
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

ORUKA THERAPEUTICS, INC.
(Exact Name of Registrant as Specified in Its Charter)**Delaware**
(State or Other Jurisdiction of
Incorporation or Organization)**36-3855489**
(I.R.S. Employer
Identification Number)**855 Oak Grove Avenue**
Suite 100
Menlo Park, CA 94025
(650) 606-7910
(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)**Paul Quinlan**
General Counsel and Corporate Secretary
Oruka Therapeutics, Inc.
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Suite 100
Menlo Park, CA 94025
(650) 606-7910
(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent For Service)*Copies to:*
Alan F. Denenberg
Elizabeth W. LeBow
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900 Middlefield Road
Redwood City, CA 94063
(650) 752-2000**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, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐Accelerated filer ☐Non-accelerated filer ☒Smaller reporting company ☒Emerging growth company ☐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, as amended, or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.**

EXPLANATORY NOTE

This registration statement contains two prospectuses:

- a base prospectus, which covers the offering, issuance and sale by the Company of shares of its common stock, preferred stock, depositary shares and/or warrants from time to time in one or more offerings, which together shall have an aggregate offering price not to exceed \$1,000,000,000; and
- a sales agreement prospectus covering the offering, issuance and sale by the Company of up to a maximum aggregate offering price of \$500,000,000 of shares of its common stock that may be issued and sold from time to time under a sales agreement, as amended, or the “Sales Agreement”, with TD Securities (USA) LLC, as sales agent.

The base prospectus immediately follows this explanatory note. The specific terms of any securities to be offered pursuant to the base prospectus will be specified in one or more prospectus supplements to the base prospectus.

The prospectus relating to the Sales Agreement immediately follows the base prospectus. The \$500,000,000 of shares of the Company’s common stock that may be offered, issued and sold pursuant to the Sales Agreement and under the sales agreement prospectus is included in the \$1,000,000,000 of securities that may be offered, issued and sold by the Company under the base prospectus. Upon termination of the Sales Agreement, any portion of the \$500,000,000 included in the sales agreement prospectus that is not sold pursuant to the Sales Agreement will be available for sale in other offerings pursuant to the base prospectus and corresponding prospectus supplements, and if no shares are sold under the Sales Agreement, the full \$1,000,000,000 of securities may be sold in other offerings pursuant to the base prospectus and corresponding prospectus supplements.

Upon effectiveness of this registration statement, no further offers or sales will be made pursuant to our prior Registration Statements on Form S-3 (Registration Nos. 333-294852 and 333-290718).

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities or accept an offer to buy these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting offers to buy these securities in any state where such offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED AUGUST 21, 2026

PROSPECTUS



\$1,000,000,000

Common Stock
Preferred Stock
Depositary Shares
Warrants

From time to time, Oruka Therapeutics, Inc. may offer and sell up to an aggregate amount of \$1,000,000,000 of any combination of the securities described in this prospectus, either individually or in combination with other securities in one or more offerings. We may also offer common stock upon conversion of preferred stock or common stock or preferred stock upon the exercise of warrants.

Our common stock is listed on the Nasdaq Global Market under the symbol “ORKA.” On August 20, 2026, the last reported sale price of our common stock was \$104.86 per share. If we decide to seek a listing of any securities offered by this prospectus, the applicable prospectus supplement will disclose the exchange or market on which such securities will be listed, if any, or where we have made an application for listing, if any.

The securities may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers or through a combination of methods, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled “Plan of Distribution” in this prospectus. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

This prospectus describes some of the general terms that may apply to the offered securities. The specific terms of any securities to be offered will be described in supplements to this prospectus, which may also add, update or change information contained in this prospectus. You should read this prospectus and the applicable prospectus supplement carefully before you make an investment decision.

Investing in our securities involves a high degree of risk. See “Risk Factors” on page 2 of this prospectus and in the documents incorporated by reference into this prospectus or any applicable prospectus supplement.

This prospectus may not be used to sell securities unless accompanied by a prospectus supplement.

Neither the Securities and Exchange Commission 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 , 2026.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission (the “SEC”) using a “shelf” registration process. Under this shelf process, we may, from time to time, sell any combination of the securities described in this prospectus in one or more offerings.

This prospectus provides you with a general description of the securities that we may offer. Each time we sell securities, we will provide a prospectus supplement that contains specific information about the terms of that offering, including the specific amounts, prices and terms of the securities offered. The prospectus supplement may also add information to this prospectus or update or change information in this prospectus. If there is any inconsistency between the information in this prospectus and any prospectus supplement, you should rely on the information in the prospectus supplement. You should read carefully this prospectus and any prospectus supplement together with the additional information described under the heading “Where You Can Find More Information and “Incorporation of Certain Information by Reference.” We have not authorized anyone to provide you with different or additional information. We are not making an offer to sell these securities in any jurisdiction where the offer or sale of these securities is not permitted. You should assume that the information in this prospectus or any prospectus supplement, as well as the information incorporated by reference herein or therein, is accurate only as of the date of the documents containing the information. Our business, financial condition, results of operations and prospects may have changed since those dates.

Unless the context indicates otherwise, as used in this prospectus and the documents incorporated by reference herein, the terms “Oruka,” “ARCA biopharma, Inc.,” “the Company,” “we,” “us,” and “our” refer to Oruka Therapeutics, Inc., a Delaware corporation, and its consolidated subsidiaries taken as a whole.

This prospectus contains trade names, trademarks and service marks of others, which are the property of their respective owners. Solely for convenience, trademarks and trade names referred to in this prospectus may appear without the ® or TM symbols.

ORUKA THERAPEUTICS, INC.

We are a clinical-stage biopharmaceutical company focused on developing novel monoclonal antibody therapeutics for psoriasis (“PsO”) and other inflammatory and immunology (“I&I”) indications. Our name is derived from *or*, for “skin,” and *arukah*, for “restoration,” and reflects our mission to deliver therapies for chronic skin diseases that provide patients the most possible freedom from their condition. Our strategy is to apply antibody engineering and format innovations to validated modes of action, which we believe will enable us to improve meaningfully upon the efficacy and dosing regimens of standard-of-care medicines while significantly reducing technical and biological risk. Our programs aim to treat and potentially modify disease by targeting mechanisms with proven efficacy and safety involved in disease pathology and the activity of pathogenic tissue-resident memory T cells.

Our lead program, ORKA-001, is designed to target the p19 subunit of interleukin-23 for the treatment of PsO. Our co-lead program, ORKA-002, is designed to target interleukin-17A and interleukin-17F for the treatment of PsO, hidradenitis suppurativa, psoriatic arthritis, and other conditions. The product candidates in these programs each bind their respective targets at high affinity and incorporate half-life extension technology with the aim to increase exposure and decrease dosing frequency. We are also developing ORKA-004, a novel extended half-life antibody designed to target TNF-like ligand 1A (“TL1A”), which we plan to pursue in combination with ORKA-001 and ORKA-002 in a variety of diseases. We believe that our focused strategy, differentiated portfolio, and deep expertise position us to set a new treatment standard in large I&I markets with continued unmet need.

Our principal executive offices are located at 855 Oak Grove Avenue, Suite 100, Menlo Park, California 94025. The telephone number of our principal executive offices is (650) 606-7910. Our website address is www.orukatz.com. Information contained on, or accessible through, our website is not incorporated by reference into this prospectus. We file our annual, quarterly and current reports, proxy statements and other information with the SEC. We make our periodic and current reports available on our website, free of charge, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. Our filings with the SEC are also available to the public on the SEC’s website at www.sec.gov. Our common stock is traded on The Nasdaq Global Market under the symbol “ORKA.”

RISK FACTORS

Investing in our securities involves a high degree of risk. Before acquiring any offered securities pursuant to this prospectus, you should carefully consider the information contained or incorporated by reference in this prospectus or in any accompanying prospectus supplement, including, without limitation, the risk factors described under “Risk Factors” in our most recent Annual Report on Form 10-K for the year ended December 31, 2025 and our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2026 and June 30, 2026, which are incorporated herein by reference (as such risk factors may be updated in our other filings with the SEC pursuant to Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act), and the risk factors described in any applicable prospectus supplement before making an investment decision. The occurrence of any of these risks might cause you to lose all or a part of your investment in the offered securities. See “Where You Can Find More Information” and “Special Note Regarding Forward-Looking Statements” included elsewhere in this prospectus.

USE OF PROCEEDS

We will set forth in the prospectus supplement our intended use for the net proceeds received from the sale of any securities. We will retain broad discretion over the use of the net proceeds from the sale of the securities offered by this prospectus.

DESCRIPTION OF CAPITAL STOCK

General

The following description summarizes the material terms of our capital stock, as well as other material terms of certain provisions of the Delaware General Corporation Law (the “DGCL”), our second amended and restated certificate of incorporation (“Certificate of Incorporation”) and amended and restated bylaws (“Bylaws”), both of which have been filed with the SEC, and are incorporated by reference herein. See “Where You Can Find More Information” for information on how to obtain copies. This summary does not purport to be complete and is qualified in its entirety by the provisions of our Certificate of Incorporation and Bylaws. We encourage you to read our Certificate of Incorporation, our Bylaws, and the applicable provisions of the DGCL for more information.

Our authorized capital stock consists of 545,000,000 shares of common stock, \$0.001 par value per share, and 5,000,000 shares of preferred stock, \$0.001 par value per share (“Preferred Stock”), of which 251,504 shares have been designated as Series B Preferred Stock, \$0.001 par value per share.

As of June 30, 2026, there were 61,069,887 shares of our common stock and 137,138 shares of Series B Preferred Stock outstanding, and no shares of Series A preferred stock outstanding.

Common Stock

Our Certificate of Incorporation authorizes the issuance of up to 545,000,000 shares of common stock. All outstanding shares of common stock are validly issued, fully paid and nonassessable.

Dividend rights

Subject to preferences that may apply to any shares of Preferred Stock outstanding at the time, the holders of our common stock are entitled to receive dividends out of funds legally available if our board of directors (“Board”), in its discretion, determines to issue dividends and then only at the times and in the amounts that our Board may determine.

Voting rights

Pursuant to our Bylaws, holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders. We have not provided for cumulative voting for the election of directors in our Certificate of Incorporation. Accordingly, pursuant to our Certificate of Incorporation, holders of a majority of the shares of our common stock are able to elect all of our directors. Our Certificate of Incorporation establishes a classified Board, divided into three classes with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms.

No preemptive or similar rights

Our common stock is not entitled to preemptive rights, and is not subject to conversion, redemption or sinking fund provisions.

Right to receive liquidation distributions

Upon our liquidation, dissolution or winding-up, the assets legally available for distribution to our stockholders would be distributable ratably among the holders of our common stock and any participating Preferred Stock outstanding at that time, subject to prior satisfaction of all outstanding debt and liabilities and the preferential rights of and the payment of liquidation preferences, if any, on any outstanding shares of Preferred Stock.

Preferred Stock

Under the terms of our Certificate of Incorporation, our Board is authorized, subject to limitations prescribed by Delaware law, to issue up to 5,000,000 shares of Preferred Stock in one or more series, to establish from time to time the number of shares to be included in each series and to fix the designation, powers, preferences and rights of the shares of each series and any of their qualifications, limitations or restrictions, in each case without further vote or action by our stockholders. Subject to any certificates of designation, the Board can also increase or decrease the number of shares of any series of Preferred Stock, but not below the number of shares of that series then outstanding, without any further vote or action by our stockholders. Our Board may authorize the issuance of Preferred Stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of our common stock. The issuance of Preferred Stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in control of our company and might adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock. We issued shares of our Series A Preferred Stock and shares of our Series B Preferred Stock in connection with the Pre-Closing Financing and the Merger, respectively, and have no current plan to issue any additional shares of Preferred Stock. The terms “Pre-Closing Financing” and “Merger,” as used in this section, have the meanings ascribed to them in our Annual Report on Form 10-K for the year ended December 31, 2025, which is incorporated herein by reference. In November 2024, all outstanding shares of Series A Preferred Stock automatically converted into shares of common stock, at which point there were no shares of Series A Preferred Stock left outstanding.

Series B Preferred Stock

Holders of our Series B Preferred Stock are entitled to receive dividends on shares of Series B Preferred Stock equal to, on an as-if-converted-to-common-stock basis, and in the same form as dividends actually paid on shares of our common stock. Except as provided in the Series B Certificate of Designation or as otherwise required by law, the Series B Preferred Stock does not have voting rights. However, as long as any shares of Series B Preferred Stock are outstanding, we will not, without the affirmative vote of the holders of a majority of the then outstanding shares of the Series B Preferred Stock: (a) (i) alter or change adversely the powers, preferences or rights given to the Series B Preferred Stock, (ii) alter or amend the Series B Certificate of Designation, or (iii) amend or repeal any provision of, or add any provision to, our Certificate of Incorporation or Bylaws in a manner that adversely affects any rights of the holders of the Series B Preferred Stock, or file any articles of amendment, certificate of designations, preferences, limitations and relative rights of any series of Preferred Stock, if such action would adversely alter or change the preferences, rights, privileges or powers of, or restrictions provided for the benefit of the Series B Preferred Stock, regardless of whether any of the foregoing actions will be by means of amendment to the Certificate of Incorporation or by merger, consolidation, recapitalization, reclassification, conversion or otherwise, (b) issue further shares of Series B Preferred Stock beyond those issued pursuant to the Merger Agreement or increase or decrease (other than by conversion) the number of authorized shares of Series B Preferred Stock, (c) at any time while at least 30% of the originally issued Series B Preferred Stock remains issued and outstanding, consummate either: (x) any Fundamental Transaction (as defined in the Series B Certificate of Designation) or (y) any merger or consolidation of the Company with or into another entity or any stock sale to, or other business combination in which the stockholders of the Company immediately before such transaction do not hold at least a majority of our capital stock immediately after such transaction, or (d) enter into any agreement with respect to any of the foregoing. The Series B Preferred Stock ranks on parity with the common stock as to the distribution of assets upon any liquidation, dissolution, or winding-up of the Company. Each share of Series B Preferred Stock is convertible at the option of the holder, at any time, and without the payment of additional consideration by the holder. As of June 30, 2026, each outstanding share of Series B Preferred Stock was convertible into common stock at a ratio of approximately 83.3332:1.

Anti-Takeover Provisions

The provisions of Delaware law, our Certificate of Incorporation and our Bylaws could have the effect of delaying, deferring or discouraging another person from acquiring control of our company. These provisions, which are summarized below, may have the effect of discouraging takeover bids. They are also designed, in part, to encourage persons seeking to acquire control of us to negotiate first with our Board. We believe that the benefits of increased protection of our potential ability to negotiate with an unfriendly or unsolicited acquirer outweigh the disadvantages of discouraging a proposal to acquire us because negotiation of these proposals could result in an improvement of their terms.

Delaware law

We are subject to the provisions of Section 203 of the DGCL regulating corporate takeovers. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years following the date on which the person became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding upon consummation of the transaction, excluding for purposes of determining the voting stock outstanding, but not the outstanding voting stock owned by the interested stockholder, (1) shares owned by persons who are directors and also officers and (2) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- at or subsequent to the date of the transaction, the business combination is approved by the board of directors of the corporation and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

Section 203 defines a “business combination” to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an “interested stockholder” as an entity or person who, together with the person’s affiliates and associates, beneficially owns, or within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

Certificate of Incorporation and Bylaw Provisions

Our Certificate of Incorporation and our Bylaws include a number of provisions that could deter hostile takeovers or delay or prevent changes in control of our company, including the following:

- **Board of Directors vacancies.** Our Certificate of Incorporation and Bylaws require that the Board, and not stockholders, fill any directorships that become vacant or are created by an increase in the authorized number of directors by the affirmative vote of a majority of the remaining directors or by the sole remaining director. In addition, pursuant to our Bylaws, the number of directors constituting our Board is permitted to be set only by a resolution adopted by a majority vote of the entire Board. These provisions prevent a stockholder from increasing the size of our Board and then gaining control of the Board by filling the resulting vacancies with its own nominees. This makes it more difficult to change the composition of the Board but promotes continuity of management.
- **Classified board.** Our Certificate of Incorporation provides that our Board is classified into three classes of directors, each with staggered three-year terms. A third party may be discouraged from making a tender offer or otherwise attempting to obtain control of us as it is more difficult and time consuming for stockholders to replace a majority of the directors on a classified board of directors.
- **Stockholder action; special meetings of stockholders.** Our Certificate of Incorporation and Bylaws provide that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. As a result, a holder controlling a majority of our capital stock would not be able to amend our Bylaws or remove directors without holding a meeting of our stockholders called in accordance with our Bylaws. Further, our Bylaws provide that special meetings of stockholders may be called only by the Board, thus prohibiting a stockholder from calling a special meeting. These provisions might delay the ability of our stockholders to force consideration of a proposal or for stockholders controlling a majority of our capital stock to take any action, including the removal of directors.
- **Advance notice requirements for stockholder proposals and director nominations.** Our Bylaws provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders or to nominate candidates for election as directors at our annual meeting of stockholders. Our Bylaws also specify certain requirements regarding the form and content of a stockholder's notice. These provisions might preclude our stockholders from bringing matters before our annual meeting of stockholders or from making nominations for directors at our annual meeting of stockholders if the proper procedures are not followed. We expect that these provisions might also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.
- **No cumulative voting.** The DGCL provides that stockholders are not entitled to the right to cumulate votes in the election of directors unless a corporation's certificate of incorporation provides otherwise. Our Certificate of Incorporation and Bylaws do not provide for cumulative voting.
- **Directors removed only for cause.** Our Bylaws provide that stockholders may remove directors only for cause, and only by the affirmative vote of the holders of at least 66 2/3% of the voting power of the stock outstanding and entitled to vote generally in the election of directors.
- **Amendment of charter provisions.** Any amendment of the above provisions in our Certificate of Incorporation requires approval by holders of at least two-thirds of our outstanding common stock.

- **Issuance of Preferred Stock.** Our Board has the authority, without further action by the stockholders, to issue up to 5,000,000 shares of Preferred Stock with rights and preferences, including voting rights, designated from time to time by our Board. The existence of authorized but unissued shares of Preferred Stock enables our Board to render more difficult or to discourage an attempt to obtain control of us by merger, tender offer, proxy contest or other means.
- **Choice of forum.** Our Certificate of Incorporation and Bylaws provide that the Court of Chancery of the State of Delaware is the sole and exclusive forum for any complaint asserting any internal corporate claims. In addition, our Bylaws also provide that the federal district courts of the United States are the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. These choice of forum provisions would not apply to suits brought to enforce any liability or duty created by the Securities Act or the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. To the extent that any such claims may be based upon federal law claims, Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. Although our Certificate of Incorporation and Bylaws contains the choice of forum provision described above, it is possible that a court could rule that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock and Series B Preferred Stock is Computershare Trust Company, N.A. The transfer agent's address is 150 Royall Street, Suite 101, Canton, MA 02021, and its telephone number is (800) 344-5128.

Exchange Listing

Our common stock is listed on The Nasdaq Global Market under the symbol "ORKA."

DESCRIPTION OF DEPOSITARY SHARES

We may issue depositary shares representing fractional interests in shares of our preferred stock of any series. The following description sets forth certain general terms and provisions of the depositary shares to which any prospectus supplement may relate. The particular terms of the depositary shares to which any prospectus supplement may relate and the extent, if any, to which the general terms and provisions may apply to the depositary shares so offered will be described in the applicable prospectus supplement. To the extent that any particular terms of the depositary shares, depositary agreements and depositary receipts described in a prospectus supplement differ from any of the terms described below, then the terms described below will be deemed to have been superseded by that prospectus supplement. We encourage you to read the applicable depositary agreement and depositary receipts for additional information before you decide whether to purchase any of our depositary shares.

In connection with the issuance of any depositary shares, we will enter into a depositary agreement with a bank or trust company, as depositary, which will be named in the applicable prospectus supplement. Depositary shares will be evidenced by depositary receipts issued pursuant to the related depositary agreement. Immediately following our issuance of the security related to the depositary shares, we will deposit the shares of our preferred stock with the relevant depositary and will cause the depositary to issue, on our behalf, the related depositary receipts. Subject to the terms of the depositary agreement, each owner of a depositary receipt will be entitled, in proportion to the fractional interest in the share of preferred stock represented by the related depositary share, to all the rights, preferences and privileges of, and will be subject to all of the limitations and restrictions on, the preferred stock represented by the depositary receipt (including, if applicable, dividend, voting, conversion, exchange, redemption, sinking fund, subscription and liquidation rights).

DESCRIPTION OF WARRANTS

We may issue warrants to purchase preferred stock or common stock. We may issue warrants independently or together with other securities. Warrants sold with other securities may be attached to or separate from the other securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and the investor(s) or a warrant agent.

The prospectus supplement relating to any warrants we offer will include specific terms relating to the offering. These terms may include some or all of the following, and such terms may differ from those described herein:

- the title of such warrants;
- the aggregate number of such warrants;
- the price or prices at which such warrants will be issued;
- the currency or currencies, including composite currencies, in which the price of such warrants may be payable;
- the designation and terms of the securities purchasable upon exercise of such warrants and the number of such securities issuable upon exercise of such warrants;
- the price at which and the currency or currencies, including composite currencies, in which the securities purchasable upon exercise of such warrants may be purchased;
- the date on which the right to exercise such warrants shall commence and the date on which such right will expire;
- whether such warrants will be issued in registered form or bearer form;
- if applicable, the minimum or maximum amount of such warrants which may be exercised at any one time;
- if applicable, the designation and terms of the securities with which such warrants are issued and the number of such warrants issued with each such security;
- if applicable, the date on and after which such warrants and the related securities will be separately transferable;
- information with respect to book-entry procedures, if any; and
- any other terms of such warrants, including terms, procedures and limitations relating to the exchange and exercise of such warrants.

The description in the prospectus supplement will not necessarily be complete and will be qualified in its entirety by reference to the applicable warrant agreement, which will be filed with the SEC.

PLAN OF DISTRIBUTION

We may offer and sell the securities being offered hereby in one or more of the following ways from time to time:

- to underwriters or dealers for resale to the public or to institutional investors;
- directly to institutional investors;
- directly to a limited number of purchasers or to a single purchaser;
- through agents to the public or to institutional investors; or
- through a combination of any of these methods of sale.

The prospectus supplement with respect to each series of securities will state the terms of the offering of the securities, including:

- the offering terms, including the name or names of any underwriters, dealers or agents;
- the purchase price of the securities and the net proceeds to be received by us from the sale;
- any underwriting discounts or agency fees and other items constituting underwriters' or agents' compensation;
- any public offering price;
- any discounts or concessions allowed or reallocated or paid to dealers; and
- any securities exchange on which the securities may be listed.

If we use underwriters or dealers in the sale, the securities will be acquired by the underwriters or dealers for their own account and may be resold from time to time in one or more transactions, including:

- privately negotiated transactions;
- at a fixed public offering price or prices, which may be changed;
- in "at the market offerings" within the meaning of Rule 415(a)(4) of the Securities Act;
- at prices related to prevailing market prices; or
- at negotiated prices.

Any initial public offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time.

If underwriters are used in the sale of any securities, the securities may be offered either to the public through underwriting syndicates represented by managing underwriters, or directly by underwriters. Generally, the underwriters' obligations to purchase the securities will be subject to certain conditions precedent. The underwriters will be obligated to purchase all of the securities if they purchase any of the securities.

We 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 short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of common shares, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of common shares. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be identified in the applicable prospectus supplement or a post-effective amendment to this registration statement.

If indicated in an applicable prospectus supplement, we may sell the securities through agents from time to time. The applicable prospectus supplement will name any agent involved in the offer or sale of the securities and any commissions we pay to them. Generally, any agent will be acting on a best efforts basis for the period of its appointment. We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase the securities from us at the public offering price set forth in the applicable prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The delayed delivery contracts will be subject only to those conditions set forth in the applicable prospectus supplement, and the applicable prospectus supplement will set forth any commissions we pay for solicitation of these delayed delivery contracts.

Offered securities may also be offered and sold, if so indicated in the applicable prospectus supplement, in connection with a remarketing upon their purchase, in accordance with a redemption or repayment pursuant to their terms, or otherwise, by one or more remarketing firms, acting as principals for their own accounts or as agents for us. Any remarketing firm will be identified and the terms of its agreements, if any, with us and its compensation will be described in the applicable prospectus supplement.

Agents, underwriters and other third parties described above may be entitled to indemnification by us against certain civil liabilities under the Securities Act, or to contribution with respect to payments which the agents or underwriters may be required to make in respect thereof. Agents, underwriters and such other third parties may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

Each series of securities will be a new issue of securities and will have no established trading market, other than our common stock, which is listed on the Nasdaq Global Market. Any common stock sold will be listed on the Nasdaq Global Market, upon official notice of issuance. The securities other than the common stock may or may not be listed on a national securities exchange and no assurance can be given that there will be a secondary market for any such securities or liquidity in the secondary market if one develops. Any underwriters to whom securities are sold by us for public offering and sale may make a market in the securities, but such underwriters will not be obligated to do so and may discontinue any market making at any time without notice.

LEGAL MATTERS

In connection with particular offerings of the securities in the future, unless otherwise stated in the applicable prospectus supplement, the validity of those securities will be passed upon for us by Davis Polk & Wardwell LLP, Redwood City, California. Any underwriters, agents, or dealers will also be advised about legal matters by their own counsel, which will be named in the applicable prospectus supplement.

EXPERTS

The financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2025 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus and any prospectus supplement is part of the registration statement that we filed with the SEC under the Securities Act and does not contain all the information set forth or incorporated by reference in the registration statement. You should review the information and exhibits in the registration statement for further information on us and the securities that we are offering. We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website at www.sec.gov that contains reports, proxy and information statements and other information we have filed electronically with the SEC. These reports, proxy statements and other information can also be read on our website at www.orukatx.com. Information contained on, or accessible through, our website is not incorporated by reference into this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to “incorporate by reference” information into this prospectus and any accompanying prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus and any accompanying prospectus supplement, except for any information superseded by information contained directly in this prospectus, any accompanying prospectus supplement or any subsequently filed document deemed incorporated by reference. This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that we have previously filed with the SEC:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2025, filed with the SEC on March 12, 2026;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2026 and June 30, 2026, filed with the SEC on [May 13, 2026](#) and [August 10, 2026](#), respectively;
- our Definitive Proxy Statement on [Schedule 14A](#) filed with the SEC on April 17, 2026 (solely with respect to those portions incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2025);
- our Current Reports on Form 8-K, filed with the SEC on [April 27, 2026](#), [April 30, 2026](#), [June 1, 2026](#) and [June 4, 2026](#); and
- the description of our capital stock which is contained in [Exhibit 4.1](#) to our Annual Report on [Form 10-K](#) for the year ended December 31, 2025, filed with the SEC on March 12, 2026, including any amendments or reports filed for the purposes of updating such description.

We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed above or filed in the future, that are not deemed “filed” with the SEC, including any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or certain exhibits furnished pursuant to Item 9.01 of Form 8-K. All documents filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of the registration statement of which this prospectus forms a part and prior to its effectiveness and before the termination of the offering of all securities under this prospectus and any prospectus supplement shall also be deemed to be incorporated herein by reference. The most recent information that we file with the SEC automatically updates and supersedes older information. The information contained in any such filing will be deemed to be a part of this prospectus, commencing on the date on which the document is filed.

We will furnish without charge to each person, including any beneficial owner, to whom a prospectus is delivered, upon written or oral request, a copy of any or all of the reports or documents incorporated by reference, including exhibits to these documents. You should direct any requests for documents to:

Oruka Therapeutics, Inc.,
Attention: Corporate Secretary
855 Oak Grove Avenue, Suite 100
Menlo Park, CA 94025
(650) 606-7910.

The documents outlined above are also available on our website at www.orukatx.com. Information contained on, or accessible through, our website is not incorporated by reference in this prospectus.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement, as well as the documents we have filed with the SEC incorporated by reference herein contain “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended (the “Securities Act”) and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). These forward-looking statements reflect our current views with respect to future events and are based on assumptions and subject to known and unknown risks and uncertainties and other factors that may cause our actual results, performance, time frames or achievements to be materially different from any future results, performance, time frames or achievements expressed or implied by the forward-looking statements. We discuss in greater detail, and incorporate by reference into this prospectus in their entirety, many of these risks and uncertainties under the section titled “Risk Factors” contained in the applicable prospectus supplement, in any free writing prospectus we may authorize for use in connection with a specific offering, and in our most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC. We caution readers that any forward-looking statement is not a guarantee of future performance and that actual results could differ materially from those contained in the forward-looking statement. These statements are based on current expectations of future events. You should evaluate all forward-looking statements made in this prospectus, the applicable prospectus supplement and the documents incorporated by reference herein in the context of these risks and uncertainties. We caution you that the risks, uncertainties and other factors referred to in this prospectus, the applicable prospectus supplement and the documents incorporated by reference herein may not contain all of the risks, uncertainties and other factors that may affect our future results and operations. Moreover, we operate in a very competitive and rapidly changing environment, and new risks and uncertainties emerge from time to time.

All statements, other than statements of historical facts contained in this prospectus, the applicable prospectus supplement and the documents incorporated by reference herein, including, without limitation, statements regarding: our future results of operations and financial position, business strategy, the length of time that we believe our existing cash resources will fund our operations, our market size, our competition, our potential growth opportunities, our clinical development activities and timeline, the efficacy and safety profile of our product candidates, the potential therapeutic benefits and economic value of our product candidates, the timing and results of preclinical studies and clinical trials, the expected impact of macroeconomic conditions, including inflation, increasing interest rates and volatile market conditions, current or potential bank failures, as well as global events, including military conflicts and geopolitical tensions on our operations, and the receipt and timing of potential regulatory designations, approvals and commercialization of product candidates, are forward-looking statements. The words “believe,” “may,” “will,” “potentially,” “estimate,” “continue,” “anticipate,” “predict,” “target,” “intend,” “could,” “would,” “should,” “project,” “plan,” “expect,” and similar expressions that convey uncertainty of future events or outcomes are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements are based on information available to us as of only the date of the document containing the applicable statement and are subject to a number of risks, uncertainties and assumptions. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties, and assumptions, the forward-looking events and circumstances discussed in this prospectus and the documents incorporated by reference herein may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. While we believe that such information provides a reasonable basis for these statements, such information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all relevant information. These statements are inherently uncertain, and investors are cautioned not to unduly rely on these statements.

All subsequent written or oral forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section. We do not undertake any obligation to release publicly any revisions to these forward-looking statements to reflect events or circumstances after the date of this prospectus herein or to reflect the occurrence of unanticipated events, except as may be required under applicable U.S. securities laws. You should read this prospectus, and the applicable prospectus supplement, together with the documents we have filed with the SEC that are incorporated by reference herein, with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect. If we do update one or more forward-looking statements, no inference should be drawn that we will make additional updates with respect to those or other forward-looking statements.

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities or accept an offer to buy these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting offers to buy these securities in any state where such offer or sale is not permitted.

Subject to Completion, Dated August 21, 2026

PROSPECTUS

\$500,000,000



Common Stock

We have entered into a sales agreement, dated October 3, 2025, with TD Securities (USA) LLC (“TD Cowen”), as amended by Amendment No. 1 to the Sales Agreement, dated August 21, 2026, relating to the sale of shares of our common stock, \$0.001 par value per share (as amended, the “Sales Agreement”). In accordance with the terms of the Sales Agreement, under this prospectus, we may offer and sell shares of our common stock having an aggregate offering price of up to \$500,000,000 from time to time through TD Cowen, acting as our agent or principal.

Sales of shares of our common stock, if any, under this prospectus will be made in negotiated transactions, including block trades or block sales, or by any method permitted by law deemed to be an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended (the “Securities Act”), including, without limitation, sales made through The Nasdaq Global Market (“Nasdaq”), or any other existing trading market for our common stock or by any other method permitted by law. TD Cowen is not required to sell any specific number or dollar amount of shares of our common stock, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices.

There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

TD Cowen will be entitled to compensation at a commission rate of up to 3.0% of the gross sales price per share sold under the Sales Agreement. See “Plan of Distribution” beginning on page 9 for additional information regarding the compensation to be paid to TD Cowen.

In connection with the sale of shares of our common stock on our behalf, TD Cowen will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of TD Cowen will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to TD Cowen with respect to certain liabilities, including liabilities under the Securities Act.

Shares of our common stock trade on the Nasdaq Global Market under the symbol “ORKA.” On August 20, 2026, the last reported sale price of our common stock as reported on the Nasdaq Global Market was \$104.86 per share.

Investing in our common stock involves a high degree of risk. See “Risk Factors” beginning on page 3 of this prospectus and in the documents incorporated by reference into this prospectus.

We are a “smaller reporting company” as defined by Rule 12b-2 of the Exchange Act and are subject to reduced public company reporting requirements.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of the securities being offered by this prospectus, or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

TD Cowen

The date of this prospectus is , 2026.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (the “SEC”) using a “shelf” registration process. Under this prospectus, we may offer and sell shares of our common stock having an aggregate offering price of up to \$500,000,000 from time to time through TD Cowen acting as our agent or principal at prices and on terms to be determined by market conditions at the time of the offering. The \$500,000,000 of shares of our common stock that may be sold under this prospectus are included in the \$1,000,000,000 of securities that may be sold under the registration statement.

We provide information to you about this offering of shares of our common stock in two separate documents that are bound together: (1) this prospectus, which describes the specific details regarding this offering; and (2) the accompanying base prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this “prospectus,” we are referring to both documents combined.

Before buying any of the common stock that we are offering, we urge you to carefully read both this prospectus together with all of the information incorporated by reference herein, as well as the additional information described under the headings “Where You Can Find More Information” and “Incorporation of Certain Documents by Reference.” These documents contain important information that you should consider when making your investment decision.

To the extent there is a conflict between the information contained in this prospectus, on the one hand, and the information contained in any document incorporated by reference in this prospectus, on the other hand, you should rely on the information in this prospectus, provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document filed after the date of this prospectus incorporated by reference in this prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

We have not, and TD Cowen has not, authorized anyone to provide any information other than that contained in or incorporated by reference in this prospectus supplement. We and TD Cowen take no responsibility for, and can provide no assurance as to, the reliability of any other information that others may give you. This prospectus does not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in this prospectus or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information in this prospectus or any prospectus supplement that we have authorized for use in connection with this offering as well as the information incorporated by reference herein or therein is accurate only as of its date. Our business, financial condition, results of operations and prospects may have changed since those dates.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreement, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Unless the context indicates otherwise, as used in this prospectus and the documents incorporated by reference herein, the terms “Oruka,” “ARCA biopharma, Inc.,” “the Company,” “we,” “us,” and “our” refer to Oruka Therapeutics, Inc., a Delaware corporation, and its consolidated subsidiaries taken as a whole.

This prospectus and the documents incorporated by reference herein contain additional trade names, trademarks and service marks of other companies, which are the property of their respective owners. We do not intend our use or display of other companies’ trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents we have filed with the SEC incorporated by reference herein contain “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). These forward-looking statements reflect our current views with respect to future events and are based on assumptions and subject to known and unknown risks and uncertainties and other factors that may cause our actual results, performance, time frames or achievements to be materially different from any future results, performance, time frames or achievements expressed or implied by the forward-looking statements. We discuss in greater detail, and incorporate by reference into this prospectus in their entirety, many of these risks and uncertainties under the section titled “Risk Factors” contained in our most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC. We caution readers that any forward-looking statement is not a guarantee of future performance and that actual results could differ materially from those contained in the forward-looking statement. These statements are based on current expectations of future events. You should evaluate all forward-looking statements made in this prospectus and the documents incorporated by reference herein in the context of these risks and uncertainties. We caution you that the risks, uncertainties and other factors referred to in this prospectus and the documents incorporated by reference herein may not contain all of the risks, uncertainties and other factors that may affect our future results and operations. Moreover, we operate in a very competitive and rapidly changing environment, and new risks and uncertainties emerge from time to time.

All statements, other than statements of historical facts contained in this prospectus and the documents incorporated by reference herein, including, without limitation, statements regarding: our future results of operations and financial position, business strategy, the length of time that we believe our existing cash resources will fund our operations, our market size, our competition, our potential growth opportunities, our clinical development activities and timeline, the efficacy and safety profile of our product candidates, the potential therapeutic benefits and economic value of our product candidates, the timing and results of preclinical studies and clinical trials, the expected impact of macroeconomic conditions, including inflation, increasing interest rates and volatile market conditions, current or potential bank failures, as well as global events, including military conflicts and geopolitical tensions on our operations, and the receipt and timing of potential regulatory designations, approvals and commercialization of product candidates, are forward-looking statements. The words “believe,” “may,” “will,” “potentially,” “estimate,” “continue,” “anticipate,” “predict,” “target,” “intend,” “could,” “would,” “should,” “project,” “plan,” “expect,” and similar expressions that convey uncertainty of future events or outcomes are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements are based on information available to us as of only the date of the document containing the applicable statement and are subject to a number of risks, uncertainties and assumptions. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties, and assumptions, the forward-looking events and circumstances discussed in this prospectus and the documents incorporated by reference herein may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. While we believe that such information provides a reasonable basis for these statements, such information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all relevant information. These statements are inherently uncertain, and investors are cautioned not to unduly rely on these statements.

All subsequent written or oral forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section. We do not undertake any obligation to release publicly any revisions to these forward-looking statements to reflect events or circumstances after the date of this prospectus herein or to reflect the occurrence of unanticipated events, except as may be required under applicable U.S. securities laws. You should read this prospectus, together with the documents we have filed with the SEC that are incorporated by reference herein, with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect. If we do update one or more forward-looking statements, no inference should be drawn that we will make additional updates with respect to those or other forward-looking statements.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus and in the documents we incorporate by reference. This summary does not contain all of the information you should consider before making an investment decision. You should read this entire prospectus carefully, especially the risks related to this offering discussed under “Risk Factors” beginning on page 3 of this prospectus, along with the other risk factors, our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus.

Acquisition of Pre-Merger Oruka

On August 29, 2024 (the “Merger Closing”), we completed our acquisition (the “Merger”) of Oruka Therapeutics, Inc. (“Pre-Merger Oruka”) pursuant to an Agreement and Plan of Merger and Reorganization, dated as of April 3, 2024 (the “Merger Agreement”). Following the transactions contemplated by the Merger Agreement, Pre-Merger Oruka merged with and into Atlas Merger Sub Corp., a wholly owned subsidiary of ARCA biopharma, Inc. (“ARCA”) and following that, Pre-Merger Oruka then merged with and into Atlas Merger Sub II, LLC (“Second Merger Sub”), with Second Merger Sub being the surviving entity. Second Merger Sub changed its corporate name to “Oruka Therapeutics Operating Company, LLC.” Pre-Merger Oruka was a pre-clinical stage biotechnology company that was incorporated on February 6, 2024 under the direction of Peter Harwin, a Managing Member of Fairmount Funds Management LLC, for the purposes of holding rights to certain intellectual property being developed by Paragon Therapeutics, Inc. On August 29, 2024, we changed our name from “ARCA biopharma, Inc.” to “Oruka Therapeutics, Inc.” and our Nasdaq ticker symbol from “ABIO” to “ORKA”.

Company Overview

We are a clinical-stage biopharmaceutical company focused on developing novel monoclonal antibody therapeutics for psoriasis (“PsO”) and other inflammatory and immunology (“I&I”) indications. Our name is derived from *or*, for “skin,” and *arukah*, for “restoration,” and reflects our mission to deliver therapies for chronic skin diseases that provide patients the most possible freedom from their condition. Our strategy is to apply antibody engineering and format innovations to validated modes of action, which we believe will enable us to improve meaningfully upon the efficacy and dosing regimens of standard-of-care medicines while significantly reducing technical and biological risk. Our programs aim to treat and potentially modify disease by targeting mechanisms with proven efficacy and safety involved in disease pathology and the activity of pathogenic tissue-resident memory T cells.

Our lead program, ORKA-001, is designed to target the p19 subunit of interleukin-23 for the treatment of PsO. Our co-lead program, ORKA-002, is designed to target interleukin-17A and interleukin-17F for the treatment of PsO, hidradenitis suppurativa, psoriatic arthritis, and other conditions. The product candidates in these programs each bind their respective targets at high affinity and incorporate half-life extension technology with the aim to increase exposure and decrease dosing frequency. We are also developing ORKA-004, a novel extended half-life antibody designed to target TNF-like ligand 1A (“TL1A”), which we plan to pursue in combination with ORKA-001 and ORKA-002 in a variety of diseases. We believe that our focused strategy, differentiated portfolio, and deep expertise position us to set a new treatment standard in large I&I markets with continued unmet need.

Corporate Information

Our principal executive offices are located at 855 Oak Grove Avenue, Suite 100, Menlo Park, California 94025. The telephone number of our principal executive offices is (650) 606-7910. Our website address is www.orukatx.com. Information contained on, or accessible through, our website is not incorporated by reference into this prospectus. We file our annual, quarterly and current reports, proxy statements and other information with the SEC. We make our periodic and current reports available on our website, free of charge, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. Our filings with the SEC are also available to the public on the SEC’s website at www.sec.gov. Our common stock is traded on The Nasdaq Global Market under the symbol “ORKA.”

This prospectus contains trade names, trademarks and service marks of others, which are the property of their respective owners. Solely for convenience, trademarks and trade names referred to in this prospectus may appear without the ® or TM symbols.

Implications of Being a Smaller Reporting Company

As of the date of this prospectus, we are a “smaller reporting company” as defined in the Exchange Act, meaning that we are permitted to rely on exemptions from certain disclosure and other requirements that are applicable to other public companies that are not smaller reporting companies. Smaller reporting companies may take advantage of certain scaled disclosures, including, among other things, providing only two years of audited financial statements in their Annual Report on Form 10-K, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and having reduced disclosure obligations regarding executive compensation. Based on the market value of our stock held by non-affiliates as of the end of the second quarter of our 2026 fiscal year, we will no longer be able to benefit from smaller reporting company status for filings or disclosure for periods beginning on or after January 1, 2027. However, until such filings, we are permitted and intend to rely on the exemptions from certain disclosure and other requirements that are applicable to smaller reporting companies.

The Offering

Common Stock Offered by Us	Shares of common stock having an aggregate offering price of up to \$500,000,000.
Common Stock to be Outstanding After this Offering	Up to 65,838,149 shares of common stock, assuming sales of 4,768,262 shares of our common stock in this offering at an offering price of \$104.86 per share, which was the last reported sale price of our common stock on Nasdaq on August 20, 2026. The actual number of shares issued will vary depending on the actual sales price of shares sold pursuant to this offering.
Plan of Distribution	“At the market offering” that may be made from time to time through TD Cowen. TD Cowen is not required to sell any specific number or dollar amount of shares of our common stock, but TD Cowen will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices. See “Plan of Distribution.”
Use of Proceeds	We currently intend to use the net proceeds from this offering for general corporate purposes, including research and development and working capital. See “Use of Proceeds” for a more complete description of the intended use of proceeds from this offering.
Nasdaq Global Market Symbol	“ORKA.”
Risk Factors	Investing in our common stock involves significant risks. You should read the “Risk Factors” section of this prospectus, as well as those risks and uncertainties identified in the documents incorporated by reference in this prospectus, including our most recent Annual Report on Form 10-K and subsequent Quarterly Reports on Form 10-Q, for a discussion of factors to consider carefully before deciding to purchase our common stock.

The number of issued and outstanding shares of common stock to be outstanding after this offering is based on 61,069,887 shares of our common stock outstanding as of June 30, 2026, and excludes:

- 11,428,149 shares of common stock issuable upon the conversion of 137,138 shares of Series B Preferred Stock outstanding as of June 30, 2026;
- 5,706,188 shares of common stock issuable upon the exercise of pre-funded warrants outstanding as of June 30, 2026;
- 5,227,356 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2026 under the 2024 Equity Incentive Plan and the 2024 Stock Incentive Plan with a weighted-average exercise price of \$20.64 per share;
- 971,930 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2026 with a weighted-average exercise price of \$23.55 per share issued in connection with the Paruka Warrant Obligation (as defined in our Annual Report on Form 10-K);
- 409,922 shares of common stock issuable upon the vesting of restricted stock units outstanding as of June 30, 2026;
- 2,619,353 shares of common stock issuable upon the exercise of employee warrants outstanding as of June 30, 2026 with a weighted-average exercise price of \$7.80 per share;
- 1,499,500 shares of common stock sold under our previous at-the-market equity offering program with TD Securities (USA) LLC subsequent to June 30, 2026;
- 5,910,376 shares of common stock reserved for issuance under our 2024 Stock Incentive Plan as of June 30, 2026; and
- 963,033 shares of common stock reserved for issuance under the Employee Stock Purchase Plan as of June 30, 2026.

RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks described below and discussed under the sections captioned “Risk Factors” contained in our most recent Annual Report on Form 10-K, as well as in any of our subsequent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K filed with the SEC, which are incorporated by reference in this prospectus in their entirety, together with other information in this prospectus and the information and documents incorporated by reference in this prospectus. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment. There may be additional risks that we do not presently know of or that we currently believe are immaterial which could also impair our business and financial position. Please also read carefully the section titled “Special Note Regarding Forward-Looking Statements.”

Risks Related to This Offering

We will have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, if any, and could spend the net proceeds in ways that do not improve our business, financial condition or results of operations or enhance the value of our common stock. You may not agree with our decisions, and our use of the proceeds may not yield any return on your investment. We currently intend to use the net proceeds from this offering for general corporate purposes, including research and development and working capital.

Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. You will not have the opportunity to influence our decisions on how to use the net proceeds from this offering. The failure by our management to apply these funds effectively could result in financial losses that could harm our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value. See “Use of Proceeds.”

If you purchase shares of common stock in this offering, you may suffer immediate and substantial dilution of your investment.

The shares sold in this offering will be sold from time to time at various prices. The price per share of our common stock sold in this offering may, at the time of sale, exceed the net tangible book value per share of our common stock outstanding prior to this offering. Therefore, if you purchase shares of our common stock in this offering, you may pay a price per share that substantially exceeds our net tangible book value per share after this offering. To the extent that shares of Series B Preferred Stock are converted into shares of common stock, warrants are exercised, options are exercised, restricted stock units vest, new options or restricted stock units are issued under our equity incentive plans, or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering.

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

To raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

The actual number of any shares we may issue and gross proceeds resulting from those sales, at any one time or in total, is uncertain.

Subject to certain limitations in the Sales Agreement and compliance with applicable law, we have the discretion to deliver a sale order to TD Cowen at any time throughout the term of the Sales Agreement. The number of shares that are sold by TD Cowen after the delivery of any sale order will fluctuate based on the market price of our common stock during the same period and limits we set with TD Cowen in any order to sell shares, and the demand for our common stock during the sale period. Because the price per share of each share sold will fluctuate based on the market price of our common stock during the sale period, it is not possible at this stage to predict the gross proceeds to be raised in connection with those sales or the number of shares, if any, that will be ultimately issued.

The common stock offered hereby will be sold in “at the market offerings,” and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices and numbers of shares sold, and subject to the final determination by our board of directors or any restrictions we may place in any applicable sale order, there is no minimum or maximum sales price. Investors may experience a decline in the value of their shares as a result of sales made at prices lower than the prices they paid.

We do not anticipate that we will pay any cash dividends in the foreseeable future.

We do not anticipate that we will pay any cash dividends in the foreseeable future. The current expectation is that we will retain our future earnings, if any, to fund the development and growth of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain, if any, for the foreseeable future.

Sales of a significant number of shares of our common stock in the public markets, or the perception that such sales could occur, could depress the market price of our common stock.

Sales of a substantial number of shares of our common stock in the public markets, or the perception that such sales could occur, could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. In addition, certain entities beneficially own a significant percentage of our Company. As of July 1, 2026, entities affiliated with Fairmount Funds Management LLC beneficially own approximately 16.9 million shares of our common stock, or approximately 22.8% of our common stock, assuming the exercise of all pre-funded warrants and options held by such entities, and the conversion of all outstanding shares of Series B Preferred Stock held by such entities into shares of common stock, without giving effect to contractual limitations contained in such securities that restrict the holder (together with its affiliates) from beneficially owning in excess of a specified percentage of our common stock, and without giving effect to the exercise or conversion of any securities exercisable or convertible into common stock owned by other stockholders. It is possible that we could issue and sell additional shares of our common stock in the public markets. We cannot predict the effect that future sales of our common stock, or the perception that such sales might occur, would have on the market price of our common stock.

Shares of our common stock that are subject to our outstanding options or warrants will become eligible for sale in the public market to the extent permitted by the provisions of various vesting agreements and Rules 144 and 701 under the Securities Act.

Moreover, certain holders of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares. Registration of these shares under the Securities Act would result in the shares becoming freely tradeable in the public market, subject to the restriction of Rule 144 in the case of our affiliates. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$500,000,000 from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that we will sell any shares under or fully utilize the Sales Agreement as a source of financing.

We currently intend to use the net proceeds from this offering for general corporate purposes, including research and development and working capital. Pending these uses, we intend to invest the net proceeds in short- and intermediate-term, investment grade interest-bearing securities.

DILUTION

Dilution is the amount by which the price paid by the purchasers of the shares of common stock sold in this offering exceeds the net tangible book value per share of common stock after the offering. Net tangible book value per share is determined by subtracting our total liabilities from the total book value of our tangible assets and dividing the difference by the number of shares of common stock deemed to be outstanding at that date.

Our historical net tangible book value as of June 30, 2026 was \$1,114.5 million, or \$18.25 per share.

After giving effect to the issuance and sale of 4,768,262 shares of common stock in this offering based on an assumed public offering price of \$104.86 per share, which is the last reported sale price of our common stock on the Nasdaq Global Market on August 20, 2026, after deducting offering commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2026 would have been \$1,599.2 million, or \$24.29 per share. This represents an immediate increase in as adjusted net tangible book value of \$6.04 per share to our existing stockholders and immediate dilution of \$80.57 per share to new investors purchasing common stock in this offering.

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

Assumed public offering price per share		\$	104.86
Historical net tangible book value per share as of June 30, 2026	\$	18.25	
Increase per share attributable to new investors		<u>6.04</u>	
As adjusted net tangible book value per share after giving effect to this offering			24.29
Dilution in adjusted net tangible book value per share to new investors		<u>\$</u>	<u>80.57</u>

The table above assumes for illustrative purposes that an aggregate of 4,768,262 shares of our common stock are sold during the term of the Sales Agreement at a price of \$104.86 per share, the last reported sale price of our common stock on the Nasdaq Global Market on August 20, 2026, for aggregate gross proceeds of \$500.0 million. The shares subject to the Sales Agreement with TD Cowen are being sold from time to time at various prices. An increase of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$104.86 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$500.0 million during the term of the Sales Agreement with TD Cowen is sold at that price, would increase our adjusted net tangible book value per share after the offering to \$24.31 per share and would increase the dilution in net tangible book value per share to new investors in this offering to \$81.55 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$104.86 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$500.0 million during the term of the Sales Agreement with TD Cowen is sold at that price, would decrease our adjusted net tangible book value per share after the offering to \$24.27 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to \$79.59 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only and will adjust based on the actual public offering price, the actual number of shares that we offer in this offering, and other terms of this offering determined at the time of each offer and sale.

To the extent that shares of Series B Preferred Stock are converted into shares of common stock, warrants are exercised, options are exercised, restricted stock units vest, new options or restricted stock units are issued under our equity incentive plans, or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering.

The number of issued and outstanding shares of common stock to be outstanding after this offering is based on 61,069,887 shares of our common stock outstanding as of June 30, 2026, and excludes:

- 11,428,149 shares of common stock issuable upon the conversion of 137,138 shares of Series B Preferred Stock outstanding as of June 30, 2026;
- 5,706,188 shares of common stock issuable upon the exercise of pre-funded warrants outstanding as of June 30, 2026;
- 5,227,356 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2026 under the 2024 Equity Incentive Plan and the 2024 Stock Incentive Plan with a weighted-average exercise price of \$20.64 per share;
- 971,930 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2026 with a weighted-average exercise price of \$23.55 per share issued in connection with the Paruka Warrant Obligation (as defined in our Annual Report on Form 10-K);
- 409,922 shares of common stock issuable upon the vesting of restricted stock units outstanding as of June 30, 2026;
- 2,619,353 shares of common stock issuable upon the exercise of employee warrants outstanding as of June 30, 2026 with a weighted-average exercise price of \$7.80 per share;
- 1,499,500 shares of common stock sold under our at-the-market equity offering program with TD Securities (USA) LLC subsequent to June 30, 2026;
- 5,910,376 shares of common stock reserved for issuance under our 2024 Stock Incentive Plan as of June 30, 2026; and
- 963,033 shares of common stock reserved for issuance under the Employee Stock Purchase Plan as of June 30, 2026.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and future earnings, if any, to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future. Any future determination to pay cash dividends will be at the discretion of our board of directors, subject to applicable limitations under Delaware law, and will be dependent upon our results of operations, financial condition, contractual restrictions and other factors deemed relevant by our board of directors.

PLAN OF DISTRIBUTION

We have entered into a Sales Agreement with TD Cowen, under which we may offer and sell from time to time shares of common stock through or to TD Cowen as our sales agent or principal. Pursuant to this prospectus, we may offer and sell up to \$500,000,000 of shares of our common stock. Sales of our common stock, if any, will be made in negotiated transactions, including block trades or block sales, or by any method permitted by law deemed to be an “at the market offering” as defined in Rule 415(a)(4) under the Securities Act, including without limitation sales made through Nasdaq or on any other existing trading market for our common stock, or by any other method permitted by law. Sales pursuant to the Sales Agreement may be made through an affiliate of TD Cowen.

TD Cowen will offer our common stock subject to the terms and conditions of the Sales Agreement on a daily basis or as otherwise agreed upon by us and TD Cowen. We will designate the maximum amount of common stock to be sold through TD Cowen on a daily basis or otherwise determine such maximum amount together with TD Cowen. Subject to the terms and conditions of the Sales Agreement, TD Cowen will use its commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us. We may instruct TD Cowen not to sell common stock if the sales cannot be effected at or above the price designated by us in any such instruction. TD Cowen or we may suspend the offering of our common stock being made through TD Cowen under the Sales Agreement upon proper notice to the other party. TD Cowen and we each have the right, by giving written notice as specified in the Sales Agreement, to terminate the Sales Agreement in each party’s sole discretion at any time.

The aggregate compensation payable to TD Cowen as sales agent is a commission rate of up to 3.0% of the gross sales price of the shares sold through it pursuant to the sales agreement. We have also agreed to reimburse TD Cowen up to \$75,000 of TD Cowen’s actual outside legal expenses incurred by TD Cowen in connection with the original execution of the Sales Agreement, in addition to amounts for certain ongoing disbursements of its legal counsel. We estimate that the total expenses of the offering payable by us, excluding commissions payable to TD Cowen under the Sales Agreement, will be approximately \$380,000.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of such common stock.

TD Cowen will provide written confirmation to us following the close of trading on The Nasdaq Global Market on each day in which common stock is sold through it as sales agent under the Sales Agreement. Each confirmation will include the number of shares of common stock sold through it as sales agent on that day, the volume weighted average price of the shares sold, the percentage of the daily trading volume and the net proceeds to us.

We will report at least quarterly the number of shares of common stock sold through TD Cowen under the Sales Agreement and the net proceeds to us in connection with the sales of common stock.

Settlement for sales of common stock will occur, unless the parties agree otherwise, on the first business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sales of our common stock on our behalf, TD Cowen will be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation paid to TD Cowen will be deemed to be underwriting commissions or discounts. We have agreed in the Sales Agreement to provide indemnification and contribution to TD Cowen against certain liabilities, including liabilities under the Securities Act. As sales agent, TD Cowen will not engage in any transactions that stabilizes our common stock.

Our common stock is listed on The Nasdaq Global Market and trades under the symbol “ORKA.” The transfer agent of our common stock is Computershare Trust Company, N.A.

TD Cowen and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received and, may in the future receive, customary fees.

LEGAL MATTERS

The validity of the common stock being offered by this prospectus will be passed upon for us by Davis Polk & Wardwell LLP, Redwood City, California. TD Securities (USA) LLC is being represented in connection with this offering by Cooley LLP, New York, New York.

EXPERTS

The financial statements incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2025 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at www.orukatx.com. Information contained on, or accessible through, our website is not incorporated by reference into this prospectus.

This prospectus is part of a registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all of the information set forth or incorporated by reference in the registration statement. You should review the information and exhibits in the registration statement for further information on us and our consolidated subsidiaries and the securities we are offering. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements.

INCORPORATION OF CERTAIN DOCUMENTS 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, except for any information superseded by information contained directly in this prospectus, or any subsequently filed document deemed incorporated by reference. This prospectus supplement incorporates by reference the documents set forth below that we have previously filed with the SEC:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2025, filed with the SEC on March 12, 2026;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2026 and June 30, 2026, filed with the SEC on [May 13, 2026](#) and [August 10, 2026](#), respectively;
- our Definitive Proxy Statement on [Schedule 14A](#) filed with the SEC on April 17, 2026 (solely with respect to those portions incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2025);
- our Current Reports on Form 8-K, filed with the SEC on [April 27, 2026](#), [April 30, 2026](#), [June 1, 2026](#) and [June 4, 2026](#); and
- the description of our capital stock which is contained in [Exhibit 4.1](#) to our Annual Report on [Form 10-K](#) for the year ended December 31, 2025, filed with the SEC on March 12, 2026, including any amendments or reports filed for the purposes of updating such description.

We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed above or filed in the future, that are not deemed “filed” with the SEC, including any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or certain exhibits furnished pursuant to Item 9.01 of Form 8-K. All documents filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of this prospectus and before the termination of the offering shall also be deemed to be incorporated herein by reference. The most recent information that we file with the SEC automatically updates and supersedes older information. The information contained in any such filing will be deemed to be a part of this prospectus, commencing on the date on which the document is filed.

We will furnish without charge to each person, including any beneficial owner, to whom a prospectus is delivered, upon written or oral request, a copy of any or all of the reports or documents incorporated by reference, including exhibits to these documents. You should direct any requests for documents to:

Oruka Therapeutics, Inc.,
Attention: Corporate Secretary
855 Oak Grove Avenue, Suite 100
Menlo Park, CA 94025
(650) 606-7910.

The documents outlined above are also available on our website at www.orukatx.com. Information contained on, or accessible through, our website is not incorporated by reference into this prospectus.



\$500,000,000

Common Stock

PROSPECTUS

TD Cowen

, 2026

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth the estimated costs and expenses, other than the underwriting discounts and commissions, payable by the registrant in connection with the issuance and distribution of the securities being registered. All the amounts shown are estimates, except for the SEC registration fee.

	Amount to be Paid
SEC registration fee	\$ 50,410.55*
Stock exchange listing fee	**
Accounting fees and expenses	**
Legal fees and expenses	**
Transfer agent and registrar fees and expenses	**
Printing and miscellaneous expenses	**
Total	\$ **

* The \$1,000,000,000 of securities registered pursuant to this registration statement includes (i) \$299,650,000.00 of unsold securities registered pursuant to the Registration Statement on Form S-3 (File No. 333-294852) declared effective on April 10, 2026 and (ii) \$335,320,666.02 of unsold securities registered pursuant to the Registration Statement on Form S-3 (File No. 333-290718) which became effective pursuant to Section 8(a) under the Act on November 3, 2025 (collectively, the “Unsold Securities”). Pursuant to Rule 415(a)(6) under the Securities Act, the amount of such registration fee associated with the offering of the Unsold Securities will be carried forward to be applied to the Unsold Securities registered under this registration statement and no additional filing fee will be due with respect to the Unsold Securities in connection with the filing of this registration statement.

** These fees cannot be estimated at this time, as they are calculated based on the securities offered and the number of issuances. An estimate of the aggregate expenses in connection with the sale and distribution of the securities being offered will be included in the applicable prospectus supplement.

Item 15. Indemnification of Directors and Officers

Section 145 of the Delaware General Corporation Law provides that a corporation may indemnify directors and officers as well as other employees and individuals against expenses (including attorneys’ fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with any threatened, pending or completed actions, suits or proceedings in which such person is made a party by reason of such person being or having been a director, officer, employee or agent to the Registrant. The Delaware General Corporation Law provides that Section 145 is not exclusive of other rights to which those seeking indemnification may be entitled under any bylaw, agreement, vote of stockholders or disinterested directors or otherwise. Article VI of the Registrant’s Bylaws provides for indemnification by the Registrant of its directors, officers and employees to the fullest extent permitted by the Delaware General Corporation Law.

Section 102(b)(7) of the Delaware General Corporation Law permits a corporation to provide in its certificate of incorporation that a director or officer of the corporation shall not be personally liable to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director or officer, except for liability (i) for any breach of the director’s or officer’s duty of loyalty to the corporation or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) for a director for unlawful payments of dividends or unlawful stock repurchases, redemptions or other distributions, (iv) for any transaction from which the director or officer derived an improper personal benefit or (v) for an officer in any action by or in the right of the corporation. The Registrant’s Certificate of Incorporation provides for such limitation of liability.

The Registrant maintains standard policies of insurance under which coverage is provided (a) to its directors and officers against loss rising from claims made by reason of breach of duty or other wrongful act, and (b) to the Registrant with respect to payments which may be made by the Registrant to such officers and directors pursuant to the above indemnification provision or otherwise as a matter of law.

The Registrant has entered into indemnification agreements with each of its executive officers and directors that provide indemnification under certain circumstances for acts and omissions that may not be covered by any directors' and officers' liability insurance.

Item 16. Exhibits

A list of exhibits filed herewith is contained in the exhibit index that immediately precedes such exhibits and is incorporated herein by reference.

Item 17. Undertakings

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 this 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 this registration statement. Notwithstanding the foregoing, any increase or decrease in the 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 Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and
 - (iii) To include any material information with respect to the plan of distribution not previously disclosed in this registration statement or any material change to such information in this registration statement; *provided, however*, that paragraphs (1)(i), (1)(ii) and (1)(iii) 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 Securities and Exchange Commission by the Registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in this registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is a part of the registration statement.
- (2) That, for purposes of determining liability under the Securities Act of 1933, 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 this offering.
 - (4) That for purposes of determining any liability under the Securities Act of 1933 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 of 1933 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.
- (6) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) 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.
- (7) Insofar as indemnification for liabilities arising under the Securities Act of 1933 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 of 1933 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 a 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 of 1933 and will be governed by the final adjudication of such issue.

EXHIBIT INDEX

Exhibit	Description	Form	Exhibit No.	Filing Date	Filed Herewith
1.1*	Form of Underwriting Agreement				
1.2	Sales Agreement between Oruka Therapeutics, Inc. and TD Securities (USA) LLC, dated October 3, 2025	S-3	1.2	10/3/2025	
1.3	Amendment No. 1 to the Sales Agreement between Oruka Therapeutics, Inc. and TD Securities (USA) LLC, dated August 21, 2026				X
2.1	Agreement and Plan of Merger and Reorganization, dated as of April 3, 2024, by and among ARCA biopharma, Inc., Atlas Merger Sub Corp., Atlas Merger Sub II, LLC and Oruka Therapeutics, Inc.	8-K	2.1	4/3/2024	
3.1	Second Amended and Restated Certificate of Incorporation	8-K	3.5	9/5/2024	
3.2	Amended and Restated Bylaws	8-K	3.6	9/5/2024	
3.3	Form of Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock	S-1/A	3.1(b)	5/24/2013	
3.4	Certificate of Elimination of Series A Convertible Preferred Stock, dated August 29, 2024	8-K	3.8	9/5/2024	
3.5	Certificate of Designation of Preferences, Rights and Limitations of Series B Non-Voting Convertible Preferred Stock	8-K	3.9	9/5/2024	
3.6	Certificate of Designation of Preferences, Rights and Limitations of Series A Non-Voting Convertible Preferred Stock	8-K	3.1	9/13/2024	
4.1	Description of Securities	10-K	4.1	3/12/2026	
4.2	Form of Pre-Funded Warrant, dated August 29, 2024	10-K	4.3	3/6/2025	
4.3	Form of Pre-Funded Warrant, dated September 13, 2024	8-K	4.1	9/13/2024	
4.4	Form of Pre-Funded Warrant, dated September 19, 2025	8-K	4.1	9/22/2025	
4.5	Paruka Warrant, dated December 31, 2024	10-Q	4.5	5/14/2025	
4.5	Paruka Warrant, dated December 12, 2025	10-K	4.6	3/12/2026	
4.7*	Specimen Preferred Stock Certificate and Form of Certificate of Designation of Preferred Stock				
4.8*	Form of Warrant Agreement				
4.9*	Form of Depositary Agreement				
5.1	Opinion of Davis Polk & Wardwell LLP relating to the base prospectus				X
5.2	Opinion of Davis Polk & Wardwell LLP relating to the sales agreement prospectus				X
23.1	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm				X
23.2	Consent of Davis Polk & Wardwell LLP (included in Exhibit 5.1)				X
23.3	Consent of Davis Polk & Wardwell LLP (included in Exhibit 5.2)				X
24.1	Power of Attorney				X
107	Filing Fee Table				X

* To be filed by amendment or as an exhibit to a Current Report on Form 8-K and incorporated herein by reference, if applicable.

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 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 the City of Menlo Park, State of California, on August 21, 2026.

ORUKA THERAPEUTICS, INC.

By: /s/ Lawrence Klein
Name: Lawrence Klein
Title: Chief Executive Officer

POWER OF ATTORNEY

Each person whose signature to this registration statement appears below hereby constitutes and appoints each of Dr. Lawrence Klein and Mr. Arjun Agarwal and each or any one of them, as such person's true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for such person and in such person's name, place and stead, in any and all capacities, to sign any and all amendments to the registration statement, including post-effective amendments, and registration statements filed pursuant to Rule 462 under the Securities Act of 1933, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, and does hereby grant unto each said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as such person might or could do in person, hereby ratifying and confirming all that each said attorney-in-fact and agents or any of them, or their substitutes, may lawfully do or cause to be done by virtue hereof.

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.

Signature	Title	Date
<u>/s/ Lawrence Klein</u> Lawrence Klein	Chief Executive Officer & Director (Principal Executive Officer)	August 21, 2026
<u>/s/ Arjun Agarwal</u> Arjun Agarwal	Senior Vice President, Finance and Treasurer (Principal Financial Officer & Principal Accounting Officer)	August 21, 2026
<u>/s/ Samarth Kulkarni</u> Samarth Kulkarni	Chairman of the Board	August 21, 2026
<u>/s/ Kristine Ball</u> Kristine Ball	Director	August 21, 2026
<u>/s/ Carl Dambkowski</u> Carl Dambkowski	Director	August 21, 2026
<u>/s/ Peter Harwin</u> Peter Harwin	Director	August 21, 2026
<u>/s/ Chris Martin</u> Chris Martin	Director	August 21, 2026

ORUKA THERAPEUTICS, INC.

COMMON STOCK
AMENDMENT NO. 1 TO SALES AGREEMENT

August 21, 2026

TD Securities (USA) LLC
1 Vanderbilt Avenue
New York, New York 10017

Ladies and Gentlemen:

Oruka Therapeutics, Inc., a Delaware corporation (the “**Company**”), and TD Securities (USA) LLC (“**TD Cowen**”), are parties to that certain Sales Agreement dated October 3, 2025 (the “**Original Agreement**”). All capitalized terms not defined herein shall have the meanings ascribed to them in the Original Agreement. The Company and TD Cowen desire to amend the Original Agreement as set forth in this Amendment No. 1 thereto (this “**Amendment**”) as follows:

1. Issuance and Sale of Shares by TD Cowen. Section 1 is hereby amended and restated in its entirety to read as follows:

“**Sale of Placement Shares**.” The Company agrees that, from time to time during the term of this Agreement, on the terms and subject to the conditions set forth herein, it may issue and sell through TD Cowen, acting as agent and/or principal, shares (the “**Placement Shares**”) of the Company’s common stock, par value \$0.001 per share (the “**Common Stock**”) having an aggregate offering price the lesser of (a) the number or dollar amount of Common Stock registered under the effective Registration Statement (defined below) pursuant to which the offering is being made, (b) the number of authorized but unissued Common Stock (less Common Stock issuable upon exercise, conversion or exchange of any outstanding securities of the Company or otherwise reserved from the Company’s authorized capital stock), (c) the number or dollar amount of Common Stock permitted to be sold under Form S-3 (including General Instruction I.B.6 thereof, if applicable), or (d) the number or dollar amount of Common Shares for which the Company has filed a Prospectus (defined below) the “**Maximum Amount**”). Notwithstanding anything to the contrary contained herein, the parties hereto agree that compliance with the limitation set forth in this Section 1 on the number of shares of Common Stock issued and sold under this Agreement shall be the sole responsibility of the Company, and TD Cowen shall have no obligation in connection with such compliance. The issuance and sale of Common Stock through TD Cowen will be effected pursuant to the Registration Statement (as defined below) filed by the Company and after such Registration Statement has been declared effective by the Securities and Exchange Commission (the “**Commission**”), although nothing in this Agreement shall be construed as requiring the Company to use the Registration Statement (as defined below) to issue the Common Stock. The Company acknowledges and agrees that sales of Common Stock under this Agreement may be made through affiliates of TD Cowen, and that TD Cowen may otherwise fulfill its obligations pursuant to this Agreement to or through an affiliated broker-dealer.

The Company shall file, in accordance with the provisions of the Securities Act of 1933, as amended, and the rules and regulations thereunder (collectively, the “**Securities Act**”), with the Commission a registration statement on Form S-3, including a base prospectus, relating to certain securities, including the Common Stock, to be issued from time to time by the Company, and which incorporates by reference documents that the Company has filed or will file in accordance with the provisions of the Securities Exchange Act of 1934, as amended, and the rules and regulations thereunder (collectively, the “**Exchange Act**”). The Company has prepared a prospectus specifically relating to the Placement Shares (the “**ATM Prospectus**”) to the base prospectus included as part of such registration statement, and shall, if necessary, prepare a prospectus supplement specifically relating to the Placement Shares (the “**Prospectus Supplement**”) to the base prospectus included as part of such registration statement. The Company shall furnish to TD Cowen, for use by TD Cowen, copies of the prospectus included as part of such registration statement, as supplemented by the Prospectus Supplement, if any, relating to the Placement Shares. The Company may file one or more additional registration statements from time to time that will contain a base prospectus and related prospectus or prospectus supplement, if applicable with respect to the Placement Shares. Except where the context otherwise requires, such registration statement, and any post-effective amendment thereto, as amended when it became or becomes effective, including all documents filed as part thereof or incorporated by reference therein, and including any information contained in a Prospectus (as defined below) subsequently filed with the Commission pursuant to Rule 424(b) under the Securities Act or deemed to be a part of such registration statement pursuant to Rule 430B or 462(b) of the Securities Act, or any subsequent registration statement on Form S-3 filed pursuant to Rule 415(a)(6) under the Securities Act by the Company to cover any Placement Shares, is herein called the “**Registration Statement**.” Any registration statement and amendments thereto filed pursuant to Rule 462(b) of the Securities Act and relating to the offering covered by the Registration Statement is herein called a “**Rule 462(b) Registration Statement**” and, after such filing, the “Registration Statement” shall include any Rule 462(b) Registration Statement. The base prospectus, including all documents incorporated therein by reference, included in the Registration Statement, as it may be supplemented by the ATM Prospectus and the Prospectus Supplement, if any, in the form in which such prospectus, ATM Prospectus and/or Prospectus Supplement have most recently been filed by the Company with the Commission pursuant to Rule 424(b) under the Securities Act, together with any “issuer free writing prospectus,” as defined in Rule 433 under the Securities Act (“**Rule 433**”), relating to the Placement Shares that (i) is consented to by TD Cowen, hereinafter referred to as a “**Permitted Free Writing Prospectus**,” (ii) is required to be filed with the Commission by the Company or (iii) is exempt from filing pursuant to Rule 433(d)(5)(i), in each case in the form filed or required to be filed with the Commission or, if not required to be filed, in the form retained in the Company’s records pursuant to Rule 433(g), is herein called the “**Prospectus**.” Any reference herein to the Registration Statement, the Prospectus or any amendment or supplement thereto shall be deemed to refer to and include the documents incorporated by reference therein, and any reference herein to the terms “amend,” “amendment” or “supplement” with respect to the Registration Statement or the Prospectus shall be deemed to refer to and include the filing after the execution hereof of any document with the Commission deemed to be incorporated by reference therein. For purposes of this Agreement, all references to the Registration Statement, the Prospectus or to any amendment or supplement thereto shall be deemed to include any copy filed with the Commission pursuant to the Electronic Data Gathering Analysis and Retrieval System (“**EDGAR**”). The Company’s obligations under this Agreement to furnish, provide, deliver or make available (and all other similar references) copies of any document shall be deemed satisfied if the same is filed with the Commission through EDGAR.

2. **Certain Definitions.** All references in the Original Agreement to the “Agreement” shall mean the Original Agreement as amended by this Amendment; *provided, however*, that all references to “date of this Agreement” in the Original Agreement shall continue to refer to the date of the Original Agreement, unless amended otherwise herein and except with respect to the first paragraph of **Section 6**, where references to the “date of this Agreement” in the Original Agreement shall refer to each of the date of the Original Agreement and the date of this Amendment.

3. Agreement Heading. The reference to “\$200,000,000” in the heading of the Original Agreement shall be removed.

4. Original Agreement Remains in Effect. Except as specifically set forth herein, all other provisions of the Original Agreement shall remain in full force and effect.

5. Entire Agreement. This Amendment, together with the Original Agreement (including all schedules and exhibits attached hereto and thereto), constitutes the entire agreement and supersedes all other prior and contemporaneous agreements and undertakings, both written and oral, among the parties hereto with regard to the subject matter hereof. Neither this Amendment nor any term hereof may be amended except pursuant to a written instrument executed by the Company and TD Cowen. In the event that any one or more of the provisions contained herein, or the application thereof in any circumstance, is held invalid, illegal or unenforceable as written by a court of competent jurisdiction, then such provision shall be given full force and effect to the fullest possible extent that it is valid, legal and enforceable, and the remainder of the terms and provisions herein shall be construed as if such invalid, illegal or unenforceable term or provision was not contained herein, but only to the extent that giving effect to such provision and the remainder of the terms and provisions hereof shall be in accordance with the intent of the parties as reflected in this Amendment.

6. Governing Law. This Amendment shall be governed by, and construed in accordance with, the internal laws of the State of New York without regard to the principles of conflicts of laws. Each party hereby irrevocably submits to the non-exclusive jurisdiction of the state and federal courts sitting in the City of New York, borough of Manhattan, for the adjudication of any dispute hereunder or in connection with any transaction contemplated hereby, and hereby irrevocably waives, and agrees not to assert in any suit, action or proceeding, any claim that it is not personally subject to the jurisdiction of any such court, that such suit, action or proceeding is brought in an inconvenient forum or that the venue of such suit, action or proceeding is improper. Each party hereby irrevocably waives personal service of process and consents to process being served in any such suit, action or proceeding by mailing a copy thereof (certified or registered mail, return receipt requested) to such party at the address in effect for notices to it under this Amendment and agrees that such service shall constitute good and sufficient service of process and notice thereof. Nothing contained herein shall be deemed to limit in any way any right to serve process in any manner permitted by law.

7. Counterparts. This Amendment may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Delivery of an executed Amendment by one party to the other may be made by facsimile transmission or other electronic transmission (including portable document format (PDF) or any electronic signature complying with the U.S. federal ESIGN Act of 2000, Uniform Electronic Transactions Act, the Electronic Signatures and Records Act or other applicable law, e.g., www.docusign.com).

[Remainder of Page Intentionally Blank]

If the foregoing correctly sets forth the understanding between the Company and TD Cowen, please so indicate in the space provided below for that purpose, whereupon this Amendment shall constitute a binding agreement between the Company and TD Cowen.

Very truly yours,

TD SECURITIES (USA) LLC

By: /s/ Michael Murphy
Name: Michael Murphy
Title: Managing Director

**ACCEPTED as of the date
first-above written:**

For and on behalf of
ORUKA THERAPEUTICS, INC.

By: /s/ Lawrence Klein
Name: Lawrence Klein
Title: President and Chief Executive Officer

[Signature Page to Amendment No. 1 to Sales Agreement]

Davis Polk

Davis Polk & Wardwell LLP
900 Middlefield Road
Redwood City, CA 94063
davispolk.com

August 21, 2026

Oruka Therapeutics, Inc.
855 Oak Grove Avenue, Suite 100
Menlo Park, CA 94025

Ladies and Gentlemen:

Oruka Therapeutics, Inc. a Delaware corporation (the “**Company**”) is filing with the Securities and Exchange Commission a Registration Statement on Form S-3 (the “**Registration Statement**”) for the purpose of registering under the Securities Act of 1933, as amended (the “**Securities Act**”), (a) shares of common stock, par value \$0.001 per share (the “**Common Stock**”) of the Company; (b) shares of preferred stock, par value \$0.001 per share (the “**Preferred Stock**”) of the Company; (c) warrants of the Company (the “**Warrants**”), which may be issued under one or more warrant agreements (each, a “**Warrant Agreement**”) to be entered into between the Company, investors, and/or the warrant agent to be named therein (the “**Warrant Agent**”); and (d) depositary shares representing fractional interests in shares or multiple shares of the Preferred Stock (the “**Depositary Shares**”), which may be issued under one or more preferred stock depositary agreements (each, a “**Depositary Agreement**”) to be entered into between the Company and the preferred stock depositary to be named therein (the “**Depositary**”).

We, as your counsel, have examined originals or copies of such documents, corporate records, certificates of public officials and other instruments as we have deemed necessary or advisable for the purpose of rendering this opinion.

In rendering the opinions expressed herein, we have, without independent inquiry or investigation, assumed that (i) all documents submitted to us as originals are authentic and complete, (ii) all documents submitted to us as copies conform to authentic, complete originals, (iii) all documents filed as exhibits to the Registration Statement that have not been executed will conform to the forms thereof, (iv) all signatures on all documents that we reviewed are genuine, (v) all natural persons executing documents had and have the legal capacity to do so, (vi) all statements in certificates of public officials and officers of the Company that we reviewed were and are accurate and (vii) all representations made by the Company as to matters of fact in the documents that we reviewed were and are accurate.

Based upon the foregoing, and subject to the additional assumptions and qualifications set forth below, we advise you that, in our opinion:

1. When the necessary corporate action on the part of the Company has been taken to authorize the issuance and sale of such shares of Common Stock proposed to be sold by the Company, and when such shares of Common Stock are issued and delivered in accordance with the applicable underwriting or other agreement against payment therefor (in excess of par value thereof) or upon conversion or exercise of any security offered under the Registration Statement (the “**Offered Security**”), in accordance with the terms of such Offered Security or the instrument governing such Offered Security providing for such conversion or exercise as approved by the Board of Directors of the Company, for the consideration approved by such Board of Directors (which consideration is not less than the par value of the Common Stock), such shares of Common Stock will be validly issued, fully-paid and non-assessable.

2. Upon designation of the relative rights, preferences and limitations of any series of Preferred Stock by the Board of Directors of the Company and the proper filing with the Secretary of State of the State of Delaware of a Certificate of Designation relating to such series of Preferred Stock, all necessary corporate action on the part of the Company will have been taken to authorize the issuance and sale of such series of Preferred Stock proposed to be sold by the Company, and when such shares of Preferred Stock are issued and delivered in accordance with the applicable underwriting or other agreement against payment therefor (in excess of par value thereof), such shares of Preferred Stock will be validly issued, fully paid and non-assessable.
3. When the Warrant Agreement to be entered into in connection with the issuance of any Warrants has been duly authorized, executed and delivered by the Company, the investor(s) and/or the Warrant Agent; the specific terms of the Warrants have been duly authorized and established in accordance with the Warrant Agreement; and such Warrants have been duly authorized, executed, issued and delivered in accordance with the Warrant Agreement and the applicable underwriting or other agreement against payment therefor, such Warrants will constitute valid and binding obligations of the Company, enforceable in accordance with their terms, subject to applicable bankruptcy, insolvency and similar laws affecting creditors' rights generally, concepts of reasonableness and equitable principles of general applicability.
4. When the Depositary Agreement to be entered into in connection with the issuance of any Depositary Shares has been duly authorized, executed and delivered by the Depositary and the Company; the specific terms of the Depositary Shares have been duly authorized and established in accordance with the Depositary Agreement; and such Depositary Shares have been duly authorized, executed, issued and delivered in accordance with the Depositary Agreement and the applicable underwriting or other agreement against payment therefor, such Depositary Shares will constitute legal and valid interests in the corresponding shares of Preferred Stock, subject to applicable bankruptcy, insolvency and similar laws affecting creditors' rights generally, concepts of reasonableness and equitable principles of general applicability.

In connection with the opinions expressed above, we have assumed that, at or prior to the time of the delivery of any such security, (i) the Board of Directors of the Company shall have duly established the terms of such security and duly authorized the issuance and sale of such security and such authorization shall not have been modified or rescinded; (ii) the Company is and shall remain, validly existing as a corporation in good standing under the laws of the State of Delaware; (iii) the Registration Statement shall have been declared effective and such effectiveness shall not have been terminated or rescinded; and (iv) the Warrant Agreement and the Depositary Agreement (collectively, the "**Documents**") are each valid, binding and enforceable agreements of each party thereto (other than as expressly covered above in respect of the Company); and (v) there shall not have occurred any change in law affecting the validity or enforceability of such security. We have also assumed that (i) the terms of any security whose terms are established subsequent to the date hereof and the issuance, execution, delivery and performance by the Company of any such security (a) require no action by or in respect of, or filing with, any governmental body, agency or official and (b) do not contravene, or constitute a default under, any provision of applicable law or public policy or regulation or any judgment, injunction, order or decree or any agreement or other instrument binding upon the Company and (ii) any Warrant Agreement will be governed by the laws of the State of New York.

We are members of the Bars of the State of New York and California and the foregoing opinion is limited to the laws of the State of New York and the General Corporation Law of the State of Delaware, except that we express no opinion as to (i) any law, rule or regulation that is applicable to the Company, the Documents or such transactions solely because such law, rule or regulation is part of a regulatory regime applicable to any party to any of the Documents or any of its affiliates due to the specific assets or business of such party or such affiliate or (ii) any law, rule or regulation relating to national security.

We hereby consent to the filing of this opinion as an exhibit to the Registration Statement referred to above and further consent to the reference to our name under the caption "Legal Matters" in the prospectus, which is a part of the Registration Statement. 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 Securities Act.

Very truly yours,

/s/ Davis Polk & Wardwell LLP

August 21, 2026

Davis Polk

Davis Polk & Wardwell LLP
900 Middlefield Road
Redwood City, CA 94063
davispolk.com

August 21, 2026

Oruka Therapeutics, Inc.
855 Oak Grove Avenue, Suite 100
Menlo Park, CA 94025

Ladies and Gentlemen:

We have acted as counsel for Oruka Therapeutics, Inc., a Delaware corporation (the “**Company**”), in connection with the (i) Registration Statement on Form S-3 (the “**Registration Statement**”) filed by the Company on August 21, 2026 with the Securities and Exchange Commission (the “**Commission**”) pursuant to the Securities Act of 1933 and (ii) the prospectus supplement (the “**Prospectus**”) of the Company, filed with the Commission on August 21, 2026, relating to the issuance and sale by the Company of shares of the Company’s common stock, par value \$0.001 per share, having an aggregate offering price of up to \$500,000,000 (the “**Shares**”) in accordance with that certain sales agreement, dated as of October 3, 2025, as amended by Amendment No. 1 to the Sales Agreement, dated as of August 21, 2026 between the Company and TD Securities (USA) LLC as agent (as amended, the “**Sales Agreement**”).

We, as your counsel, have examined originals or copies of such documents, corporate records, certificates of public officials and other instruments as we have deemed necessary or advisable for the purpose of rendering this opinion.

In rendering the opinion expressed herein, we have, without independent inquiry or investigation, assumed that (i) all documents submitted to us as originals are authentic and complete, (ii) all documents submitted to us as copies conform to authentic, complete originals, (iii) all signatures on all documents that we reviewed are genuine, (iv) all natural persons executing documents had and have the legal capacity to do so, (v) all statements in certificates of public officials and officers of the Company that we reviewed were and are accurate and (vi) all representations made by the Company as to matters of fact in the documents that we reviewed were and are accurate.

Based upon the foregoing, we are of the opinion that the Shares to be sold by the Company have been duly authorized and, assuming the terms of any sales of Shares pursuant to the Sales Agreement are approved by the Company’s board of directors or a properly constituted and authorized committee thereof (or any of them delegates such approval to officers and such terms are approved by such officers), when issued and delivered by the Company and paid for (which consideration is not less than the par value of the common stock) pursuant to the Sales Agreement, the Shares will be validly issued, fully paid and non-assessable.

In connection with the opinion expressed above, we have assumed that the Company is validly existing as a corporation in good standing under the laws of the State of Delaware.

We are members of the Bars of the State of New York and California, and the foregoing opinion is limited to the laws of the State of New York and the General Corporation Law of the State of Delaware, except that we express no opinion as to (i) any law, rule or regulation that is applicable to the Company, the Sales Agreement, the Shares or such transactions solely because such law, rule or regulation is part of a regulatory regime applicable to any party to the Sales Agreement or any of its affiliates due to the specific assets or business of such party or such affiliate or (ii) any law, rule or regulation relating to national security.

We hereby consent to the filing of this opinion as an exhibit to the Registration Statement referred to above and further consent to the reference to our name under the caption “Legal Matters” in the prospectus, which is a part of the Registration Statement. 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 Securities Act.

Very truly yours,

/s/ Davis Polk & Wardwell LLP

August 21, 2026

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of Oruka Therapeutics, Inc. of our report dated March 12, 2026 relating to the financial statements, which appears in Oruka Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2025. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
August 21, 2026

Calculation of Filing Fee Tables

S-3

Oruka Therapeutics, Inc.

Table 1: Newly Registered and Carry Forward Securities

☐ Not Applicable

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial Effective Date	Filing Fee Previously Paid in Connection with Unsold Securities to be Carried Forward
Newly Registered Securities												
	Equity	Common Stock, \$0.001 par value per share	457(o)									
	Equity	Preferred Stock, \$0.001 par value per share	457(o)									
	Other	Depository Shares	457(o)									
	Other	Warrants	457(o)									
Fees to be Paid	1 Unallocated (Universal) Shelf		457(o)			\$ 365,029,333.98	0.0001381	\$ 50,410.55				
Fees Previously Paid												
Carry Forward Securities												
Carry Forward Securities	Equity	Common Stock, \$0.001 par value per share	415(a)(6)						S-3	333-290718	11/03/2025	\$ 0.00
Carry Forward Securities	Equity	Preferred Stock, \$0.001 par value per share	415(a)(6)						S-3	333-290718	11/03/2025	\$ 0.00
Carry Forward Securities	Other	Depository Shares	415(a)(6)						S-3	333-290718	11/03/2025	\$ 0.00
Carry Forward Securities	Other	Warrants	415(a)(6)						S-3	333-290718	11/03/2025	\$ 0.00
Carry Forward Securities	2 Other	Unallocated (Universal) Shelf	415(a)(6)			\$ 335,320,666.02			S-3	333-290718	11/03/2025	\$ 46,307.78
Carry Forward Securities	Equity	Common Stock, \$0.001 par value per share	415(a)(6)						S-3	333-294852	04/10/2026	\$ 0.00
Carry Forward Securities	Equity	Preferred Stock, \$0.001 par value per share	415(a)(6)						S-3	333-294852	04/10/2026	\$ 0.00
Carry Forward Securities	Other	Depository Shares	415(a)(6)						S-3	333-294852	04/10/2026	\$ 0.00
Carry Forward Securities	Other	Warrants	415(a)(6)						S-3	333-294852	04/10/2026	\$ 0.00
Carry Forward Securities	3 Other	Unallocated (Universal) Shelf	415(a)(6)			\$ 299,650,000.00			S-3	333-294852	04/10/2026	\$ 41,381.67
Total Offering Amounts:						\$ 1,000,000,000.00		\$ 50,410.55				
Total Fees Previously Paid:								\$ 0.00				
Total Fee Offsets:								\$ 0.00				
Net Fee Due:								\$ 50,410.55				

Offering Note

1

There are being registered hereunder such indeterminate number of shares of common stock, such indeterminate number of shares of preferred stock, such

indeterminate number of depositary shares and such indeterminate number of warrants to purchase preferred stock or common stock as shall have an aggregate initial offering price not to exceed \$1,000,000,000. The securities registered also include such indeterminate number of shares of preferred stock and common stock as may be issued upon exercise of warrants. In addition, pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Act"), the shares being registered hereunder include such indeterminate number of shares of common stock and preferred stock as may be issuable with respect to the shares being registered hereunder as a result of stock splits, stock dividends or similar transactions.

The proposed maximum aggregate offering price per class of security will be determined from time to time by Oruka Therapeutics, Inc. or the Registrant, in connection with the issuance by the Registrant of the securities registered hereunder and is not specified as to each class of security pursuant to Instruction 2.A.iii.b of the Instructions to the Calculation of Filing Fee Tables and Related Disclosure on Form S-3 under the Securities Act.

2

Pursuant to Rule 415(a)(6) under the Securities Act, the securities registered pursuant to this registration statement include (i) \$335,320,666.02 of unsold securities (the "2025 Unsold Securities") previously registered pursuant to the Registration Statement on Form S-3 (File No. 333-290718), which became effective pursuant to Section 8(a) under the Act on November 3, 2025 (the "2025 Registration Statement") and (ii) \$299,650,000.00 of unsold securities (the "2026 Unsold Securities", and together with the 2025 Unsold Securities, the "Unsold Securities") previously registered pursuant to the Registration Statement on Form S-3 (File No. 333-294852), which was declared effective on April 10, 2026 (the "2026 Registration Statement", and together with the 2025 Registration Statement, the "Prior Registration Statements"). The filing fees associated with the offerings of the Unsold Securities are hereby carried forward to be applied to the Unsold Securities registered hereunder. The registrant is also registering new securities under this registration statement with an aggregate initial offering price of \$365,029,333.98 (the "New Securities"), which aggregate offering price is not specified as to each class of securities. A filing fee of \$50,410.55 with respect to the New Securities is being paid in connection with the filing of this registration statement. To the extent that, after the filing date hereof and prior to the effectiveness of this registration statement, the registrant sells any Unsold Securities pursuant to the Prior Registration Statements, the registrant will identify in a pre-effective amendment to this registration statement the updated dollar amount of Unsold Securities from the Prior Registration Statements to be included in this registration statement pursuant to Rule 415(a)(6) and the updated amount of New Securities to be registered on this registration statement. Pursuant to Rule 415(a)(6), the offerings of the Unsold Securities under the Prior Registration Statements will be deemed terminated as of the date of effectiveness of this registration statement.

3

See Offering Note 2.

Table 2: Fee Offset Claims and Sources

☒Not Applicable

		Registrant or Filer Name	Form or Filing Type	File Number	Initial Filing Date	Filing Date	Fee Offset Claimed	Security Type Associated with Fee Offset Claimed	Security Title Associated with Fee Offset Claimed	Unsold Securities Associated with Fee Offset Claimed	Unsold Aggregate Offering Amount Associated with Fee Offset Claimed	Fee Paid with Fee Offset Source
Rules 457(b) and 0-11(a)(2)												
Fee Offset Claims												
Fee Offset Sources												
Rule 457(p)												
Fee Offset Claims												
Fee Offset Sources												

Table 3: Combined Prospectuses

☒Not Applicable

	Security Type	Security Class Title	Amount of Securities Previously Registered	Maximum Aggregate Offering Price of Securities Previously Registered	Form Type	File Number	Initial Effective Date
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