

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

**AMENDMENT NO. 1 TO FORM S-3  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933**

**CLENE INC.**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or Other Jurisdiction  
of Incorporation or Organization)

**85-2828339**  
(I.R.S. Employer  
Identification Number)

**6550 South Millrock Drive, Suite G50  
Salt Lake City, Utah 84121  
Tel: (801) 676-9695**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Robert Etherington  
President and Chief Executive Officer  
6550 South Millrock Drive, Suite G50  
Salt Lake City, Utah 84121  
Tel: (801) 676-9695**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

**Copies to:**

**Jerry Miraglia, Esq.  
General Counsel and Corporate Secretary  
500 Principio Parkway West, Suite 400  
North East, Maryland 21901  
Tel: (443) 273-1645**

**Tom McAleavey  
Holland & Knight LLP  
200 South Orange Avenue, Suite 2600  
Orlando, Florida 32801  
Tel: (407) 244-5108**

**Approximate date of commencement of proposed sale to the public:** From time to time after this Registration Statement becomes effective.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box:

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box:

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input checked="" type="checkbox"/>

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

**The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.**

**The information contained herein is not complete and may be changed. These securities may not be sold nor may offers to buy be accepted prior to the time the Registration Statement becomes effective. This prospectus shall not constitute an offer to sell or the solicitation of an offer to buy nor shall there be any sale of these securities in any jurisdiction in which such offer, solicitation or sale is not permitted.**

**SUBJECT TO COMPLETION, DATED SEPTEMBER 29, 2023**

**PRELIMINARY PROSPECTUS**



## **Clene Inc.**

### **Up to 3,000,000 Shares of Common Stock**

This prospectus relates to the offer and resale from time to time by the Selling Securityholder, of up to an aggregate of 3,000,000 shares of Clene Inc. common stock, par value \$0.0001 per share, that may be issued upon the exercise of a warrant to purchase common stock at an exercise price of \$0.80 per share (the "Warrant"). The Warrant was issued as part of an amendment to a loan and security agreement (the "Loan Agreement") between us and Avenue Venture Opportunities Fund, L.P. ("Avenue").

This prospectus also includes an indeterminable number of additional shares of common stock as may be issued to prevent dilution resulting from stock splits, stock dividends or other similar transactions.

We will not receive any proceeds from the sale of shares of common stock by the Selling Securityholder pursuant to this prospectus, except with respect to amounts received by us upon exercise of the Warrant to the extent such Warrant is exercised for cash. However, we have paid, and will continue to pay, the expenses, other than underwriting discounts and commissions and certain expenses incurred by the Selling Securityholder in disposing of the common stock, associated with the sale of common stock pursuant to this prospectus.

We are registering the offer and resale of the common stock described above by the Selling Securityholder to satisfy certain registration rights we have granted. Our registration of the common stock covered by this prospectus does not mean that the Selling Securityholder will offer or sell any of the common stock. The Selling Securityholder and any of its permitted transferees may offer and sell the common stock covered by this prospectus in a number of different ways and at varying prices. Additional information on the Selling Securityholder, and the times and manner in which it may offer and sell the common stock under this prospectus, is provided under "Selling Securityholders" and "Plan of Distribution" in this prospectus.

You should read this prospectus and any additional prospectus supplement or amendment carefully before you invest in our securities.

Our common stock and public warrants are listed on the Nasdaq Capital Market ("Nasdaq") under the symbol "CLNN" and "CLNNW," respectively. On September 20, 2023, the last reported sale price of our common stock and public warrants on Nasdaq was \$0.4822 and \$0.0683, respectively.

**Investing in our securities involves a high degree of risk. See "Risk Factors" section on page 10 of this prospectus and other risk factors contained in any applicable prospectus supplement and in the documents incorporated by reference herein and therein.**

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 \_\_\_\_\_, 2023.

---

## TABLE OF CONTENTS

	<b>Page</b>
<a href="#"><u>ABOUT THIS PROSPECTUS</u></a>	1
<a href="#"><u>CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS</u></a>	2
<a href="#"><u>MARKET AND INDUSTRY DATA</u></a>	4
<a href="#"><u>PROSPECTUS SUMMARY</u></a>	5
<a href="#"><u>THE OFFERING</u></a>	9
<a href="#"><u>RISK FACTORS</u></a>	10
<a href="#"><u>USE OF PROCEEDS</u></a>	11
<a href="#"><u>DESCRIPTION OF CAPITAL STOCK</u></a>	12
<a href="#"><u>SELLING SECURITYHOLDERS</u></a>	13
<a href="#"><u>PLAN OF DISTRIBUTION</u></a>	14
<a href="#"><u>LEGAL MATTERS</u></a>	17
<a href="#"><u>EXPERTS</u></a>	17
<a href="#"><u>WHERE YOU CAN FIND MORE INFORMATION</u></a>	17
<a href="#"><u>INFORMATION INCORPORATED BY REFERENCE</u></a>	18

## 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, the Selling Securityholder and its permitted transferees may, from time to time, offer and sell, as applicable, the common stock issuable upon exercise of the Warrant, through any means as described under “Plan of Distribution.” More specific terms of any shares of common stock that the Selling Securityholder and its permitted transferees offer and sell may be provided in a prospectus supplement that describes, among other things, the specific amounts and prices of the common stock being offered and the terms of the offering.

We may also provide a prospectus supplement or post-effective amendment to the Registration Statement to 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 under “Where You Can Find More Information.”

Neither we nor the Selling Securityholder have authorized anyone to provide you with any information or to make any representations other than those contained in, or incorporated by reference into, this prospectus, or any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. Neither we nor the Selling Securityholder take responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. Neither we nor the Selling Securityholder will make an offer to sell this common stock 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.

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.”

For investors outside of the United States: We have not, and the Selling Securityholder has 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 the shares of common stock and the distribution of this prospectus outside of the United States.

**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:

- our future financial performance, including our ability to continue as a going concern;
- our plans and strategies to raise additional funding;
- the clinical results of our drug candidates;
- the likelihood of commercial success for our drug candidates;
- our plans and strategies 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 marketed products and drug candidates, if approved;
- our ability to obtain and maintain protection of intellectual property for our technology and drugs;
- our reliance on third parties to conduct drug development, manufacturing and other services;
- our limited operating history and our ability to obtain additional funding for operations and to complete the licensing or development and commercialization of our drug candidates;
- the impact of the COVID-19 pandemic on our clinical development, commercial and other operations;
- changes in applicable laws or regulations;

- the 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<sup>®</sup>”) therapeutics. CSN<sup>®</sup> 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 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 in central nervous system disorders including Amyotrophic Lateral Sclerosis (“ALS”), Multiple Sclerosis (“MS”), and Parkinson’s Disease (“PD”). We currently have no drugs approved for commercial sale and have not generated any revenue from drug sales. We have never been profitable and have incurred operating losses in each year since inception. We generate revenue from sales of dietary supplements through our wholly owned subsidiary, dOrbital, Inc., or through an exclusive license with 4Life Research LLC, a stockholder and related party. We anticipate these revenues to be small compared to our operating expenses and to the revenue we expect to generate from potential future sales of our drug candidates, for which we are currently conducting clinical trials.

### Recent Developments of Our Clinical Programs

#### *Amyotrophic Lateral Sclerosis*

On June 15, 2023, we reported new data demonstrating a statistically significant reduction of plasma neurofilament light chain (“NfL”) levels for CNM-Au8 treated participants compared to placebo after 24 weeks of treatment in the double-blind, placebo-controlled period of the Phase 2/3 HEALEY ALS Platform Trial, which evaluated the safety and efficacy of CNM-Au8 in patients with ALS. NfL is a key biomarker of neurodegeneration. NfL is released from neurons following axonal injury, especially in people living with ALS, where higher levels of NfL have been found to predict more rapid decline in clinical function and increased mortality risk. Surrogate biomarkers such as NfL have recently been used to support an approval by the U.S. Food and Drug Administration (“FDA”) for the treatment of ALS. Analyses of NfL from serum samples specified as the primary blood matrix for analysis are underway. Additional biomarker and long-term survival data from the HEALEY ALS Platform Trial double-blind and open label extension (“OLE”) periods have been collected and are undergoing testing preparatory for analysis, and we expect to report the data as follows: (i) plasma NfL data from the OLE in the third quarter of 2023, (ii) initial long-term survival data from the OLE in the third quarter of 2023, (iii) exploratory results for time to clinical worsening events and ALSFRS-R for the OLE in the fourth quarter of 2023, and (iv) data from additional biomarkers in late 2023.

On August 29, 2023, we reported updated data from the long-term OLE of the Phase 2 RESCUE-ALS clinical trial, which evaluated the efficacy, safety, and pharmacokinetics of CNM-Au8 in patients with early symptomatic ALS. The 24-month data cut, as of July 2023, showed a significant median survival benefit of 19.3 months using the rank-preserving structural failure time model (“RPSFTM”). The RPSFTM analysis method estimates the survival gained by receiving active treatment using the data from all study participants and then subtracts the benefit from ex-placebo participants switched to CNM-Au8 during the OLE to provide a comparison of CNM-Au8 versus placebo across the entire study period. This well-recognized method has been used to estimate cross-over treatment effects in a recent ALS trial, and oncology and other rare disease trials. The 24-month data cut also showed a significant 52% decreased risk of ALS clinical worsening (defined as the first occurrence of death, tracheostomy, assisted ventilation, or feeding tube placement) with CNM-Au8 treatment. The full data cut is as follows:

- Cross-over adjusted median survival (RPSFTM, all study participants, post hoc):
  - 19.3 month median survival benefit (CNM-Au8 median survival of 34.2 months, placebo-adjusted median survival of 14.9 months).
  - 75% decreased risk of long-term all-cause mortality in participants originally randomized to treatment with CNM-Au8 compared to those originally randomized to placebo after adjusting for benefit received by placebo after switching to CNM-Au8 (HR: 0.252, 95% CI: 0.106 to 0.597; bootstrap log-rank  $p < 0.001$ ).



- Unadjusted median survival (without adjusting for the benefit received in ex-placebo participants; analyses include all study participants):
  - 10.1 month median survival benefit when not accounting for the improvement by ex-placebo treated participants who switched to CNM-Au8 at the start of the OLE (CNM-Au8 median survival of 34.2 months; placebo median survival of 24.1 months).
  - 46% decreased risk of all-cause mortality in participants originally randomized to treatment with CNM-Au8 compared to those originally randomized to placebo (HR: 0.54, 95% CI: 0.25-1.1, log-rank p=0.09).
- Observed survival versus ALS historical placebo controls:
  - 70% decreased risk of long-term mortality in participants originally randomized to treatment with CNM-Au8 compared to matched placebo participants derived from the PRO-ACT database (Cox adjusted HR: 0.300, 95% CI: 0.09 to 0.79; p=0.03). PRO-ACT contains approximately 12,000 ALS patient records from multiple completed clinical trials.
- 52% decreased risk of ALS clinical worsening events (HR: 0.48, 95% CI: 0.23-1.0, log-rank p=0.049) in the participants originally randomized to CNM-Au8 treatment versus original placebo.

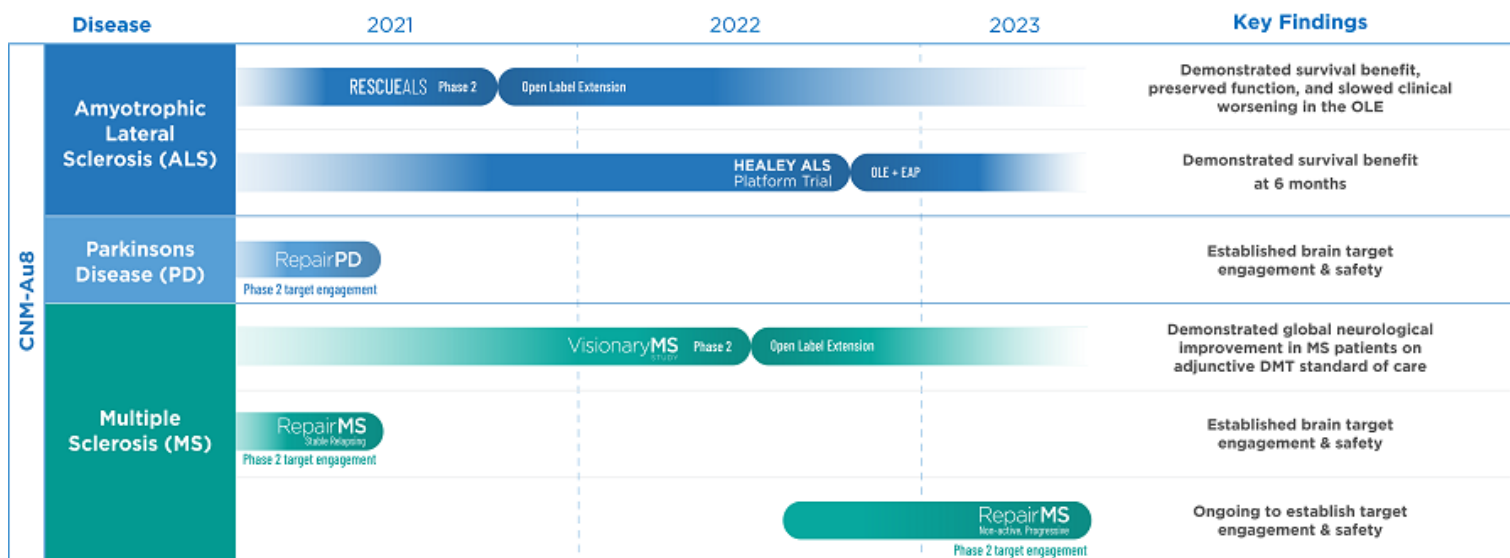
CNM-Au8 was well-tolerated without long term safety concerns in both RESCUE-ALS and the HEALEY ALS Platform Trial, with over 475 collective years of exposure across ALS, MS, and PD participants in CNM-Au8 clinical trials and Expanded Access Protocol (compassionate use) programs without any observed safety signals. No serious adverse events have been assessed as related to CNM-Au8 treatment; adverse events observed with CNM-Au8 have been characterized as transient and predominantly mild-to-moderate in severity.

We are presently discussing the design of an international Phase 3 study, RESTORE-ALS, with expert ALS clinical advisors and expect to initiate the trial in the first half of 2024. We plan to work closely with regulatory health authorities from the FDA and European Medicines Agency (“EMA”), 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 to discuss the totality of our long-term survival data and NFL data. We anticipate meeting with the FDA in the fourth quarter of 2023. Based on the outcome of the FDA meeting, we believe we could file an NDA with the FDA in the first half of 2024 with a potential accelerated approval Prescription Drug User Fee Act (“PDUFA”) action date by the end of 2024.

### Multiple Sclerosis

In February and March 2023, we reported updated exploratory data from our Phase 2 VISIONARY-MS clinical trial, which evaluated the efficacy and safety of CNM-Au8 in stable relapsing remitting MS patients. We expect additional results up to 144 weeks from the OLE in the fourth quarter of 2023. 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 first half of 2024. We plan to work closely with regulatory health authorities from the FDA and EMA, MS experts, and patient representatives to determine the proper path to advance our assets into Phase 3 and potential future approval. We expect to meet with the FDA in an end of Phase 2 meeting in the first half of 2024. We are presently discussing the design of an international Phase 3 MS study with expert MS clinical advisors and expect to initiate the trial in the second half of 2024, contingent on funding.

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.

On June 6, 2023, BrainStorm Cell Therapeutics Inc. announced the FDA will hold a meeting of the FDA Cellular, Tissue and Gene Therapies Advisory Committee on September 27, 2023, to review the Biologics License Application for its investigational therapeutic NurOwn for the treatment of ALS, with a PDUFA action date by December 8, 2023.

On April 25, 2023, the FDA granted accelerated approval of tofersen, branded as QALSODY, a 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 and 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. sought accelerated approval of tofersen based on the use of plasma NfL as a surrogate biomarker that is reasonably likely to predict clinical benefit. Tofersen study results suggest reductions in plasma NfL preceded and predicted slowing of decline in measures of clinical and respiratory function, strength, and quality of life. Previously in March 2023, the Peripheral and Central Nervous System Drugs Advisory Committee voted 9 (yes) and 0 (no) as to whether a reduction in plasma NfL concentration in tofersen-treated patients is reasonably likely to predict clinical benefit of tofersen for treatment of patients with SOD1-ALS, and 3 (yes), 5 (no), and 1 (abstain) as to whether the clinical data from the placebo-controlled study and available long-term extension study results, with additional supporting results from the effects on relevant biomarkers (i.e. changes in plasma NfL concentration and/or reductions in SOD1), provide substantial evidence of the effectiveness of tofersen in the treatment of patients with SOD1-ALS. Additionally, in December 2022, the EMA accepted the Marketing Authorization Application for review of tofersen.

## ***Going Concern***

We incurred a loss from operations of \$21.1 million and \$26.9 million for the six months ended June 30, 2023 and 2022, respectively. Our accumulated deficit was \$230.1 million and \$193.2 million as of June 30, 2023 and December 31, 2022, respectively. Our cash, cash equivalents, and marketable securities totaled \$49.2 million and \$23.3 million as of June 30, 2023 and December 31, 2022, respectively, and net cash used in operating activities was \$16.2 million and \$22.8 million for the six months ended June 30, 2023 and 2022, 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 subsequent to the quarter ended June 30, 2023 and 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. We expect 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 unless we obtain additional financing. Additionally, pursuant to our term loan with Avenue, we are required to 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 plan 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 and equity purchase agreement and potential proceeds from the exercise of outstanding warrants. 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. During the three months ended June 30, 2023, we raised approximately \$37.4 million of net proceeds in an underwritten public equity offering. We have implemented cost-saving initiatives, including delaying and 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 quarter ended June 30, 2023, were issued and through the date of this prospectus.

Our financial statements incorporated by reference herein 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 incorporated by reference herein 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, 2022. 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 and became a public company on December 30, 2020 (the “Closing Date”) when it completed a merger and reverse recapitalization (the “Reverse Recapitalization”) with Tottenham and Tottenham’s wholly-owned subsidiary and our predecessor, Chelsea Worldwide Inc., and Creative Worldwide Inc., a wholly-owned subsidiary of Chelsea Worldwide Inc. On the Closing Date, Chelsea Worldwide Inc. changed its name 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 Reverse Recapitalization was \$543.4 million, paid in the form of 54,339,012 newly issued shares of common stock valued at \$10.00 per share. Prior to the Reverse Recapitalization, 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 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

Shares of common stock offered by the Selling Securityholder 3,000,000 shares issuable upon exercise of the Warrant at an exercise price of \$0.80 per share.

Shares of common stock outstanding prior to exercise of all warrants 128,408,358 shares of common stock, based on total shares outstanding as of September 20, 2023.

Use of proceeds All shares of common stock offered and sold by the Selling Securityholder pursuant to this prospectus will be sold by the Selling Securityholder for its respective accounts. We will not receive any proceeds from the sale of shares of common stock by the Selling Securityholder pursuant to this prospectus, except with respect to amounts received by us upon exercise of the Warrant to the extent such Warrant is exercised for cash. See “Use of Proceeds” for additional information.

Risk Factors Any investment in the common stock offered hereby is speculative and involves a high degree of risk. You should read carefully the information set forth in “Risk Factors” and other information included elsewhere in this prospectus for a discussion of factors that you should consider before deciding to invest in our common stock.

Nasdaq Capital Market Symbol “CLNN”

The number of shares of our common stock outstanding as of September 20, 2023 excludes the following:

- 21,228,397 shares of common stock issuable upon exercise of stock options outstanding as of September 20, 2023 with a weighted-average exercise price of \$2.32 per share;
- 1,477,795 shares of common stock reserved as of September 20, 2023, for future grant under our 2020 Amended Stock Plan;
- 105,432,083 shares of common stock issuable upon exercise of warrants outstanding as of September 20, 2023 with a weighted-average exercise price of \$1.52 per share;
- 793,756 shares of common stock issuable upon vesting of rights to restricted stock awards and restricted stock units outstanding as of September 20, 2023;
- 6,592,334 shares of common stock issuable upon vesting of earn-out shares outstanding as of September 20, 2023; and
- up to 1,732,703 shares of common stock issuable upon conversion of our convertible notes payable outstanding as of September 20, 2023.

Except as otherwise indicated, all information in this prospectus assumes no exercise of the outstanding options or warrants, vesting of restricted stock awards, restricted stock units, or earn-out shares, or conversion of convertible notes payable referred to above.

## 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

All of the shares of common stock offered by the Selling Securityholder pursuant to this prospectus will be sold by the Selling Securityholder for its own account. We will not receive any proceeds from these sales.

We will receive the proceeds from the exercise of the Warrant. If the Warrant is exercised in full for cash, we would receive \$2.4 million in gross proceeds, and intend to use any proceeds received from the exercise of the Warrant to meet general working capital needs. There is no assurance that the holder of the Warrant will elect to exercise any or all of such Warrant. To the extent that the Warrant is exercised on a net or "cashless" basis, the amount of cash we would receive from the exercise of the Warrant will decrease. We will bear all other costs, fees and expenses incurred in effecting the registration of the common stock covered by this prospectus, including, without limitation, all registration and filing fees, Nasdaq listing fees and professional fees and expenses. The Selling Securityholder will pay any underwriting fees, discounts, selling commissions, stock transfer taxes and certain legal expenses incurred by the Selling Securityholder when disposing of its common stock.

## DESCRIPTION OF SECURITIES

*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 incorporated by reference as Exhibits 3.1 and 3.2, respectively, to this prospectus.

Our amended and restated certificate of incorporation authorizes a total number of shares of all classes of stock of 301,000,000 shares, consisting of: (i) 1,000,000 shares of preferred stock, par value \$0.0001 per share, and (ii) 300,000,000 shares of common stock, par value \$0.0001 per share.

### 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 (the "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.

### Avenue Warrant

The Warrant was issued on June 27, 2023 pursuant to an amendment to the Loan Agreement. The Warrant is exercisable for 3,000,000 shares of common stock at an exercise price of \$0.80 per share. Avenue may exercise the Warrant (i) by making a cash payment equal to the exercise price multiplied by the number of shares or (ii) on a net or "cashless" basis. The Warrant may be exercised in whole or in part, from time to time up to and including on June 30, 2028. In the event of certain transactions which constitute a change of control of the Company, the Warrant shall be automatically exchanged for the number of shares of Common Stock which remain exercisable thereunder immediately prior to the change of control transaction, for no payment of any form of consideration by Avenue for such shares, and the Warrant shall be terminated.

As of the date of this prospectus, we had 105,432,083 warrants outstanding.

### 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.

## SELLING SECURITYHOLDERS

This prospectus relates to the possible resale by the Selling Securityholder from time to time of up to 3,000,000 shares of our common stock that the Selling Securityholder may acquire upon the exercise of the Warrant. When we refer to the “Selling Securityholder” in this prospectus, we mean the persons listed in the table below, and the pledgees, donees, transferees, assignees, successors, designees and others who later come to hold any of the Selling Securityholder’s interest in the common stock other than through a public sale.

The following table sets forth, as of the date of this prospectus, information concerning the shares of our common stock that may be offered from time to time by the Selling Securityholder. The Selling Securityholder is not obligated to exercise the Warrant nor sell any of the shares of common stock received upon exercise of the Warrant and offered by this prospectus. The Selling Securityholder may also offer and sell less than the number of shares of common stock indicated. The Selling Securityholder is not making any representation that any shares of common stock covered by this prospectus will or will not be offered for sale.

The number of shares of common stock and percentages of beneficial ownership set forth below are based on 128,408,358 shares of our common stock issued and outstanding as of the date of this prospectus, and assumes the full exercise of the Warrant for 3,000,000 shares of our common stock.

Name of Selling Securityholder	Shares Beneficially Owned Prior to the Offering		Shares Being Offered	Shares Beneficially Owned After the Offering	
	Shares	%		Shares	%
Avenue Venture Opportunities Fund, L.P.	3,000,000	2.3%	3,000,000	—	0.0%
Total Shares	3,000,000	2.3%	3,000,000	—	0.0%

Except for the Loan Agreement, the Selling Securityholder has not had any material relationship with us within the past three years.



## PLAN OF DISTRIBUTION

We are registering the offer and resale by the Selling Securityholder of up to 3,000,000 shares of common stock that are issuable upon the exercise of the Warrant. We are required to pay all fees and expenses incident to the registration of the shares of our common stock that may be offered and sold pursuant to this prospectus.

The shares of common stock beneficially owned by the Selling Securityholder covered by this prospectus may be offered and sold from time to time by the Selling Securityholder. The term "Selling Securityholder" includes donees, pledgees, transferees or other successors in interest selling securities received after the date of this prospectus from a Selling Securityholder as a gift, pledge, partnership distribution or other transfer. The Selling Securityholder will act independently of us in making decisions with respect to the timing, manner and size of each sale. Such sales may be made on one or more exchanges or in the over-the-counter market or otherwise, at prices and under terms then prevailing or at prices related to the then-current market price or in negotiated transactions. The Selling Securityholder may sell their shares by one or more of, or a combination of, the following methods:

- purchases by a broker-dealer as principal and resale by such broker-dealer for its own account pursuant to this prospectus;
- ordinary brokerage transactions and transactions in which the broker solicits purchasers;
- block trades in which the broker-dealer so engaged will attempt to sell the securities as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- an over-the-counter distribution in accordance with the rules of Nasdaq;
- through trading plans entered into by a Selling Securityholder pursuant to Rule 10b5-1 under the Exchange Act that are in place at the time of an offering pursuant to this prospectus and any applicable prospectus supplement hereto that provide for periodic sales of their securities on the basis of parameters described in such trading plans;
- through one or more underwritten offerings on a firm commitment or best efforts basis;
- settlement of short sales entered into after the date of this prospectus;
- agreements with broker-dealers to sell a specified number of the securities at a stipulated price per share or warrant;
- in "at the market" offerings, as defined in Rule 415 under the Securities Act, at negotiated prices, at prices prevailing at the time of sale or at prices related to such prevailing market prices, including sales made directly on a national securities exchange or sales made through a market maker other than on an exchange or other similar offerings through sales agents;
- directly to purchasers, including through a specific bidding, auction or other process or in privately negotiated transactions;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- through a combination of any of the above methods of sale; or
- any other method permitted pursuant to applicable law.

In addition, a Selling Securityholder that is an entity may elect to make a pro rata in-kind distribution of securities to its members, partners or shareholders pursuant to the Registration Statement of which this prospectus is a part by delivering a prospectus with a plan of distribution. Such members, partners or shareholders would thereby receive freely tradeable securities pursuant to the distribution through a registration statement. To the extent a distributee is an affiliate of ours (or to the extent otherwise required by law), we may file a prospectus supplement in order to permit the distributees to use the prospectus to resell the securities acquired in the distribution.

There can be no assurance that the Selling Securityholder will sell all or any of the securities offered by this prospectus. In addition, the Selling Securityholder may also sell securities under Rule 144 under the Securities Act, if available, or in other transactions exempt from registration, rather than under this prospectus. The Selling Securityholder have the sole and absolute discretion not to accept any purchase offer or make any sale of securities if they deem the purchase price to be unsatisfactory at any particular time.

The Selling Securityholder also may transfer the securities in other circumstances, in which case the transferees, pledgees or other successors-in-interest will be the selling beneficial owners for purposes of this prospectus. Upon being notified by a Selling Securityholder that a donee, pledgee, transferee, or other successor-in-interest intends to sell our securities, we will, to the extent required, promptly file a supplement to this prospectus to name specifically such person as a selling shareholder.

With respect to a particular offering of the securities held by the Selling Securityholder, to the extent required, an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the Registration Statement of which this prospectus is part, will be prepared and will set forth the following information:

- the specific securities to be offered and sold;

- the name of the selling securityholder;
- the respective purchase prices and public offering prices, the proceeds to be received from the sale, if any, and other material terms of the offering;
- settlement of short sales entered into after the date of this prospectus;
- the names of any participating agents, broker-dealers or underwriters; and
- any applicable commissions, discounts, concessions and other items constituting compensation from the selling shareholders.

In connection with distributions of the securities or otherwise, the Selling Securityholder may enter into hedging transactions with broker-dealers or other financial institutions. In connection with such transactions, broker-dealers or other financial institutions may engage in short sales of the securities in the course of hedging the positions they assume with Selling Securityholder. The Selling Securityholder may also sell the securities short and redeliver the securities to close out such short positions. The Selling Securityholder may also enter into option or other transactions with broker-dealers or other financial institutions which require the delivery to such broker-dealer or other financial institution of securities offered by this prospectus, which securities such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). The Selling Securityholder may also pledge securities to a broker-dealer or other financial institution, and, upon a default, such broker-dealer or other financial institution, may effect sales of the pledged securities pursuant to this prospectus (as supplemented or amended to reflect such transaction).

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 over-allotments 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.

The Selling Securityholder may solicit offers to purchase the securities directly from, and it may sell such securities directly to, institutional investors or others. In this case, no underwriters or agents would be involved. The terms of any of those sales, including the terms of any bidding or auction process, if utilized, will be described in the applicable prospectus supplement.

It is possible that one or more underwriters may make a market in our securities, but such underwriters will not be obligated to do so and may discontinue any market making at any time without notice. We cannot give any assurance as to the liquidity of the trading market for our securities.

The Selling Securityholder may authorize underwriters, broker-dealers or agents to solicit offers by certain purchasers to purchase the securities at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions we or the Selling Securityholder pay for solicitation of these contracts.

A Selling Securityholder may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by the Selling Securityholder or borrowed from the Selling Securityholder or others to settle those sales or to close out any related open borrowings of stock and may use securities received from the Selling Securityholder in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and will be identified in the applicable prospectus supplement (or a post-effective amendment). In addition, the Selling Securityholder may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

In effecting sales, broker-dealers or agents engaged by the Selling Securityholder may arrange for other broker-dealers to participate. Broker-dealers or agents may receive commissions, discounts or concessions from the Selling Securityholder in amounts to be negotiated immediately prior to the sale.

In compliance with the guidelines of the Financial Industry Regulatory Authority ("FINRA"), the aggregate maximum discount, commission, fees or other items constituting underwriting compensation to be received by any FINRA member or independent broker-dealer will not exceed 8% of the gross proceeds of any offering pursuant to this prospectus and any applicable prospectus supplement.

If at the time of any offering made under this prospectus a member of FINRA participating in the offering has a "conflict of interest" as defined in FINRA Rule 5121 ("Rule 5121"), that offering will be conducted in accordance with the relevant provisions of Rule 5121.

To our knowledge, there are currently no plans, arrangements or understandings between the Selling Securityholder and any broker-dealer or agent regarding the sale of the securities by the Selling Securityholder. Upon our notification by the Selling Securityholder that any material arrangement has been entered into with an underwriter or broker-dealer for the sale of securities through a block trade, special offering, exchange distribution, secondary distribution or a purchase by an underwriter or broker-dealer, we will file, if required by applicable law or regulation, a supplement to this prospectus pursuant to Rule 424(b) under the Securities Act disclosing certain material information relating to such underwriter or broker-dealer and such offering.

Underwriters, broker-dealers or agents may facilitate the marketing of an offering online directly or through one of their affiliates. In those cases, prospective investors may view offering terms and a prospectus online and, depending upon the particular underwriter, broker-dealer or agent, place orders online or through their financial advisors.

In offering the securities covered by this prospectus, the Selling Securityholder and any underwriters, broker-dealers or agents who execute sales for the Selling Securityholder may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. Any discounts, commissions, concessions or profit they earn on any resale of those securities may be underwriting discounts and commissions under the Securities Act.

The underwriters, broker-dealers and agents may engage in transactions with us or the Selling Securityholder, or perform services for us or the Selling Securityholder, in the ordinary course of business.

In order to comply with the securities laws of certain states, if applicable, the securities must be sold in such jurisdictions only through registered or licensed brokers or dealers. In addition, in certain states the securities may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

The Selling Securityholder and any other persons participating in the sale or distribution of the securities will be subject to applicable provisions of the Securities Act and the Exchange Act, and the rules and regulations thereunder, including, without limitation, Regulation M. These provisions may restrict certain activities of, and limit the timing of purchases and sales of any of the securities by, the Selling Securityholder or any other person, which limitations may affect the marketability of the shares of the securities.

We will make copies of this prospectus available to the Selling Securityholder for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The Selling Securityholder may indemnify any agent, broker-dealer or underwriter that participates in transactions involving the sale of the securities against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the Selling Securityholder against certain liabilities, including certain liabilities under the Securities Act, the Exchange Act or other federal or state law. Agents, broker-dealers and underwriters may be entitled to indemnification by us and the Selling Securityholder against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments which the agents, broker-dealers or underwriters may be required to make in respect thereof.

## LEGAL MATTERS

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

## EXPERTS

The financial statements of Clene Inc. as of and for the years ended December 31, 2022 and 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.

## 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 by the Selling Securityholder 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 the Selling Securityholder pursuant to 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 <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, 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 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, 2022, filed with the SEC on March 13, 2023;
- our Quarterly Reports on Form 10-Q for the quarter ended [March 31, 2023](#), filed with the SEC on May 12, 2023, and the quarter ended [June 30, 2023](#), filed with the SEC on August 14, 2023;
- our Current Reports on Form 8-K filed with the SEC on [February 17, 2023](#), [February 27, 2023](#) (first of two reports filed on February 27, 2023), [March 3, 2023](#), [March 6, 2023](#) (second of two reports filed on March 6, 2023), [March 9, 2023](#), [March 17, 2023](#), [May 11, 2023](#), [June 2, 2023](#), [June 15, 2023](#), [June 16, 2023](#) (first of two reports filed on June 16, 2023), [June 16, 2023](#) (second of two reports filed on June 16, 2023), [June 30, 2023](#), [August 4, 2023](#), [August 29, 2023](#), [September 19, 2023](#), and [September 25, 2023](#);
- the information specifically incorporated by reference into our Annual Report on [Form 10-K](#) for the year ended December 31, 2022 from our Definitive Proxy Statement on [Schedule 14A](#), filed with the SEC on March 28, 2023; 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 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.



# Clene Inc.

Up to 3,000,000 Shares of Common Stock

PRELIMINARY PROSPECTUS

, 2023

---

## PART II

### INFORMATION NOT REQUIRED IN PROSPECTUS

#### ITEM 14. *Other Expenses of Issuance and Distribution.*

The following table sets forth the expenses that will be paid by us in connection with the distribution of the securities being registered, other than underwriting discounts and commissions and certain expenses incurred by the Selling Securityholder in disposing of the securities.

All amounts are estimates, except for the SEC registration fee.

	<u>Amount to Be Paid</u>
SEC registration fee	\$ 169
Accounting fees and expenses	10,000
Legal fees and expenses	7,500
Total	<u>\$ 17,669</u>

#### ITEM 15. *Indemnification of Directors and Officers.*

Section 145(a) of the DGCL provides, in general, that a corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation), because he or she is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding, if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful.

Section 145(b) of the DGCL provides, in general, that a corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor because the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees) actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, except that no indemnification shall be made with respect to any claim, issue or matter as to which he or she shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, he or she is fairly and reasonably entitled to indemnity for such expenses that the Court of Chancery or other adjudicating court shall deem proper.

Section 145(g) of the DGCL provides, in general, that a corporation may purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any liability asserted against such person and incurred by such person in any such capacity, or arising out of his or her status as such, whether or not the corporation would have the power to indemnify the person against such liability under Section 145 of the DGCL.

Our Certificate of Incorporation provides that no director of ours shall be personally liable to us or our shareholders for monetary damages for any breach of fiduciary duty as a director, except for liability (1) for any breach of the director's duty of loyalty to us or our shareholders, (2) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (3) in respect of unlawful dividend payments or stock redemptions or repurchases, or (4) for any transaction from which the director derived an improper personal benefit. In addition, our Certificate of Incorporation provides that if the DGCL is amended to authorize the further elimination or limitation of the liability of directors, then the liability of a director of ours shall be eliminated or limited to the fullest extent permitted by the DGCL, as so amended.

Our Certificate of Incorporation further provides that any repeal or modification of such article by its shareholders or amendment to the DGCL will not adversely affect any right or protection existing at the time of such repeal or modification with respect to any acts or omissions occurring before such repeal or modification of a director serving at the time of such repeal or modification.

Our Bylaws provide that we will indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding whether civil, criminal, administrative or investigative (other than an action by or in the right of the Company) by reason of the fact that he or she is or was, or has agreed to become, the Company's director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture or other enterprise (all such persons being referred to as an Indemnitee), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), judgments, fines, and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding and any appeal therefrom, if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in or not opposed to our best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful. Our Bylaws also provides that we will advance expenses to Indemnitees in connection with a legal proceeding, subject to limited exceptions.

We have entered into indemnification agreements with each of our directors and executive officers. These agreements provide that we will indemnify each of our directors and such officers to the fullest extent permitted by law and our Certificate of Incorporation and our Bylaws.

We will also maintain a general liability insurance policy, which will cover certain liabilities of directors and officers of ours arising out of claims based on acts or omissions in their capacities as directors or officers.

#### ITEM 16. Exhibits.

Exhibit Number	Exhibit Description
3.1	<a href="#">Fourth Amended and Restated Certificate of Incorporation of Clene Inc. (incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K filed by the Registrant on May 11, 2023).</a>
3.2	<a href="#">Bylaws of Clene Inc. (incorporated by reference to Exhibit 3.2 to the Current Report on Form 8-K filed by the Registrant on January 5, 2021).</a>
4.1	<a href="#">Form of Avenue Venture Opportunities Fund, L.P. Warrant to Purchase Shares of Common Stock (incorporated by reference to Exhibit 4.1 to the Current Report on Form 8-K filed by the Registrant on June 30, 2023).</a>
5.1**	<a href="#">Opinion of Holland &amp; Knight LLP.</a>
10.1#	<a href="#">Second Amendment to Supplement to Loan and Security Agreement, dated June 27, 2023, by and among Avenue Venture Opportunities Fund, L.P., Clene Inc., and Clene Nanomedicine, Inc. (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed by the Registrant on June 30, 2023).</a>
23.1**	<a href="#">Consent of Holland &amp; Knight LLP (included as part of Exhibit 5.1).</a>
23.2**	<a href="#">Consent of Deloitte &amp; Touche LLP.</a>
24.1	<a href="#">Power of Attorney (included on signature page of the Registration Statement).</a>
107*	<a href="#">Filing Fee Table.</a>

\* Previously filed.

\*\* Filed herewith.

# Schedules and similar attachments to this exhibit have been omitted pursuant to Item 601(a)(5) of Regulation S-K. We agree to furnish supplementally a copy of such omitted materials to the SEC upon request.

#### ITEM 17. Undertakings.

(a) The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement:

- (i) To include any prospectus required by Section 10(a)(3) of the Securities Act;
- (ii) To reflect in the prospectus any facts or events arising after the effective date of the Registration Statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the Registration Statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20% change in the maximum aggregate offering price set forth in the "Calculation of Filing Fee Tables" or "Calculation of Registration Fee" table, as applicable, in the effective Registration Statement.
- (iii) To include any material information with respect to the plan of distribution not previously disclosed in the Registration Statement or any material change to such information in the Registration Statement;

provided, however, that paragraphs (a)(1)(i), (ii), and (iii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in the Registration Statement or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of this Registration Statement.



- (2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That, for the purpose of determining liability under the Securities Act to any purchaser:
  - (i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the Registration Statement as of the date the filed prospectus was deemed part of and included in the Registration Statement; and
  - (ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i),(vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.
- (5) That, for the purpose of determining liability of the registrant under the Securities Act to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this Registration Statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:
  - (i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
  - (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
  - (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
  - (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.
- (b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the Registration Statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (c) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

## SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in Salt Lake City, Utah, on September 29, 2023.

### CLENE INC.

By: /s/ Robert Etherington  
Robert Etherington  
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Robert Etherington</u> Robert Etherington	President, Chief Executive Officer, and Director (Principal Executive Officer)	September 29, 2023
<u>/s/ Morgan R. Brown</u> Morgan R. Brown	Chief Financial Officer (Principal Financial and Accounting Officer)	September 29, 2023
<u>*</u> David J. Matlin	Chairman of the Board	September 29, 2023
<u>*</u> Arjun Desai	Director	September 29, 2023
<u>*</u> Jonathon T. Gay	Director	September 29, 2023
<u>*</u> Shalom Jacobovitz	Director	September 29, 2023
<u>*</u> Matthew Kiernan	Director	September 29, 2023
<u>*</u> Vallerie V. McLaughlin	Director	September 29, 2023
<u>*</u> Alison H. Mosca	Director	September 29, 2023
<u>*</u> Reed Neil Wilcox	Director	September 29, 2023

\*By: /s/ Robert Etherington  
Robert Etherington  
Attorney-in-Fact

# Holland & Knight

200 South Orange Avenue, Suite 2600 | Orlando, FL 32801 | T 407.425.8500 | F 407.244.5288  
Holland & Knight LLP | www.hkllaw.com

September 29, 2023

Clene Inc.  
6550 South Millrock Drive, Suite G50  
Salt Lake City, Utah 84121

Re: Clene Inc. – Registration Statement on Form S-3

Ladies and Gentlemen:

We have acted as special counsel for Clene Inc., a Delaware corporation (the “Company”), in connection with the preparation and filing with the Securities and Exchange Commission (the “Commission”) of a Registration Statement on Form S-3 (as amended, the “Registration Statement”), under the Securities Act of 1933, as amended (the “Act”), including a prospectus (the “Prospectus”). The Registration Statement relates to the offer and resale by a selling shareholder of the Company of up to 3,000,000 shares (the “Warrant Shares”) of common stock of the Company, par value \$0.0001 per share (the “Common Stock”), upon exercise of a warrant to purchase Common Stock (the “Warrant”).

Capitalized terms in this opinion letter that are not otherwise defined herein have the meanings ascribed to them in the Registration Statement. This opinion letter is being issued pursuant to the requirements of the Act.

In connection with the foregoing, we have examined certain records of the Company, certificates of public officials and officers of the Company, and such other documents as we have deemed relevant for purposes of the opinion expressed below.

With respect to various factual matters material to the opinion expressed below, we have relied upon certificates and information furnished by public officials and representatives of the Company. We have assumed without inquiry or other investigation: (i) the legal capacity of each natural person executing the agreements described herein; (ii) the full power and authority of each entity other than the Company to execute, deliver and perform such agreements and each document executed and delivered or to be executed and delivered in connection therewith; (iii) the due authorization, execution and delivery by each entity other than the Company of each such agreement and each document executed and delivered or to be executed and delivered by such entity; (iv) that there have been no undisclosed modifications of any provision of any document reviewed by us in connection with the rendering of this opinion letter and no undisclosed prior waiver of any right or remedy contained in any of the documents; (v) the genuineness of each signature; (vi) the completeness of each document submitted to us; (vii) the authenticity of each document reviewed by us as an original; (viii) the conformity to the original of each document reviewed by us as a copy and the authenticity of the original of each document received by us as a copy; (ix) that each certificate or copy of a public record furnished by public officials is accurate, complete and authentic; (x) the valid, legal, binding and enforceable nature of the obligations of all parties under the transaction documents other than the Company; and (xi) that each transaction complies with all tests of good faith, fairness and conscionability required by law.

---

We have also assumed that prior to the issuance of the Warrant Shares: (i) the Registration Statement, and any amendments thereto (including post-effective amendments), will have become effective and such effectiveness shall not have been terminated or rescinded; and (ii) after the issuance of any Warrant Shares, the total number of issued shares of Common Stock, together with the total number of shares of Common Stock reserved for issuance upon the exercise, exchange or conversion, as the case may be, of any exercisable, exchangeable or convertible security, as the case may be, then outstanding, will not exceed the total number of authorized shares of Common Stock under the Company's Certificate of Incorporation (the "Certificate of Incorporation").

Based upon the foregoing and subject to the assumptions, limitations, qualifications and exceptions set forth herein, we are of the opinion that when the Warrant Shares are issued and delivered upon exercise of the Warrant in accordance with the terms and conditions of the Warrant and following payment of the exercise price in accordance with the terms and conditions of the Warrant, the Warrant Shares will be duly authorized, validly issued, fully paid, and non-assessable.

Our opinion is limited to matters governed by the General Corporation Law of the State of Delaware, and we are expressing no opinion as to the effect of the laws of any other jurisdiction or, in the case of Delaware, any other laws, or as to any matters of municipal law or the laws of any local agencies within any state. This opinion letter is rendered as of the date hereof, and we undertake no, and hereby disclaim any, obligation to advise you of any change in any matter set forth herein. Our opinion is limited to the matters stated herein, and no opinion is to be implied or inferred beyond the matters stated herein.

We hereby consent to the filing of this opinion letter as an exhibit to the above-referenced Registration Statement and further consent to the reference to our name under the caption "Legal Matters" in the Prospectus. In giving this consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Act or the rules and regulations of the Commission.

Very truly yours,

HOLLAND & KNIGHT LLP

*/s/ Holland & Knight LLP*

We consent to the incorporation by reference in this Registration Statement No. 333-274651 on Form S-3 of our report dated March 13, 2023 relating to the financial statements of Clene Inc. appearing in the Annual Report on Form 10-K of Clene Inc. for the year ended December 31, 2022. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ Deloitte & Touche LLP  
Salt Lake City, UT  
September 29, 2023