. Contingent earn-out payments involve certain assumptions requiring significant judgment and actual results may differ from assumed and estimated amounts.

Preferred Stock Warrant Liability

Prior to the Reverse Recapitalization with Tottenham, the Company accounted for freestanding warrants to purchase shares of Preferred Stock as liabilities on the balance sheet at their estimated fair value as the underlying redeemable convertible Preferred Stock was considered contingently redeemable and may obligate the Company to transfer assets to the holders at a future date upon the occurrence of a deemed liquidation event. At the end of each reporting period, changes in the estimated fair value of the warrants to purchase shares of Preferred Stock were recorded in change in fair value of Preferred Stock warrant liability in the consolidated statements of operations and comprehensive loss. Changes in the estimated fair value of the Preferred Stock warrant liability were ($14.6) million and ($0.4) million for the years ended December 31, 2020 and 2019, respectively. In connection with the Reverse Recapitalization, all Clene Nanomedicine Preferred Stock was converted to the Company's Common Stock and the Clene Nanomedicine Preferred Stock warrants were converted to warrants to purchase the Company's Common Stock. The Company assessed the features of these warrants and determined that they qualify for classification as permanent equity. Accordingly, the Company remeasured the warrants to fair value upon the closing of the Reverse Recapitalization and reclassified the resulting warrant liability to additional paid-in capital (See Note 16).

Common Stock Warrants

The Company accounts for common stock warrants as either equity instruments or liabilities in accordance with ASC 480, *Distinguishing Liabilities from Equity* ("ASC 480"), depending on the specific terms of the warrant agreement (See Note 10).

Revenue Recognition

Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration to which it is entitled in exchange for the goods or services it transfers to the customer.

Once a contract is determined to be within the scope of ASC 606 at contract inception, the Company reviews the contract to determine which performance obligations it must deliver and which of these performance obligations are distinct. The Company recognizes as revenue the amount of the transaction price that is allocated to each performance obligation when that performance obligation is satisfied or as it is satisfied. The Company typically satisfies its performance obligations via delivery of dietary supplements to the customer. Payments are due upon receipt for commercial transactions or a prepayment is collected for online retail sales. The Company's revenue for the year ended December 31, 2020 was comprised of sales of dietary supplements.

The Company recorded deferred revenue of $0.1 million as of December 31, 2020 from the dietary supply agreement with the related party discussed in Note 20. The deferred revenue is expected to be recognized in the first half of 2021.

Grant Funding

The Company may submit applications to receive grant funding from governmental and non-governmental entities. Grant funding received that involves no conditions or continuing performance obligations of the Company is recognized upon receipt. Grant funding with conditions or obligations of the Company is recognized as the conditions or obligations are fulfilled. The Company has made an accounting policy election to record such unconditional grants, such as the Australian Research and Development Credit, as other income in the consolidated statements of operations and comprehensive loss. Income from grants is recognized in the period during which the related qualifying expenses are incurred, provided that the conditions under which the grants were provided have been met. The Company recognizes Australian Research and Development Credit in an amount equal to the qualifying expenses incurred in each period multiplied by the applicable reimbursement percentage. During the years ended December 31, 2020 and 2019, the Company recognized $3.2 million and $0.6 million, respectively, of Australian Research and Development Credit within other income (expense), net in the consolidated statement of operations and comprehensive loss. As of December 31, 2020 and 2019, the Company recorded $2.1 million and $0, respectively, of Australian Research and Development Credit receivable in prepaid expenses and other current assets on the consolidated balance sheets.

Any amount received in advance of fulfilling such conditions or obligations is recorded in accrued liabilities in the consolidated balance sheets if the conditions or obligations are expected to be met within the next twelve months. As of December 31, 2020 and 2019, the Company recorded $0.3 million and $0.1 million, respectively, of Australian Research and Development Credit received in advance in accrued liabilities.

Grant funding recognized on conditional grants is included as a reduction in research and development expenses in the consolidated statements of operations and comprehensive loss as the conditions are tied to the Company's research and development efforts, and as the arrangement between the Company and the organizations are not part of the Company's on-going, major, or central operations. During the years ended December 31, 2020 and 2019, the Company recorded $0.8 million and $0.1 million, respectively of grant funding as a reduction of research and development expenses.

Fair Value of Financial Instruments

Certain assets and liabilities are carried at fair value under U.S. GAAP. Fair value is defined as the price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy:

Level 1 — Inputs based upon quoted market prices for identical assets or liabilities in active markets at the measurement date.

Level 2 — Observable inputs other than quoted market prices included in Level 1, such as quoted prices for similar assets and liabilities in active markets; quoted prices for identical or similar assets and liabilities in markets that are not active; or other inputs that are observable or can be corroborated by observable market data.

Level 3 — Inputs that are management's best estimate of what market participants would use in pricing the asset or liability at the measurement date. The inputs are unobservable in the market and significant to the instrument's valuation.

The Company reviews the fair value hierarchy classification as of the actual date of the event or change in circumstances that caused the transfer. There was a transfer to Level 1 from Level 3 as of December 31, 2020 for the Notes payable.

See Note 16 for information on the Company's assets and liabilities measured at fair value as of December 31, 2020 and 2019.

Foreign Currency Translation and Transactions

The functional currency of the Company is the United States dollar. The Company's Australian subsidiary determined its functional currency to be the Australian dollar. The Company uses the United States dollar as its reporting currency for the consolidated financial statements. The results of its non-U.S. dollar based functional currency operations are translated to U.S. dollars at the average exchange rates during the period. The Company's assets and liabilities are translated using the current exchange rate as of the consolidated balance sheet date and shareholders' equity is translated using historical rates.

Adjustments resulting from the translation of the consolidated financial statements of the Company's foreign functional currency subsidiaries into U.S. dollars are excluded from the determination of net loss and are accumulated in a separate component of shareholders' equity. These foreign currency translation gains and losses are currently the only component of other comprehensive income.

The Company also incurs foreign exchange transaction gains and losses for purchases denominated in foreign currencies. Foreign exchange transaction gains and losses are included in other income (expense) in the Company's consolidated results of operations as incurred.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. The Company's only element of other comprehensive income (loss) in any period presented was translation of Australian dollar denominated balances of the Company's Australian subsidiary to U.S. dollars for consolidation.

Net Loss Per Share Attributable to Common Shareholders

The Company calculated basic and diluted net loss per share attributable to common shareholders in conformity with the two-class method required for companies with participating securities. The Company considered all series of redeemable convertible Preferred Stock to have been participating securities as the holders were entitled to receive non-cumulative dividends on a pari passu basis in the event that a dividend had been paid on common stock. See Note 19, Net Loss Per Share Attributable to Common Shareholders, for further details on the Company's historical participating securities, including warrants to purchase redeemable convertible Preferred Stock and common stock.

Under the two-class method, basic net loss per share attributable to common shareholders was calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period, less shares subject to repurchase. The net loss attributable to common shareholders was not allocated to the redeemable convertible Preferred Stock as the holders of redeemable convertible Preferred Stock did not have a contractual obligation to share in losses. Diluted net loss per share attributable to common shareholders was computed by giving effect to all potentially dilutive common stock equivalents outstanding for the period. For purposes of this calculation, redeemable convertible Preferred Stock, stock options to purchase common stock, early exercised stock options, and warrants to purchase redeemable convertible Preferred Stock and common stock were considered common shares equivalents but had been excluded from the calculation of diluted net loss per share attributable to common shareholders as their effect was anti-dilutive. In periods in which the Company reports a net loss attributable to common shareholders, diluted net loss per share attributable to common shareholders is the same as basic net loss per share attributable to common shareholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. The Company reported a net loss attributable to common shareholders during the years ended December 31, 2020 and 2019.

Segment Information

The Company has determined that its chief executive officer is the chief operating decision maker ("CODM"). Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the CODM in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business in two operating segments, the first being that of the development and commercialization of proprietary nanotechnology drug suspensions, and the second being the development and commercialization of dietary supplements (See Note 21).

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined on the basis of the differences between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Stock-Based Compensation

The Company accounts for stock-based compensation arrangements with employees using a fair value-based method for costs related to all share-based payments including stock options and restricted common stock. Stock-based compensation expense is recorded in research and development and general and administrative expenses based on the classification of the work performed by the grantees.

Prior to the Reverse Recapitalization, there was not a public market for the shares of Clene Nanomedicine, Inc. common stock. The Company's determination of the fair value of stock options on the date of grant utilized the Black-Scholes option-pricing model and was impacted by its common stock price, as determined by the Board of Directors with input from the Company's management, as well as changes in assumptions regarding a number of subjective variables. These variables included, but were not limited to, the expected term that options remained outstanding, the expected common stock price volatility over the term of the option awards, risk-free interest rates, and expected dividends.

The fair value was recognized over the period during which an optionee was required to provide services in exchange for the option award and service-based RSUs, known as the requisite service period (usually the vesting period), on a straight-line basis. For the RSUs with market conditions, the fair value is recognized over the period based on the expected milestone achievement dates as the derived service period (usually the vesting period), on a straight-line basis. For the RSUs with performance conditions, the grant date fair value of these awards is the market price on the applicable grant date, and compensation expense will be recognized when the conditions become probable of being satisfied. The Company will recognize a cumulative true-up adjustment once the conditions become probable of being satisfied as the related service period had been completed in a prior period.

Stock-based compensation expense recognized at fair value included the impact of estimated forfeitures. The Company elected to account for forfeitures as they occurred, rather than estimating expected forfeitures.

After the closing of the Reverse Recapitalization, the Company determined the fair value of each share of Common Stock underlying stock-based awards based on the closing price of the Company's Common Stock as reported by Nasdaq on the date of grant. The fair value of the RSUs with market conditions are determined using a Monte Carlo valuation model. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

Research and Development

Research and development costs are charged to expense as incurred. The Company accounts for nonrefundable advance payments for goods and services that will be used in future research and development activities as expenses when the goods have been received or when the service has been performed. Research and development expenses consist of costs incurred by the Company for the discovery and development of the Company's product candidates. Research and development costs include, but are not limited to, payroll and personnel expenses including stock-based compensation, clinical trial supplies, fees for clinical trial services, consulting costs, and allocated overhead, including rent, equipment, and utilities.

Clinical Trial Accrual

The Company's clinical trial accrual process accounts for expenses resulting from obligations under contracts with CROs, consultants, and under clinical site agreements in connection with conducting clinical trials. Clinical trial costs are charged to research and development expense as incurred. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to the Company under such contracts. The Company reflects the appropriate clinical trial expense in the consolidated financial statements by matching the appropriate expenses with the period in which services and efforts are expended. In the event advance payments are made to a CRO, the payments will be recorded as a prepaid asset which will be amortized over the period of time the contracted services are performed. In addition to pass-through costs, the Company generally incurs costs in clinical trials in four distinct groups as follows:

CRO Start-up — These costs include the initial set-up of the clinical trial and usually occurs within a few months after the contract has been executed and includes costs which are expensed ratably over the start-up period when such period is identifiable and expensed as incurred when no such period exists. Start-up phase activities include study initiation, site recruitment, regulatory applications, investigator meetings, screening, preparation, pre-study visits, and training.

CRO Site and Study Management — These costs include medical and safety monitoring, and patient administration and data management. These costs are usually calculated on a per patient basis and expensed ratably over the treatment period beginning on the date that the patient enrolls.

CRO Close Down and Reporting — These costs include analyzing the data obtained and reporting results, which occurs after patients have ceased treatment and the database of information collected is locked. These costs are expensed as incurred over the course of any close down and reporting period.

Third Party Contracts — These costs include fees charged by third parties for various support services which are not provided by CROs and include such items as lab fees, data quality review costs, and fees incurred for investigational product monitoring and inventory control. These items are expensed ratably over any identifiable service period with the engaged third-party vendors.

The CRO contracts generally include pass-through fees including, but not limited to, regulatory expenses, investigator fees, travel costs and other miscellaneous costs, including shipping and printing fees. The Company determines accrual estimates through reports from and discussion with applicable personnel and outside services providers as to the progress or state of completion of trials, or the services completed. The Company makes estimates of accrued expenses as of each balance sheet date in the consolidated financial statements based on the facts and circumstances known to the Company at that time.

Recently Adopted Accounting Pronouncements

In March 2020, the FASB issued ASU 2020-04, Reference Rate Reform (Topic 848): Facilitating of the Effects of Reference Rate Reform on Financial Reporting, which provides optional expedients and exceptions for applying U.S. GAAP to contracts, hedging relationships, and other transactions in which the reference LIBOR or another reference rate is expected to be discontinued as a result of the Reference Rate Reform. This ASU is intended to ease the potential burden in accounting for (or recognizing the effects of) reference rate reform on financial reporting. The new guidance was effective immediately, and through December 31, 2022. As a result of the Company having elected the extended transition period for complying with new or revised accounting standards pursuant to Section 107(b) of the JOBS Act, ASU 2016-02 is effective for the Company for fiscal years beginning after December 15, 2020, and all interim periods thereafter. Early adoption is permitted. The Company early adopted this guidance on March 1, 2020. The adoption of this guidance did not have a material impact on its consolidated financial statements.

Recent Accounting Pronouncements Not Yet Adopted

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*. The amendments in this ASU, among other things, require the measurement of all expected credit losses for financial assets held at the reporting date based on historical experience, current conditions, and reasonable and supportable forecasts. Financial institutions and other organizations will now use forward-looking information to better inform their credit loss estimates. The guidance is effective for fiscal years beginning after December 15, 2022. The Company is currently evaluating the expected impact of the new guidance.

In August 2018, the FASB issued ASU No. 2018-15, *Intangibles – Goodwill and Other – Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That is a Service Contract*. The new guidance provides for the deferral of implementation costs for cloud computing arrangements and expensing those costs over the term of the cloud services arrangement. The new guidance is effective for fiscal years beginning after December 15, 2020. The Company is currently evaluating the expected impact of the new guidance.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes* (Topic 740), which amends the existing guidance relating to the accounting for income taxes. This ASU is intended to simplify the accounting for income taxes by removing certain exceptions to the general principles of accounting for income taxes and to improve the consistent application of GAAP for other areas of accounting for income taxes by clarifying and amending existing guidance. The new guidance is effective for fiscal years beginning after December 15, 2021. The Company does not expect that the adoption of this new guidance will have a material impact on its consolidated statements.

3. Reverse Recapitalization with Tottenham and Clene Nanomedicine

On December 30, 2020, the Company consummated the Reverse Recapitalization, pursuant to which Tottenham merged with and into PubCo in connection with the Reincorporation Merger and PubCo merged with and into Clene Nanomedicine, resulting in Clene Nanomedicine becoming a wholly owned subsidiary of PubCo. On the Closing Date, PubCo changed its name from Chelsea Worldwide, Inc. to Clene Inc. (see Note 1).

Upon the consummation of the Reverse Recapitalization, each Tottenham ordinary share issued and outstanding immediately prior to the effective time of the Reincorporation Merger was automatically cancelled and ceased to exist and (i) for each Tottenham ordinary share, the Company issued one validly issued share of the Company's Common Stock; (ii) each warrant to purchase one half of one Tottenham Ordinary Share was converted into a warrant to purchase one-half of one share of the Company's Common Stock; and (iii) each Tottenham right exchangeable into one-tenth (1/10) of one Tottenham ordinary share was converted into a right exchangeable for one-tenth (1/10) of one share of the Company's Common Stock. As a result of the Reverse Recapitalization, all outstanding shares of Tottenham ordinary shares of 2,303,495 held by the Initial Shareholders and Tottenham public shareholders were converted into the same number of the Company's Common Stock. In addition, pursuant to the Merger Agreement, the Initial Shareholders are entitled to receive up to 750,000 of the company common shares as earn-out shares upon the achievement of certain milestones described in below. The contingent earn-out with the Initial Shareholders is accounted for as a contingent liability and is included in the line item of "Contingent Earn-out" on the consolidated balance sheets.

In accordance with the Merger Agreement, on the closing of the Reverse Recapitalization, each share of Clene Nanomedicine preferred stock and common stock then issued and outstanding was automatically cancelled, extinguished and exchanged for 0.1389 newly issued shares of Clene Inc. Common Stock. At the closing of the Reverse Recapitalization, Clene Inc. acquired 100% of the issued and outstanding Clene Nanomedicine common stock, in exchange for 54,339,012 shares of Clene Inc. Common Stock issued to the Clene Nanomedicine common shareholders, among which 2,716,958 shares of the Clene Inc. Common Stock are to be issued and held in escrow to satisfy any indemnification obligations incurred under the Merger Agreement. In addition, all outstanding warrants (other than warrants that expired, were exercised or were deemed automatically net exercised immediately prior to the Acquisition Merger) exercisable for common stock in Clene Nanomedicine were assumed by the Company with no changes to the terms and conditions of the awards. The awards have been retroactively restated to reflect the Exchange Ratio established in the Reverse Recapitalization.

In connection with the Reverse Recapitalization, a total of 53,286,115 stock options of Clene Nanomedicine common stock was cancelled and the holders thereof in exchange received 0.1320 newly issued stock options of Clene Inc. Common Stock for a total of 7,032,590, which is 95% of the Exchange Ratio. Pursuant to the Merger Agreement, the Company issued RSUs to the option holders which complements the 5% closing payment shares held in escrow for Clene Nanomedicine common shareholders. In addition, the Company issued 1,136,961 RSUs to option holders to complement the earn-out payments that would contingently be issued to certain current Clene Nanomedicine's shareholders upon the achievement of milestones described in below.

Also, in connection with the Reverse Recapitalization, Clene Nanomedicine entered into a letter agreement with LifeSci Capital LLC ("LifeSci") on July 2, 2020, according to which LifeSci was engaged to act as Clene Nanomedicine's financial advisor with respect to identifying and soliciting special purpose acquisition companies for the purpose of entering into a merger or similar transaction with Clene Nanomedicine and its shareholders. Under this agreement, Clene Nanomedicine agreed that if it consummated a merger with Tottenham, LifeSci would receive consideration of (i) 3% of the amount by which the total transaction consideration exceeded $350 million, plus (ii) 7% of cash and cash-equivalents received by Clene Nanomedicine from the Tottenham's trust account. Clene Nanomedicine could elect to pay LifeSci either in cash, equity interests of the surviving company, or a combination of the two. Upon the consummation of the Reverse Recapitalization, 644,164 shares of the Company's Common Stock were issued to LifeSci as consideration for its services as pursuant to the letter agreement (see Note 18).

Immediately after giving effect to the Reverse Recapitalization, there were 59,526,171 shares of Common Stock issued and outstanding, and warrants to purchase 5,566,363 shares of Common Stock issued and outstanding (see Note 10).

During Tottenham's IPO, Tottenham incurred deferred underwriters' fees which were payable to Chardan from the amounts held in the trust account upon completion of the Reverse Recapitalization. Upon the closing of the Reverse Recapitalization, the Company paid $2.1 million to Chardan as the settlement of the deferred underwriting and advisory fees which amount was included in the total offering costs of the Reverse Recapitalization transaction.

During the year ended December 31, 2020, the Company recorded $5.9 million of offering costs, which excludes the fair value of common shares issued as a payment of related offering costs and Chardan underwriting fees discussed above. Those offering costs were related to third-party legal, accounting services and other professional services to consummate the Reverse Recapitalization. These offering costs are recorded in additional paid-in capital upon the close of the Reverse Recapitalization in the Company's consolidated balance sheets.

On December 28, 2020 and prior to the close of the Reverse Recapitalization on December 30, 2020, various PIPE investors purchased 2,239,500 shares of the Company's Common Stock at a price of $10.00 per share and 1,119,750 warrants with an exercise price of $0.01 per share, to purchase one share of the Company's Common Stock, for net proceeds of $22.2 million (see Notes 10 and 18).

Earn-out shares

Certain of Clene Nanomedicine's current stockholders are entitled to receive earn-out shares as follows (the "Clene Nanomedicine Contingent Earn-Out"): (i) 3,333,333 shares of the Company's Common Stock if (A) the volume-weighted average price ("VWAP") of the shares of the Company's Common Stock equals or exceeds $15.00 (or any foreign currency equivalent) (the "Milestone 1 Price") in any twenty trading days within a thirty trading day period within the three years following the closing of the Reverse Recapitalization on any securities exchange or securities market on which the shares of the Company's Common Stock are then traded or (B) the change of control price equals or exceeds the Milestone 1 Price if a change of control transaction occurs within the three years following the closing of the Reverse Recapitalization (the requirements set forth in clause (A) and (B), "Milestone 1"); (ii) 2,500,000 shares of the Company's Common Stock if (A) the VWAP of the shares of the Company's Common Stock equals or exceeds $20.00 (or any foreign currency equivalent) (the "Milestone 2 Price") in any twenty trading days within a thirty trading day period within the five years following the closing of the Reverse Recapitalization on any securities exchange or securities market on which the shares of the Company's Common Stock are then traded or (B) the change of control price equals or exceeds the Milestone 2 Price if a change of control transaction occurs within the five years following the closing of the Reverse Recapitalization (the requirements set forth in clause (A) or (B), "Milestone 1"); and (iii) 2,500,000 shares of the Company's Common Stock if Clene Nanomedicine completes a randomized placebo-controlled study for treatment of COVID-19 which results in a statistically significant finding of clinical efficacy within twelve months after the closing of the Reverse Recapitalization ("Milestone 3"). If Milestone 1 is not achieved but Milestone 2 is achieved, the Clene Nanomedicine stockholders will receive a catch-up issuance equal to the shares issued upon satisfaction of Milestone 1. Upon the consummation of the Reverse Recapitalization, the earn-out shares that certain Clene Nanomedicine stockholders are entitled to receive increased by 12,852 as a result of the exercise of stock options during November 2020. Therefore, the total Clene Nanomedicine earn-out shares has increased to 8,346,185 shares of the Company's Common Stock.

The Initial Shareholders of Tottenham may be entitled to receive earn-out shares as follows (the "Initial Shareholders Contingent Earn-Out"): (i) 375,000 shares of the Company's Common Stock upon satisfaction of the requirements of Milestone 1; and (ii) another 375,000 shares of the Company's Common Stock upon satisfaction of the requirements of Milestone 2. If Milestone 1 is not achieved but Milestone 2 is achieved, the Initial Shareholders shall receive a catch-up issuance equal to the shares granted upon satisfaction of the requirements of Milestone 1.

Clene Nanomedicine and Initial Shareholders earn-out payments (collectively, referred to as "Earn-out Shares") have been classified as liabilities in the consolidated balance sheets as of December 31, 2020 and were initially measured at fair value on the date of the Reverse Recapitalization and will be subsequently remeasured to fair value at each reporting date (see Note 16).

As a result of the Reverse Recapitalization and the PIPE offering, Clene Nanomedicine's stockholders own approximately 91% of the Common Stock of the Company, Tottenham public stockholders own approximately 4% of the Common Stock of the Company, and investors from the PIPE own approximately 4% of the Common Stock of the Company, based on the number of shares of Clene Inc. Common Stock outstanding on December 30, 2020 (in each case, not giving effect to any shares issuable upon exercise of Clene Inc. warrants, options, or earn-out shares).

4. Prepaid expenses and other current assets

Prepaid expenses and other current assets consisted of the following as of December 31, 2020 and 2019:

(in thousands)	2020	2019
Australia research and development credit receivable	$ 2,148	$ -
CRO prepayments	1,211	413
Accounts receivable	21	-
Metals to be used in research and development	31	191
Other	112	57
	$ 3,523	$ 661

5. Property and Equipment, Net

Property and equipment, net consisted of the following as of December 31, 2020 and 2019:

(in thousands)	2020	2019
Lab equipment	$ 3,077	$ 2,707
Furniture and fixtures	147	162
Leasehold improvements	3,889	3,430
Construction in progress	490	410
	7,603	6,709
Less accumulated depreciation	(3,378)	(2,390)
Total property and equipment, net	$ 4,225	$ 4,319

Depreciation expense related to property and equipment, net for the years ended December 31, 2020 and 2019 was approximately $1.0 million ($0.9 million in Research and Development expense and $0.1 million in General and Administrative expense) and $0.9 million ($0.8 million in Research and Development expense and $0.1 million in General and Administrative expense), respectively.

6. Accrued Liabilities

Accrued liabilities consisted of the following as of December 31, 2020 and 2019:

(in thousands)	2020	2019
Accrued professional fees	$ 189	$ 1,826
Accrued compensation and benefits	1,225	817
Accrued CRO fees	788	95
Deferred grant funds	301	80
Accrued expense reimbursements	33	36
Accrued transaction costs	1,354	-
Other	70	24
	$ 3,960	$ 2,878

7. Leases

The Company adopted ASC 842 on January 1, 2019 using the modified retrospective approach. Upon adoption of the new leasing standards, the Company (i) recognized an operating lease right of use asset of approximately $1.2 million and a corresponding operating lease liability of approximately $1.7 million, which are included in the Company's consolidated balance sheet, and with a $14 thousand cumulative adjustment to accumulated deficit and (ii) elected the package of transition practical expedients, which allowed the Company to carry forward prior conclusions related to whether any expired or existing contracts are or contain leases, the lease classification for any expired or existing leases and initial direct costs for existing leases.

The Company also made an accounting policy election not to recognize leases with an initial term of 12 months or less within its consolidated balance sheets and to recognize those lease payments on a straight-line basis in its consolidated statements of operations and comprehensive loss over the lease term.

At the lease commencement date, the discount rate implicit in the lease is used to discount the lease liability if readily determinable. If not readily determinable or leases do not contain an implicit rate, the Company's incremental borrowing rate is used as the discount rate.

In April 2020, the Company terminated an existing operating lease for office space. At the time of termination, the Company removed the remaining right-of-use asset of $0.3 million, lease liability of $0.3 million, and recognized a gain of $51 thousand. Further, in April 2020, the Company commenced a new operating lease. At the time of commencement, the Company recorded the right-of-use asset value of $0.4 million, leasehold improvements of $0.4 million, and a lease liability of $0.8 million. The net effect of the change in leases being an increase in right-of-use assets of $56 thousand, an increase in leasehold improvements of $0.5 million, an increase in lease liability of $0.4 million, and a gain on termination of $51 thousand.

The Company has noncancelable operating lease arrangements primarily for office and lab space. The Company also has noncancelable finance leases for certain lab equipment. The maturity analysis of finance and operating lease liabilities as of December 31, 2020 are as follows:

(in thousands)	Finance Leases	Operating Leases
2021	$ 165	$ 376
2022	135	421
2023	82	433
2024	20	442
2025	-	454
Thereafter	-	530
Total undiscounted cash flows	403	2,656
Less amount representing interest/discounting	(8)	(677)
Present value of future lease payments	395	1,979
Less lease obligations, current portion	(190)	(194)
Lease obligations – long term portion	$ 205	$ 1,785

The Company expects that, in the normal course of business, the existing leases will be renewed or replaced by similar leases.

Finance Leases

Assets recorded under finance lease obligations and included with property and equipment as of December 31, 2020 and 2019 are summarized as follows:

(in thousands)	2020	2019
Lab equipment	$ 920	$ 920
Furniture and fixtures	46	46
Work in process	228	228
Total	1,194	1,194
Less accumulated depreciation	(593)	(418)
Net	$ 601	$ 776

As of December 31, 2020, the Company's finance lease obligations had a weighted-average interest rate of 8.1% and had a weighted-average remaining term of 2.7 years. As of December 31, 2019, the Company's finance lease obligations had a weighted-average interest rate of 8.1% and had a weighted-average remaining term of 3.7 years.

Operating Leases

The Company's balance of right-of-use assets on the face of the balance sheet pertain to operating leases. As of December 31, 2020, the Company's operating lease obligations had a weighted-average discount rate of 9.6% and had a weighted-average remaining term of 6.3 years. As of December 31, 2019, the Company's operating lease obligations had a weighted-average discount rate of 9.6% and a weighted-average remaining term of 6.0 years.

Components of Lease Cost

The components of finance and operating lease costs for the years ended December 31, 2020 and 2019 were as follows:

(in thousands)	**2020**	**2019**
Finance lease costs:		
Amortization	$ 175	$ 182
Interest on lease liabilities	37	29
Operating lease costs	293	325
Short-term lease costs	249	283
Variable lease costs	92	103
Total lease costs	$ 846	$ 922

Supplemental Cash Flow Information

(in thousands)	**2020**	**2019**
Operating cash flows from operating leases	$ (635)	$ (711)
Operating cash flows from finance leases	$ (37)	$ (29)
Finance cash flows from finance leases	$ (194)	$ (176)

8. Notes Payable

In February 2019, the Company entered into a loan agreement (the "2019 MD Loan") with the Department of Housing and Community Development, a principal department of the State of Maryland ("Maryland"). Pursuant to the 2019 MD Loan, Maryland agreed to provide a $0.5 million term loan. Amounts outstanding under the 2019 MD Loan bear simple interest at an annual rate of 8.00%. Under the 2019 MD Loan, the Company has agreed to affirmative and negative covenants to which it will remain subject until maturity. These covenants include providing information about the Company and its operations; limitations on the Company's ability to retire, repurchase, or redeem the Company's common or preferred stock, options, and warrants other than per the terms of the securities; and limitations on the Company's ability to pay dividends of cash or property. There are no financial covenants associated with the Loan Agreement. Events of default under the Loan Agreement include failure to make payments when due, insolvency events, failure to comply with covenants, and material adverse effects with respect to the Company. The Company is not in violation of any affirmative or negative covenants. Repayment of the full balance outstanding is due on February 22, 2034. The 2019 MD Loan establishes "Phantom Shares," based on 119,906 shares of the Company's common stock (based on 863,110 Series C Preferred Shares prior to the Reverse Recapitalization), determined at issuance. The Loan Agreement states the repayment amount is to be the greater of the balance of principal and accrued interest or the Phantom Share value. The Company determined that the note should be accounted for at fair value. The Company records the fair value of the debt at the end of each reporting period. In order to value the note, the Company considers the amount of the simple interest expense that would be due and considers the value of Phantom Shares. Expense of $0.5 million and $34 thousand was recognized during the years ended December 31, 2020 and 2019, respectively. The fair value of $1.1 million and $0.5 million of principal and accrued interest is included in long-term notes payable as of December 31, 2020 and December 31, 2019, respectively.

In April 2019, the Company entered into a loan agreement (the "2019 Cecil Loan") with Cecil County, Maryland ("Cecil"). Pursuant to the 2019 Cecil Loan, Cecil agreed to provide a $0.1 million term loan. Amounts outstanding under the 2019 Cecil Loan bear simple interest at an annual rate of 8.00%. Under the 2019 Cecil Loan, the Company has agreed to affirmative and negative covenants to which it will remain subject until maturity. These covenants include providing information about the Company and its operations; limitations on the Company's ability to retire, repurchase, or redeem the Company's common or preferred stock, options, and warrants other than per the terms of the securities; and limitations on the Company's ability to pay dividends of cash or property. There are no financial covenants associated with the Loan Agreement. Events of default under the Loan Agreement include failure to make payments when due, insolvency events, failure to comply with covenants, and material adverse effects with respect to the Company. The Company is not in violation of any affirmative or negative covenants. Repayment of the full balance outstanding is due on April 30, 2034. The 2019 Cecil Loan establishes "Phantom Shares," based on 23,981 shares of the Company's common stock (based on 172,622 Series C Preferred Shares prior to the Reverse Recapitalization), determined at issuance. The 2019 Cecil Loan states the repayment amount is to be the greater of the balance of principal and accrued interest or the Phantom Share value. The Company determined that the note should be accounted for at fair value. The Company records the fair value of the debt at the end of each reporting period. In order to value the note, the Company considers the amount of the simple interest expense that would be due and considers the value of Phantom Shares. Expense of $0.1 million and $6 thousand was recognized during the years ended December 31, 2020 and 2019, respectively. The fair value of $0.2 million and $0.1 million of principal and accrued interest is included in long-term notes payable as of December 31, 2020 and December 31, 2019, respectively.

In May 2020, the Company entered into a note payable in the amount of $0.6 million (the "PPP Note") under the Paycheck Protection Program of the CARES Act (the "PPP"). As amended, the PPP permits forgiveness of amounts loaned for payments of payroll and other qualifying expenses within 24 weeks of receipt of loaned funds, given that at least 60% of the total loan is used for payroll. Amounts not forgiven by the PPP have a repayment period of five years. The Company expects the full $0.6 million balance of the PPP Note to be forgiven. The Company will record any forgiveness after approval by the issuer. Until then, the PPP balance is included in long-term notes payable as of December 31, 2020. On January 11, 2021, the U.S. Small Business Administration notified the Company that the Company's PPP loan of $0.6 million had been forgiven (see Note 22).

9. Preferred Stock Warrant Liability

Prior to the Reverse Recapitalization, the Company issued Series A Preferred Stock Warrants in 2013 in connection with certain note purchase agreements. The warrants expire 10 years from issuance. These warrants are exercisable at a fixed exercise price of $1.97, which is equal to the price per share of the Series A Preferred Stock by the Company. As of December 31, 2019, these warrants were exercisable into 1,608,672 shares of the Series A Preferred Stock.

Prior to the Reverse Recapitalization, on April 8, 2013, the Company issued 10-year warrants to purchase units of the Company's most senior equity equal to 0.50% of the Company's fully diluted equity at the time of exercise in connection with certain note purchase agreements. As of December 31, 2019, these warrants were exercisable into 271,439 shares of the Company's most senior equity, Series C Preferred Stock, at a fixed exercise price of $1.97 per share. On August 11, 2020, in connection with the Company's issuance of Series D Preferred Stock, these warrants became exercisable into 320,441 shares of the Company's most senior equity, Series D Preferred Stock, at a fixed exercise price of $1.97 per share.

Prior to the Reverse Recapitalization, the Company classified its Preferred Stock warrants as a liability on its consolidated balance sheet because the warrants are freestanding financial instruments that may have required to the Company to transfer assets upon exercise. The liability associated with each of these warrants was initially recorded at fair value upon the issuance date of each warrant and is subsequently remeasured to fair value as a component of other income (expense), net in the consolidated statement of operations and comprehensive loss. Upon the closing of the Reverse Recapitalization (see Note 1), and as pursuant to the Merger Agreement, all of the outstanding Clene Nanomedicine Preferred Stock was converted to the Company's Common Stock and the Clene Nanomedicine Preferred Stock warrants to purchase Clene Nanomedicine Preferred Stock were converted to warrants to purchase the Company's Common Stock (see Note 10). Upon conversion, the Company assessed the features of the warrants and determined that they qualify for classification as permanent equity upon the closing of the Reverse Recapitalization. Accordingly, the Company remeasured the warrants to fair value one final time upon the close of the Reverse Recapitalization, and recognized a loss of $14.6 million for the year ended December 31, 2020, within other income, (expense), net on the consolidated statements of operations and comprehensive loss. Upon the closing of the Reverse Recapitalization, the warrant liability was reclassified to additional paid-in capital (see Notes 1 and 17).

As of December 31, 2020, the Company does not have any Preferred Stock warrants outstanding.

As of December 31, 2019, the fair value of the outstanding warrants was $3.2 million with the changes in fair value recorded as a component of other income (expense), net on the consolidated statements of operations and comprehensive loss. As of December 31, 2019, the Company had Preferred Stock warrants outstanding and exercisable as follows:

	Expiration Date	Exercise Price Per Share[1]	Warrants Outstanding[1]
Series C preferred stock warrants[2]	April 2023	$ 1.9658	271,439
Series A preferred stock warrants	April 2023	$ 1.9658	1,608,672

(1) The exercise price per share and warrants outstanding, prior to the Reverse Recapitalization, have been retroactively restated as shares reflecting the Exchange Ratio established in the Reverse Recapitalization (See Note 1).

(2) As of December 31, 2019, the most senior equity preferred stock warrants were convertible into Series C Preferred Stock.

10. Common Stock Warrants

As of December 31, 2020, outstanding warrants to purchase shares of the Company's Common Stock consisted of the following:

Date Exercisable	Number of Shares Issuable	Exercise Price	Exercisable for	Classification	Expiration
June 2021	1,119,750	$ 0.01	Common Stock	Equity	December 2021
December 2020	2,407,500	$ 11.50	Common Stock	Equity	December 2025
December 2020	110,000	$ 11.50	Common Stock	Equity	December 2025
December 2020	1,929,113	$ 1.97	Common Stock	Equity	April 2023
Total	5,566,363				

On December 28, 2020, the Company entered into a subscription agreement (the "Subscription Agreement") with various investors for the private purchase of 2,239,500 shares of the Company's Common Stock at a price of $10.00 per share with net proceeds of $22.2 million. Investors in the PIPE offering also received warrants ("PIPE Warrants") to purchase a number of shares equal to one-half (1/2) of the number of PIPE Shares, totaling 1,119,750 shares of the Company's Common Stock, at an exercise price of $0.01 per share. Also, pursuant to the Subscription Agreement, the 1,119,750 PIPE Warrants are subject to a 180-day holding period. A holder of the PIPE Warrants may not exercise the PIPE Warrant if the holder, together with its affiliates, would beneficially own more than 9.99% of the number of shares of the Company's Common Stock outstanding immediately after giving effect to such exercise. As of December 31, 2020, none of the warrants had been exercised.

In connection with the Reverse Recapitalization, all of Tottenham's issued and outstanding warrants to purchase one-half (1/2) of one share of Tottenham's ordinary shares totaling 4,815,000 shares issued in connection with Tottenham's initial public offering, were automatically converted into 2,407,500 warrants to purchase the Company's Common Stock. The warrants became exercisable upon the completion of the Reverse Recapitalization and will expire five years after the consummation of the Reverse Recapitalization (i.e., December 2025). The Company may redeem those outstanding warrants, in whole and not in part, at a price of $0.01 per warrant if, and only if, the last sales price of the Company's Common Stock equals or exceeds $16.50 per share for any 20 trading days within a 30-trading day period ending three business days before the Company sends the notice of redemption. As of December 31, 2020, none of the warrants had been exercised.

In connection with Tottenham's initial public offering in August 2018, Tottenham issued to Chardan options to purchase 220,000 units at $10.00 per unit. Each of Tottenham's units consists of one and one-tenth shares of Tottenham's ordinary shares for $10.00 per share and one warrant to purchase one-half of one Tottenham ordinary share at an exercise price of $11.50 per share. In connection with the Reverse Recapitalization, the Chardan Unit Purchase Option was converted into one Company unit purchase option. The Chardan Unit Purchase Option Warrants are exercisable upon the completion of the Reverse Recapitalization and will expire in December 2025. As of December 31, 2020, no Chardan Unit Purchase Options were exercised.

In connection with the Reverse Recapitalization, all of the 1,929,113 outstanding Series A and Series D Preferred Stock Warrants were converted automatically into 1,929,113 warrants to purchase shares of the Company Common Stock at $1.97 per share (See Note 9).

11. Convertible Notes

In February through July 2020, the Company issued convertible promissory notes (the "2020 Convertible Notes") in an aggregate principal amount of $6.1 million, bearing interest at an annual rate of 5%. The 2020 Convertible Notes were convertible at the earlier of (i) one year, at which point the notes would be convertible into Series C preferred shares at the Series C preferred share issuance price, and (ii) next equity financing of no less than $10.0 million, at which point the notes would be convertible into shares issued in the next equity financing at 90% of the per share issuance price of the next equity financing. The 2020 Convertible Notes contained redemption features that met the requirements for separate accounting and were accounted for as a single derivative instrument. Accordingly, the 2020 derivative instrument of $0.7 million was recorded at fair value at inception as redeemable convertible preferred stock derivative liability in the consolidated balance sheets (see Note 12).

The Company recognized interest expense of $0.2 million, including amortization of debt discount of $0.2 million during the year ended December 31, 2020, in connection with the 2020 Convertible Notes.

On August 11, 2020, in connection with the Company's issuance and sale of Series D Preferred Stock, all of the outstanding principal and accrued interest under the 2020 Convertible Notes, totaling $6.9 million, was automatically converted into 1,497,135 shares of Series D Preferred Stock at a price equal to 90% of $4.60 per share, the per share price paid in cash by investors in the Series D preferred stock financing.

The Company accounted for the conversion of the 2020 Convertible Notes as a debt extinguishment and recognized a loss on extinguishment of debt of $0.5 million within other income (expense), net in the consolidated statement of operations and comprehensive loss. As of the date of conversion, the unamortized discount on the 2020 Convertible Notes was $0.5 million. The loss on extinguishment was calculated as the difference between (i) the fair value of the 1,497,135 shares of Series D Preferred Stock issued to settle the 2020 Convertible Notes of $6.9 million and (ii) the carrying value of the 2020 Convertible Notes, including the principal balance of the 2020 Convertible Notes of $6.1 million and accrued but unpaid interest of $76 thousand, net of the unamortized debt discount of $5.7 million, plus the then-current fair value of derivative liability associated with the 2020 Convertible Notes at the time of the extinguishment of $0.7 million.

12. Derivative Instruments

Derivative instrument in connection with the 2020 Convertible Notes

One of the redemption features of the 2020 Convertible Notes met the requirements for separate accounting and was accounted for as a derivative instrument. The 2020 Derivative Instrument was recorded at fair value, which was $0.7 million at issuance. In August 2020, in connection with the Company's issuance and sale of Series D Preferred Stock, all of the outstanding principal and accrued interest under the 2020 Convertible Notes was automatically converted into shares of Series D Preferred Stock and the derivative liability was extinguished. Prior to the extinguishment of derivative liability, the 2020 Derivative Instrument was marked at fair value and the Company recorded the change in the 2020 Derivative Instrument of ($29) thousand in the consolidated statements of operations and comprehensive loss (see Note 11).

Derivative instrument in connection with the Contingent Earn-out

The Earn-out Shares issued in connection with the Reverse Recapitalization met the requirements for separate accounting and is therefore accounted for as a derivative instrument. Accordingly, upon the consummation of the Reverse Recapitalization, the Company recorded a liability in the consolidated balance sheets and a debit to additional paid-in capital for the earn-out provision associated with the Initial Shareholders Contingent Earn-out and a debit to accumulated deficit for the earn-out provisions associated with the Clene Nanomedicine Contingent Earn-out. The contingent shares to be issued to the Clene Nanomedicine shareholders immediately prior to the Reverse Capitalization were treated as a deemed distribution. The contingent earn-out was subsequently remeasured to fair value at each reporting date as a component of other income (expense), net in the Company's consolidated statements of operations and comprehensive loss.

Upon the closing of the Reverse Recapitalization, the Company recognized the contingent earn-out liability at its fair value of $72.1 million in the consolidated balance sheets. As of December 31, 2020, the carrying value of the contingent earn-out was $58.0 million. During the year ended of December 31, 2020, the Company recognized a gain of $14.1 million in change in fair value of contingent earn-out as a component of other income (expense), net in the Company's consolidated statements of operations and comprehensive loss. To date, none of the milestones has been achieved.

13. Commitments and Contingencies

Litigation — From time to time, the Company may have certain contingent liabilities that arise in the ordinary course of business activities. The Company accrues a liability for such matters when it is probable that future expenditures will be made and such expenditures can be reasonably estimated. The Company is not aware of any current pending legal matters or claims.

14. Income Taxes

The Company has not recorded income tax benefits for the net operating losses incurred during the years ended December 31, 2020 and 2019 nor for research and development tax credits and other deferred tax assets generated, due to its uncertainty of realizing a benefit from those items.

The components of income (loss) before income taxes for the years ended December 31, 2020 and 2019 were as follows (in thousands):

	2020	2019
United States	$ (18,985)	$ (13,812)
Foreign	114	(2,343)
Loss before provision for income taxes	$ (18,871)	$ (16,155)

Income tax expense (benefit) for the years ended December 31, 2020 and 2019 were as follows (in thousands):

Provision for income taxes:	2020	2019
Current tax expense:		
Federal	-	-
State	-	-
Foreign	146	-
Total current tax expense (benefit)	146	-
Deferred tax expense:		
Federal	-	-
State	-	-
Foreign	260	-
Total deferred tax expense (benefit)	260	-
Total income tax expense (benefit)	406	-

A reconciliation of the income tax computed at the U.S. federal statutory rate of 21% to the expense for income taxes for the years ended December 31, 2020 and 2019 is as follows (in thousands):

	2020	2019
Income tax expense (benefit) at federal statutory rate	(3,963)	(3,393)
State income taxes (net of federal benefit)	(917)	(721)
Warrant liability	3,069	-
Contingent consideration	(2,966)	-
Research and development credits	(425)	326
Other	242	1,205
Change in valuation allowance	5,366	2,583
Income tax expense (benefit)	406	-

The Company's effective tax rate was (2.15)% and 0.00% for the years ended December 31, 2020 and 2019, respectively. Significant components of the Company's deferred tax assets (liabilities) as of December 31, 2020 and 2019 were as follows (in thousands):

	2020	2019
Deferred tax assets (liabilities):		
Net operating loss carryforwards	17,958	13,502
Depreciation and amortization	1,810	1,814
Research & development credits	1,682	882
Lease liability	520	436
Right-of-use asset	(270)	(48)
Accrued interest	160	-
Non-qualified stock options	146	130
Accrued compensation	115	62
Other	(260)	(23)
Total	21,861	16,755
Less: valuation allowance	(22,121)	(16,755)
Net deferred tax assets (liabilities)	(260)	-

In assessing the realizability of deferred tax assets, management considers whether it is more-likely-than-not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during periods in which those temporary differences become deductible. Management considers the scheduled reversal of deferred tax liabilities, projected future taxable income, carry back opportunities and tax planning strategies in making the assessment. The Company believes it is more likely than not it will not realize the benefits of these deductible differences and has applied a full valuation allowance against them. As the Company has no deferred tax assets in Australia, it has recognized a deferred tax liability and expense for $0.3 million for temporary differences that will reverse in future periods.

The Company has federal and state net operating losses (NOLs) of approximately $72.2 million and $59.8 million as of December 31, 2020, respectively that, subject to limitation, may be available in future tax years to offset taxable income. Of the available federal NOLs, approximately $38.8 million can be carried forward indefinitely but utilization is limited to 80% of the Company's taxable income in any given tax year based on current federal tax laws. The remaining balance of $33.4 million will begin to expire after 2034. Of the available state NOLs, approximately $39.4 million can be carried forward indefinitely but utilization is limited to 80% of the Company's taxable income in any given tax year based on current tax laws. The remaining balance of $20.4 million will begin to expire after 2032. Additionally, the Company has approximately $1.7 million of research and development (R&D) credit carryforwards that will begin to expire after 2034 if not utilized.

Under the provisions of §382 of the Internal Revenue Code, substantial changes in the Company's ownership may result in limitations on the amount of NOL carryforwards and R&D credits that can be utilized in future years. NOL carryforwards and R&D credits are subject to examination in the year they are utilized regardless of whether the tax year in which they are generated has been closed by statute. The amount subject to disallowance is limited to the amount utilized. Accordingly, the Company may be subject to examination for prior NOLs and credits generated as such tax attributes are utilized.

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2020 and 2019. The Company’s practice is to recognize interest and penalties related to income tax matters in income tax expense. The Company had no accrual of interest and penalties on the Company’s balance sheets and has not recognized interest and penalties in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2020 and 2019.

The Company is subject to taxation in the United States and Australia. The Company’s tax returns from 2014 to present are subject to examination by the United States and state authorities due to the carry forward of unutilized net operating losses and R&D credits. There are currently no pending examinations.

15. Stock-Based Compensation

2020 Stock Plan

In December 2020, in connection with the Reverse Recapitalization, the Company’s board of directors approved the 2020 Stock Plan (the “2020 Stock Plan”) and reserved 12,000,000 shares of Common Stock for issuance thereunder, all of which may be issued pursuant to incentive stock options or any other type of award under the 2020 Stock Plan. The 2020 Stock Plan became effective immediately upon the closing of the Reverse Recapitalization. The maximum number of shares of Common Stock that may be issued pursuant to the exercise of incentive stock options under the 2020 Stock Plan is 12,000,000. The Company’s selected employees, officers, directors and consultants are eligible to participate in the traditional stock option grants, stock appreciation rights, restricted stock awards, restricted stock unit awards, other stock awards, and performance awards under the 2020 Stock Plan. The purpose of this 2020 Stock Plan is to enable the Company to offer competitive equity compensation packages in order to attract and retain the talent necessary for the Combined Company.

The 2020 Stock Plan is administered by the Company’s Board of Directors. The exercise prices, vesting periods and other restrictions are determined at the discretion of the Company’s Board of Directors, except that the exercise price per share of options may not be less than 100% of the fair market value of the Common Stock on the date of grant. Stock options awarded under the 2020 Stock Plan expire ten years after the grant date, unless the Company’s Board of Directors sets a shorter term. Stock options and restricted stock granted to employees, officers, members of the Company’s Board of Directors and consultants generally vest over a four-year period. If an option or other award granted under the 2020 Stock Plan expires, terminates or is cancelled, the unissued shares subject to that option or award shall again be available under the 2020 Stock Plan. If shares awarded pursuant to the 2020 Stock Plan are forfeited to or repurchased at original cost by the Company, the number of shares forfeited or repurchased at original cost shall again be available under the 2020 Stock Plan.

On December 30, 2020, the Company granted 1,507,062 restricted stock units under the 2020 Stock Plan. As of December 31, 2020, 10,492,938 shares remained available for future grant.

2014 Stock Plan

Following the closing of the Reverse Recapitalization, the 2014 Stock Plan is administered by the Company’s Board of Directors. Stock options awarded under the 2014 Stock Plan expire ten years after the grant date. Stock options and restricted stock granted to employees, officers, members of the Company’s Board of Directors and consultants typically vest over a four-year period.

As a result of the Reverse Recapitalization (as described in Note 1), stock options outstanding under the 2014 Stock Plan of 53,286,115 were converted into 7,032,590 of stock options of the Company based on the Exchange Ratio determined in accordance with the terms of the Merger Agreement. The exchange of Clene Nanomedicine’s stock options for Clene Inc. stock options was treated as a modification of the awards. The modification of the stock options did not result in a material incremental compensation expense to be recognized at the closing of the Reverse Recapitalization.

During the year ended December 31, 2020, the Company granted stock options for 270,555 shares under the 2014 Stock Plan.

As of December 31, 2019, there were 6,720,065 common shares authorized for grant to employees, officers, directors, and consultants under the 2014 Stock Plan. Effective as of the closing of the Reverse Recapitalization on December 30, 2020, no additional awards may be made under the 2014 Stock Plan and as a result, (i) any shares in respect of stock options that are expired or terminated under the 2014 Stock Plan without having been fully exercised will not be available for future awards; (ii) any shares in respect of restricted stock that are forfeited to, or otherwise repurchased by the Company, will not be available for future awards; and (iii) any shares of Common Stock that are tendered to the Company by a participant to exercise an award will not be available for future awards.

During the year ended December 31, 2019, the Company granted stock options for 1,440,717 shares under the 2014 Stock Plan. There were 388,283 shares available for grant under the 2014 Stock Plan as of December 31, 2019.

Stock-based compensation for the years ended December 31, 2020 and 2019 was approximately $0.8 million and $0.4 million, respectively, and is recorded in research and development and general and administrative expenses in the consolidated statement of operations and comprehensive loss as follows:

(In thousands)	**2020**	**2019**
General and administrative	$ 281	$ 161
Research and development	480	238
Total stock-based compensation	$ 761	$ 399

As of December 31, 2020, the Company had approximately $2.4 million of unrecognized stock-based compensation costs related to non-vested awards which is expected to be recognized over a weighted-average period of 2.04 years.

The following sets forth the outstanding Common Stock options and related activity for the year ended December 31, 2020 (in thousands, except share and per share data):

Equity	**Number of Options**	**Weighted Average Exercise Price Per Share**	**Weighted Average Remaining Term (Years)**	**Instrinsic Value**
Outstanding - December 31, 2018	5,698,090	$ 0.38	6.62	$ 11,089
Granted	1,440,717	2.42	9.66	-
Exercised	(11,878)	0.83	-	31
Forfeited	(248,757)	1.44	-	-
Outstanding - December 31, 2019	6,878,172	0.83	6.36	18,105
Granted	270,555	5.48	5.32	-
Exercised	(83,232)	0.94	-	740
Forfeited	(32,904)	1.65	-	-
Outstanding - December 31, 2020	7,032,591	$ 0.97	5.34	$ 62,462
Options vested and exercisable - December 31, 2020	5,896,034	$ 0.55	4.86	$ 52,694
Options vested and exercisable - Stock options vested and expected to vest December 31, 2020	7,032,591	$ 0.97	5.34	$ 62,462

Prior to the consummation of the Reverse Recapitalization, the exercise price of the stock options granted was based on the fair market value of the common shares of the Company as of the grant date as determined by the Board of Directors, with input from the Company's management. The Board of Directors determined the fair value of the common stock at the time of grant of the options by considering a number of objective and subjective factors, including third-party valuation reports, valuations of comparable companies, sales of redeemable convertible Preferred Stock, sales of common stock to unrelated third parties, operating and financial performance, the lack of liquidity of the Company's capital stock, and general and industry-specific economic outlook.

Stock options are valued using the Black-Scholes option pricing model. Since the Company has limited trading history of its common stock, the expected volatility is derived from the average historical stock volatilities of several unrelated public companies within the Company's industry that the Company considers to be comparable to its own business over a period equivalent to the expected term of the stock option grants. The risk-free interest rate for periods within the contractual life of the stock options is based on the U.S. Treasury yield curve in effect at the time of the grant. The expected dividend is assumed to be zero as the Company has never paid dividends and has no current plans to do so. The expected term represents the period that stock-based awards are expected to be outstanding. For option grants that are considered to be "plain vanilla," the Company determines the expected term using the simplified method. The simplified method deems the term to be the average of the time-to-vesting and the contractual life of the options. For other option grants, the Company estimates the expected term using historical data on employee exercises and post-vesting employment termination behavior taking into account the contractual life of the award.

The assumptions used to calculate the value of the stock option awards granted in 2020 and 2019 are presented as follows:

	2020	2019
Expected stock price volatility	75.00% - 119.30%	75.00%
Risk-free interest rate	0.39% - 0.53%	1.46%
Expected dividend yield	0%	0%
Expected term of options	6 years	6 years

The weighted average grant-date fair value of options granted during the years ended December 31, 2020 and 2019 was $2.3923 and $1.5806, respectively.

Restricted Stock Units

On December 30, 2020, the Company granted the following shares of restricted common stock under the 2020 Stock Plan:

- 370,101 shares to various employees and non-employee directors, which vest on June 30, 2021, subject to the employee's continuous employment through such vesting date. The award represents 5% of the converted stock options under 2014 Stock Plan as a result of the Reverse Recapitalization and complements the 5% closing payment shares held in escrow for Clene Nanomedicine common shareholders (as described in Note 1). The grant-date fair value of these awards was $4.0 million.

- 454,781 shares to various employees and non-employee directors, which were eligible to vest based on certain market conditions, subject to the employee's continuous employment through such vesting date. The award complements the Milestone 1 earn-out share entitlement of Clene Nanomedicine shareholders and vests based on the same market condition (as described in Note 3). The grant-date fair value of these awards, using a Monte Carlo simulation, was $4.3 million. Based on the outcome of the market condition as of the December 31, 2020 measurement date, no shares were vested.

- 341,090 shares to various employees and non-employee directors, which were eligible to vest based on certain market conditions, subject to the employee's continuous employment through such vesting date. The award complements the Milestone 2 earn-out share entitlement of Clene Nanomedicine. shareholders and vests based on the same market condition (as described in Note 3). The grant-date fair value of these awards, using a Monte Carlo simulation, was $3.5 million. Based on the outcome of the market condition as of the December 31, 2020 measurement date, no shares were vested.

- 341,090 shares to various employees and non-employee directors, which were eligible vest based on certain performance conditions tied to the completion of the COVID-19 coronavirus treatment study, subject to the employee's continuous employment through such vesting date. The award complements the Milestone 3 earn-out share entitlement of Clene Nanomedicine shareholders and vests based on the same performance condition (as described in Note 3). The grant-date fair value of these awards was $3.7 million based on a weighted average grant date fair value of $10.82 per share. The Company did not recognize compensation expense because the occurrence of achieving this milestone was not probable. As of the December 31, 2020 measurement date, no shares were vested.

The following table summarizes the restricted common stock activity during the year ended December 31, 2020:

	Number of RSUs	Weighted Average Grant Date Fair Value
Unvested balance as of December 31, 2019	-	$ -
Granted	1,507,062	10.30
Vested	-	-
Unvested balance as of December 31, 2020	1,507,062	$ 10.30

The assumptions used to calculate the value of the restricted stock units granted in 2020 in the Monte Carlo valuation model include projected stock price, volatility and risk-free rate based on the achievement of certain stock price milestones. Our significant unobservable inputs as of December 31, 2020 were as follows: (i) 85% of expected stock price volatility, (ii) risk-free interest rate of 0.4%, and (iii) expected term of 5 years. The weighted average grant-date fair value of RSUs granted during the years ended December 31, 2020 and 2019 was $10.3034 and $0, respectively.

The stock-based compensation expense associated with the RSUs were immaterial for the years ended December 31, 2020 and 2019. As of December 31, 2020, total unrecognized compensation cost related to the unvested stock-based awards was $15.5 million, which is expected to be recognized over a weighted average period of 8 months.

16. Fair Value

The carrying amount of cash and accounts payable approximates fair value because of the immediate, short-term maturity of these financial instruments.

Liabilities with Fair Value Measurements on a Recurring Basis — The following tables present the Company's fair value hierarchy for its liabilities measured at fair value on a recurring basis as of December 31, 2020 and 2019 (in thousands):

	Fair Value Measurements on a Recurring Basis December 31, 2020			
	Level 1	Level 2	Level 3	Total
Notes payable	$ 1,296	$ -	$ -	$ 1,296
Clene Nanomedicine contingent earn-out	-	-	52,053	52,053
Initial Shareholders contingent earn-out	-	-	5,906	5,906

	Fair Value Measurements on a Recurring Basis December 31, 2019			
	Level 1	Level 2	Level 3	Total
Redeemable convertible preferred stock warrant liability	$ -	$ -	$ 3,213	$ 3,213
Notes payable	-	-	640	640

For the year ended December 31, 2020, there was a transfer to Level 1 from Level 3 of the Company's notes payable as the fair value of the notes payable is determined based on the Company's stock price listed on the Nasdaq. There were no other transfers between Level 1, Level 2 or Level 3. For the years ended December 31, 2019, there were no transfers between Level 1, Level 2, or Level 3.

Valuation of the Notes Payable

The carrying value of the notes payable includes certain notes remeasured at fair value on a recurring basis in the balance sheet as of December 31, 2020 and 2019. In order to value the note, the Company considers the amount of simple interest expense that would be due and considers the value of Phantom Shares.

Prior to becoming a public company, the Company's notes payable contained unobservable inputs that reflected the Company's own assumptions. Accordingly, the Company's notes payable were measured at fair value on a recurring basis using unobservable inputs. Significant unobservable inputs as of December 31, 2019 were the fair value of Series C Preferred Stock of $4.1699 per share.

As of December 31, 2020, the fair value of the Company's Notes payable is determined based on the closing price of $9.01 per share for CLNN listed on the Nasdaq.

Valuation of Warrants to Purchase Preferred Stock

The Company's Preferred Stock warrant liabilities contain unobservable inputs that reflect the Company's own assumptions. Accordingly, the Company's Preferred Stock warrant liabilities were measured at fair value on a recurring basis using unobservable inputs. Prior to the extinguishment of the Preferred Stock warrant liabilities on December 30, 2020 and on December 31, 2019, the Preferred Stock warrant liability was valued using a Black-Scholes valuation model.

Significant unobservable inputs at December 30, 2020 were the fair value of Series D Preferred Stock warrants of $10.82 per share, the fair value of Series A Preferred Stock warrants of $10.82 per share, expected term of 2.3 years, expected volatility of Series D Preferred Stock warrants of 101%, and expected volatility of Series A Preferred Stock warrants of 101%. Significant unobservable inputs at December 31, 2019 were the fair value of Series C Preferred Stock warrants of $4.1699 per share, the fair value of Series A Preferred Stock warrants of $3.1046 per share, expected term of 2 years, expected volatility of Series C Preferred Stock warrants of 49%, and expected volatility of Series A Preferred Stock warrants of 71%.

The Board of Directors determines the fair value of the Preferred Stock by considering a number of objective and subjective factors, including third-party valuations, valuations of comparable companies, sales of redeemable convertible Preferred Stock, sales of common stock to unrelated third parties, operating and financial performance, the lack of liquidity of the Company's capital stock, and general and industry-specific economic outlook. The Company estimated the volatility of its Preferred Stock based on comparable peer companies' historical volatility. The risk-free interest rate for periods within the contractual life of the warrants is based on the U.S. Treasury yield curve in effect at the valuation date. The Company has no plans to declare any future dividends. The determination of the fair value of the Preferred Stock warrant liability could change in future periods based upon changes in the value of the Company's Preferred Stock and other assumptions as presented above. The Company records any such change in fair value to the change in fair value of Preferred Stock warrant liability expense line in the consolidated statements of operations and comprehensive loss.

Upon the closing of the Reverse Recapitalization (see Note 1), all of the outstanding Clene Nanomedicine Preferred Stock was converted to Clene Inc. Common Stock and the Clene Nanomedicine Preferred Stock warrants were converted to warrants for the purchase of Clene Inc. Common Stock. Accordingly, the Preferred Stock warrant liabilities were extinguished in connection with the conversion of Clene Nanomedicine Preferred Stock on December 30, 2020 (see Note 9).

Valuation of the Contingent Earn-out

Pursuant to the Merger Agreement, Clene Nanomedicine's common shareholders immediately prior to the Reverse Recapitalization and Initial Shareholders of Totttenham were entitled to receive additional shares of up to 8,333,333 shares and 750,000 shares of the Company's Common Stock, respectively, upon the Company achieving certain milestones described in Note 3. Upon the consummation of the Reverse Recapitalization, Clene Nanomedicine and the Initial Shareholders are entitled to receive additional shares up to 8,346,185 shares as a result of the exercise of the stock options in November 2020, and 750,000 shares of the Company's Common Stock. The Clene Nanomedicine Contingent Earn-out and the Initial Shareholders Contingent Earn-out are recorded at fair value as contingent earn-out on the closing of the Reverse Recapitalization on December 30, 2020 and remeasured at each reporting period. As of December 31, 2020, no milestone has been achieved.

The estimated fair value of the initial contingent earn-out is determined using a Monte Carlo analysis in order to simulate the future path of the Company's stock price over the earn-out period. The carrying amount of the liability may fluctuate significantly and actual amounts paid may be materially different from the liability's estimated value. As of December 31, 2020, the contingent earn-out was revalued using a similar Monte Carlo analysis. The unobservable inputs to the model were as follows:

	2020	2019
Expected stock price volatility	85.00%	N/A
Risk-free interest rate	0.40%	N/A
Expected term	5 years	N/A

The following is a summary of changes in the fair value of the Company's financial liability related to the notes payable, the derivative instrument, the Preferred Stock warrants, and the contingent earn-out measured at fair value as of December 31, 2020 and 2019 (in thousands):

	Notes Payable	Derivative Instrument	Preferred Stock Warrants	Clene Nanomedicine Contingent Earn-out	Initial Shareholders Contingent Earn-out
Balance - December 31, 2018	$ -	$ -	$ 4,518	$ -	$ -
Issuance of notes payable	600	-	-	-	-
Change in fair value	40	-	361	-	-
Exercise of Series C preferred stock warrants	-	-	(1,666)	-	-
Balance - December 31, 2019	640	-	3,213	-	-
Issuance of convertible promissory notes	-	705	-	-	-
Initial fair value of instrument	-	-	-	64,712	7,371
Change in fair value	656	(29)	14,615	(12,659)	(1,465)
Extinguishment of preferred stock warrant liability in connection with the conversion of redeemable convertible preferred stock	-	-	(17,828)	-	-
Extinguishment of derivative liability in connection with extinguishment of the 2020 Convertible Notes (Note 12)	-	(676)	-	-	-
Balance - December 31, 2020	$ 1,296	$ -	$ -	$ 52,053	$ 5,906

17. Redeemable Convertible Preferred Stock

Prior to the Reverse Recapitalization, the Company had issued Series A, B, C, and D Preferred Stock to various investors. Preferred stock is convertible into common stock at the option of the holder at the conversion price. The Company evaluated the Preferred Stock and concluded that it did not meet the criteria for being classified as a liability. However, the Company had determined that the Preferred Stock should be classified as temporary equity, as the Company might be required to redeem the outstanding Preferred Stock in cash. The Company had concluded that a redemption event is not probable. Accordingly, the value of Preferred Stock had not been adjusted to its redemption amount.

Holders of Preferred Stock vote together with the holders of common stock as a single class. Voting rights are in proportion to the number of votes equal to common stock shares into which preferred shares would be converted.

Redeemable Preferred Stock

Between February and April 2015, the Company issued 16,066,503 shares of Series A Preferred Stock to several investors, at a price of $1.9658 per share, for proceeds of $9.5 million in cash and $18.0 million by conversion of convertible promissory notes.

In December 2016, the Company issued 4,168,815 shares of Series B Preferred Stock at a price of $4.0778 per share and a buyout option for proceeds of $16.6 million, net of issuance costs of $0.4 million. The Agreement provided the buyer with an exclusive right and option to acquire all of the issued and outstanding stock of the Company on a fully diluted basis at a set price and provides for future milestone payments to be made to existing shareholders of the Company based on achievement of certain milestones defined within the Agreement. The purchase option was not exercised and was terminated by written notice received from the buyer on September 21, 2017. The Company allocated the total cash consideration received of $16.6 million between the Series B Preferred Stock and the buyout option based on the relative fair value of each instrument. The $3.4 million assigned to the buyout option was treated as a contribution and recorded into additional paid-in capital.

Between August and October 2018, the Company issued 4,929,718 shares of Series C Preferred Stock to several investors. The Company issued 3,849,011 shares, at a price of $4.1699 per share, for proceeds of $15.9 million in cash, net of issuance costs of $0.2 million. $1.5 million of the proceeds were allocated to the Series C Preferred Stock Warrants issued (see Note 9). The Company issued 1,080,707 shares upon conversion of the convertible promissory notes (see Note 11).

Between March and July 2019, the Company issued 2,334,801 shares of Series C Preferred Stock to several investors. The Company issued 1,935,111 shares, at a price of $4.1699 per share, for proceeds of $8.1 million in cash, net of immaterial issuance costs. The Company issued 399,690 shares on exercise of Series C Preferred Stock Warrants (see Note 9).

In August 2020, the Company issued 9,394,057 shares of Series D Preferred Stock to several investors. The Company issued 7,896,922 shares, at a price of $4.6018 per share, for proceeds of $35.1 million in cash, net of $1.3 million issuance costs. In addition, in connection with the Company's issuance and sale of Series D preferred stock, all of the outstanding principal and accrued interest under the 2020 Convertible Notes was automatically converted into an aggregate of 1,497,135 shares of Series D Preferred Stock. The Company determined the fair value of the shares issued upon conversion to be $6.9 million, based on the preferred stock financing cash price per share (see Note 11).

The Series A Preferred Stock, Series B Preferred Stock, Series C Preferred Stock, and Series D Preferred Stock are collectively referred as the "Preferred Stock." In connection with the closing of the Reverse Recapitalization, the Preferred Stock converted into 36,893,894 shares of Common Stock on a 1:0.1389 basis (see Note 1).

As of December 31, 2020, there was no Preferred Stock outstanding.

Preferred Stock consisted of the following as of December 31, 2019 (in thousands, except share amounts):

	December 31, 2019				
	Preferred Shares Authorized	Preferred Shares Issued and Outstanding	Carrying Value	Liquidation Value	Common Stock Issuable Upon Conversion
Series A Preferred Stock	17,675,175	16,066,503	$ 27,485	$ 31,584	16,066,503
Series B Preferred Stock	4,168,815	4,168,815	16,582	16,999	4,168,815
Series C Preferred Stock	9,192,018	7,264,519	28,594	30,292	7,264,519
Total	31,036,008	27,499,837	$ 72,661	$ 78,875	27,499,837

The rights and preferences of Series A, Series B, Series C, and Series D Preferred Stock are as follows:

Voting Rights — The holder of each share of Series A, Series B, Series C, and Series D Preferred Stock shall have the right to one vote for each share of common stock into which such Series A, Series B, Series C, and Series D Preferred Stock could then be converted.

Right to Elect Directors — As long as the majority of the Series A Preferred Stock issued remains outstanding, its holders shall be entitled to elect two directors of the Company. The holders of Series B Preferred Stock are entitled to elect one director of the Company. The holders of Series C Preferred Stock are entitled to elect one director of the Company. The holders of Preferred Stock and common stock (voting together as a single class and not as separate series and on as-converted basis) shall be entitled to elect any remaining director of the Company.

Dividend Rights — The holders of Preferred Stock are entitled to receive, when, as and if declared by the Board of Directors, out of any assets of the Company legally available therefore, any dividends as may be declared from time to time by the Board of Directors. No dividend may be declared or paid on the common stock (other than dividends payable in shares of common stock) unless any and all such dividends or distributions are distributed among all holders of common stock and Preferred Stock in proportion as if the Preferred Stock were converted to common stock at the effective conversion rate. The debt covenants of the Company's outstanding note payable prohibit the issuance of dividends, see Note 8.

Preferred Stock Protective Provisions — As long as Preferred Stock originally issued remains outstanding, the Company shall not without first obtaining the approval of the holders of at least a majority of the outstanding shares of Preferred Stock: (i) consummate a liquidation event or effect any other merger or consolidation, (ii) amend, alter, or repeal any provision of the Certificate of Incorporation, (iii) increase or decrease (other than redemption or conversion) the total number of authorized shares of common stock or Preferred Stock, (iv) authorize or issue any equity security having a preference over, or being on a parity of any series of Preferred Stock, (v) redeem, purchase, or acquire any shares of Preferred Stock or common stock, (vi) pay or declare any dividend on any shares of capital stock of the Company, other than dividends payable in shares of common stock, (vii) create or hold capital stock in any subsidiary that is not wholly owned by the Company or permit any direct or indirect subsidiary to sell, lease, transfer, exclusively license, or otherwise dispose the assets of such subsidiary.

In addition, Series B, Series C, and Series D Preferred Stock have protective provisions that prevent the Company from amending, altering, or repealing any provision of the Certificate of Incorporation or Bylaws to adversely alter or change the powers, preferences or special rights without first obtaining the approval of the holders of at least a majority of the outstanding shares of Series B, Series C, and Series D Preferred Stock, respectively.

Liquidation Preference — In case of any liquidation event, either voluntary or involuntary, the holders of Series D Preferred Stock shall be entitled to receive out of the proceeds or assets of the Company available for distribution to its shareholders prior and in preference to any distribution of the proceeds of such liquidation event to the holders of Series C Preferred Stock, Series B Preferred Stock, Series A Preferred Stock, and common stock by reason of their ownership thereof, an amount per share equal to the sum of the applicable original issue price for the Series D Preferred Stock plus declared but unpaid dividends on such share. If, upon the occurrence of such event, the proceeds thus distributed among the holders of the Series D Preferred Stock shall be insufficient to permit the payment to such holders of the full amounts, then the entire Proceeds legally available for distribution shall be distributed ratably among the holders of the Series D Preferred Stock in proportion to the full preferential amount that each such holder is entitled to receive.

In case of any liquidation event, either voluntary or involuntary, the holders of Series C Preferred Stock shall be entitled to receive out of the proceeds or assets of the Company available for distribution to its shareholders prior and in preference to any distribution of the proceeds of such liquidation event to the holders of Series B Preferred Stock, Series A Preferred Stock, and common stock by reason of their ownership thereof, an amount per share equal to the sum of the applicable original issue price for the Series C Preferred Stock plus declared but unpaid dividends on such share. If, upon the occurrence of such event, the proceeds thus distributed among the holders of the Series C Preferred Stock shall be insufficient to permit the payment to such holders of the full amounts, then the entire Proceeds legally available for distribution shall be distributed ratably among the holders of the Series C Preferred Stock in proportion to the full preferential amount that each such holder is entitled to receive.

In case of any liquidation event, either voluntary or involuntary, the holders of Series B Preferred Stock shall be entitled to receive out of the proceeds or assets of the Company available for distribution to its shareholders prior and in preference to any distribution of the proceeds of such liquidation event to the holders of Series A Preferred Stock, and common stock by reason of their ownership thereof, an amount per share equal to the sum of the applicable original issue price for the Series B Preferred Stock plus declared but unpaid dividends on such share. If, upon the occurrence of such event, the proceeds thus distributed among the holders of the Series B Preferred Stock shall be insufficient to permit the payment to such holders of the full preferential amounts, then the remaining Proceeds legally available for distribution after distribution to holders of the Series D Preferred Stock and Series C Preferred Stock shall be distributed ratably among the holders of the Series B Preferred Stock in proportion to the full preferential amount that each such holder is entitled to receive.

In case of any liquidation event, either voluntary or involuntary, the holders of Series A Preferred Stock shall be entitled to receive out of the proceeds or assets of the Company available for distribution to its shareholders prior and in preference to any distribution of the proceeds of such liquidation event to the holders of common stock by reason of their ownership thereof, an amount per share equal to the sum of the applicable original issue price for the Series A Preferred Stock plus declared but unpaid dividends on such share. If, upon the occurrence of such event, the proceeds thus distributed among the holders of the Series A Preferred Stock shall be insufficient to permit the payment to such holders of the full preferential amounts, then the remaining Proceeds legally available for distribution after distribution to holders of the Series D Preferred Stock, Series C Preferred Stock and Series B Preferred Stock shall be distributed ratably among the holders of the Series A Preferred Stock in proportion to the full preferential amount that each such holder is entitled to receive For purposes of determining the amount each holder of shares of Preferred Stock is entitled to receive in a liquidation event, each such holder shall be deemed to have converted into shares of common stock immediately prior to the Liquidation Event if, as a result of an actual conversion, such holder would receive, in the aggregate, an amount greater than the amount that would be distributed otherwise.

Redemption — The Series A, Series B, Series C, and Series D Preferred Stock are not redeemable at the option of the holder. However, so long as a majority of the Preferred Stock originally issued remains outstanding, the Company shall not, without first obtaining the approval of the holders of at least a majority of the then outstanding shares of Preferred Stock, redeem, purchase, or acquire any share or shares of Preferred Stock or common stock, except the repurchase, if any, of shares of common stock from employees, officers, directors, consultants, or other persons performing services for the Company.

Conversion Rights —

(a) Right to Convert. Each share of Preferred Stock shall be convertible, at the option of the holder thereof, at any time, into such number of fully paid and non-assessable shares of common stock as is determined by dividing the applicable original issue price by the applicable conversion price. The initial conversion price per share of Series A, Series B, Series C, and Series D Preferred Stock shall be $1.9658, $4.0778, $4.1699, and $4.6018, respectively, provided, however, that the conversion price shall be subject to adjustment as set forth below.

(b) Automatic Conversion. Each share of Series A, Series B, Series C, and Series D Preferred Stock shall automatically be converted into shares of common stock upon the earlier of (i) the closing of the sale of common stock in an underwritten public offering pursuant to a registration statement under the Securities Act of 1933, the public offering price of which is not less than $30.0 million in the aggregate, (ii) the date, or the occurrence of an event, specified by vote or written consent, or agreement of the holders of a majority of the then outstanding shares of Preferred Stock (voting together as a single class and not as separate series and on an as-converted basis), or (iii) a closing of a merger with a publicly-traded entity that has no operations other than searching for an operating company with which to merge (a "SPAC") at a value per share in accordance with the restated certification incorporation, resulting in at least $30.0 million of proceeds to the Company (including any cash acquired in the merger with the SPAC).

(c) Conversion Price Adjustment. The conversion Price of Preferred Stock shall be subject to adjustment as follows: If the Company shall issue any additional stock (as defined in the associated agreement) without consideration or for a consideration per share less than the Conversion Price in effect immediately prior to the issuance of such additional stock, the Conversion Price shall be adjusted.

18. Common Stock

As of December 31, 2020, the Company's certificate of incorporation, as amended and restated, authorized the Company to issue 100,000,000 shares of the Company's Common Stock, par value $0.0001 per share and 1,000,000 shares of the Company's Preferred Stock, par value $0.0001 per share.

The Company's common shareholders are entitled to one vote per share and to notice of any shareholders' meeting. Voting, dividend and liquidation rights of the holders of Common Stock are subject to the prior rights of holders of all classes of stock and are qualified by the rights, powers, preferences and privileges of the holders of Preferred Stock. No distributions shall be made with respect to Common Stock until all declared dividends to Preferred Shares have been paid or set aside for payment to the holders of Preferred Stock. Common Stock is not redeemable at the option of the holder.

On the closing of the Reverse Recapitalization, the total 2,303,495 of the Tottenham ordinary shares held by the Initial Shareholders and public shareholders were converted into the same number of Company's Common Stock (see Note 3).

On the closing of the Reverse Recapitalization, 644,164 shares of the Company's Common Stock were issued to LifeSci as financial advisor to the Reverse Recapitalization (see Note 3).

On December 28, 2020 and prior to the closing of the Reverse Recapitalization, various PIPE investors purchased 2,239,500 shares of the Company's Common Stock at a price of $10.00 per share and 1,119,750 warrants to purchase, at an exercise price of $0.01 per share, one share of the Company's Common Stock for net proceeds of $22.2 million (see Notes 1 and 3).

As of December 31, 2020, the Company's common shares issued and outstanding are 59,526,171 and there are no preferred shares issued and outstanding (see Note 17).

19. Net Loss Per Share Attributable to Common Shareholders

The following table sets forth the computation of basic and diluted net loss per share attributable to common shareholders (in thousands, except share and per share data):

	As of December 31,	
	2020	**2019**
Numerator:		
Net loss attributable to common shareholders	$ (19,277)	$ (16,155)
Denominator:		
Weighted average shares outstanding	17,503,992	17,357,505
Net loss per share attributable to common shareholders, basic and diluted	$ (1.10)	$ (0.93)

Included within weighted average common shares outstanding are 1,119,750 common shares issuable upon the exercise of the PIPE warrants as the warrants are exercisable at any time for nominal consideration, and as such, the shares are considered outstanding for the purpose of calculating basic and diluted net loss per share attributable to common shareholders.

The Company has not considered the effect of the Chardan Unit Purchase Option that would convert to 242,000 shares of the Company's Common Stock and warrants to purchase 110,000 shares of the Company's Commons Stock, in the calculation of diluted loss per share, since the conversion of the Chardan Unit Purchase Option and the exercise of the Chardan Unit Purchase Option Warrants into the Company's Commons Stock would be anti-dilutive (see Notes 1 and 10).

The following outstanding shares of potentially dilutive securities were excluded from the computation of diluted net loss per share attributable to common shareholders for the periods presented because including them would have been antidilutive:

	As of December 31,	
	2020	**2019**
Series C redeemable convertible preferred stock	-	7,264,519
Series B redeemable convertible preferred stock	-	4,168,815
Series A redeemable convertible preferred stock	-	16,066,503
Series C redeemable convertible preferred stock warrants	-	271,439
Series A redeemable convertible preferred stock warrants	-	1,608,672
Common stock warrants (see Note 10)	4,336,613	-
Options to purchase common stock	7,032,591	6,878,172
Chardan Unit Purchase Option to purchase common stock (see Note 1)	242,000	-
Chardan Unit Purchase Option Warrants (see Notes 1 and 10)	110,000	-
Earn-out shares (see Note 3 and 12)	9,096,185	-
Total	20,817,389	36,258,120

20. Related Party Transactions

Related Party Payables

During years prior to 2020, the Company incurred expenses for compensation for consulting services provided by a member of the Board of Directors. These expenses were fully paid as of December 31, 2020. As of December 31, 2019, the outstanding balance of $0.1 million was recorded in accounts payable.

Supply Agreement

In August 2018, in conjunction with an investment made in the Company's Series C Preferred Stock and Series C Preferred Stock Warrants by 4Life, LLC, an investor, the Company entered into a supply agreement with the investor. Under the terms of this agreement, the Company granted the investor an exclusive license to pursue development of dietary supplements using certain of the Company's intellectual property (IP). The exclusive rights to the IP will be for a term of 5 years from the commencement of sales of licensed product by the investor, with a deemed commencement date of January 1, 2023 if sales have not yet commenced, and is subject to annual minimum sales. The agreement may be renewed for additional 5-year terms. If the investor fails to meet the annual minimum sales requirements, the investor may pay an additional fee to maintain exclusivity or have the investor's license converted to non-exclusive rights. As part of this agreement, the Company will provide non-pharmaceutical product to the investor for development efforts and potential future production, and the investor is to pay royalties of 3% of incremental sales, as defined in the agreement. As of December 31, 2020, the Company had sold $70 thousand of product under this agreement, as well as $62 thousand of product not under this agreement, and received $0.1 million in advance to be applied against future sales of product under this agreement. The Company recorded this advanced amount as deferred revenue as of December 31, 2020 within accrued liabilities, and the Company expects to fulfil the performance obligations to release the deferred revenue in the first half of 2021 as the investor purchases product. As of December 31, 2020, the investor has made commercial sales of their products under the agreement which the Company recognized as royalty revenues of $30 thousand. As of and for the year ended December 31, 2019, the Company had not sold any product under this agreement, and there were no balances outstanding due to or from the investor.

21. Geographic and Segment Information

Geographic Information

The Company's long-lived assets, which were composed of property and equipment, net by location was as follows (in thousands):

	As of December 31,	
	2020	2019
United States	$ 3,997	$ 3,908
Australia	228	411
Total property and equipment, net	$ 4,225	$ 4,319

Segment Information

As of December 31, 2019, the Company had a single operating segment, development and commercialization of proprietary nanotechnology drug suspensions ("Drugs"). The Company identified a second segment, development and commercialization of proprietary dietary supplements ("Supplements"), in January 2020. The Company's chief operating decision maker, the CEO, now obtains and reviews separate financial information for Supplements in deciding how to allocate resources to the segments and in assessing performance.

The operating results of the Company's Drugs and Supplements segments for the years ended December 31, 2020 and 2019 were as follows (in thousands):

	As of December 31, 2020		
	Drugs	Supplements	Total
Revenue from external customers	$ -	$ 206	$ 206
(Loss) Income from operations	$ (20,355)	$ 141	$ (20,214)

	As of December 31, 2019		
	Drugs	Supplements	Total
Revenue from external customers	$ -	$ -	$ -
Loss from operations	$ (16,332)	$ -	$ (16,332)

The Company's long-lived assets, which were composed of property and equipment, net by segment was as follows (in thousands):

	As of December 31,	
	2020	2019
Drugs	$ 3,990	$ 4,319
Supplements	235	—
Total property and equipment, net	$ 4,225	$ 4,319

22. Subsequent Events

On January 11, 2021, the U.S. Small Business Administration notified the Company that the PPP loan of $0.6 million was forgiven. On that date, the Company recorded a gain on forgiveness of the PPP loan of $0.6 million in its consolidated statement of operations and comprehensive loss.

On January 27, 2021, the Company was awarded the Michael J. Fox Foundation grant for $0.5 million and funding is milestone based. On that date, the grant was recorded in accrued liabilities in the consolidated balance sheets, and as the associated conditions or obligations are met, the grant funding will be recognized as a reduction in research and development expenses in the consolidated statements of operations and comprehensive loss.

On February 16, 2021, the Company filed a registration statement on Form S-1 to register 4,541,481 shares of Common Stock underlying outstanding warrants that the Company had issued, among which 2,517,500 and 904,231 warrants were originally issued by Tottenham and Clene Nanomedicine, respectively, prior to the closing of the Reverse Recapitalization, and 1,119,750 warrants were issued as part of the PIPE offering in connection with the closing of the Reverse Recapitalization. The Company will receive aggregate gross proceeds of $30.7 million if all of these warrants are exercised. In addition, the registration statement on Form S-1 included 23,251,553 shares of the Common Stock to be registered for possible sale by the selling shareholders. The Company will not receive any proceeds from the sales by the selling shareholders. Incident to the registration of the Common Stock, the Company incurred certain offering costs, which will be recognized as an expense within general and administrative expenses on the consolidated statement of operations and comprehensive loss in the first quarter of 2021.

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 conducted an evaluation of the effectiveness of our disclosure controls and procedures as of December 31, 2020, as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2020, our disclosure controls and procedures were not effective due to the material weaknesses in internal control over financial reporting described below. Notwithstanding the identified material weaknesses, management, including our Chief Executive Officer and Chief Financial Officer, believes the consolidated financial statements included in this Annual Report on Form 10-K fairly represent in all material respects our financial condition, results of operations and cash flows at and for the periods presented in accordance with U.S. GAAP.

Disclosure controls and procedures are designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosure.

Material Weaknesses in Internal Control over Financial Reporting

In connection with the audit of Clene's financial statements as of and for the years ended December 31, 2020 and 2019, Clene's management identified material weaknesses in its internal control over financial reporting. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. The material weaknesses identified relate to the fact that Clene did not design or maintain an effective control environment commensurate with its financial reporting requirements, including (a) lack of a sufficient number of trained professionals with an appropriate level of accounting knowledge, training and experience to appropriately analyze, record and disclose accounting matters timely and accurately, and (b) lack of structures, reporting lines and appropriate authorities and responsibilities to achieve financial reporting objectives. This deficiency in Clene's control environment contributed to the following additional deficiencies (each of which individually represents a material weakness) in Clene's internal control over financial reporting:

- Clene did not design and maintain formal accounting policies, procedures and controls to achieve complete, accurate and timely financial accounting, reporting and disclosures, including controls over the preparation and review of account reconciliations and journal entries;

- Clene did not design and maintain effective controls over segregation of duties related to manual journal entries. Specifically, certain personnel have the ability to both prepare and post manual journal entries without an independent review by someone without the ability to prepare and post manual journal entries;

- Clene did not design and maintain formal accounting policies, processes and controls to analyze, account for and disclose complex transactions. Specifically, Clene did not design and maintain controls to analyze, account for and disclose warrants to purchase preferred stock and convertible promissory notes with embedded derivatives, including ensuring complete and accurate data was used in the valuations;

- Clene did not design and maintain effective controls over certain information technology ("IT") general controls for IT systems that are relevant to the preparation of the financial statements. Specifically, Clene did not design and maintain: (a) user access controls to ensure appropriate segregation of duties and that adequately restrict user and privileged access to financial applications, programs, and data to appropriate personnel of Clene, (b) program change management controls to ensure that IT program and data changes affecting financial IT applications and underlying accounting records are identified, tested, authorized and implemented appropriately, (c) computer operations controls to ensure that data backups are authorized and monitored, and (d) testing and approval controls for program development to ensure that new software development is aligned with business and IT requirements.

The control deficiencies described above resulted in the misstatement of Clene's redeemable convertible preferred stock warrant liability, accrued liabilities, general and administrative expenses, Australian research and development credit, and amounts and classification within our statement of cash flows and related financial disclosures as of and for the year ended December 31, 2019 and in the misstatement of Clene's prepaid expenses and other current assets, accrued liabilities, earn-out liabilities, redeemable convertible preferred stock warrant liability, general and administrative expenses, amounts and classification within our statement of equity, and amounts and classification within our statement of cash flows and related financial disclosures as of and for the year ended December 31, 2020. Additionally, each of the control deficiencies described above could result in a misstatement of one or more account balances or disclosures that would result in a material misstatement to the annual or interim consolidated financial statements that would not be prevented or detected. Accordingly, Clene's management has determined that each of the control deficiencies described above constitute material weaknesses.

Material Weakness Remediation

Management is actively engaged and committed to taking the steps necessary to remediate the control deficiencies that constituted the above material weakness. During 2020, we made the following enhancements to our control environment:

- We added finance personnel to the organization to strengthen our internal accounting team, to provide oversight, structure and reporting lines, and to provide additional review over our disclosures to include a Chief Financial Officer and a Manager of SEC Reporting;

- We engaged outside consultants to assist in the design, implementation, and documentation of internal controls that address the relevant risks, are properly designed, and provide for appropriate evidence of performance of the internal control; and

- We engaged outside consultants to assist us in the evaluation of a new Enterprise Resource Planning (" ERP") system in order to mitigate the internal control gaps and limitations that cannot be addressed by the current ERP around segregation of duties, and to enhance the information technology general controls environment.

Our remediation activities are continuing during 2021. In addition to the above actions, we expect to engage in additional activities, including, but not limited to:

- Adding more technical accounting resources to enhance our control environment;

- Until we have sufficient technical accounting resources, engaging external consultants to provide support and to assist us in our evaluation of more complex applications of GAAP, and to assist us with documenting and assessing our accounting policies and procedures;

- Implementing a new ERP to enhance the accuracy of our financial records, enable the enforcement of systematic segregation of duties, and to improve our information technology general controls environment.

We continue to enhance corporate oversight over process-level controls and structures to ensure that there is appropriate assignment of authority, responsibility, and accountability to enable remediation of our material weaknesses.

We believe that our remediation plan will be sufficient to remediate the identified material weakness and strengthen our internal control over financial reporting.

As we continue to evaluate, and work to improve, our internal control over financial reporting, management may determine that additional measures to address control deficiencies or modifications to the remediation plan are necessary.

Changes in Internal Control over Financial Reporting

We are engaged in the process of the design and implementation of our internal control over financial reporting in a manner commensurate with the scale of our operations following the Reverse Recapitalization. During the quarter ended December 31, 2020, there were changes in our internal control over financial reporting which are described under "Material Weakness Remediation" above.

Management's Report on Internal Control Over Financial Reporting

This report does not include a report of management's assessment regarding internal control over financial reporting ("ICFR") as allowed by the SEC for reverse acquisitions between an issuer and a private operating company when it is not possible to conduct an assessment of the private operating company's ICFR in the period between the consummation date of the reverse acquisition and the date of management's assessment of ICFR (see Section 215.02 of the SEC Division of Corporation Finance's Regulation S-K Compliance & Disclosure Interpretations). As discussed elsewhere in this Annual Report on Form 10-K, we completed the Reverse Recapitalization among the registrant and Tottenham Acquisition I Limited on December 30, 2020. Prior to the Reverse Recapitalization, we were a special purpose acquisition company formed for the purpose of effecting a merger, capital stock exchange, asset acquisition, stock purchase, reorganization, or similar business combination involving one or more businesses. As a result, previously existing internal controls are no longer applicable or comprehensive enough as of the assessment date as our operations prior to the Reverse Recapitalization were insignificant compared to those of the consolidated entity post-Reverse Recapitalization. The design of ICFR for the Company post-Reverse Recapitalization has required and will continue to require significant time and resources from management and other personnel. As a result, management was unable, without incurring unreasonable effort or expense, to conduct an assessment of our ICFR as of December 31, 2020. If management were to conduct an assessment regarding the Company's ICFR, however, its scope would include the criteria set forth by the Internal Control Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of The Treadway Commission.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Information required by this Item regarding the Company's directors and corporate governance, including information with respect to our corporate governance guidelines, Code of Business Conduct and Ethics and beneficial ownership reporting compliance, will appear in the Proxy Statement we will deliver to our stockholders in connection with our 2021 Annual Meeting of Stockholders. Such information is incorporated herein by reference. Information relating to our executive officers is included in Item 1 of Part I, "Business—Executive Officers."

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item will appear in the Proxy Statement we will deliver to our stockholders in connection with our 2021 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this Item regarding security ownership of certain beneficial owners and management will appear in the Proxy Statement we will deliver to our stockholders in connection with our 2021 Annual Meeting of Stockholders. Such information is incorporated herein by reference. Information relating to securities authorized for issuance under the Company's equity compensation plans is included in Part II of this Annual Report under "Item 5–Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities."

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

The information required by this Item will appear in the Proxy Statement we will deliver to our stockholders in connection with our 2021 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this Item will appear in the Proxy Statement we will deliver to our stockholders in connection with our 2021 Annual Meeting of Stockholders. Such information is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) The following are filed with this Annual Report:

(1) The following financial statements are included in Item 8 of this Annual Report

(2) Not applicable

(b) Exhibits

The following exhibits are filed as part of this Annual Report or are incorporated by reference.

EXHIBIT INDEX

Exhibit	Description
2.1	Merger Agreement, dated as of September 1, 2020 (incorporated by reference to Annex A-1 to the Proxy Statement/Consent Solicitation Statement/Prospectus on Form S-4 filed by the Registrant on September 10, 2020).
3.1	Amended and Restated Certificate of Incorporation of Clene Inc. (incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K filed by the Registrant on January 5, 2021).
3.2	Bylaws of Clene Inc. (incorporated by reference to Exhibit 3.2 to the Current Report on Form 8-K filed by the Registrant on January 5, 2021).
4.1	Specimen TOTA Warrant Certificate (incorporated by reference to Exhibit 4.4 to the Tottenham Registration Statement on Form S-1 filed with the Securities & Exchange Commission on July 5, 2018)
4.2	Warrant Agreement, dated August 1, 2018, by and between Continental Stock Transfer & Trust Company and the Registrant (incorporated by reference to Exhibit 4.5 to the Current Report on Form 8-K filed with the Securities and Exchange Commission on August 7, 2018).
10.1	Form of Registration Rights Agreement (incorporated by reference to Exhibit 10.10 to the Registration Statement on Form S-4 filed by Chelsea Worldwide Inc. with the Securities and Exchange Commission on December 15, 2020)
10.2	Escrow Agreement, by and among Clene Inc., Fortis Advisors LLC and Continental Stock Transfer & Trust Company, as the escrow agent (incorporated by reference to Exhibit 10.8 to the Registration Statement on Form S-4 filed by Chelsea Worldwide Inc. with the Securities and Exchange Commission on December 15, 2020)
10.3	Form of Indemnification Agreement between the Registration and its directors and executive officers (incorporated by reference to Exhibit 10.18 to the Registration Statement on Form S-4 filed by Chelsea Worldwide Inc. with the Securities and Exchange Commission on December 15, 2020)
10.4*	License Agreement, effective August 31, 2018, between Clene Nanomedicine, Inc. and 4Life Research, LLC (incorporated by reference to Exhibit 10.14 to the Registration Statement on Form S-4 filed by Chelsea Worldwide Inc. with the Securities and Exchange Commission on December 15, 2020)
10.5*	Exclusive Supply Agreement, dated August 31, 2018, between Clene Nanomedicine, Inc. and 4Life Research, LLC (incorporated by reference to Exhibit 10.15 to the Registration Statement on Form S-4 filed by Chelsea Worldwide Inc. with the Securities and Exchange Commission on December 15, 2020)
10.6*	Lease Agreement, dated May 9, 2016, and First Amendment of Lease Agreement, dated January 6, 2017, between Upper Chesapeake Flex One, LLC and Clene Nanomedicine, Inc. (incorporated by reference to Exhibit 10.16 to the Registration Statement on Form S-4 filed by Chelsea Worldwide Inc. with the Securities and Exchange Commission on December 15, 2020)
10.7*	Clinical Research Support Agreement, dated September 27, 2019, between Clene Nanomedicine, Inc. and The General Hospital Corporation (incorporated by reference to Exhibit 10.17 to the Registration Statement on Form S-4 filed by Chelsea Worldwide Inc. with the Securities and Exchange Commission on December 15, 2020)
10.8**	2020 Equity Incentive Plan (Incorporated by reference to Exhibit 10.4 to the registrant's Registration Statement on Form 8-K filed by the registrant on January 5, 2021)
21.1	Subsidiaries of Registrant (Incorporated by reference to Exhibit 21.1 to the registrant's Current Report on Form 8-K filed by the registrant on January 5, 2021)
31.1	Certification of Chief Executive Officer pursuant to Rule 13a-14 and Rule 15d-14(a), promulgated under the Securities and Exchange Act of 1934, as amended.
31.2	Certification of Chief Financial Officer pursuant to Rule 13a-14 and Rule 15d-14(a), promulgated under the Securities and Exchange Act of 1934, as amended.
32.1	Certification of Chief 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 Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.1	XBRL Instance Document
101.2	XBRL Taxonomy Extension Schema Document
101.3	XBRL Taxonomy Extension Calculation Linkbase Document
101.4	XBRL Taxonomy Extension Definition Linkbase Document
101.5	XBRL Taxonomy Extension Label Linkbase Document
101.6	XBRL Taxonomy Extension Presentation Linkbase Document

* Portions of this exhibit have been omitted pursuant to Rule 601(b)(10) of Regulation S-K. The omitted information is not material and would likely cause competitive harm to the registrant if publicly disclosed.

** Indicates a management contract or a compensatory plan or agreement.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Exchange Act of 1934, the registrant caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

CLENE INC.

Dated: March 26, 2021

By: /s/ Robert Etherington
Name: Robert Etherington
Title: President, Chief Executive Officer and Director

Pursuant to the requirements of the Securities Act, this Annual Report on Form 10-K has been signed by the following persons in the capacities and on the dated indicated.

Signature	Title	Date
/s/ Robert Etherington Robert Etherington	President, Chief Executive Officer and Director (Principal Executive Officer)	March 26, 2021
/s/ Ted (Tae Heum) Jeong Ted (Tae Heum) Jeong	Chief Financial Officer (Principal Financial and Accounting Officer)	March 26, 2021
/s/ Shalom Jacobovitz Shalom Jacobovitz	Chairman of the board	March 26, 2021
/s/ Alison Mosca Alison Mosca	Director	March 26, 2021
/s/ Jonathon Gay Jonathon Gay	Director	March 26, 2021
/s/ John Henry Stevens John Henry Stevens	Director	March 26, 2021
/s/ Reed Neil Wilcox Reed Neil Wilcox	Director	March 26, 2021
/s/ Chidozie Ugwumba Chidozie Ugwumba	Director	March 26, 2021
/s/ David Matlin David Matlin	Director	March 26, 2021
/s/ Fiona Costello Fiona Costello	Director	March 26, 2021

Exhibit 31.1

CERTIFICATION

I, Robert Etherington, certify that:

1. I have reviewed this Annual Report on Form 10-K of Clene Inc.;

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 presented in this report;

4. The registrant's other certifying officer 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 subsidiaries, 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 financial 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 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 involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 26, 2021

/s/ Robert Etherington
Robert Etherington
Chief Executive Officer

Exhibit 31.2

CERTIFICATION

I, Ted (Tae Heum) Jeong, certify that:

1. I have reviewed this Annual Report on Form 10-K of Clene Inc.;

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 presented in this report;

4. The registrant's other certifying officer 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 subsidiaries, 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 financial 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 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 involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 26, 2021

/s/ Ted (Tae Heum) Jeong
Ted (Tae Heum) Jeong
Chief Financial Officer

Exhibit 32.1

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Robert Etherington, Chief Executive Officer of Clene Inc. (the "Company"), hereby certifies that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K for the period ended December 31, 2020, to which this Certification is attached as Exhibit 32.1 (the "Annual Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

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

Dated: March 26, 2021

/s/ Robert Etherington
Robert Etherington
Chief Executive Officer

A signed original of this written statement required by Section 906 of 18 U.S.C. § 1350 has been provided to the Company, and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Exchange Act (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.

Exhibit 32.2

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Ted (Tae Heum) Jeong, Chief Financial Officer of Clene Inc. (the "Company"), hereby certifies that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K for the period ended December 31, 2020, to which this Certification is attached as Exhibit 32.1 (the "Annual Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

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

Dated: March 26, 2021

/s/ Ted (Tae Heum) Jeong
Ted (Tae Heum) Jeong
Chief Financial Officer

A signed original of this written statement required by Section 906 of 18 U.S.C. § 1350 has been provided to the Company, and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Exchange Act (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.