

Up to \$18,880,000



Clene Inc.

Common Stock

This prospectus supplement supplements, modifies and supersedes, only to the extent indicated herein, certain information contained in our prospectus supplement dated April 28, 2025 (the “First Supplement”) as supplemented by our prospectus supplement no. 1 dated July 3, 2025 (the “Second Supplement”) and prospectus supplement no. 2 dated September 5, 2025 (the “Third Supplement,” and together with the First Supplement and Second Supplement, the “Prior Supplements”), which together with the accompanying prospectus dated April 25, 2025, contained in our Registration Statement on Form S-3 (Registration No. 333-286058) (the “Base Prospectus”), relating to the sale of shares of common stock, par value \$0.0001 per share, of Clene Inc., from time to time through Canaccord Genuity LLC (“Canaccord”) acting as our sales agent pursuant to the terms of the equity distribution agreement dated April 28, 2025 (the “Equity Distribution Agreement”) by and between us and Canaccord.

This prospectus supplement should be read in conjunction with, is not complete without, and may not be delivered or utilized except in connection with, the Prior Supplements and the Base Prospectus, including all supplements thereto and documents incorporated by reference therein. If there is any inconsistency between the information in the Prior Supplements, Base Prospectus and this prospectus supplement, you should rely on the information in this prospectus supplement. Any information that is modified or superseded in the Prior Supplements or Base Prospectus shall not be deemed to constitute a part of the Prior Supplements or Base Prospectus, respectively, except as modified or superseded by this prospectus supplement.

We are no longer subject to the sales limitations of General Instruction I.B.6 of Form S-3 with respect to our Registration Statement on Form S-3 (Registration No. 333-286058) of which the Prior Supplements, as amended by this prospectus supplement, form a part.

Under the Equity Distribution Agreement we may issue and sell shares of our common stock having an aggregate gross sales price of up to \$25,000,000 from time to time through Canaccord acting as sales agent. In accordance with the terms of the Equity Distribution Agreement, we are filing this prospectus supplement to supplement and amend, as of October 17, 2025, the maximum aggregate gross sales price of our common stock that may be offered, issued and sold under the Equity Distribution Agreement. Accordingly, we may offer and sell shares of our common stock having a maximum aggregate gross sales price of up to \$18,880,000 from time to time through Canaccord, which does not include the shares of our common stock having a maximum aggregate gross sales price of \$6,119,859 that were sold pursuant to the Prior Supplements to date.

Sales of our common stock, if any, under this prospectus supplement may be deemed to be an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended (the “Securities Act”). Canaccord is not required to sell any specific number or dollar amount of securities, but will act as our sales agent and use commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us, consistent with its normal trading and sales practices, on mutually agreed terms between us and Canaccord. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Canaccord will be entitled to a commission of up to 3.0% of the gross sales price per share of common stock sold under the Equity Distribution Agreement. In connection with the sale of our common stock on our behalf, Canaccord will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of Canaccord will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Canaccord with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended (the “Exchange Act”).

You should read this prospectus supplement, the Prior Supplements, the Base 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 symbols “CLNN” and “CLNNW,” respectively. On October 15, 2025, the last reported sale price of our common stock and public warrants on Nasdaq was \$8.89 and \$0.0102, respectively.

Investing in our securities involves a high degree of risk. See “Risk Factors” section on page S-10 of the First Supplement and other risk factors contained in any applicable prospectus supplement and in the documents incorporated by reference herein and therein.

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

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

Canaccord Genuity

The date of this prospectus supplement is October 17, 2025.