

PROSPECTUS SUPPLEMENT
To Prospectus dated February 7, 2025

Up to 12,146,988 Shares of Common Stock
Up to 9,098,727 Shares of Common Stock Issuable Upon Exercise of Warrants
Up to 46,717,980 Shares of Common Stock Issuable Upon Conversion of Notes

Adagio Medical Holdings, Inc.

This prospectus supplement updates and supplements the information contained in the prospectus dated February 7, 2025 (as may be supplemented or amended from time to time, the “Prospectus”), which forms part of our registration statement on Form S-1 (File No. 333-284266) with the information contained in our Current Report on Form 8-K that was filed with the Securities and Exchange Commission on October 15, 2025 (the “Current Report”). Accordingly, we have attached the Current Report to this prospectus supplement.

The Prospectus and this prospectus supplement relate to the offer, sale or other disposition from time to time of up to 67,963,695 shares of our common stock, \$0.0001 par value per share (the “Common Stock”), by the selling stockholders named in the Prospectus or their permitted transferees (collectively, the “selling stockholders”), consisting of (i) up to 7,951,913 shares of Common Stock (excluding the shares of Common Stock underlying the PIPE Warrants (as defined below)) (the “PIPE Shares”) and 110,000 shares of Common Stock (the “Registration Delay Shares”) issued pursuant to the terms of the Convert Waivers (as defined below), (ii) up to 670,000 shares of Common Stock issuable upon exercise of pre-funded warrants to purchase shares (the “Pre-Funded Warrant Shares”) of Common Stock, with an exercise price of \$0.01 per share (the “Pre-Funded Warrants”), (iii) up to 7,528,727 shares of Common Stock (the “PIPE Warrant Shares”) issuable upon exercise of warrants to purchase shares of Common Stock, with an exercise price of \$10.00 per share (the “PIPE Warrants”), in each of cases (i) through (iii), issued pursuant to those certain amended and restated subscription agreements, dated July 31, 2024 (the “Subscription Agreements”), by and among us, ARYA Sciences Acquisition Corp IV, a Cayman Islands exempted company (“ARYA”), and certain selling stockholders named therein (the “PIPE Investors”) at an effective price of approximately \$7.10 per PIPE Share and/or Pre-Funded Warrant, (iv) up to 46,717,980 shares of Common Stock (excluding the shares of Common Stock underlying the Convert Warrants (as defined below)) (the “Convertible Note Shares”) issuable upon the conversion of those certain 13% senior secured convertible notes, with a conversion price of \$10.00 per share, subject to adjustment as provided in the Convertible Security Subscription Agreement (as defined below), (the “Convert Notes”), (v) up to 900,000 shares of Common Stock (the “Convert Warrant Shares”) issuable upon exercise of warrants to purchase shares of Common Stock, with an exercise price of \$24.00 per share, subject to adjustment as provided in such warrants (the “Convert Warrants” and, together with the PIPE Warrants, the “Warrants”), in each of cases (iv) and (v), issued pursuant to that certain securities purchase agreement, dated February 13, 2024, by and among us and certain investors named therein (the “Convert Investors”), and any assignment thereunder (the “Convertible Security Subscription Agreement”), and that certain note purchase agreement, dated February 13, 2024, by and among us, Adagio Medical, Inc., a Delaware corporation, and Perceptive Life Sciences Master Fund, Ltd, a Cayman Islands exempted company (the “2024 Bridge Financing Note Subscription Agreement”), (vi) up to 2,354,100 shares issued to ARYA Sciences Holdings IV, a Cayman Islands exempted company (the “Sponsor”), consisting of 499,000 shares of Common Stock that were initially issued to Sponsor in a private placement as Class A ordinary shares of ARYA at a price of \$10.00 per share and exchanged for shares of Common Stock at Closing (as defined below) (the “Sponsor Class A Conversion Shares”), 1,500,000 shares of Common Stock that were initially issued to Sponsor as Class B ordinary shares of ARYA at an effective price of approximately \$0.007 per share and exchanged for shares of Common Stock at Closing (the “Sponsor Class B Conversion Shares”), and 355,100 shares of Common Stock that were originally issued to Sponsor as Class A ordinary shares of ARYA upon the conversion of certain convertible promissory notes issued by ARYA at an effective price of \$10.00 per share and exchanged for shares of Common Stock at Closing (the “Sponsor Working Capital Shares”), (vii) up to 582,475 shares of Common Stock, consisting of 492,475 shares of Common Stock issued to certain of our affiliates as consideration in connection with the Business Combination (as defined below) at an equity consideration value of approximately \$9.23 per share and 30,000 shares of Common Stock issued to each of Michael Henderson, Todd Wider and Leslie Trigg (collectively, the “Independent ARYA Directors”), which were originally issued as Class B ordinary shares of ARYA, valued at approximately \$0.007 per share, (viii) up to 1,147,500 shares of Common Stock issuable to the Sponsor that are subject to share trigger price vesting and will vest if, prior to the tenth anniversary of the Closing, the post-Closing share price of Common Stock equals or exceeds \$24.00 per share for any 20 trading days within any 30 trading day period (the “Share Trigger Price Vesting”), which were originally issued as Class B ordinary shares of ARYA, valued at approximately \$0.007 per share and exchanged for shares of Common Stock at Closing; and (ix) 1,000 shares of Common Stock issuable upon exercise of certain stock options assumed by us in connection with the consummation of the Business Combination held by our Chief Operating Officer with an exercise price of \$1.67 per share.

You should read this prospectus supplement in conjunction with the Prospectus. This prospectus supplement is qualified by reference to the Prospectus except to the extent that the information in this prospectus supplement supersedes the information contained in the Prospectus. This prospectus supplement is not complete without, and may not be delivered or utilized except in connection with, the Prospectus. If there is any inconsistency between the information in the Prospectus and this prospectus supplement, you should rely on the information in this prospectus supplement. Terms used in this prospectus supplement but not defined herein shall have the meanings given to such terms in the Prospectus.

Our Common Stock is listed on The Nasdaq Capital Market under the symbol “ADGM”. On October 14, 2025, the last reported sales price of our Common Stock was \$1.71 per share.

We are an “emerging growth company” as defined under U.S. federal securities laws and, as such, have elected to comply with reduced public company reporting requirements. This prospectus complies with the requirements that apply to an issuer that is an emerging growth company.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described in the section titled “Risk Factors” beginning on page 15 of the prospectus, and under similar headings in any amendments or supplements to the prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities, or passed upon the accuracy or adequacy of the prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus supplement is October 15, 2025.
