

PROSPECTUS SUPPLEMENT
(To Prospectus dated April 26, 2022)



Clene Inc.

Up to \$25,000,000 and 499,002 Shares of Common Stock

This prospectus supplement relates to the offer and sale of shares of our common stock that we may issue and sell to Lincoln Park Capital Fund, LLC ("Lincoln Park") from time to time, in our sole discretion, from and after the date of this prospectus supplement, pursuant to a purchase agreement that we entered into with Lincoln Park on March 3, 2023 (the "Purchase Agreement").

The shares of our common stock to which this prospectus supplement relates include:

- up to \$25,000,000 of shares of our common stock (the "Purchase Shares") that we may, in our sole discretion, sell to Lincoln Park from time to time over a 36-month period commencing on the date of this prospectus supplement, pursuant to and in accordance with the Purchase Agreement;
- 332,668 shares of our common stock that we are issuing to Lincoln Park on the date of this prospectus supplement as an initial fee for its commitment to purchase shares of our common stock at our direction from time to time under the Purchase Agreement (the "Initial Commitment Shares"); and
- up to 166,334 additional shares of our common stock that we will issue to Lincoln Park on a pro rata basis upon each purchase by Lincoln Park of Purchase Shares from us under the Purchase Agreement, up to an aggregate amount of shares for which the total aggregate purchase price paid by Lincoln Park equals its \$25,000,000 total purchase commitment under the Purchase Agreement, if and when we determine, in our sole discretion, to sell such Purchase Shares to Lincoln Park under the Purchase Agreement from time to time from and after the date of this prospectus supplement (the "Additional Commitment Shares" and, together with the Initial Commitment Shares, the "Commitment Shares").

This prospectus supplement and the accompanying prospectus also cover the resale of these shares of common stock by Lincoln Park to the public. See "The Lincoln Park Transaction" for a description of the Purchase Agreement and additional information regarding Lincoln Park. Lincoln Park is an "underwriter" within the meaning of Section 2(a)(11) of the Securities Act of 1933, as amended, or the Securities Act. See "Plan of Distribution."

The purchase price to be paid by Lincoln Park for the Purchase Shares that we may elect to issue and sell to Lincoln Park under the Purchase Agreement will be based upon the market prices of our common stock at the time of such sales and calculated in accordance with the pricing terms set forth in the Purchase Agreement. We will pay the expenses incurred in connection with the issuance of the shares of our common stock. See "Plan of Distribution."

Our common stock and public warrants are listed on The Nasdaq Capital Market ("Nasdaq") under the symbols "CLNN" and "CLNNW," respectively. On March 3, 2023, the last reported sale price of our common stock and public warrants on Nasdaq was \$1.20 and \$0.1286, respectively.

Investing in our securities involves a high degree of risk. See "Risk Factors" section beginning on page S-10 and in the documents incorporated by reference herein.

We are an "emerging growth company," as that term is defined under the federal securities laws and, as such, we have elected to comply with certain reduced public company reporting requirements and may elect to do so in future filings.

Neither the SEC nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus supplement is March 7, 2023.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement is part of a Registration Statement on Form S-3 (the “Registration Statement”) that we filed with the U.S. Securities and Exchange Commission (“SEC”) using the “shelf” registration process. By using a shelf registration statement, we may offer and sell securities having an aggregate offering price of up to \$175,000,000 from time to time under this prospectus supplement at prices and on terms to be determined by market conditions at the time of offering.

This prospectus supplement provides you with a description of the offering. You should read this prospectus supplement together with the additional information to which we refer you in the section of this prospectus supplement entitled “Where You Can Find More Information,” and together with the information incorporated by reference as described in the section of this prospectus supplement entitled “Information Incorporated By Reference.”

We provide information to you about this offering in two separate documents that are bound together: (i) this prospectus supplement, which describes the specific details regarding this offering; and (ii) the accompanying base prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this “prospectus,” we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying base prospectus, you should rely on this prospectus supplement. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in any document incorporated by reference in this prospectus supplement, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus supplement—the statement in the document having the later date modifies or supersedes the earlier statement.

You should rely only on the information incorporated by reference or set forth in this prospectus supplement. We have not, and Lincoln Park has not, authorized anyone to provide you with any information or to make any representations other than those contained in this prospectus supplement. We and Lincoln Park do not take responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We will not, and Lincoln Park will not, make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement is accurate only as of the date on the front cover of this prospectus supplement. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside of the United States: We have not, and Lincoln Park has not, done anything that would permit this offering or possession or distribution of this prospectus supplement in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus supplement must inform themselves about, and observe any restrictions relating to, the offering of securities and the distribution of this prospectus supplement outside of the United States.

We urge you to read carefully this prospectus supplement, together with information incorporated by reference herein, before deciding whether to invest in the securities being offered.

This prospectus supplement and the accompanying base prospectus contain summaries of certain provisions contained in some of the documents described herein or therein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein or therein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus supplement is a part, and you may obtain copies of those documents as described under “Where You Can Find More Information.”

We use various trademarks and trade names in our business, including without limitation our corporate name and logo. All other trademarks or trade names referred to in this prospectus supplement are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus supplement may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the other documents we have filed with the SEC that are incorporated by reference herein contain forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), and Section 27A of the Securities Act. Certain statements in this prospectus supplement may constitute “forward-looking statements” for purposes of the federal securities laws. 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 our future operations. 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 prospectus supplement may include, for example, statements about:

- the future financial performance of the Company;
- the clinical results of our drug candidates;
- the likelihood of commercial success for our drug candidates;
- our plans and strategy to obtain and maintain regulatory approvals of our drug candidates;
- the size and growth potential of the markets for our drug candidates, and our ability to serve those markets, either alone or in combination with others;
- changes in the market for our drug candidates;
- expansion plans and opportunities; and
- other factors detailed under “Risk Factors” in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q

These forward-looking statements represent our views as of the date of this prospectus supplement and involve a number of judgments, risks and uncertainties. We anticipate that subsequent events and developments will cause our views to change. 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. Accordingly, forward-looking statements should not be relied upon as representing our views as of any subsequent date.

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:

- our substantial dependence on the successful commercialization of our drug candidates, if approved, in the future;
- our inability to maintain the listing of our common stock on Nasdaq;
- our significant net losses and net operating cash outflows;
- 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 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 effects of inflation;
- the effects of staffing and materials shortages;
- the possibility that we may be adversely affected by other economic, business, and/or competitive factors; and
- other risks and uncertainties set forth in “Risk Factors” in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus supplement, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to rely unduly upon these statements.

MARKET AND INDUSTRY DATA

We obtained the industry and market data used throughout this prospectus supplement from our own internal estimates and research, as well as from independent market research, industry and general publications and surveys, governmental agencies, publicly available information and research, surveys, and studies by third parties. Internal estimates are derived from publicly available information released by industry analysts and third-party sources, our internal research and our industry experience, and are based on assumptions made by us based on such data and our knowledge of our industry and market, which we believe to be reasonable. In some cases, we do not expressly refer to the sources from which this data is derived. In addition, while we believe the industry and market data included in this prospectus supplement is reliable and based on reasonable assumptions, such data involve material risks and other uncertainties and are subject to change based on various factors, including those discussed in "Risk Factors." These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties or by us.

This summary highlights selected information from this prospectus supplement and does not contain all of the information that is important to you in making an investment decision. This summary is qualified in its entirety by the more detailed information included elsewhere in this prospectus supplement. Before making your investment decision with respect to our securities, you should carefully read this entire prospectus supplement, the accompanying base prospectus and the information incorporated herein and therein by reference. Unless the context otherwise requires, references to “we,” “us,” “our,” “the Company,” “Clene” and similar designations are intended to mean the business and operations of Clene Inc. and its consolidated subsidiaries.

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 nanocrystal form, possess unusually high, unique catalytic activities not present in those same elements in bulk form. These catalytic activities drive, support, and maintain beneficial metabolic and energetic cellular 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 electro-crystal-chemistry 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 primarily in neurology. Our development and clinical efforts are currently focused on addressing the high unmet medical needs related to central nervous system disorders including Amyotrophic Lateral Sclerosis (“ALS”), Multiple Sclerosis (“MS”), and Parkinson’s Disease (“PD”).

Clinical Development Pipeline and Recent Developments

CNM-Au8[®] for the Treatment of ALS

We recently reported data from the open label extension (“OLE”) of our Phase 2 RESCUE-ALS clinical trial, which evaluated the efficacy, safety, pharmacokinetics, and pharmacodynamics of CNM-Au8 in patients with early symptomatic ALS. The data showed preserved ALS Functional Rating Scale Revised (“ALSFRS-R”) score in patients and delayed time to clinical worsening from the most recent 12-month data cut of the OLE, which represents a 12-month minimum follow-up for OLE participants from the last-patient last-visit from the 36-week double-blind treatment period through July 14, 2022. The rate of change for ALSFRS-R was compared *post hoc* with a random slopes model.

- Statistically significant difference in ALSFRS-R slope from day 1 (randomization) to week 48: among participants originally randomized to active compared to participants originally randomized to placebo (p=0.0159; 2.6-point difference in ALSFRS-R at week 48). This represents an extension of the original double-blind period in which placebo-to-CNM-Au8 OLE participants had not yet reached effective drug concentrations.
- Statistically significant difference in ALSFRS-R slope from week 60 to week 120 comparing participants originally randomized to active or placebo. Analyses were conducted starting at 24-weeks in open-label to ensure that ex-placebo participants who switched to CNM-Au8 in the OLE were at steady-state CNM-Au8 concentrations (p=0.0057; 6.0-point difference in ALSFRS-R at week 120).
- Statistically significant delay in time to ALS clinical worsening including death, tracheostomy, initiation of ventilatory support, or feeding tube insertion through 120 weeks (Cox hazard ratio 0.478, 95% CI: 0.225 to 1.015, log-rank p=0.0494). The risk of ALS progression was less than half for those originally receiving CNM-Au8 compared to those originally receiving placebo.

CNM-Au8 was well-tolerated without long term safety concerns.

We also reported topline data in October 2022 from the Phase 2/3 Healey ALS Platform Trial, which evaluated the safety and efficacy of CNM-Au8 in patients with ALS. The full analyses, including data on a subject level basis and exploratory efficacy parameters, are expected to be received from the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital by mid-2023. Additionally, we expect data on biomarkers of neurodegeneration in mid-2023. The open-label extension will continue to follow participants for an additional 52-week treatment period and we expect matured survival data in mid-2023. We are presently discussing the design of an international Phase 3 study, RESTORE-ALS, with expert ALS clinical advisors with the 30 mg dose.

We plan to work closely with regulatory health authorities from the U.S. Food and Drug Administration (“FDA”) and European Medicines Agency, ALS experts, and patient representatives to determine the proper path to support potential approval. We do not know when or if we will be able to file a New Drug Application (“NDA”) with the FDA based on our accumulation of clinical evidence until we meet with the FDA in an end of Phase 2 meeting which is expected in the third quarter of 2023 after we receive the biomarker data and efficacy parameters that is forthcoming from the Healey ALS Platform Trial.

CNM-Au8 for the Treatment of MS

We recently reported updated data from our Phase 2 VISIONARY-MS clinical trial, which evaluated the efficacy and safety of CNM-Au8 in stable relapsing remitting MS patients. These exploratory results support the previously reported statistically significant clinical improvements in low contrast vision and global neurological function in stable relapsing MS patients reported in the modified intent to treat population. Exploratory MRI findings provide evidence of brain neuronal structural integrity assessed by diffusion tensor imaging that demonstrated statistically significant results for key metrics of axonal integrity and white matter integrity. Preservation of white matter integrity is associated with decreased cognitive functional decline in MS patients. Results included all participants with advanced MRI data collection (n=68):

- Fractional Anisotropy change within the whole brain (Cerebrum): 0.0029, 95% CI: 0.0048 to 0.0054, p = 0.0199;
- Fractional Anisotropy change within total Cerebral White Matter – Week 48 least squares (“LS”) Mean Difference: 0.0026, 95% CI: -0.0003 to 0.0055, p = 0.0805; and
- Fractional Anisotropy change within total Cerebral Normal Appearing White Matter – Week 48 LS Mean Difference: 0.0025, 95% CI: -0.00034 to 0.0054, p = 0.0823.

Exploratory multi-focal Visual Evoked Potential (“mf-VEP”) findings provide evidence of improved information transmission in the visual system (from the eye to the visual cortex) supported by statistically significant increases in amplitude. The VEP least affected eye was defined as the eye with the shortest latency delay at baseline. Results included all participants with recorded VEP data (n=64):

- mf-VEP amplitude percent change in the least affected eye at baseline – Week 48 LS mean difference: 9.7%, 95% CI: 3.1% to 16.3%, p=0.0047;
- mf-VEP amplitude percent change in the most affected eye at baseline – Week 48 LS mean difference: 6.1%, 95% CI: -0.6% to 12.7%, p=0.0730; and
- mf-VEP amplitude percent change across both eyes – Week 48 LS mean difference: 7.9%, 95% CI: 1.4% to 14.4%, p=0.0184.

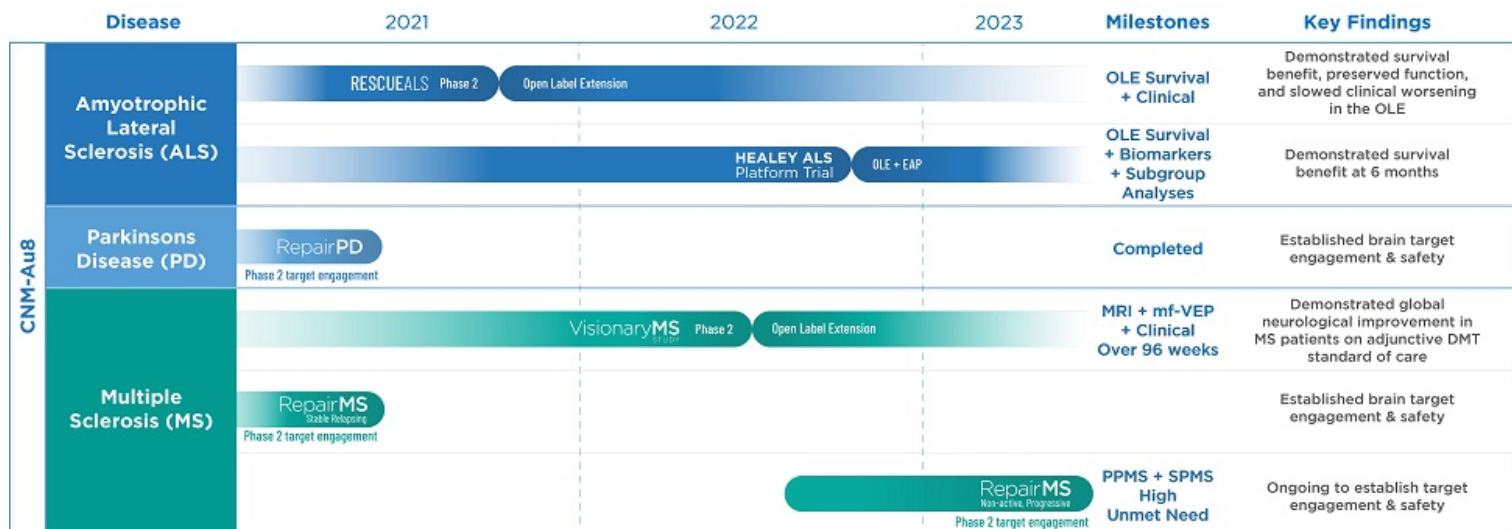
The increased amplitude signal suggests previously impaired neurons subsequently increase information transmission following CNM-Au8 treatment, supporting improved axonal integrity.

We also completed the first dosing cohort of REPAIR-MS, an open-label, investigator blinded Phase 2 clinical trial, and have initiated a second dosing cohort in non-active progressive MS patients which is expected to be complete in the second half of 2023.

CNM-ZnAg

We recently reported topline data from the Phase 2 clinical trial to investigate the efficacy and safety of CNM-ZnAg for the treatment of COVID-19. The trial was a randomized double-blind placebo-controlled trial of CNM-ZnAg with a primary endpoint of the time to substantial alleviation of COVID-19 symptoms through 28 days, confirmed over a continuous period greater than or equal to 48 hours, in the mITT population (all participants with PCR documented SARS-CoV-2 infection, n=288). The trial evaluated two different doses of CNM-ZnAg, which were combined for analyses versus placebo. No clinical benefit was observed versus placebo. CNM-ZnAg was safe and well-tolerated, and no safety signals were identified. As a result, we have ceased further clinical development of CNM-ZnAg for treatment of COVID-19.

The chart below reflects the growing body of evidence for CSN therapeutics from our completed and ongoing clinical programs.



Recent Competition Update

Despite the great need for an effective disease-modifying treatment for ALS 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. In May 2022, the FDA approved an orally administered version of edaravone, which has been available since 2017 as an intravenous infusion for the treatment of ALS. In September 2022, the FDA approved AMX0035, branded as Relyvrio, a drug from Amylyx Pharmaceuticals, Inc. for the treatment of ALS. AMX0035 previously received a conditional approval by Health Canada in June 2022.

In July 2022, the FDA accepted an NDA for tofersen, an investigational drug from Biogen Inc., for the treatment of SOD1 ALS. While tofersen did not meet the primary endpoint in the Phase 3 VALOR trial, trends favoring tofersen were seen across multiple secondary and exploratory measures of biologic activity and clinical function. Additional 12-month integrated data from the Phase 3 VALOR trial and its OLE showed that earlier initiation of tofersen compared to delayed initiation slowed declines in clinical function, respiratory function, muscle strength, and quality of life in people with SOD1-ALS. Biogen Inc. is seeking approval of tofersen under the FDA’s accelerated approval pathway, based on the use of neurofilament as a surrogate biomarker that is reasonably likely to predict clinical benefit. Neurofilaments are normal proteins found in healthy neurons, that are increased in blood and cerebrospinal fluid when damage has been done to neurons or their axons and are a marker of neurodegeneration. In ALS, higher levels of neurofilaments have been found to predict more rapid decline in clinical function and shortened survival. Tofersen study results suggest reductions in neurofilament preceded and predicted slowing of decline in measures of clinical and respiratory function, strength, and quality of life. The NDA has been granted priority review and the FDA will convene a meeting of the Peripheral and Central Nervous System Drugs Advisory Committee for the NDA on March 22, 2023. The NDA has a Prescription Drug User Fee Act action date of April 25, 2023. Additionally, in December 2022 the European Medicines Agency accepted the Marketing Authorization Application for review of tofersen.

In December 2022, BrainStorm Cell Therapeutics Inc. (“BrainStorm”) was granted a Type A meeting with the FDA to discuss a refusal to file letter previously issued by the FDA regarding a New Biologics License Application for NurOwn for the treatment of ALS. The Type A Meeting was scheduled to occur on January 11, 2023. BrainStorm completed a Phase 3 trial in ALS which did not meet the primary and secondary endpoints. However, a pre-specified subgroup of participants showed a trend to a meaningful increase in the clinical response with NurOwn compared to placebo and met the secondary endpoint of average ALSFRS-R change from baseline to week 28. Additional post-hoc sensitivity analyses also showed a statistical trend towards a clinically meaningful treatment effect with NurOwn across subgroups. Finally, biomarker data in all trial participants also showed consistent patterns of NurOwn reducing markers of inflammation and neurodegeneration, and increasing neuroprotective and anti-inflammatory markers relative to placebo.

In February 2023, Prilenia Therapeutics B.V. announced the pridopidine arm of the Healey ALS Platform Trial did not meet the primary and key secondary endpoints, but beneficial effects were observed across several pre-specified secondary and exploratory endpoints.

Going Concern

We incurred a loss from operations of \$9.8 million and \$10.5 million for the three months ended September 30, 2022 and 2021, respectively; and \$36.7 million and \$35.9 million for the nine months ended September 30, 2022 and 2021, respectively. Our accumulated deficit was \$192.2 million and \$163.3 million as of September 30, 2022 and December 31, 2021, respectively. Our cash, cash equivalents, and marketable securities totaled \$16.2 million and \$50.3 million as of September 30, 2022 and December 31, 2021, respectively, and net cash used in operating activities was \$31.3 million and \$25.0 million for the nine months ended September 30, 2022 and 2021, respectively.

We have incurred significant losses and negative cash flows from operations since our inception. We have not generated significant revenues since our inception, and we do not anticipate generating significant revenues unless we successfully complete development and obtain regulatory approval for commercialization of a drug candidate. We expect to incur additional losses in the future, particularly as we advance the development of our clinical-stage drug candidates, continue research and development of our preclinical drug candidates, and initiate additional clinical trials of, and seek regulatory approval for, these and other future drug candidates.

Our management performs strategic reviews of our operating plans and budgets, considering the status of our product development programs, human capital, capital needs and resources, and current capital market conditions. Based on these reviews, our Board of Directors and management make adjustments to our operating plans and budgets to allocate our projected cash expenditures. Notwithstanding these ongoing adjustments, we project that within the next twelve months, we will not have sufficient cash and other resources on hand to sustain our current operations or meet our obligations as they become due, and we must obtain additional financing. Additionally, pursuant to our term loan with Avenue Venture Opportunities Fund, L.P., we must maintain unrestricted cash and cash equivalents of at least \$5.0 million to avoid acceleration of the full balance of the loan. These conditions raise substantial doubt about the Company's ability to continue as a going concern.

To mitigate our funding needs, we intend to implement plans to raise additional funding, including exploring equity financing and offerings, debt financing, licensing or collaboration arrangements with third parties, as well as utilizing our existing at-the-market facility. These plans are subject to market conditions and reliance on third parties, and there is no assurance that effective implementation of our plans will result in the necessary funding to continue current operations. In October 2022, we announced an equity offering which provided net cash proceeds of \$10.8 million. In December 2022, we raised \$5.0 million in a term loan with the Maryland Department of Housing and Community Development ("DHCD"). Subsequent to September 30, 2022, we have raised \$3.6 million of net cash proceeds through our at-the-market facility. We have implemented cost-saving initiatives, including delaying or reducing research and development programs and commercialization efforts, reduction in executive compensation, a hiring freeze, and elimination of certain staff positions. We have concluded that our plans do not alleviate the substantial doubt about our ability to continue as a going concern beyond one year from the date the condensed consolidated financial statements for the period ended September 30, 2022 were issued.

Our financial statements incorporated by reference have been prepared assuming we will continue as a going concern, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business. As a result, our financial statements do not include any adjustments relating to the recoverability and classification of assets and their carrying amounts, or the amounts and classification of liabilities that may result should we be unable to continue as a going concern.

Implications of Being an Emerging Growth Company and a Smaller Reporting Company

We qualify as an "emerging growth company" as defined in Section 2(a)(19) of the Securities Act, as modified by the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"). As such, we are eligible for and may 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 of 2002, (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 earlier of: (i) the last day of the fiscal year (a) following the fifth anniversary of the closing of the initial public offering of Tottenham Acquisition I Limited ("Tottenham"), a British Virgin Islands exempted company and our predecessor, (b) in which we have total annual gross revenue of at least \$1.07 billion, or (c) in which we are deemed to be a "large accelerated filer" under the Exchange Act, which would occur if the market value of the shares of our common stock held by non-affiliates exceeds \$700.0 million as of the last business day of our most recently completed second fiscal quarter; or (ii) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this extended transition period and, as a result, we may adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-public companies instead of the dates required for other public companies. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

In addition, we are also a “smaller reporting company” because the market value of our stock held by non-affiliates plus the proposed aggregate amount of gross proceeds to us as a result of this offering is less than \$700 million as of June 30, 2022 and our annual revenue was less than \$100 million during the fiscal year ended December 31, 2021. We may continue to be a smaller reporting company after this offering in any given year if either (i) the market value of our stock held by non-affiliates is less than \$250 million as of June 30 in the most recently completed fiscal year or (ii) our annual revenue is less than \$100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than \$700 million as of June 30 in the most recently completed fiscal year. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

For risks related to our status as an emerging growth company and a smaller reporting company, see the disclosure in “Risk Factors.”

Corporate History and Information

Clene Nanomedicine, Inc. was incorporated in the state of Delaware in December 2012. On December 30, 2020 (the “Closing Date”), we 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 the Company (which was at such time doing business as Clene Nanomedicine, Inc.), Tottenham, 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 shareholders. Prior to the Reincorporation Merger discussed below, Tottenham was a British Virgin Islands company incorporated 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”); and (ii) promptly following the Reincorporation Merger, Merger Sub was merged with and into Clene Nanomedicine, Inc. (“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 Nasdaq under the symbol “CLNN.” The aggregate consideration for the Acquisition Merger was \$543.4 million, paid in the form of 54,339,012 newly issued shares of Common Stock valued at \$10.00 per share.

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 <https://clene.com>. The information contained in or accessible from our website is not incorporated into this prospectus supplement, and you should not consider it part of this prospectus supplement. We have included our website address in this prospectus supplement solely as an inactive textual reference.

THE OFFERING

Shares of common stock being offered by us:	<p>Up to \$25,000,000 of shares of our common stock that we may, in our sole discretion, issue and sell to Lincoln Park as Purchase Shares, from time to time over a 36-month period commencing on the date of this prospectus supplement, pursuant to and in accordance with the Purchase Agreement.</p> <p>332,668 shares of our common stock that we are issuing as Initial Commitment Shares to Lincoln Park on the date of this prospectus supplement in consideration for Lincoln Park's commitment to purchase shares of our common stock at our direction under the Purchase Agreement, from time to time during the term of the Purchase Agreement. We will not receive any cash proceeds for our issuance of the Initial Commitment Shares to Lincoln Park pursuant to the Purchase Agreement.</p> <p>Up to 166,334 additional shares of our common stock that we will issue to Lincoln Park as Additional Commitment Shares, on a pro rata basis upon each purchase by Lincoln Park of Purchase Shares from us under the Purchase Agreement, up to an aggregate amount of shares for which the total aggregate purchase price paid by Lincoln Park equals its \$25,000,000 total purchase commitment under the Purchase Agreement, if and when we determine, in our sole discretion, to sell such Purchase Shares to Lincoln Park under the Purchase Agreement. We will not receive any cash proceeds for our issuance of the Additional Commitment Shares, if any, to Lincoln Park pursuant to the Purchase Agreement.</p>
Shares of common stock to be outstanding immediately after this offering	<p>97,921,205 shares of common stock, assuming our sale of 20,833,333 Purchase Shares at a price of \$1.20 per share, which was the closing price of our common stock on Nasdaq on March 3, 2023, and our issuance of 499,002 Commitment Shares to Lincoln Park under the Purchase Agreement. The actual number of shares issued by us to Lincoln Park under the Purchase Agreement, if any, will vary depending on the prices at which we sell shares of common stock to Lincoln Park pursuant to the Purchase Agreement; however, we will not issue to Lincoln Park more than 15,310,115 shares of common stock (including Purchase Shares and Commitment Shares), representing 19.99% of the shares of our common stock outstanding immediately prior to the execution of the Purchase Agreement (subject to certain reductions and pro rata adjustments as set forth in the Purchase Agreement), unless (i) we first obtain stockholder approval in accordance with applicable Nasdaq listing rules to issue shares in excess of such amount to Lincoln Park under the Purchase Agreement or (ii) the average price paid by Lincoln Park for all shares of common stock issued by us under the Purchase Agreement is equal to or greater than \$1.2404, such that the above maximum share issuance limitation will not apply to issuances and sales of our common stock to Lincoln Park pursuant to the Purchase Agreement under applicable Nasdaq listing rules.</p>
Use of proceeds	<p>We currently intend to use the net proceeds from this offering, if any, together with our existing cash, for expenses primarily related to general corporate purposes, including to fund the clinical development of our lead drug candidate, CNM-Au8, including for conducting our on-going and planned clinical trials and potential future commercialization efforts; and for additional early-stage research and development activities, business development activities, working capital and other general corporate purposes. See "Use of Proceeds" for additional information.</p>
Risk factors	<p>Any investment in the securities offered hereby is speculative and involves a high degree of risk. You should read carefully the information set forth in "Risk Factors" in this prospectus supplement and the accompanying base prospectus, together with other information included elsewhere in this prospectus supplement, or incorporated by reference into this prospectus supplement, for a discussion of factors that you should consider before deciding to invest in our securities.</p>
Nasdaq Capital Market symbol	<p>"CLNN"</p>
	<p>The number of shares of our common stock outstanding immediately after this offering is based on 76,588,870 shares of common stock outstanding as of March 3, 2023 and excludes the following:</p> <ul style="list-style-type: none">• 16,169,566 shares of common stock issuable upon exercise of stock options outstanding as of March 3, 2023 with a weighted-average exercise price of \$2.87 per share;• 145,958 shares of common stock reserved as of March 3, 2023, for future grant under our 2020 Stock Plan;• 4,477,045 shares of common stock issuable upon exercise of warrants outstanding as of March 3, 2023 with a weighted-average exercise price of \$7.32 per share;• 769,139 shares of common stock issuable upon vesting of rights to restricted stock awards outstanding as of March 3, 2023;• 6,592,334 shares of common stock issuable upon vesting of earn-out shares outstanding as of March 3, 2023;• 482,703 shares of common stock issuable upon conversion of \$5.0 million of the principal amount of the 2021 Avenue Loan at the right and discretion of Avenue;• up to 1,250,000 shares of common stock issuable upon conversion of \$5.0 million of the principal amount of a loan with DHCD, at the right and discretion of DHCD subject to certain conditions; and <p>Except as otherwise indicated, all information in this prospectus supplement assumes no exercise of the outstanding options, warrants, or restricted stock awards, vesting of earn-out shares, or conversion of convertible notes payable referred to above.</p>

RISK FACTORS

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should carefully consider the risks and uncertainties described below and under “Risk Factors” in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, which are incorporated herein by reference, together with the information contained in this prospectus supplement, the accompanying base prospectus and any other information that has been or will be incorporated herein or therein by reference. The occurrence of one or more of the events or circumstances described in these risk factors, alone or in combination with other events or circumstances, may have a material adverse effect on our business, reputation, revenue, financial condition, results of operations and future prospects, in which event the market price of our common stock could decline, and you could lose part or all of your investment. The risk factors are not intended to be exhaustive and are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. This prospectus supplement also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially and adversely from those anticipated in the forward-looking statements as a result of a number of factors. See “Cautionary Note Regarding Forward-Looking Statements.”

Risks Related to Our Common Stock and this Offering

Our management will have broad discretion over the use of the net proceeds, if any, we receive in this offering and may not apply the proceeds in ways that increase the value of your investment, which could cause the market price of our common stock to decline.

Our management will have broad discretion to use the net proceeds, if any, payable to us from this offering and you will be relying on the judgment of our management regarding the application of these net proceeds. Our management might not apply the net proceeds, if any, from this offering in ways that increase the value of your investment. Until we use the net proceeds, if any, payable to us from this offering, we plan to invest them, and these investments may not yield a favorable rate of return. If we do not invest or apply the net proceeds, if any, from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause the market price of our common stock to decline.

Sales of shares to Lincoln Park under the Purchase Agreement may affect the price of our common stock and make it more difficult to raise additional equity capital.

On March 3, 2023, we entered into the Purchase Agreement with Lincoln Park, pursuant to which Lincoln Park has committed to purchase up to \$25,000,000 of our common stock. In connection with the execution of the Purchase Agreement, we are issuing 332,668 shares of common stock to Lincoln Park as Initial Commitment Shares for no cash consideration as an initial fee for its commitment to purchase shares of our common stock at our direction under the Purchase Agreement from time to time after the date of this prospectus supplement and during the term of the Purchase Agreement. We may also issue up to 166,334 additional shares of our common stock to Lincoln Park as Additional Commitment Shares, on a pro rata basis upon each purchase by Lincoln Park of Purchase Shares from us under the Purchase Agreement, up to an aggregate amount of shares for which the total aggregate purchase price paid by Lincoln Park equals its \$25,000,000 total purchase commitment under the Purchase Agreement, if and when we determine, in our sole discretion, to sell such Purchase Shares to Lincoln Park under the Purchase Agreement. The remaining shares of our common stock that may be issued under the Purchase Agreement may be sold by us to Lincoln Park at our discretion from time to time over a 36-month period commencing after the satisfaction of certain conditions set forth in the Purchase Agreement, which we anticipate will occur on the date of this prospectus supplement. The purchase price for the shares that we may sell to Lincoln Park under the Purchase Agreement will fluctuate based on the market prices of our common stock at the time we elect to make sales of shares of our common stock, if any, to Lincoln Park under the Purchase Agreement. Depending on market liquidity at the time, sales of such shares may cause the trading price of our common stock to fall.

Sales of shares of our common stock, if any, to Lincoln Park will depend upon market conditions and other factors to be determined by us. Therefore, Lincoln Park may ultimately purchase all, some or none of the shares of our common stock that may be sold pursuant to the Purchase Agreement and, after it has acquired shares, Lincoln Park may sell all, some or none of those shares. Sales to Lincoln Park by us could result in substantial dilution to the interests of other holders of our common stock. Additionally, the sale of a substantial number of shares of our common stock to Lincoln Park, or the anticipation of such sales, could make it more difficult for us to sell equity or equity-related securities in the future at a time and at a price that we might otherwise wish to effect sales, which could have a materially adverse effect on our business and operations.

Future sales or issuances of our common stock in the public markets, or the perception of such sales, could depress the trading price of our common stock.

The sale of a substantial number of shares of our common stock or other equity-related securities in the public markets, or the perception that such sales could occur, could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. We may sell large quantities of our common stock pursuant to this prospectus supplement and/or in one or more separate offerings. We cannot predict the effect that future sales of common stock or other equity-related securities would have on the market price of our common stock.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be lower than the price per share paid by investors in this offering.

We may require additional financing to sustain our operations, without which we may not be able to continue operations, and the terms of subsequent financings may adversely impact our stockholders.

We may direct Lincoln Park to purchase up to \$25,000,000 worth of shares of our common stock under our agreement over a 36-month period, in amounts up to 75,000 to 200,000 shares of our common stock depending on market prices, subject to a maximum limit of \$2,000,000 per purchase, on any single business day.

Our ability to sell shares to Lincoln Park and obtain funds under the Purchase Agreement is limited by the terms and conditions in the Purchase Agreement, including restrictions on the amounts we may sell to Lincoln Park at any one time, and a limitation on our ability to sell shares to Lincoln Park to the extent that it would cause Lincoln Park to beneficially own more than 4.99% of our outstanding shares of common stock (the "**Beneficial Ownership Cap**"), which Lincoln Park may, in its sole discretion, increase to up to 9.99% of our outstanding shares of common stock by delivering written notice thereof to us, which shall not be effective until the 61st day after such written notice is delivered to us. Additionally, we are prohibited under applicable Nasdaq listing rules from issuing to Lincoln Park more than 15,310,115 shares of common stock under the Purchase Agreement (including Purchase Shares and Commitment Shares), such maximum number of shares representing 19.99% of the outstanding shares of our common stock immediately prior to the execution of the Purchase Agreement (such maximum share issuance limitation subject to certain reductions and pro rata adjustments as set forth in the Purchase Agreement, the "**Exchange Cap**"), unless (i) we first obtain stockholder approval in accordance with applicable Nasdaq listing rules to issue shares in excess of the Exchange Cap to Lincoln Park under the Purchase Agreement or (ii) the average price paid by Lincoln Park for all shares of common stock issued by us under the Purchase Agreement is equal to or greater than \$1.2404, such that the Exchange Cap will not apply under applicable Nasdaq listing rules to limit issuances and sales of our common stock to Lincoln Park pursuant to the Purchase Agreement. Therefore, we may not in the future have access to the full amount available to us under the Purchase Agreement, depending on the price of our common stock. In addition, any amounts we sell under the Purchase Agreement may not satisfy all of our funding needs, even if we are able and choose to sell and issue all of our common stock currently registered.

The extent we rely on Lincoln Park as a source of funding will depend on a number of factors including the prevailing market price of our common stock and the extent to which we are able to secure working capital from other sources. If obtaining sufficient funding from Lincoln Park were to prove unavailable or prohibitively dilutive, we will need to secure another source of funding in order to satisfy our working capital needs. Even if we sell all \$25,000,000 of common stock under the Purchase Agreement to Lincoln Park, we may still need additional capital to finance our future plans and working capital needs, and we may have to raise funds through the issuance of equity or debt securities. Depending on the type and the terms of any financing we pursue, stockholders' rights and the value of their investment in our common stock could be reduced. A financing could involve one or more types of securities including common stock, convertible debt or warrants to acquire common stock. These securities could be issued at or below the then prevailing market price for our common stock. In addition, the holders of our outstanding debt would have a claim to our assets that would be prior to the rights of stockholders until the debt is paid. If the issuance of new securities results in diminished rights to holders of our common stock, the market price of our common stock could be negatively impacted. Should the financing we require to sustain our working capital needs be unavailable or prohibitively expensive when we require it, the consequences could be a material adverse effect on our business, operating results, financial condition and prospects.

USE OF PROCEEDS

We may receive up to \$25,000,000 in aggregate gross proceeds under the Purchase Agreement from any sales we make to Lincoln Park pursuant to the Purchase Agreement after the date of this prospectus supplement. We estimate that the net proceeds to us from the sale of our common stock to Lincoln Park pursuant to the Purchase Agreement will be up to \$24.9 million up to an approximate 36-month period, assuming that we sell the full amount of our common stock that we have the right, but not the obligation, to sell to Lincoln Park under the Purchase Agreement, and after other estimated fees and expenses. We will not receive any cash proceeds from our issuance of the Commitment Shares to Lincoln Park pursuant to the Purchase Agreement. We may sell fewer than all of the shares offered by this prospectus supplement, in which case our net offering proceeds will be less. Because we are not obligated to sell any shares of our common stock under the Purchase Agreement, the actual total offering amount and proceeds to us, if any, are not determinable at this time. See “Plan of Distribution” elsewhere in this prospectus supplement for more information.

The principal purposes of this offering are to increase our financial flexibility and to obtain additional capital to support our operations. We currently intend to use the net proceeds from this offering, if any, together with our existing cash, for expenses primarily related to general corporate purposes, including to fund the clinical development of our lead drug candidate, CNM-Au8, including for conducting our on-going and planned clinical trials and potential future commercialization efforts; for additional early-stage research and development activities; and for business development activities, working capital, and other general corporate purposes.

The expected use of net proceeds represents our intentions, based upon our present plans and business conditions. We cannot specify with certainty all of the particular uses for the net proceeds. Due to uncertainties inherent in the drug development process, it is difficult to estimate the exact amounts of the net proceeds that will be used for any particular purpose. We may use our existing cash and the future payments, if any, generated from any future collaboration agreements to fund our operations, either of which may alter the amount of net proceeds used for a particular purpose. In addition, the amount, allocation and timing of our actual expenditures will depend upon numerous factors, including the results of our research and development efforts, the timing and success of clinical trials, and the timing of regulatory submissions. Accordingly, we will have broad discretion in using these net proceeds.

We intend to invest the net proceeds we receive that are not used as described above in a variety of capital preservation investments, including investment-grade, interest-bearing instruments and certificates of deposit or direct or guaranteed obligations of the U.S. government.

DIVIDEND POLICY

We have not declared or paid any cash dividends on our capital stock. We currently intend to retain any future earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

DILUTION

If you invest in our common stock in this offering, you will experience immediate and substantial dilution to the extent of the difference between the public offering price per share of our common stock, and the adjusted net tangible book value per share of our common stock immediately upon the consummation of this offering. Net tangible book value per share represents the book value of our tangible assets less the book value of our total liabilities divided by the number of shares of common stock then issued and outstanding.

Our historical net tangible book value (deficit) as of September 30, 2022 was \$(9.3) million, or \$(0.15) per share of our common stock. Our historical net tangible book value (deficit) is the amount of our total tangible assets less our total liabilities. Historical net tangible book value (deficit) per share represents historical net tangible book value (deficit) divided by 63,541,984 shares of our common stock outstanding as of September 30, 2022.

After giving effect to our issuance and sale of 20,833,333 shares of our common stock in this offering (which excludes the 332,668 Initial Commitment Shares and the 166,334 Additional Commitment Shares) at an assumed offering price of \$1.20 per share, which was the last reported sale price of our common stock on Nasdaq on March 3, 2023, and without giving effect to the Exchange Cap, and after deducting estimated offering expenses payable by us, our as adjusted net tangible book value (deficit) as of September 30, 2022 would have been \$15.7 million, or \$0.19 per share. This represents an immediate increase in as adjusted net tangible book value (deficit) per share of \$0.34 to existing stockholders and an immediate dilution of \$1.01 in as adjusted net tangible book value (deficit) per share to investors purchasing common stock in this offering. Dilution per share to investors purchasing common stock in this offering is determined by subtracting as adjusted net tangible book value (deficit) per share after this offering from the public offering price per share paid by investors.

The following table illustrates this dilution on a per share basis:

Public offering price per share		\$	1.20
Historical net tangible book value (deficit) per share		\$	(0.15)
Increase in historical net tangible book value per share attributable to this offering		\$	0.34
As adjusted net tangible book value (deficit) per share after this offering		\$	0.19
Dilution per share to investors participating in this offering		\$	1.01

The dilution information discussed above is illustrative only and will change based on the actual offering price or prices if and when we sell shares of our common stock to Lincoln Park. A \$1.00 increase in the assumed offering price of \$1.20 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$25,000,000 during the term of the Purchase Agreement is sold as that price, would result in an as adjusted net tangible book value per share after this offering of approximately \$0.43 and dilution per share to investors participating in this offering of approximately \$1.77, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. A \$1.00 decrease in the assumed offering price of \$1.20 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$25,000,000 during the term of the Purchase Agreement is sold at that price, would result in an as adjusted net tangible book value per share after this offering of approximately \$(0.06) and dilution per share to investors participating in this offering of approximately \$0.26, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

The foregoing tables and calculations (other than the historical net tangible book value (deficit) calculations) are based on 63,541,984 shares of common stock outstanding as of September 30, 2022, which excludes:

- 12,173,570 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2022 with a weighted-average exercise price of \$3.53 per share;
- 4,316,862 shares of common stock reserved as of September 30, 2022, for future grant under our 2020 Stock Plan;
- 4,477,045 shares of common stock issuable upon exercise of warrants outstanding as of September 30, 2022 with a weighted-average exercise price of \$7.32 per share;
- 769,139 shares of common stock issuable upon vesting of rights to restricted stock awards outstanding as of September 30, 2022;
- 6,592,334 shares of common stock issuable upon vesting of earn-out shares outstanding as of September 30, 2022;
- 482,703 shares of common stock issuable upon conversion of \$5.0 million of the principal amount of the 2021 Avenue Loan at the right and discretion of Avenue;

To the extent that stock options, warrants, restricted stock awards, earn-out shares, or convertible notes payable outstanding as of September 30, 2022 are exercised, vested, or converted to shares of common stock at prices below the prices paid by investors participating in this offering, investors in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

General

On March 3, 2023, we entered into the Purchase Agreement with Lincoln Park, pursuant to which Lincoln Park has agreed to purchase from us, at our direction from time to time, in our sole discretion, from and after the date of this prospectus supplement and over a period of up to 36 months thereafter, shares of our common stock having a total maximum aggregate purchase price to Lincoln Park of \$25,000,000 (subject to certain limitations contained in the Purchase Agreement), upon the terms and subject to the conditions contained in the Purchase Agreement. Concurrently with the execution of the Purchase Agreement on March 3, 2023, we also entered into a registration rights agreement, or the Registration Rights Agreement, with Lincoln Park, pursuant to which we have filed with the SEC this prospectus supplement, together with the accompanying prospectus, relating to the offer and sale of the Purchase Shares and Commitment Shares that may be issued and sold by us to Lincoln Park, from time to time in our sole discretion, from and after the date of this prospectus supplement, and to take such other specified actions to maintain the registration under the Securities Act of the offer and sale of the Purchase Shares and Commitment Shares that may be issued and sold by us to Lincoln Park under the Purchase Agreement and that are included in this prospectus supplement.

Pursuant to the terms of the Purchase Agreement, on the date of this prospectus, we are issuing 332,668 Initial Commitment Shares to Lincoln Park as an initial fee for its commitment to purchase shares of our common stock at our direction under the Purchase Agreement, from time to time during the term of the Purchase Agreement, and to issue up to 166,334 Additional Commitment Shares to Lincoln Park on a pro rata basis upon each purchase by Lincoln Park of Purchase Shares from us under the Purchase Agreement, up to an aggregate amount of shares for which the total aggregate purchase price paid by Lincoln Park equals its \$25,000,000 total purchase commitment under the Purchase Agreement, if and when we determine, in our sole discretion, to sell such Purchase Shares to Lincoln Park under the Purchase Agreement from time to time from and after the date of this prospectus supplement. We will not receive any cash proceeds for our issuance of the Initial Commitment Shares and, as applicable, the Additional Commitment Shares to Lincoln Park pursuant to the Purchase Agreement.

We may, from time to time and at our sole discretion, direct Lincoln Park to purchase shares of our common stock upon the satisfaction of certain conditions set forth in the Purchase Agreement at a purchase price per share based on the market price of our common stock at the time of sale as computed under the Purchase Agreement. We will control the timing and amount of any sales of our common stock to Lincoln Park, and Lincoln Park has no right to require us to sell any shares to it under the Purchase Agreement. Lincoln Park may not assign or transfer its rights and obligations under the Purchase Agreement.

Under applicable Nasdaq listing rules, we are prohibited from issuing to Lincoln Park more than the Exchange Cap of 15,310,115 shares of common stock under the Purchase Agreement (including Purchase Shares and Commitment Shares), representing 19.99% of the outstanding shares of our common stock immediately prior to the execution of the Purchase Agreement (subject to certain reductions and pro rata adjustments as set forth in the Purchase Agreement), unless (i) we first obtain stockholder approval in accordance with applicable Nasdaq listing rules to issue shares in excess of the Exchange Cap to Lincoln Park under the Purchase Agreement or (ii) the average price paid by Lincoln Park for all shares of common stock issued by us under the Purchase Agreement is equal to or greater than \$1.2404 (which represents the lower of (A) the official closing price of our common stock on Nasdaq on the date of the Purchase Agreement and (B) the average official closing price of our common stock on Nasdaq for the five consecutive trading days ending on the date of the Purchase Agreement, as adjusted to take into account our issuance of the Commitment Shares to Lincoln Park for non-cash consideration), such that the Exchange Cap will not apply under applicable Nasdaq listing rules to limit issuances and sales of our common stock to Lincoln Park pursuant to the Purchase Agreement. In any event, the Purchase Agreement specifically provides that we may not issue or sell any shares of our common stock under the Purchase Agreement if such issuance or sale would breach any applicable Nasdaq listing rules.

The Purchase Agreement also prohibits us from directing Lincoln Park to purchase any shares of our common stock if those shares of our common stock, when aggregated with all other shares of our common stock then beneficially owned by Lincoln Park and its affiliates (as calculated pursuant to Section 13(d) of the Securities Exchange Act of 1934, as amended, and Rule 13d-3 thereunder), would result in Lincoln Park having beneficial ownership of shares of our common stock in excess of the 4.99% Beneficial Ownership Cap, which Beneficial Ownership Cap Lincoln Park may, in its sole discretion, increase to up to 9.99% of our outstanding shares of common stock by delivering written notice thereof to us, which shall not be effective until the 61st day after such written notice is delivered to us.

Purchase of Shares Under the Purchase Agreement***Regular Purchases***

Under the Purchase Agreement, we may, from time to time over a 36-month period commencing after the satisfaction of certain conditions set forth in the Purchase Agreement, direct Lincoln Park to purchase up to 75,000 shares of our common stock (such amount, the “Regular Purchase Amount” and such purchase, the “Regular Purchase”), on such business day (or the purchase date), provided, however, that Lincoln Park’s committed obligations under each Regular Purchase cannot exceed \$2,000,000. The Regular Purchase Amount may be increased to up to (i) 100,000 shares if the closing price of our common stock is not below \$1.00, (ii) 150,000 shares if the closing price of our common stock is not below \$2.00 and (iii) 200,000 shares if the closing price of our common stock is not below \$4.00. We may direct Lincoln Park to purchase shares in a Regular Purchase on any business day. The foregoing share amounts and per share prices will be adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction occurring after the date of the Purchase Agreement.

The purchase price per share for each such Regular Purchase will be equal to the lesser of:

- the lowest sale price for our common stock on the purchase date of such shares; or
- the arithmetic average of the three lowest closing sale prices for our common stock during the 10 consecutive business days ending on the business day immediately preceding the purchase date of such shares.

The parties may mutually agree to increase the number of shares to be purchased by Lincoln Park pursuant to any Regular Purchase.

Accelerated Purchases

We also have the right to direct Lincoln Park, on any business day on which we have properly submitted a Regular Purchase notice for the maximum amount allowed for such Regular Purchase to purchase an additional amount of our common stock (an "Accelerated Purchase"), of up to the lesser of:

- 300% of the number of shares purchased pursuant to such prior business day Regular Purchase; and
- 30% of the aggregate shares of our common stock traded on Nasdaq during the period on the trading day immediately following the purchase date for such Regular Purchase (the "Accelerated Purchase Date"), beginning at the commencement of regular trading on Nasdaq (or such later time on such Accelerated Purchase Date as mutually agreed by us and Lincoln Park specified in the Accelerated Purchase notice for such Accelerated Purchase), and ending at the close of regular trading on Nasdaq on such Accelerated Purchase Date, or, if certain trading volume or market price thresholds specified in the Purchase Agreement are crossed prior to the close of regular trading on Nasdaq on the applicable Accelerated Purchase Date, ending at such earlier time that any one of such thresholds is crossed, which period of time on the applicable Accelerated Purchase Date (the "Accelerated Purchase Measurement Period").

The purchase price per share for each such Accelerated Purchase will be equal to 97% of the lesser of:

- the volume-weighted average price of our common stock on Nasdaq during the applicable Accelerated Purchase Measurement Period on the applicable Accelerated Purchase date; and
- the closing sale price of our common stock on the applicable Accelerated Purchase date.

The parties may mutually agree to increase the number of shares to be purchased by Lincoln Park pursuant to any Accelerated Purchase.

Additional Accelerated Purchases

We also have the right to direct Lincoln Park, prior to 1:00 p.m., Eastern Time, on any business day on which an Accelerated Purchase has been completed (an "Additional Accelerated Purchase Date") and all of the shares to be purchased thereunder have been properly delivered to Lincoln Park in accordance with the Purchase Agreement to purchase an additional amount of our common stock (an "Additional Accelerated Purchase") of up to the lesser of:

- 300% of the number of shares purchased pursuant to such prior business day Regular Purchase; and
- 30% of the aggregate shares of our common stock traded on Nasdaq during the period on the applicable Additional Accelerated Purchase Date beginning at the time mutually agreed by us and Lincoln Park and specified in the Additional Accelerated Purchase notice for such Additional Accelerated Purchase, and ending at the close of regular trading on Nasdaq on such Additional Accelerated Purchase Date, or, if certain trading volume or market price thresholds specified in the Purchase Agreement are crossed prior to the close of regular trading on Nasdaq on such date, ending at such earlier time that any one of such thresholds is crossed, which period of time on the applicable Additional Accelerated Purchase Date (the "Additional Accelerated Purchase Measurement Period").

We may, in our sole discretion, submit multiple Additional Accelerated Purchase notices to Lincoln Park on a single Additional Accelerated Purchase Date, provided that (i) such Additional Accelerated Purchase notice is received by Lincoln Park prior to 1:00 p.m., Eastern Time, on such Additional Accelerated Purchase Date and (ii) all prior Accelerated Purchases and Additional Accelerated Purchases (including those that have occurred earlier on the same trading day) have been completed and all of the shares to be purchased thereunder have theretofore been properly delivered to Lincoln Park in accordance with the Purchase Agreement.

The purchase price per share for each such Additional Accelerated Purchase will be equal to 97% of the lower of:

- the volume-weighted average price of our common stock on Nasdaq during the applicable Additional Accelerated Purchase Measurement Period on the applicable Additional Accelerated Purchase Date; and
- the closing sale price of our common stock on the applicable Additional Accelerated Purchase Date.

The parties may mutually agree to increase the number of shares to be purchased by Lincoln Park pursuant to any Additional Accelerated Purchase.

In the case of Regular Purchases, Accelerated Purchases and Additional Accelerated Purchases, the purchase price per share will be adjusted for any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction as set forth in the Purchase Agreement.

Other than as set forth above, there are no trading volume requirements or restrictions under the Purchase Agreement, and we will control the timing and amount of any sales of our common stock to Lincoln Park.

Suspension Events

Suspension events under the Purchase Agreement include the following:

- the effectiveness of the registration statement of which this prospectus supplement and accompanying prospectus form a part lapses for any reason (including, without limitation, the issuance of a stop order or similar order by the SEC), or such registration statement (or the prospectus forming a part thereof) is unavailable for the sale by us or the resale by Lincoln Park of our common stock under the Purchase Agreement, and such lapse or unavailability continues for a period of 10 consecutive business days or for more than an aggregate of 30 business days in any 365-day period, but excluding a lapse or unavailability where (i) we terminate the registration statement after Lincoln Park has confirmed in writing that all of the shares of our common stock covered thereby have been resold or (ii) we supersede the registration statement with a new registration statement, including, without limitation, when the prior registration statement is effectively replaced with a new registration statement covering the shares of our common stock covered by the Purchase Agreement (provided in the case of this clause (ii) that all of the shares of our common stock covered by the superseded or terminated registration statement that have not theretofore been sold to Lincoln Park are included in the superseding or new registration statement);
- suspension by Nasdaq of our common stock from trading or the failure of the common stock to be listed on Nasdaq for a period of one business day;
- the delisting of our common stock from Nasdaq Capital Market, provided, however, that the common stock is not immediately thereafter trading on the Nasdaq Global Market, the Nasdaq Global Select Market, the New York Stock Exchange, the NYSE American, the NYSE Arca, or the OTCQX or OTCQB operated by the OTC Markets Group, Inc. (or any nationally recognized successors thereto);
- the failure for any reason by our transfer agent to issue (i) the Initial Commitment Shares to Lincoln Park within two business days after the commencement date of the Purchase Agreement, (ii) the Additional Commitment Shares to Lincoln Park within two business days after the date on which Lincoln Park is entitled to receive such Additional Commitment Shares, or (iii) Purchase Shares to Lincoln Park within two business days after any Regular Purchase date, Accelerated Purchase Date or Additional Accelerated Purchase Date, as applicable, on which Lincoln Park is entitled to receive such shares;
- if we breach any representation, warranty, covenant, or other term or condition contained in the Purchase Agreement or Registration Rights Agreement if such breach would reasonably be expected to have a Material Adverse Effect (as defined in the Purchase Agreement) and, except, in the case of a breach of a covenant that is reasonably curable, only if such breach continues for a period of at least five business days;
- if any person commences a proceeding against the us pursuant to or within the meaning of any bankruptcy law;
- if we, pursuant to or within the meaning of any bankruptcy law, (i) commence a voluntary case, (ii) consent to the entry of an order for relief against us in an involuntary case, (iii) consent to the appointment of a custodian of the Company or for all or substantially all of our property, or (iv) makes a general assignment for the benefit of our creditors or are generally unable to pay our debts as the same become due;
- a court of competent jurisdiction enters an order or decree under any bankruptcy law that (i) is for relief against us in an involuntary case, (ii) appoints a custodian of the Company or for all or substantially all of our property, or (iii) orders the liquidation of us or any of our subsidiaries;
- if, at any time, we are not eligible to transfer our common stock electronically as DWAC shares; or
- if, at any time after the commencement date of the Purchase Agreement, the Exchange Cap is reached (to the extent such Exchange Cap is applicable) and the stockholder approval to issue in excess of such amount has not been obtained in accordance with the applicable rules of Nasdaq.

In addition to any other rights and remedies under applicable law and the Purchase Agreement, so long as a suspension event has occurred and is continuing, or if any event which, after notice and/or lapse of time, would become a suspension event has occurred and is continuing, we shall not deliver to Lincoln Park any Regular Purchase notice, Accelerated Purchase notice or Additional Accelerated Purchase notice. Lincoln Park does not have the right to terminate the Purchase Agreement upon any of the suspension events set forth above, however, the Purchase Agreement will automatically terminate (i) if, pursuant to or within the meaning of any bankruptcy law, we commence a voluntary case or if any person commences a proceeding against us which is not discharged within 90 days, or a custodian is appointed for the Company or for substantially all of our property, or we make a general assignment for the benefit of our creditors; (ii) we sell and Lincoln Park purchases the full amount of shares available under the Purchase Agreement; or (iii) the full amount of shares available under the Purchase Agreement has not been purchased by the end of the 36-month period commencing after the satisfaction of certain conditions set forth in the Purchase Agreement.

Our Termination Rights

We have the unconditional right, at any time, for any reason and without any payment or liability to us, to give notice to Lincoln Park to terminate the Purchase Agreement with effect one business day after the notice has been received by Lincoln Park.

No Short-Selling or Hedging by Lincoln Park

Lincoln Park has represented and warranted that neither it nor any of its agents, representatives or affiliates has engaged in any direct or indirect short-selling or hedging of our common stock, and has agreed that neither it nor any of its agents, representatives or affiliates will engage in any direct or indirect short-selling or hedging of our common stock during any time prior to the termination of the Purchase Agreement.

Prohibitions on Variable Rate Transactions

Subject to specified exceptions included in the Purchase Agreement, we are limited in our ability to enter into specified variable rate transactions until the 36-month anniversary of the date of the Purchase Agreement, irrespective of any earlier termination of the Purchase Agreement. Such transactions include an equity line of credit, at-the-market offering, or other continuous offering or similar offering in which we may offer or issue or sell our common stock or other securities that entitle the holder thereof to acquire shares of our common stock at a future determined price. However, we are permitted to enter into certain at-the-market offerings exclusively through a registered broker-dealer acting as agent of the Company pursuant to a written agreement between the Company and such registered broker-dealer, including our existing at-the-market offering.

Effect of Performance of the Purchase Agreement on our Stockholders

All shares registered in this offering that have been or may be issued or sold by us to Lincoln Park under the Purchase Agreement are expected to be freely tradable. Shares registered in this offering may be sold over a period of up to approximately 36 months commencing on the date of this prospectus supplement. The sale by Lincoln Park of a significant number of shares registered in this offering at any given time could cause the market price of our common stock to decline and to be highly volatile. Sales of our common stock to Lincoln Park, if any, will depend upon market conditions and other factors to be determined by us, in our sole discretion. We may ultimately decide to sell to Lincoln Park all, some or none of the additional shares of our common stock that may be available for us to sell pursuant to the Purchase Agreement. If and when we do sell shares to Lincoln Park, after Lincoln Park has acquired the shares, Lincoln Park may resell all, some or none of those shares at any time or from time to time in its discretion. Therefore, sales to Lincoln Park by us under the Purchase Agreement may result in substantial dilution to the interests of other holders of our common stock. In addition, if we sell a substantial number of shares to Lincoln Park under the Purchase Agreement, or if investors expect that we will do so, the actual sales of shares or the mere existence of our arrangement with Lincoln Park may make it more difficult for us to sell equity or equity-related securities in the future at a time and at a price that we might otherwise wish to effect such sales. However, we have the right to control the timing and amount of any additional sales of our shares to Lincoln Park and the Purchase Agreement may be terminated by us at any time at our discretion without any cost to us.

Pursuant to the terms of the Purchase Agreement, we have the right, but not the obligation, to direct Lincoln Park to purchase up to \$25,000,000 of our common stock, exclusive of the Initial Commitment Shares being issued to Lincoln Park as consideration for its commitment to purchase shares of our common stock under the Purchase Agreement and the Additional Commitment Shares that may be issued to Lincoln Park in connection with each purchase under the Purchase Agreement. The Purchase Agreement generally prohibits us from issuing or selling to Lincoln Park under the Purchase Agreement (i) shares of our common stock in excess of the Exchange Cap, unless we obtain stockholder approval to issue shares in excess of the Exchange Cap or the shares we desire to sell in excess of the Exchange Cap must be sold for an average price that equals or exceeds \$1.2404 per share (subject to adjustment for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction that occurs on or after the date of the Purchase Agreement), such that the transactions contemplated by the Purchase Agreement are exempt from the Exchange Cap limitation under applicable Nasdaq rules and (ii) any shares of our common stock if those shares, when aggregated with all other shares of our common stock then beneficially owned by Lincoln Park and its affiliates, would exceed the Beneficial Ownership Limitation of our then issued and outstanding shares of common stock.

The following table sets forth the amount of gross proceeds we would receive from Lincoln Park from our sale of shares to Lincoln Park under the Purchase Agreement at varying purchase prices:

Assumed Average Purchase Price Per Share	Number of Shares to be Issued if Full Purchase ⁽¹⁾	Percentage of Outstanding Shares After Giving Effect to the Issuance to Lincoln Park ⁽²⁾	Gross Proceeds from the Sale of Shares Under the Purchase Agreement Registered in this Offering
\$ 0.50	14,811,113	19.24%	\$ 7,405,557
\$ 1.00	14,811,113	19.23%	\$ 14,811,113
\$ 1.20 ⁽³⁾	14,811,113	19.23%	\$ 17,773,336
\$ 2.00	12,500,000	16.22%	\$ 25,000,000
\$ 4.00	6,250,000	8.11%	\$ 25,000,000

- (1) Includes the total number of Purchase Shares that we would have sold under the Purchase Agreement at the corresponding assumed average purchase price set forth in the first column, up to the aggregate purchase price of \$25,000,000, if available, while giving effect to the Exchange Cap and without regard for the Beneficial Ownership Limitation, and excludes the Commitment Shares. We may only issue shares of our common stock in excess of the Exchange Cap if we obtain stockholder approval to do so, or if the average price of applicable sales of our common stock to Lincoln Park under the Purchase Agreement equals or exceeds \$1.2404 per share.
- (2) The denominator is based on 76,588,870 shares of common stock outstanding as of March 3, 2023, adjusted to include the number of registered shares to be issued if full purchase issuance, plus (i) 332,668 Initial Commitment Shares being issued to Lincoln Park as consideration for its commitment to purchase shares of our common stock under the Purchase Agreement, and (ii) the proportional amount of 166,334 Additional Commitment Shares as consideration for purchases of shares of our common stock under the Purchase Agreement, assuming the average purchase price in the first column. The Exchange Cap represents 19.99% of the aggregate number of shares of common stock outstanding prior to execution of the Purchase Agreement. The numerator is based on the number of shares of our common stock issued set forth in the second column.
- (3) The closing sale price of our shares on March 3, 2023.

PLAN OF DISTRIBUTION

Pursuant to this prospectus supplement and the accompanying prospectus, we are offering up to \$25,000,000 in shares of our common stock that may be issued by us directly to Lincoln Park from time to time over the 36-month term of the Purchase Agreement, 332,668 shares of our common stock to Lincoln Park as Initial Commitment Shares, and 166,334 shares of common stock that may be issued to Lincoln Park in connection with each purchase of Purchase Shares, pursuant to the Purchase Agreement and subject to the terms and subject to the conditions set forth therein. This prospectus supplement and the accompanying prospectus also cover the resale of these shares by Lincoln Park to the public. See “The Lincoln Park Transaction.”

The Purchase Agreement provides that, from time-to-time over the term of the Purchase Agreement, on any business day, and at our sole discretion, we may require Lincoln Park to purchase up to 75,000 shares of our common stock as a Regular Purchase, which may be increased to up to 200,000 shares, if the closing price of our common stock exceeds certain threshold prices set forth in the Purchase Agreement, subject to a maximum of purchase commitment of Lincoln Park of \$2,000,000 per Regular Purchase. The foregoing share amounts and related market prices will be adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction occurring after the date of this prospectus supplement. We and Lincoln Park may mutually agree to increase such limit. In addition, under certain circumstances set forth in the Purchase Agreement, we may, upon notice to Lincoln Park, from time to time and at our sole discretion, direct Lincoln Park to purchase additional shares of our common stock in Accelerated Purchases and Additional Accelerated Purchases as set forth in the Purchase Agreement. The purchase price per share is based on the market price of our common stock at the time of sale as computed under the Purchase Agreement. Lincoln Park may not assign or transfer its rights and obligations under the Purchase Agreement. See the section entitled “The Lincoln Park Transaction” above.

Lincoln Park is an “underwriter” within the meaning of Section 2(a)(11) of the Securities Act. Lincoln Park has informed us that it will use an unaffiliated broker-dealer to effectuate all sales, if any, of the common stock that it may purchase from us pursuant to the Purchase Agreement. Such sales will be made on Nasdaq at prices and at terms then prevailing or at prices related to the then current market price. Each such unaffiliated broker-dealer will be an underwriter within the meaning of Section 2(a)(11) of the Securities Act. Lincoln Park has informed us that each such broker-dealer will receive commissions from Lincoln Park that will not exceed customary brokerage commissions.

We know of no existing arrangements between Lincoln Park and any other stockholder, broker, dealer, underwriter, or agent relating to the sale or distribution of the shares offered by this prospectus supplement.

We will pay \$25,000 to Lincoln Park as Lincoln Park’s full and complete expense reimbursement in connection with entering into the transaction, including any legal fees.

We have agreed to indemnify Lincoln Park and certain other persons against certain liabilities in connection with the offering of shares of common stock offered hereby, including liabilities arising under the Securities Act or, if such indemnity is unavailable, to contribute amounts required to be paid in respect of such liabilities.

Lincoln Park represented to us that at no time prior to the date of the Purchase Agreement has Lincoln Park or its agents, representatives or affiliates engaged in or effected, in any manner whatsoever, directly or indirectly, any short sale (as such term is defined in Rule 200 of Regulation SHO of the Exchange Act) of our common stock or any hedging transaction, which establishes a net short position with respect to the common stock. Lincoln Park agreed that during the term of the Purchase Agreement, it, its agents, representatives or affiliates will not enter into or effect, directly or indirectly, any of the foregoing transactions.

We have advised Lincoln Park that it is required to comply with Regulation M promulgated under the Exchange Act. With certain exceptions, Regulation M precludes Lincoln Park, any affiliated purchasers, and any broker-dealer or other person who participates in the distribution from bidding for or purchasing, or attempting to induce any person to bid for or purchase any security which is the subject of the distribution until the entire distribution is complete. Regulation M also prohibits any bids or purchases made in order to stabilize the price of a security in connection with the distribution of that security. All of the foregoing may affect the marketability of the shares offered by this prospectus supplement.

American Stock Transfer & Trust Company, LLC is the transfer agent and registrar for our common stock. Our common stock is listed on the Nasdaq Capital Market under the symbol “CLNN.”

LEGAL MATTERS

The validity of the securities offered pursuant to this prospectus supplement will be passed upon by Holland & Knight LLP.

EXPERTS

The financial statements of Clene Inc. as of and for the year ended December 31, 2021 incorporated by reference in this prospectus have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report. Such financial statements are incorporated by reference in reliance upon the report of such firm given their authority as experts in auditing and accounting.

The financial statements as of December 31, 2020 and for the year ended December 31, 2020 incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2021 have been so incorporated in reliance on the report (which contains an emphasis of matter paragraph relating to the Company's requirement for additional financing or a collaboration agreement to fund planned future operations as described in Note 1 to the financial statements) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3, including exhibits, under the Securities Act, with respect to the securities offered pursuant to this prospectus supplement. This prospectus supplement is part of the registration statement, but does not contain all of the information included in the registration statement or the exhibits. For further information with respect to us and the securities offered by this prospectus supplement, we refer you to the registration statement and its exhibits. Statements contained in this prospectus supplement as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

In addition, we file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains an internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, including our SEC filings, located at <https://www.sec.gov>. We also maintain a website at <https://clene.com>. The information contained in or accessible from our website is not incorporated into this prospectus supplement, and you should not consider it part of this prospectus supplement. We have included our website address in this prospectus supplement solely as an inactive textual reference. You may access, free of charge, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus supplement, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in this prospectus supplement or a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement or a subsequently filed document incorporated by reference modifies or replaces that statement.

This prospectus supplement incorporates by reference the documents set forth below that have previously been filed with the SEC:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on March 11, 2022;
- our Quarterly Reports on Form 10-Q for the quarters ended [March 30, 2022](#), [June 30, 2022](#), and [September 30, 2022](#), filed with the SEC on May 9, 2022, August 15, 2022, and November 7, 2022, respectively;
- our Current Reports on Form 8-K filed with the SEC on [January 18, 2022](#), [February 2, 2022](#), [April 14, 2022](#), [May 6, 2022](#), [May 19, 2022](#), [October 31, 2022](#), [December 14, 2022](#), [December 20, 2022](#), [February 17, 2023](#), [February 27, 2023](#) (first of two reports filed on February 27, 2023), [March 3, 2023](#), and [March 6, 2023](#) (second of two reports filed on March 6, 2023);
- the information specifically incorporated by reference into our Annual Report on [Form 10-K](#) for the year ended December 31, 2021 from our Definitive Proxy Statement on [Schedule 14A](#), filed with the SEC on March 24, 2022; and
- the description of our common stock contained in the registration statement on [Form 8-A](#), dated December 30, 2020, filed pursuant to Section 12(b) of the Exchange Act, as amended by Amendment No. 1 to [Form 8-A](#), dated February 9, 2021.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus supplement and deemed to be part of this prospectus supplement from the date of the filing of such reports and other documents.

We will provide to each person, including any beneficial owner, to whom a prospectus supplement is delivered, a copy of any or all of the information that has been incorporated by reference in the prospectus but not delivered with the prospectus. You may request a copy of any documents incorporated by reference in this prospectus supplement and the accompanying base prospectus, at no cost, by writing or telephoning us at:

Clene Inc.
Attention: Investor Relations
6550 South Millrock Drive, Suite G50
Salt Lake City, Utah 84121
Telephone: 801-676-9695

Exhibits to the filings will not be sent, however, unless those exhibits have been specifically incorporated by reference in this prospectus supplement.

\$175,000,000



Clene Inc.

**Common Stock
Preferred Stock
Debt Securities
Warrants
Units**

From time to time, we may offer and sell up to \$175,000,000 aggregate dollar amount of our common stock, preferred stock, debt securities, warrants to purchase our common stock, preferred stock or debt securities, and/or units consisting of some or all of these securities, in any combination, together or separately, in one or more offerings, in amounts, at prices and on the terms that will be determined at the time of the offering and which will be set forth in a prospectus supplement. The prospectus supplement may also add, update or change information contained in this prospectus.

The securities may be sold directly to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. If any agents, underwriters or dealers are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents, underwriters or dealers and any applicable fees, commissions, discounts and over-allotment options will be set forth in a prospectus supplement.

You should read this prospectus and any prospectus supplement or amendment carefully before you invest in our securities. This prospectus may not be used to consummate sales of these securities unless it is accompanied by a prospectus supplement.

Our common stock and Public Warrants are listed on the Nasdaq Capital Market ("Nasdaq") under the symbols "CLNN" and "CLNNW," respectively. On April 11, 2022, the last reported sale price of our common stock and Public Warrants on Nasdaq was \$3.16 and \$0.32, respectively.

Investing in our securities involves a high degree of risk. See "Risk Factors" section beginning on page 7.

We are an "emerging growth company," as that term is defined under the federal securities laws and, as such, we have elected to comply with certain reduced public company reporting requirements and may elect to do so in future filings.

Neither the SEC nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is April 26, 2022.

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ABOUT THIS PROSPECTUS

This prospectus is part of a Registration Statement on Form S-3 (the “Registration Statement”) that we filed with the U.S. Securities and Exchange Commission (“SEC”) using the “shelf” registration process. Under this shelf registration process, we may offer and sell shares of our common stock, preferred stock, debt securities, warrants to purchase our common stock, preferred stock or debt securities, and/or units, either individually or in combination with other securities, in one or more offerings, up to a total dollar amount of \$175,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we offer securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that offering. The prospectus supplement may also add information to, or update or change information contained in, this prospectus. You should read both this prospectus and any applicable prospectus supplement or post-effective amendment to the Registration Statement, together with the additional information to which we refer you in the section of this prospectus entitled “Where You Can Find More Information,” and together with the information incorporated by reference as described in the section of this prospectus entitled “Information Incorporated By Reference.”

You should rely only on the information incorporated by reference or set forth in this prospectus or the applicable prospectus supplement. We have not authorized anyone to provide you with any information or to make any representations other than those contained in this prospectus, or any applicable prospectus supplement or post-effective amendment to the Registration Statement. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We will not make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside of the United States: We have not done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of securities and the distribution of this prospectus outside of the United States.

We urge you to read carefully this prospectus, before deciding whether to invest in the securities being offered.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described under “Where You Can Find More Information.”

We use various trademarks and trade names in our business, including without limitation our corporate name and logo. All other trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement and the other documents we have filed with the SEC that are incorporated by reference herein contain forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), and Section 27A of the Securities Act of 1933, as amended (the “Securities Act”). Certain statements in this prospectus may constitute “forward-looking statements” for purposes of the federal securities laws. 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 our future operations. 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 prospectus may include, for example, statements about:

- the future financial performance of the Company;
- the clinical results of our drug candidates;
- the likelihood of commercial success for our drug candidates;
- our plans and strategy to obtain and maintain regulatory approvals of our drug candidates;
- the size and growth potential of the markets for our drug candidates, and our ability to serve those markets, either alone or in combination with others;
- changes in the market for our drug candidates;
- expansion plans and opportunities; and
- other factors detailed under “Risk Factors” in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q.

These forward-looking statements represent our views as of the date of this prospectus and involve a number of judgments, risks and uncertainties. We anticipate that subsequent events and developments will cause our views to change. 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. Accordingly, forward-looking statements should not be relied upon as representing our views as of any subsequent date.

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:

- our substantial dependence on the successful commercialization of our drug candidates, if approved, in the future;
- our inability to maintain the listing of our common stock on Nasdaq;
- our significant net losses and net operating cash outflows;
- 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 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 effects of inflation;
- the effects of staffing and materials shortages;
- the possibility that we may be adversely affected by other economic, business, and/or competitive factors; and
- other risks and uncertainties set forth in “Risk Factors” in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to rely unduly upon these statements.

MARKET AND INDUSTRY DATA

We obtained the industry and market data used throughout this prospectus from our own internal estimates and research, as well as from independent market research, industry and general publications and surveys, governmental agencies, publicly available information and research, surveys, and studies by third parties. Internal estimates are derived from publicly available information released by industry analysts and third-party sources, our internal research and our industry experience, and are based on assumptions made by us based on such data and our knowledge of our industry and market, which we believe to be reasonable. In some cases, we do not expressly refer to the sources from which this data is derived. In addition, while we believe the industry and market data included in this prospectus is reliable and based on reasonable assumptions, such data involve material risks and other uncertainties and are subject to change based on various factors, including those discussed in "Risk Factors." These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties or by us.

PROSPECTUS SUMMARY

This summary highlights selected information from this prospectus and does not contain all of the information that is important to you in making an investment decision. This summary is qualified in its entirety by the more detailed information included elsewhere in this prospectus. Before making your investment decision with respect to our securities, you should carefully read this entire prospectus and the information incorporated herein by reference. Unless the context otherwise requires, references to “we,” “us,” “our,” “the Company,” “Clene” and similar designations are intended to mean the business and operations of Clene Inc. and its consolidated subsidiaries.

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 nanocrystal form, possess unusually high, unique catalytic activities not present in those same elements in bulk form. These catalytic activities drive, support, and maintain beneficial metabolic and energetic cellular 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 electro-crystal-chemistry 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 Amyotrophic Lateral Sclerosis (“ALS”), Multiple Sclerosis (“MS”), and Parkinson’s Disease (“PD”); and second, those related to COVID-19, a highly infectious viral respiratory disease with serious and sometimes fatal co-morbidities.

Clinical Development Pipeline

CNM-Au8®: We have one Phase 2/3 registrational clinical trial, the Healey ALS Platform Trial, which is currently ongoing to establish the safety and efficacy of CNM-Au8® in patients with ALS. We completed RESCUE-ALS, a Phase 2 proof of concept clinical trial to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of CNM-Au8® in patients with early symptomatic ALS. We also completed REPAIR-PD and the first dosing cohort of REPAIR-MS, two open-label, investigator blinded Phase 2 clinical trials which demonstrated target engagement of CNM-Au8® on the brain’s energy metabolites. REPAIR-MS will continue with the initiation of a second dosing cohort. In addition, we have a Phase 2 clinical trial, VISIONARY-MS, for the treatment of visual pathway deficits in chronic optic neuropathy to assess the efficacy, safety, tolerability, and pharmacokinetics of CNM-Au8® for remyelination in stable relapsing MS. We support two Expanded Access Programs (“EAPs”) for patients with ALS. The initial EAP was launched in partnership with the Sean M. Healey & AMG Center (“Healey Center”) for ALS at Massachusetts General Hospital in September 2019, which is closed to new enrollment, but remains ongoing for current participants. A second EAP was implemented in conjunction with the Healey ALS Platform Trial at three participating clinical sites. Finally, we anticipate launching RESCUE-PD, a Phase 2 clinical trial for the treatment of patients with PD, in mid-2022.

CNM-ZnAg: We have one Phase 2 clinical trial presently underway to establish the efficacy and safety of ZnAg liquid solution for the treatment of COVID-19.

The chart below reflects the respective stages of our main drug candidates.



Implications of Being an Emerging Growth Company and a Smaller Reporting Company

We qualify as an “emerging growth company” as defined in Section 2(a)(19) of the Securities Act, as modified by the Jumpstart Our Business Startups Act of 2012 (the “JOBS Act”). As such, we are eligible for and may 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 of 2002 (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 earlier of: (i) the last day of the fiscal year (a) following the fifth anniversary of the closing of the initial public offering of Tottenham Acquisition I Limited, a British Virgin Islands exempted company and our predecessor (“Tottenham”), (b) in which we have total annual gross revenue of at least \$1.07 billion, or (c) in which we are deemed to be a “large accelerated filer” under the Exchange Act, which would occur if the market value of the shares of our common stock held by non-affiliates exceeds \$700.0 million as of the last business day of our most recently completed second fiscal quarter; or (ii) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this extended transition period and, as a result, we may adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-public companies instead of the dates required for other public companies. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

In addition, we are also a “smaller reporting company” because the market value of our stock held by non-affiliates plus the proposed aggregate amount of gross proceeds to us as a result of this offering is less than \$700 million as of June 30, 2021 and our annual revenue was less than \$100 million during the fiscal year ended December 31, 2021. We may continue to be a smaller reporting company after this offering in any given year if either (i) the market value of our stock held by non-affiliates is less than \$250 million as of June 30 in the most recently completed fiscal year or (ii) our annual revenue is less than \$100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than \$700 million as of June 30 in the most recently completed fiscal year. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

For risks related to our status as an emerging growth company and a smaller reporting company, see the disclosure in “Risk Factors.”

Corporate History and Information

Clene Nanomedicine, Inc. was incorporated in the state of Delaware in December 2012. On December 30, 2020 (the "Closing Date"), we 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 the Company (which was at such time doing business as Clene Nanomedicine, Inc.), Tottenham, 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 shareholders. Prior to the Reincorporation Merger discussed below, Tottenham was a British Virgin Islands company incorporated 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"); and (ii) promptly following the Reincorporation Merger, Merger Sub was merged with and into Clene Nanomedicine, Inc. ("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." The aggregate consideration for the Acquisition Merger was \$543.4 million, paid in the form of 54,339,012 newly issued shares of common stock valued at \$10.00 per share.

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 <https://clene.com>. The information contained in or accessible from our website is not incorporated into this prospectus, and you should not consider it part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

The Offering

Under this prospectus, we may offer and sell to the public in one or more series or issuances of common stock, preferred stock, debt securities, warrants to purchase our common stock, preferred stock or debt securities, and/or units consisting of some or all of these securities with an aggregate offering price not to exceed \$175,000,000.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should carefully consider the risks and uncertainties described under “Risk Factors” in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, which are incorporated herein by reference, together with the information contained in this prospectus and any other information that has been or will be incorporated herein by reference. The occurrence of one or more of the events or circumstances described in these risk factors, alone or in combination with other events or circumstances, may have a material adverse effect on our business, reputation, revenue, financial condition, results of operations and future prospects, in which event the market price of our common stock could decline, and you could lose part or all of your investment. The risk factors are not intended to be exhaustive and are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. This prospectus also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially and adversely from those anticipated in the forward-looking statements as a result of a number of factors. See “Cautionary Note Regarding Forward-Looking Statements.”

USE OF PROCEEDS

Unless otherwise indicated in the applicable prospectus supplement, we will use the net proceeds from the sale of securities offered by this prospectus for expenses primarily related to general corporate purposes, including to fund the clinical development and commercialization of our drug candidates; to in-license, acquire or invest in new businesses, technology or assets (although we have no such agreements, commitments or understandings with respect to any such in-license or acquisition as of the date of this prospectus); for additional early-stage research and development activities; and for business development activities, working capital, and other general corporate purposes. Any specific allocation of the net proceeds of an offering of securities to a specific purpose will be determined at the time of such offering and will be described in the related supplement to this prospectus.

The expected use of net proceeds represents our intentions based upon our present plans and business conditions. We cannot specify with certainty all of the particular uses for the net proceeds. Due to uncertainties inherent in the drug development process, it is difficult to estimate the exact amounts of the net proceeds that will be used for any particular purpose. We may use our existing cash and the future payments, if any, generated from any future collaboration agreements to fund our operations, either of which may alter the amount of net proceeds used for a particular purpose. In addition, the amount, allocation and timing of our actual expenditures will depend upon numerous factors, including the results of our research and development efforts, the timing and success of clinical trials, and the timing of regulatory submissions. Accordingly, we will have broad discretion in using these net proceeds.

We intend to invest the net proceeds we receive that are not used as described above in a variety of capital preservation investments, including investment-grade, interest-bearing instruments and certificates of deposit or direct or guaranteed obligations of the U.S. government.

DESCRIPTION OF CAPITAL STOCK

The following is a summary of the rights and preferences of our capital stock. While we believe that the following description covers the material terms of our capital stock, the description may not contain all of the information that is important to you. We encourage you to read carefully this entire prospectus, any future related prospectus supplement and certificates of designation relating to the securities, as applicable, our amended and restated certificate of incorporation (the “certificate of incorporation”) and amended and restated bylaws (the “bylaws”) and the other documents we refer to for a more complete understanding of our capital stock. Copies of our certificate of incorporation and bylaws are incorporated by reference as exhibits to the registration statement of which this prospectus is a part. See “Where You Can Find More Information” and “Information Incorporated by Reference.”

General

We are governed by the certificate of incorporation, as amended and restated from time to time, and the Delaware General Corporation Law (“DGCL”), and the common law of the state of Delaware. The following summary of certain provisions of our securities does not purport to be complete and is subject to our amended and restated certificate of incorporation, our amended and restated bylaws and the provisions of the DGCL. Copies of our amended and restated certificate of incorporation or our amended and restated bylaws are attached to this prospectus as Exhibits 3.1 and 3.2, respectively.

Our amended and restated certificate of incorporation authorizes a total number of shares of all classes of stock of 151,000,000 shares, consisting of (i) 1,000,000 shares of preferred stock, par value \$0.0001 per share, and (ii) 150,000,000 shares of common stock, par value \$0.0001 per share.

As of April 11, 2022, there were 63,246,545 issued and outstanding shares of our common stock held by 77 stockholders of record.

Common Stock

Our common stock is listed on Nasdaq under the symbol “CLNN.” The holders of our common stock are entitled to one vote for each share held on all matters to be voted on by shareholders and do not have cumulative voting rights. The holders of our common stock are entitled to receive dividends, if and when declared by our Board of Directors (“Board”) out of funds legally available therefor. In the event of a liquidation, dissolution or winding up of the Company, our shareholders are entitled to share ratably in all assets remaining available for distribution to them after payment of liabilities and after provision is made for each class of stock, if any, having preference over our common stock. Holders of our common stock have no preemptive or other subscription rights. Our Board is classified.

Preferred Stock

Our preferred stock is currently undesignated and no shares of preferred stock are outstanding. The Board has the authority to issue shares of preferred stock from time to time on terms it may determine, to divide shares of preferred stock into one or more series and to fix the designations, preferences, privileges, and restrictions of preferred stock, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preference, sinking fund terms, and the number of shares constituting any series or the designation of any series to the fullest extent permitted by the DGCL. The issuance of preferred stock could have the effect of decreasing the trading price of common stock, restricting dividends on our capital stock, diluting the voting power of the common stock, impairing the liquidation rights of our capital stock or delaying or preventing a change in control of us. There is no restriction on the repurchase or redemption of shares by us while there is any arrearage in the payment of dividends or sinking fund installments.

Warrants

As of April 11, 2022, we had warrants outstanding that were exercisable into a total of 4,477,045 shares of common stock, as outlined below.

Public Warrants

The Public Warrants originally issued by Tottenham are listed on Nasdaq under the symbol “CLNNW.” Each Public Warrant entitles the holder thereof to purchase one-half (1/2) of one share of our common stock at a price of \$11.50 per full share. We will not issue fractional shares. As a result, a Public Warrant holder must exercise warrants in multiples of two, at a price of \$11.50 per full share, subject to adjustment, to validly exercise the warrants. The Public Warrants became exercisable upon the completion of the Reverse Recapitalization and will expire on December 30, 2025. As of April 11, 2022, we had 4,815,000 Public Warrants outstanding exercisable into 2,407,500 shares of common stock. The Public Warrants are currently exercisable.

We may redeem the outstanding Public Warrants (excluding the private warrants that are part of the private units), in whole and not in part, at a price of \$0.01 per warrant:

- at any time while the warrants are exercisable;

- upon a minimum of 30 days' prior written notice of redemption;
- if, and only if, the last sales price of our 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 we send the notice of redemption; and
- if, and only if, (i) there is a current registration statement in effect with respect to our common stock underlying the warrants at the time of redemption and for the entire 30-day trading period referred to above and continuing each day thereafter until the date of redemption or (ii) the warrants may be exercised on cashless basis as set forth in the Warrant Agreement and such cashless exercise is exempt from registration under the Securities Act.

If the foregoing conditions are satisfied and we issue a notice of redemption, each warrant holder can exercise his, her or its warrant prior to the scheduled redemption date. However, the price of our common stock may fall below the \$16.50 trigger price as well as the \$11.50 warrant exercise price per full share after the redemption notice is issued and not limit our ability to complete the redemption.

If we call the Public Warrants for redemption as described above, our management will have the option to require all warrant holders that wish to exercise the warrants to do so on a "cashless" basis. In such event, each warrant holder would pay the exercise price by surrendering the whole warrant for that number of shares of our common stock equal to the quotient obtained by dividing (x) the product of the number of our common stock underlying the warrants, multiplied by the difference between the exercise price of our warrants and the "fair market value" (as defined below) by (y) the fair market value. The "fair market value" means the average reported last sale price of our common stock for the ten trading days ending on the third trading day prior to the date on which the notice of redemption is sent to the warrant holders. Whether we will exercise the option to require all warrant holders to exercise their warrants on a "cashless basis" will depend on a variety of factors, including the price of our common stock at the time the warrants are called for redemption, our cash needs at such time and concerns regarding dilutive share issuances.

Founder Warrants

Prior to the Reverse Recapitalization, in April 2013, we issued Series A preferred stock warrants in connection with certain note purchase agreements. The warrants expire 10 years from issuance and became exercisable upon completion of a previous equity financing of Clene Nanomedicine. At the close of the Reverse Recapitalization and as of April 11, 2022, these warrants are exercisable and entitle the holder thereof to purchase one share of our common stock at a fixed exercise price of \$1.97 into 1,608,670 aggregate shares of common stock.

Prior to the Reverse Recapitalization, in April 2013, Clene Nanomedicine issued warrants to purchase units of its most senior equity equal to 0.25% of the company's fully diluted equity at the time of exercise in connection with certain note purchase agreements. The warrants expire 10 years from issuance and became exercisable upon issuance. At the close of the Reverse Recapitalization and as of April 11, 2022, these warrants are exercisable and entitle the holder thereof to purchase one share of our common stock at a fixed exercise price of \$1.97 into 320,441 aggregate shares of our common stock.

Option Warrants

In July 2021, Chardan exercised the Chardan Unit Purchase Option originally issued in connection with Tottenham's initial public offering in August 2018 for 220,000 units, each unit consisting of one and one-tenth shares of common stock and one warrant to purchase one-half of one share of common stock at an exercise price of \$11.50 per share. Chardan elected to perform a cashless or net exercise, which resulted in a net issuance of 49,166 Option Warrants to purchase one-half of one share of common stock. The Option Warrants became exercisable upon issuance and are subject to the same expiration and redemption terms as the Public Warrants. As of April 11, 2022, the Option Warrants are exercisable into 24,583 shares of common stock at a fixed exercise price of \$11.50 per share.

Avenue Warrant

In May 2021, we issued the a warrant to purchase shares of our common stock in connection with a loan agreement by and among the Company and our wholly owned subsidiary, Clene Nanomedicine, and Avenue Venture Opportunities Fund, L.P. ("Avenue"), a Delaware limited partnership within the Avenue Capital Group, and its affiliates. The exercise price per share of the warrant is \$8.63. The warrant became exercisable upon issuance and expires on May 21, 2026. As of April 11, 2022, the warrant is exercisable into 115,851 shares of common stock.

Stock Options

As of December 31, 2021, we had outstanding options to purchase an aggregate of 10,395,027 shares, with a weighted average exercise price of \$3.35 per share. Subsequent to December 31, 2021, we granted 2,492,515 shares issuable upon exercise of stock options, with a weighted average exercise price of \$3.03 per share.

Restricted Stock Awards

As of December 31, 2021, we had 916,603 outstanding and unvested rights to restricted stock awards, which were subject to time- and market-based vesting conditions.

Contingent Earn-Outs

As of December 31, 2021, we had outstanding and unvested earn-outs to issue an aggregate of 6,592,334 shares, which were subject to market- and performance-based vesting conditions.

Convertible Notes Payable

As of December 31, 2021, we had outstanding convertible notes payable under the Loan Agreement with Avenue, which was convertible into 482,703 shares of common stock at the discretion, but not the obligation, of Avenue at any time from May 21, 2022 through May 21, 2024.

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and executive officers. Each indemnification agreement provides for indemnification and advancement by us of certain expenses and costs relating to claims, suits or proceedings arising from service to us or, at our request, service to other entities, as officers or directors to the maximum extent permitted by applicable law.

Dividends

We currently intend to retain all available funds and any future earnings to fund the growth and development of our business. We have never declared or paid any cash dividends on our capital stock. We do not intend to pay cash dividends to our shareholders in the foreseeable future. Our ability to declare dividends is limited by the terms of financing or other agreements that we have entered into. Future debt or other financing arrangements also may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Investors should not purchase our common stock with the expectation of receiving cash dividends.

Any future determination to declare dividends will be made at the discretion of our Board and will depend on our financial condition, operating results, capital requirements, general business conditions, and other factors that our Board may deem relevant.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent and registrar's address is 6201 15th Avenue, Brooklyn, New York 11219.

DESCRIPTION OF DEBT SECURITIES

This section describes the general terms and provisions of our debt securities that we may issue from time to time. We may issue debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any future debt securities we may offer under this prospectus, the applicable prospectus supplement will describe the specific terms of any debt securities offered through that prospectus supplement. The terms of any debt securities we offer under a prospectus supplement may differ from the terms we describe below, and to the extent the terms set forth in a prospectus supplement differ from the terms described below, the terms set forth in the prospectus supplement shall control. Unless the context requires otherwise, whenever we refer to the “indentures,” we are also referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue any senior debt securities under the senior indenture that we will enter into with the trustee named in the senior indenture. We will issue any subordinated debt securities under the subordinated indenture that we will enter into with the trustee named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The indentures will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We use the term “trustee” to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplement related to the debt securities that we may offer under this prospectus, as well as the complete applicable indenture that contains the terms of the debt securities. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

General

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title;
- the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;
- any limit on the amount that may be issued;
- whether or not we will issue the series of debt securities in global form, and, if so, the terms and who the depository will be;
- the maturity date;
- whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;
- the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- the terms of the subordination of any series of subordinated debt;
- the place where payments will be payable;
- restrictions on transfer, sale or other assignment, if any;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- the date, if any, after which, the conditions upon which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder’s option, to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- whether the indenture will restrict our ability or the ability of our subsidiaries, if any at such time, to:
 - o incur additional indebtedness;

- o issue additional securities;
- o create liens;
- o pay dividends or make distributions in respect of our capital stock or the capital stock of our subsidiaries;
- o redeem capital stock;
- o place restrictions on our subsidiaries' ability to pay dividends, make distributions or transfer assets;
- o make investments or other restricted payments;
- o sell or otherwise dispose of assets;
- o enter into sale-leaseback transactions;
- o engage in transactions with stockholders or affiliates;
- o issue or sell stock of our subsidiaries; or
- o effect a consolidation or merger;
- whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;
- a discussion of certain material U.S. federal income tax considerations applicable to the debt securities;
- information describing any book-entry features;
- provisions for a sinking fund purchase or other analogous fund, if any;
- the applicability of the provisions in the indenture on discharge;
- whether the debt securities are to be offered at a price such that they will be deemed to be offered at an "original issue discount" as defined in paragraph (a) of Section 1273 of the Internal Revenue Code, as amended;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any additional events of default or covenants provided with respect to the debt securities, and any terms that may be required by us or advisable under applicable laws or regulations or advisable in connection with the marketing of the debt securities.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock, our preferred stock or other securities (including securities of a third party). We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock, our preferred stock or other securities (including securities of a third-party) that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indentures will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate. If the debt securities are convertible into or exchangeable for other securities of ours or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property must make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Events of Default Under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indentures with respect to any series of debt securities that we may issue:

- if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended;
- if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable at maturity, upon redemption or repurchase or otherwise, and the time for payment has not been extended;
- if we fail to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

We will describe in each applicable prospectus supplement any additional events of default relating to the relevant series of debt securities.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of not less than a majority in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the unpaid principal, premium, if any, and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity or security satisfactory to it against any loss, liability or expense. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the trustee or security satisfactory to it against any loss, liability or expense or to be incurred in compliance with instituting the proceeding as trustee; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities, or other defaults that may be specified in the applicable prospectus supplement.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indentures.

Modification of Indenture; Waiver

Subject to the terms of the indenture for any series of debt securities that we may issue, we and the trustee may change an indenture without the consent of any holders with respect to the following specific matters:

- to fix any ambiguity, defect or inconsistency in the indenture;
- to comply with the provisions described above under “—Consolidation, Merger or Sale”;

- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act;
- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided under “Description of Debt Securities—General,” to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment hereunder by a successor trustee;
- to provide for uncertificated debt securities and to make all appropriate changes for such purpose;
- to add to our covenants such new covenants, restrictions, conditions or provisions for the benefit of the holders, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred to us in the indenture; or
- to change anything that does not materially adversely affect the interests of any holder of debt securities of any series.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, subject to the terms of the indenture for any series of debt securities that we may issue or as otherwise provided in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the stated maturity of the series of debt securities;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption or repurchase of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that, subject to the terms of the indenture and any limitation otherwise provided in the prospectus supplement applicable to a particular series of debt securities, we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement with respect to that series.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series. If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs.

Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the Debt Security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Ranking of Debt Securities

The subordinated debt securities will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of subordinated debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

The senior debt securities will rank equally in right of payment to all our other senior unsecured debt. The senior indenture does not limit the amount of senior debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement, which includes this prospectus.

General

We may issue warrants for the purchase of common stock, preferred stock or debt securities, in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities.

We plan to evidence each series of warrants by warrant certificates that we will issue under a separate warrant agreement. We will enter into the warrant agreement with a warrant agent. We will indicate the name and address of the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

We will describe in the applicable prospectus supplement the terms of the series of warrants, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- the number of shares of common stock purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreement and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the periods during which, and places at which, the warrants are exercisable;
- the manner of exercise;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreement and warrants may be modified;
- if applicable, a discussion of certain material U.S. federal income tax considerations of holding or exercising the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

DESCRIPTION OF UNITS

General

We may issue units comprised of common stock, preferred stock, debt securities and warrants to purchase common stock, preferred stock or debt securities in any combination. We may issue units in such amounts and in as many distinct series as we wish. This section outlines certain provisions of the units that we may issue. If we issue units, they will be issued under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. The information described in this section may not be complete in all respects and is qualified entirely by reference to the unit agreement with respect to the units of any particular series. The specific terms of any series of units offered will be described in the applicable prospectus supplement. If so described in a particular supplement, the specific terms of any series of units may differ from the general description of terms presented below. We urge you to read any prospectus supplement related to any series of units we may offer, as well as the complete unit agreement and unit certificate that contain the terms of the units. If we issue units, forms of unit agreements and unit certificates relating to such units will be incorporated by reference as exhibits to the registration statement, which includes this prospectus.

Each unit that we may issue will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date. The applicable prospectus supplement may describe:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement;
- the price or prices at which such units will be issued;
- the applicable U.S. federal income tax considerations relating to the units;
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- any other terms of the units and of the securities comprising the units.

The provisions described in this section, as well as those described under “Description of Capital Stock,” “Description of Debt Securities” and “Description of Warrants” will apply to the securities included in each unit, to the extent relevant and as may be updated in any prospectus supplements. We may issue units in such amounts and in as many distinct series as we wish. This section summarizes terms of the units that apply generally to all series. Most of the financial and other specific terms of a particular series of units will be described in the applicable prospectus supplement.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, “at the market offerings,” negotiated transactions, block trades, or a combination of these methods or any other method permitted pursuant to applicable law. We may sell the securities to or through one or more underwriters or dealers (acting as principal or agent), through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

- at a fixed price or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

A prospectus supplement or supplements will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of the underwriters, dealers or agents, if any;
- the purchase price of the securities or other consideration therefor, and the proceeds, if any, we will receive from the sale;
- any over-allotment or other options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents’ or underwriters’ compensation;
- any public offering price;
- any discounts or concessions allowed or reallocated or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

At-the-Market Offerings

If we reach an agreement with an underwriter on a placement, including the number of shares of stock to be offered in the placement and any minimum price below which sales may not be made, such underwriter would agree to use its commercially reasonable efforts, consistent with its normal trading and sales practices, to try to sell such shares on such terms. Underwriters could make sales in privately negotiated transactions and/or any other method permitted by law, including sales deemed to be an “at-the-market” offering as defined in Rule 415 promulgated under the Securities Act, sales made directly on the Nasdaq Capital Market, the existing trading market for our stock, or sales made to or through a market maker other than on an exchange. The name of any such underwriter or agent involved in the offer and sale of our stock, the amounts underwritten, and the nature of its obligations to take our stock will be described in the applicable prospectus supplement.

Underwriters and Agents

Only underwriters named in the prospectus supplement will be underwriters of the securities offered by the prospectus supplement. Dealers and agents participating in the distribution of the securities may be deemed to be underwriters, and compensation received by them on resale of the securities may be deemed to be underwriting discounts. If such dealers or agents were deemed to be underwriters, they may be subject to statutory liabilities under the Securities Act.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. If a dealer is used in the sale of securities, we or an underwriter will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale. To the extent required, we will set forth in the prospectus supplement the name of the dealer and the terms of the transaction. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time.

We may use underwriters, dealers or agents with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, dealer or agent, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We may also designate agents to solicit offers to purchase the securities from time to time and may enter into arrangements for “at-the-market,” equity line or similar transactions. We will name any agent involved in the offering and sale of securities and we will describe any commissions payable to the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, the agent will act on a best-efforts basis for the period of its appointment.

We may provide agents, underwriters and dealers with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents, underwriters or dealers may make with respect to these liabilities. Agents, underwriters and dealers, or their affiliates, may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

In order to facilitate the offering of the securities, any underwriters or agents, as the case may be, involved in the offering of such securities may engage in transactions that stabilize, maintain or otherwise affect the price of our securities. Specifically, the underwriters or agents, as the case may be, may over-allot in connection with the offering, creating a short position in our securities for their own account. In addition, to cover overallocments or to stabilize the price of our securities, the underwriters or agents, as the case may be, may bid for, and purchase, such securities in the open market. Finally, in any offering of securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allotted to an underwriter or a broker-dealer for distributing such securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. The underwriters or agents, as the case may be, are not required to engage in these activities, and may end any of these activities at any time.

Any underwriters that are qualified market makers on the Nasdaq Capital Market may engage in passive market making transactions in the common stock on the Nasdaq Capital Market in accordance with Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker’s bid, however, the passive market maker’s bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, the validity of the securities offered pursuant to this prospectus will be passed upon by Holland & Knight LLP. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The financial statements of Clene Inc. as of and for the year ended December 31, 2021 incorporated by reference in this prospectus have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report. Such financial statements are incorporated by reference in reliance upon the report of such firm given their authority as experts in auditing and accounting.

The financial statements as of December 31, 2020 and for the year ended December 31, 2020 incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2021 have been so incorporated in reliance on the report (which contains an emphasis of matter paragraph relating to the Company's requirement for additional financing or a collaboration agreement to fund planned future operations as described in Note 1 to the financial statements) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3, including exhibits, under the Securities Act, with respect to the securities offered pursuant to this prospectus. This prospectus is part of the registration statement, but does not contain all of the information included in the registration statement or the exhibits. For further information with respect to us and the securities offered by this prospectus, we refer you to the registration statement and its exhibits. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

In addition, we file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains an internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, including our SEC filings, located at <http://www.sec.gov>. We also maintain a website at <https://clene.com>. The information contained in or accessible from our website is not incorporated into this prospectus, and you should not consider it part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference. You may access, free of charge, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in this prospectus or a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or a subsequently filed document incorporated by reference modifies or replaces that statement.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on March 11, 2022;
- our Current Reports on Form 8-K filed with the SEC on [January 18, 2022](#), [February 2, 2022](#), and [April 14, 2022](#);
- the information specifically incorporated by reference into our Annual Report on [Form 10-K](#) for the year ended December 31, 2021 from our Definitive Proxy Statement on [Schedule 14A](#), filed with the SEC on March 24, 2022; and
- the description of our common stock contained in the registration statement on [Form 8-A](#), dated December 30, 2020, filed pursuant to Section 12(b) of the Exchange Act, as amended by Amendment No. 1 to [Form 8-A](#), dated February 9, 2021.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including all such reports and other documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and other documents.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, a copy of any or all of the information that has been incorporated by reference in the prospectus but not delivered with the prospectus. You may request a copy of any documents incorporated by reference in this prospectus, at no cost, by writing or telephoning us at:

Clene Inc.
Attention: Investor Relations
6550 South Millrock Drive, Suite G50
Salt Lake City, Utah 84121
Telephone: 801-676-9695

Exhibits to the filings will not be sent, however, unless those exhibits have been specifically incorporated by reference in this prospectus or any accompanying prospectus supplement.



Clene Inc.

Up to \$25,000,000 and 499,002 Shares of Common Stock

PROSPECTUS SUPPLEMENT

March 7, 2023