PROSPECTUS SUPPLEMENT (To Prospectus dated April 26, 2022 and Prospectus Supplement dated April 26, 2022)

December 20, 2022

Up to \$50,000,000



Clene Inc.

Common Stock

This prospectus supplement (the "Supplement") supplements the prospectus supplement (the "Prospectus Supplement"), dated April 26, 2022, providing for the offer and sale of shares of our common stock, par value \$0.0001 per share, having an aggregate offering price of up to \$50,000,000 from time to time through the agents named therein. Sales of our common stock, if any, under this Supplement, the Prospectus Supplement and the base prospectus will be made by any method that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended. This Supplement should be read in conjunction with the Prospectus Supplement, the base prospectus, and any additional prospectus supplement or amendment.

This Supplement is being filed to reflect the amendment of the equity distribution agreement with Canaccord Genuity LLC and Oppenheimer & Co. Inc., pursuant to which the offering is being conducted, to remove Oppenheimer & Co. Inc.

Accordingly, each reference in the Prospectus Supplement to the term "agents" or "sales agents" is hereby amended to remove Oppenheimer & Co. Inc.

In addition, the list of agents on the front cover of the Prospectus Supplement is hereby amended and restated as follows:

Canaccord Genuity

In addition, the list of agents on the back cover of the Prospectus Supplement is hereby amended and restated as follows:

Canaccord Genuity