

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 August 27, 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		<u>24.29</u>
Dilution in adjusted net tangible book value per share to new investors	\$	<u><u>80.57</u></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](#), [June 4, 2026](#) and [August 24, 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

August 27, 2026
