Filed Pursuant to Rule 424b(5)
Registration No. 333-290777

PROSPECTUS SUPPLEMENT
(to Prospectus dated October 8, 2025)

Zenas BioPharma, Inc.

Up to $200,000,000

Common Stock

We have previously entered into an Open Market Sale Agreement℠, or the Sales Agreement, dated October 8, 2025, with Jefferies LLC, or Jefferies, as sales agent, relating to the sale of shares of our common stock, par value $0.0001 per share, or the shares of common stock. We previously filed a prospectus supplement on October 8, 2025, relating to the offer and sale of shares of our common stock having an aggregate offering price of up to $200,000,000 from time to time through Jefferies, acting as our sales agent, or the Prior Prospectus Supplement. As of the date of this prospectus supplement, we have sold an aggregate amount of approximately $153.2 million of shares of our common stock under the Prior Prospectus Supplement pursuant to the Sales Agreement. We are terminating the offering pursuant to the Prior Prospectus Supplement and we will not make any further offer or sale of shares of our common stock pursuant to the Prior Prospectus Supplement.

We are filing this prospectus supplement in accordance with the terms of the Sales Agreement, relating to the offer and sale of shares of our common stock having an aggregate offering price of up to $200,000,000 from time to time through Jefferies, acting as our sales agent, from and after the date hereof.

Sales of shares of common stock, if any, under this prospectus supplement will be made by any method permitted that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended, or the Securities Act. The sales agent will use its commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us, consistent with its normal trading and sales practices, on mutually agreed terms between the sales agent and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "ZBIO." The last reported sale price of shares of our common stock on the Nasdaq Global Select Market on November 4, 2026 was $28.46 per share.

Jefferies will be entitled to compensation at a commission rate of up to 3.0% of the gross proceeds of shares of common stock sold pursuant to the Sales Agreement. In connection with the sale of shares of common stock on our behalf, the sales agent may be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of the sales agent may be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to the sales agent with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act. See "Plan of Distribution" beginning on page S-10 regarding the compensation to be paid to the sales agent.

An investment in our common stock involves significant risks. You should carefully consider the Risk Factors beginning on page S-5 of this prospectus supplement and "Item 1A—Risk Factors" of our most recent report on Form 10-K or Form 10-Q that is incorporated by reference in this prospectus supplement, before investing in our common stock.

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

Jefferies

The date of this prospectus supplement is November 6, 2026.

Table of Contents

Prospectus Supplement

	Page
ABOUT THIS PROSPECTUS SUPPLEMENT	S-i
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS	S-ii
PROSPECTUS SUPPLEMENT SUMMARY	S-1
THE OFFERING	S-3
RISK FACTORS	S-5
USE OF PROCEEDS	S-6
DILUTION	S-7
DIVIDEND POLICY	S-9
PLAN OF DISTRIBUTION	S-10
LEGAL MATTERS	S-12
EXPERTS	S-12
WHERE YOU CAN FIND MORE INFORMATION	S-12
INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE	S-13
Prospectus	
ABOUT THIS PROSPECTUS	1
ABOUT THE COMPANY	3
RISK FACTORS	5
FORWARD-LOOKING STATEMENTS	6
USE OF PROCEEDS	8
PLAN OF DISTRIBUTION	9
DESCRIPTION OF COMMON STOCK	11
DESCRIPTION OF PREFERRED STOCK	12
DESCRIPTION OF WARRANTS	13
DESCRIPTION OF DEBT SECURITIES	14
WHERE YOU CAN FIND MORE INFORMATION	22
INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE	23
LEGAL MATTERS	24
EXPERTS	24

You should rely only on the information contained in or incorporated by reference into this prospectus supplement, the accompanying prospectus and any free writing prospectuses prepared by us or on our behalf. We have not authorized any person to provide any information or make any statement that differs from what is contained in this prospectus supplement and any free writing prospectuses prepared by us or on our behalf. If any person does make a statement that differs from what is in this prospectus supplement or any free writing prospectuses, you should not rely on it. This prospectus supplement is not an offer to sell, nor is it a solicitation of an offer to buy, these securities in any jurisdiction in which the offer or sale is not permitted. You should assume that the information contained in this prospectus supplement, the accompanying prospectus, any free writing prospectus and the documents incorporated by reference is accurate only as of its respective date, regardless of the time of delivery of this prospectus supplement, the accompanying prospectus and any free writing prospectus or of any sale of shares of common stock in this offering. Our business, financial condition, results of operations and prospects may have subsequently changed.

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of an automatic shelf registration statement on Form S-3 (File No. 333-290777) that we filed with the U.S. Securities and Exchange Commission, or the SEC, on October 8, 2025, as a "well-known seasoned issuer" as defined in Rule 405 under the Securities Act, utilizing a "shelf" registration process. Under this shelf registration process, we may, from time to time, sell shares of common stock and other securities in one or more offerings. This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of our shares of common stock and also adds to and updates the information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part is the accompanying prospectus, which provides more general information about us and related matters. To the extent the information contained in this prospectus supplement differs from the information contained in the accompanying prospectus or any document filed with the SEC prior to the date of this prospectus supplement and incorporated herein by reference, the information in this prospectus supplement shall control. Generally, when we refer to this "prospectus," we are referring to both this prospectus supplement and the accompanying prospectus combined. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus, or any documents incorporated by reference, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus, including the documents incorporated by reference therein. Information in any document we subsequently file that is incorporated by reference shall modify or supersede the information in this prospectus supplement, the accompanying prospectus and documents incorporated by reference prior to such subsequent filing.

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein include important information about us, our shares of common stock and other information you should know before investing. This prospectus supplement describes the specific details regarding this offering, including the price, the amount of shares of common stock being offered and the risks of investing in our common stock.

You should carefully read this prospectus supplement and the accompanying prospectus together with the additional information described under the headings "Where You Can Find More Information" and "Incorporation of Certain Documents by Reference."

This prospectus supplement and the accompanying prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the shares of common stock to which it relates, nor do this prospectus supplement and the accompanying prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

References in this prospectus supplement to "Zenas," "the Company," "we," "us" and "our" refer to Zenas BioPharma, Inc. and our subsidiaries on a consolidated basis, as appropriate, unless we state otherwise or the context otherwise requires. The Zenas BioPharma word mark, logo mark, and the "lightning bolt" design are trademarks of Zenas BioPharma, Inc. or its affiliated companies. This prospectus and the other documents incorporated by reference contain references to our trademarks and to trademarks belonging to other entities. Each of the other trademarks, trade names and service marks included in this prospectus belongs to its respective holder. Solely for convenience, trademarks, trade names and service marks referred to in this prospectus, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to those trademarks, trade names and service marks. We do not intend our use or display of other entities' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein include forward-looking statements. All statements other than statements of historical facts contained in this prospectus supplement, the accompanying prospectus, and in the documents incorporated by reference herein and therein, are forward-looking statements. In some cases, forward-looking statements can be identified by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. Forward-looking statements include, but are not limited to, statements concerning:

- the commercial opportunities stemming from the development of our product candidates for multiple immunology and inflammation (“I&I”) diseases;
- our ability to develop and, if approved, ultimately commercialize our product candidates and, with partners, our other programs;
- our ability to obtain or maintain orphan drug designation for certain of our product candidates;
- the initiation, timing, progress, results, and cost of our development programs, and our current and future preclinical and clinical studies, including statements regarding the timing of initiation and completion of our clinical trials, and the period during which the results of the trials will become available;
- the success, cost and timing of our clinical development of our product candidates, including the extent to which interim, topline or preliminary data may be predictive of final results or of the results of future clinical trials;
- our ability to establish clinical differentiation of our product candidates;
- our ability to develop product candidates that have broad therapeutic potential;
- our ability to utilize our business development strategy and expertise to build a balanced portfolio;
- our ability to build our operational and commercial capabilities for supplying and marketing our products, if approved, in key markets;
- market conditions in the biopharmaceutical sector and issuance of securities analysts’ reports or recommendations;
- the trading volume of our common stock;
- an inability to obtain additional funding and make future royalty payments under our Revenue Participation Right Purchase and Sale Agreement with Royalty Pharma Investments 2019 ICAV;
- an inability to obtain additional funding and make borrowings under our agreement with BioPharma Credit PLC, BPCR Limited Partnership and BioPharma Credit Investments V (Master) LP, which are funds managed by Pharmakon Advisors, LP (collectively, “Pharmakon”), and the guarantors party to such agreement;
- our ability to initiate, recruit and enroll patients in and conduct our clinical trials at the pace that we project;
- our ability to obtain regulatory approval of our product candidates, including our plans with respect to regulatory submissions and the timing and outcome with respect to such regulatory submissions and reviews by the U.S. Food and Drug Administration (the “FDA”) or comparable foreign regulatory authorities and with respect to any regulatory approvals we may receive, and any related restrictions, limitations or warnings in the label of any of our product candidates, if approved;
- our reliance on third parties to manufacture drug substance and drug product for use in our clinical trials;
- our ability to retain and recruit key personnel;
- our ability to obtain and maintain adequate intellectual property rights;
- our expectations regarding government and third-party payor coverage and reimbursement;

- the impact of current and future healthcare reforms, including those affecting the delivery of or payment for healthcare products and services;
- our expectations regarding federal, state and foreign regulatory requirements;
- other governmental legislation and regulation, as well as adverse effects from a shutdown of the U.S. government;
- our estimates of our expenses, ongoing losses, capital requirements and our needs for or ability to obtain additional financing;
- our existing cash and the sufficiency of our existing cash and proceeds from future capital-raising efforts, if any, to fund our future operating expenses and capital expenditure requirements;
- the potential benefits of strategic collaboration agreements;
- our ability to identify and enter into strategic collaborations or arrangements, including potential business development opportunities and potential licensing partnerships, and our ability to attract collaborators with development, regulatory and commercialization expertise;
- sales of our stock by us, our insiders or our stockholders;
- our expectations regarding the time during which we will be an emerging growth company and smaller reporting company under the Jumpstart Our Business Startups Act of 2012, as amended;
- general economic, industry, geopolitical and market conditions, such as military conflict or war, inflation and financial institution instability, tariffs and other trade measures, or pandemic or epidemic disease outbreaks, many of which are beyond our control;
- additions or departures of senior management, directors or key personnel;
- our financial performance;
- developments and projections relating to our competitors or our industry; and
- other risks and uncertainties, including those included under the section titled “Risk Factors” contained in this prospectus supplement. See “Where You Can Find More Information.”

The forward-looking statements in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein may prove incorrect. These forward-looking statements speak only as of the date of this prospectus supplement and are subject to a number of known and unknown risks, uncertainties and assumptions, including those described under the sections titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” contained in our Annual Report on Form 10-K for the fiscal year ended December 31, 2025, as filed with the SEC on March 16, 2026, any subsequent Quarterly Report on Form 10-Q, and as described or may be described in any subsequent Annual Report on Form 10-K, each incorporated by reference in this prospectus supplement and in other documents we file with the SEC that are deemed incorporated by reference into this prospectus supplement. In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus supplement and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and should not be unduly relied upon. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, these forward-looking statements should not be relied upon as guarantees of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual future results, levels of activity, performance and events and circumstances could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risks and uncertainties may emerge from time to time, and management cannot predict all risks and uncertainties. Except as required by applicable law, we do not undertake to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information included or incorporated by reference in this prospectus supplement and does not contain all of the information that may be important to you. This prospectus supplement includes or incorporates by reference information about the shares of common stock we are offering as well as information regarding our business, risks and detailed financial data. You should read this prospectus supplement in its entirety, including the information incorporated by reference, which is described under the headings "Where You Can Find More Information" and "Incorporation of Certain Documents by Reference" herein and therein. In particular, you should consider the risks and uncertainties described under the heading "Risk Factors" in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein and in any related free writing prospectus.

Company Overview

We are a clinical-stage global biopharmaceutical company committed to being a leader in the development and commercialization of transformative immunology-based therapies for patients in need. With the evolving understanding of the pathogenesis of autoimmune diseases, along with the expansion of promising immunology-based pharmacologic targets, we are building an I&I focused biopharmaceutical company. Our core business strategy combines disciplined product candidate acquisition with strategic deployment of internal expertise and effective use of external resources. We leverage our experienced executive management team and our established networks throughout the biopharmaceutical industry to identify, acquire and develop product candidates that we believe can provide superior clinical benefits to patients living with autoimmune diseases.

Our lead I&I product candidate, obexelimab, is a bifunctional monoclonal antibody designed to bind both CD19 and FcγRIIb, which are broadly present across B cell lineage, in order to inhibit the activity of cells that are implicated in many autoimmune diseases without depleting them. Based on existing clinical data generated to date, we believe that targeting B cell lineage via CD19 and FcγRIIb can inhibit B cells and has been shown to be well-tolerated.

We are developing obexelimab as a potential I&I franchise for patients in several autoimmune diseases, representing substantial commercial opportunities individually and in the aggregate. We are conducting clinical trials in IgG4-RD through a registration-directed Phase 3 trial which reported topline data in January 2026, relapsing multiple sclerosis ("RMS") through an ongoing Phase 2, double-blind, randomized, placebo-controlled trial which reported topline data in October 2025 and systemic lupus erythematosus ("SLE") through an ongoing Phase 2, double-blind, randomized, placebo-controlled trial, for which we expect to report topline results, including biomarker data, in the fourth quarter of 2026.

In January 2026, we reported positive results from the Phase 3 trial of obexelimab in patients with IgG4-RD. Obexelimab met the primary endpoint, demonstrating a highly statistically significant and clinically meaningful 56% reduction in the risk of IgG4-RD flare compared to placebo (Hazard Ratio 0.44, p=0.0005) and also met and demonstrated highly statistically significant activity compared to placebo on all four key secondary endpoints. Obexelimab was well tolerated with a safety profile consistent with that observed in previously completed clinical trials. Based on these results, we submitted the obexelimab Biologics License Application ("BLA") to the FDA for the treatment of IgG4-RD in May 2026. In August 2026, the FDA accepted the Company's BLA and assigned a Prescription Drug User Fee Act ("PDUFA") target date of May 27, 2027. In October 2026, the European Medicines Agency validated the recently submitted Marketing Authorization Application for the treatment of IgG4-RD.

In October 2026, we announced interim data from the ongoing INDIGO open-label extension ("OLE"). Based on a data cutoff of May 2026, the 12-month probability of remaining flare-free was 0.93 based upon investigator- and adjudication committee-confirmed flares requiring rescue therapy, and 0.87 based upon investigator-determined flares requiring rescue therapy; adjudication was pending for five patients as of the data cutoff. Adverse event rates were comparable to or lower than those observed during the randomized, controlled period.

In October 2025, we entered into an exclusive license agreement (the "License Agreement") dated October 7, 2025, with InnoCare Pharma Inc. ("InnoCare"), pursuant to which we were granted exclusive rights to develop, manufacture, and commercialize orelabrutinib, a Bruton's Tyrosine Kinase inhibitor ("BTK"), for

multiple sclerosis (“MS”) worldwide, and in all non-oncology indications worldwide excluding mainland China, Hong Kong, Macau and Taiwan (“greater China”), and Brunei, Burma, Cambodia, Timor-Leste, Indonesia, Laos, Malaysia, Philippines, Singapore, Thailand and Vietnam (“Southeast Asia”), as well as two early development product candidates: ZB021, an IL-17AA/AF inhibitor, in all fields of use worldwide excluding greater China and Southeast Asia, and ZB022, a TYK2 inhibitor, in all fields of use worldwide. Orelabrutinib is a highly selective and central nervous system (“CNS”) penetrant, oral small molecule BTK inhibitor. Orelabrutinib is designed to bind irreversibly to BTK with minimal off-target effects, which may potentially reduce certain side effects. We believe orelabrutinib is designed to efficiently cross the blood brain barrier, reaching therapeutic levels within the CNS to directly target inflammation in diseases like MS.

In September 2025, the Phase 3 PriMroSe trial of orelabrutinib in patients with primary progressive multiple sclerosis (“PPMS”) was initiated. The PriMroSe trial is a global, multicenter, randomized, double blind, placebo-controlled clinical trial evaluating the safety and efficacy of orelabrutinib dosed 80 mg once daily (“QD”) compared to placebo in patients with PPMS, with a primary endpoint of time to onset of 12 week composite confirmed disability progression. In March of 2026, we initiated a second global, Phase 3, multicenter, randomized, double-blind, placebo-controlled clinical trial evaluating orelabrutinib dosed 80 mg QD compared to placebo in patients with non-active secondary progressive multiple sclerosis, with a primary endpoint of time to onset of 24-week CDP. ZB021 is an oral IL-17AA/AF inhibitor designed to block both IL-17AA homodimer and IL-17AF heterodimer signaling. Preclinical studies for ZB021 have shown favorable PK and ADME properties. ZB021 achieved comparable activity in vivo to a reference anti-IL-17 biologic in a rat CIA model. We, along with our partner, InnoCare, initiated a Phase 1 clinical study in the second quarter of 2026. ZB022 is an oral, brain-penetrant TYK2-JH2 inhibitor, currently in Investigational New Drug (“IND”) enabling studies. Subject to the results of these IND-enabling studies, we expect to initiate a Phase 1 clinical study in 2027.

We are also advancing ZB014, a half-life extended anti-CD-19 and FcγRIIb monoclonal antibody, currently in IND-enabling studies. Subject to the results of IND-enabling studies, we expect to initiate a Phase 1 clinical study in 2027.

Termination of ATM Prospectus

In connection with this offering, we terminated the Prior Prospectus Supplement filed with our registration statement on Form S-3ASR (File No. 333-290777) and related to the shares of our common stock issuable pursuant to the Sales Agreement. As of the date hereof, we have sold an aggregate of 5,474,099 shares of common stock pursuant to the Prior Prospectus Supplement. Other than the termination of the Prior Prospectus Supplement, the Sales Agreement remains in full force and effect.

Risk Factors Summary

This investment involves a high degree of risk. See “Risk Factors” beginning on page S-5 of this prospectus supplement and the similarly titled sections in the documents incorporated by reference into this prospectus supplement.

Corporate Information

Our principal executive offices are located at 852 Winter Street, Suite 250, Waltham, MA 02451, and our telephone number is (857) 271-2954. Our website address is: www.zenasbio.com. We have included our website address as a factual reference and do not intend it to be an active link to our website. The information that can be accessed through our website is not part of this prospectus, and investors should not rely on any such information in deciding whether to purchase our common stock.

THE OFFERING

Common stock offered by us	Shares of our common stock having an aggregate offering price of up to $200,000,000.
Common stock to be outstanding after this offering	Up to 74,822,461 shares of common stock, assuming a sales price of $28.46 per share, which was the last reported sale price per share of our common stock on the Nasdaq Global Select Market on November 4, 2026. The actual number of shares of common stock issued will vary depending on the sales price under this offering.
Plan of Distribution	"At the market offering" that may be made from time to time on the Nasdaq Global Select Market, if at all, through Jefferies. See "Plan of Distribution" on page S-10 of this prospectus supplement.
Use of Proceeds	We intend to use the net proceeds from the sale of shares of common stock offered by this prospectus supplement, together with other available funds, primarily for general corporate purposes, including, without limitation, research and development expenditures, preclinical and clinical development and commercialization of our product candidates, the acquisition or in-licensing of products or product candidates, business or technologies, collaborations, working capital and capital expenditures. See "Use of Proceeds" on page S-6 of this prospectus supplement.
Risk Factors	This investment involves a high degree of risk. See "Risk Factors" beginning on page S-5 of this prospectus supplement and the similarly titled sections in the documents incorporated by reference herein.
Nasdaq Global Select Market symbol	Our common stock is listed on Nasdaq under the symbol "ZBIO."

The number of shares of common stock that will be outstanding after this offering as shown above is based on 67,795,055 shares of common stock outstanding as of September 30, 2026, which number excludes:

- 11,667,480 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of $14.78 per share;
- 1,350,759 shares of common stock issuable upon the vesting of restricted stock units outstanding;
- 1,583,621 shares of common stock reserved for issuance pursuant to future equity awards under our 2024 Equity Incentive Plan (the "2024 Plan"), as well as any future increases in the number of shares of common stock reserved for future issuance under the 2024 Plan;
- 592,500 shares of common stock reserved for issuance pursuant to future equity awards under our 2026 Inducement Plan, as amended (the "2026 Plan"), as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2026 Plan;
- 1,241,412 shares of common stock reserved for future issuance under our 2024 Employee Stock Purchase Plan (the "2024 ESPP"), as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2024 ESPP;

- 142,431 shares of common stock issued after September 30, 2026 upon the exercise of outstanding stock options having a weighted-average exercise price of $15.49 per share;
- 11,797 shares of common stock issued upon the vesting of restricted stock units after September 30, 2026; and
- 8,679,234 shares of common stock issuable upon conversion of our outstanding 2.50% Convertible Senior Notes due 2032 (the “Notes”), based on the initial conversion rate of 37.7358 shares of common stock per $1,000 principal amount of the Notes.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before purchasing our securities, you should carefully consider the risk factors relating to Zenas BioPharma, Inc. set forth below along with those in our most recent Annual Report on Form 10-K incorporated by reference in this prospectus supplement and in any subsequent Quarterly Reports on Form 10-Q, as may be updated by subsequent annual, quarterly and other reports that are incorporated by reference into this prospectus supplement. For a description of these reports and documents, and information about where you can find them, see "Where You Can Find More Information" and "Incorporation of Certain Documents by Reference." Additional risks not presently known or that we presently consider to be immaterial could subsequently materially and adversely affect our financial condition, results of operations, business and prospects.

Risks Related to This Offering

You will incur immediate and substantial dilution as a result of the completion of this offering.

The price per share of common stock being offered may be higher than the net tangible book value per share of our outstanding shares of common stock prior to this offering. Assuming that an aggregate of 7,027,406 shares of our common stock are sold at an assumed offering price of $28.46 per share, the last reported sale price of our shares of common stock on the Nasdaq Global Select Market on November 4, 2026, for aggregate gross proceeds of approximately $200.0 million, and after deducting commissions and estimated offering expenses payable by us, new investors in this offering will incur immediate dilution of $23.03 per share of common stock. For a more detailed discussion of the foregoing, see the section entitled "Dilution" below.

We will have broad discretion over the use of the net proceeds from this offering.

We will have broad discretion to use the net proceeds from the sale of shares of common stock in this offering, and investors in our common stock will be relying on the judgment of our board of directors and management regarding the application of these proceeds. Although we intend to use the net proceeds from this offering primarily for general corporate purposes, including, without limitation, research and development expenditures, preclinical and clinical development and commercialization of our product candidates, the acquisition or in-licensing of products or product candidates, business or technologies, collaborations, working capital and capital expenditures, we have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion of the allocation of net proceeds, and investors will not have the opportunity, as part of their investment decision, to assess whether the proceeds are being used appropriately. Our use of the proceeds may not improve our operating results or increase the value of the securities being offered hereby.

It is not possible to predict the aggregate proceeds resulting from sales made under the Sales Agreement.

Subject to certain limitations in the Sales Agreement and compliance with applicable law, we have the discretion to deliver an issuance notice to Jefferies at any time throughout the term of the Sales Agreement. The number of shares that are sold through Jefferies after delivering an issuance notice, if any, will fluctuate based on a number of factors, including the market price of shares of our common stock during the sales period, the limits we set with Jefferies in any applicable issuance notice and the demand for shares of our common stock during the sales period. Because the price per share of each share of common stock sold pursuant to the Sales Agreement will fluctuate during this offering, it is not currently possible to predict the number of shares of common stock that will be sold or the aggregate proceeds we will raise in connection with those sales under the Sales Agreement, and we may not sell any shares of common stock.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of shares of common stock offered by this prospectus, together with other available funds, primarily for general corporate purposes, including, without limitation, research and development expenditures, preclinical and clinical development and commercialization of our product candidates, the acquisition or in-licensing of products or product candidates, business or technologies, collaborations, working capital and capital expenditures. The amount of net proceeds from this offering will depend upon the number of shares of common stock sold and the market prices at which they are sold. There can be no assurance that we will be able to sell any shares of common stock under or fully utilize the Sales Agreement as a source of financing.

We have not determined the amount of net proceeds to be used specifically for such purposes or the timing of these expenditures. The amounts actually expended for each purpose may vary significantly depending upon numerous factors, including the amount and timing of the proceeds from the sale of shares of common stock offered by this prospectus, the progress of our clinical trials, pre-commercialization efforts and other product development activities. In addition, expenditures may also depend on the establishment of new collaborative arrangements with other partners, the availability of other financing and other factors. Pending these uses, we plan to invest these net proceeds in treasury bills, corporate bonds, commercial paper, term deposits, bankers acceptances or deposit-based investments including, but not limited to, interest savings accounts. The goal with respect to the investment of these net proceeds is capital preservation and liquidity so that such funds are readily available to fund our operations.

We anticipate that we will be required to raise substantial additional capital to continue to fund the clinical development of our product candidates. If we are able to gain marketing approval for product candidates that we develop, we will require significant additional amounts of capital in order to launch and commercialize such product candidates to the extent that such launch and commercialization are not the responsibility of a collaborator. We expect to finance our future cash needs through public or private equity offerings, debt financings, royalty-based financing, collaborations, licensing arrangements or other sources, or any combination of the foregoing.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the public offering price per share of common stock you will pay in this offering and the as adjusted net tangible book value per share of common stock after this offering. Net tangible book value per share of common stock represents our total tangible assets less total liabilities, divided by the number of shares of common stock outstanding.

As of September 30, 2026, our historical net tangible book value was $212.3 million, or $3.13 per share of common stock. Historical net tangible book value per share represents historical net tangible book value divided by the 67,795,055 shares of our common stock outstanding as of September 30, 2026.

After giving effect to the sale of 7,027,406 shares of our common stock in the aggregate amount of $200.0 million at an assumed offering price of $28.46 per share, the last reported sale price of our shares of common stock on November 4, 2026 on the Nasdaq Global Select Market, and after deducting estimated commissions and estimated offering expenses, our as adjusted net tangible book value as of September 30, 2026 would have been approximately $406.2 million, or approximately $5.43 per share. This represents an immediate increase in the net tangible book value of $2.30 per share to existing stockholders and an immediate dilution of $23.03 per share to new investors purchasing shares of common stock in this offering.

The following table illustrates this per share dilution to the new investors purchasing shares of common stock in this offering:

Assumed public offering price per share		$ 28.46
Net tangible book value per share at September 30, 2026	$3.13	
Increase in net tangible book value per share attributable to this offering	$2.30	
As adjusted net tangible book value per share after this offering		$ 5.43
Dilution per share to new investors in this offering		$ 23.03

The number of shares of common stock that will be outstanding after this offering as shown above is based on 67,795,055 shares of common stock outstanding as of September 30, 2026, which number excludes:

- 11,667,480 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of $14.78 per share;
- 1,350,759 shares of common stock issuable upon the vesting of restricted stock units outstanding;
- 1,583,621 shares of common stock reserved for issuance pursuant to future equity awards under the 2024 Plan, as well as any future increases in the number of shares of common stock reserved for future issuance under the 2024 Plan;
- 592,500 shares of common stock reserved for issuance pursuant to future equity awards under the 2026 Plan, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2026 Plan;
- 1,241,412 shares of common stock reserved for future issuance under the 2024 ESPP, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2024 ESPP;
- 142,431 shares of common stock issued after September 30, 2026 upon the exercise of outstanding stock options having a weighted-average exercise price of $15.49 per share;
- 11,797 shares of common stock issued upon the vesting of restricted stock units after September 30, 2026; and
- 8,679,234 shares of common stock issuable upon conversion of our outstanding Notes, based on the initial conversion rate of 37.7358 shares of common stock per $1,000 principal amount of the Notes.

To the extent the stock options outstanding as of September 30, 2026 have been or are exercised, or other shares of common stock are issued, investors purchasing shares of common stock in this offering could experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

DIVIDEND POLICY

We have never declared or paid any dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors our board of directors deems relevant, and subject to the restrictions contained in any future financing instruments. Our ability to pay cash dividends on our capital stock in the future may also be limited by the terms of any preferred securities we may issue or agreements governing any indebtedness we may incur.

PLAN OF DISTRIBUTION

We have previously entered into the Sales Agreement on October 8, 2025, under which we may offer and sell common stock from time to time through Jefferies acting as agent. Pursuant to this prospectus supplement, we may offer and sell shares of our common stock having an aggregate offering price of up to $200,000,000. Sales of our shares of common stock, if any, under this prospectus supplement and the accompanying prospectus will be made by any method that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act.

Each time we wish to issue and sell shares of our common stock under the Sales Agreement, we will notify Jefferies of the number of shares to be issued, the dates on which such sales are anticipated to be made, any limitation on the number of shares to be sold in any one day and any minimum price below which sales may not be made. Once we have so instructed Jefferies, unless Jefferies declines to accept the terms of such notice, Jefferies has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligations of Jefferies under the Sales Agreement to sell our shares of common stock are subject to a number of conditions that we must meet.

The settlement of sales of shares between us and Jefferies is generally anticipated to occur on the first trading day following the date on which the sale was made. Sales of our shares of common stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Jefferies may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

We will pay Jefferies a commission of up to 3.0% of the gross proceeds of shares of common stock sold pursuant to the Sales Agreement. 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. In addition, we have agreed to reimburse Jefferies for certain ongoing fees and disbursements of its legal counsel, except as otherwise agreed to in writing between us and Jefferies. We estimate that the total expenses for the offering, excluding any commissions or expense reimbursement payable to Jefferies under the terms of the Sales Agreement in connection with sales pursuant to this prospectus supplement, will be approximately $0.2 million. The remaining sale proceeds, after deducting any other transaction fees, will equal our net proceeds from the sale of such shares.

Jefferies will provide written confirmation to us before the open on the Nasdaq Global Select Market on the day following each day on which our shares of common stock are sold under the Sales Agreement. Each confirmation will include the number of shares sold on that day, aggregate gross proceeds of such sales and the proceeds to us.

In connection with the sale of our shares of common stock on our behalf, Jefferies may be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation of Jefferies may be deemed to be underwriting commissions or discounts. We have agreed to indemnify Jefferies against certain civil liabilities, including liabilities under the Securities Act and the Exchange Act. We have also agreed to contribute to payments Jefferies may be required to make in respect of such liabilities.

The offering of our shares of common stock pursuant to the Sales Agreement will terminate as permitted therein.

This summary of the material provisions of the Sales Agreement does not purport to be a complete statement of its terms and conditions. A copy of the Sales Agreement was filed as an exhibit to the registration statement of which this prospectus supplement forms part and is incorporated herein by reference.

Jefferies and its affiliates have in the past and may in the future provide various investment banking, commercial banking, financial advisory and other financial services for us and our affiliates, for which services they may in the future receive customary fees. For example, Jefferies acted as an underwriter in our initial public offering in September 2024, as a placement agent in our private placement in October 2025, and as an underwriter in our concurrent public offerings of convertible notes and common stock in March 2026, and Jefferies received compensation in connection with each transaction. Further, in the course of its business,

Jefferies may actively trade our securities for its own account or for the accounts of customers, and, accordingly, Jefferies may at any time hold long or short positions in such securities.

A prospectus supplement and the accompanying prospectus in electronic format may be made available on a website maintained by Jefferies, and Jefferies may distribute the prospectus supplement and the accompanying prospectus electronically.

LEGAL MATTERS

The validity of the shares of common stock being offered by this prospectus supplement will be passed upon for us by Ropes & Gray LLP, Boston, Massachusetts. Jefferies LLC is being represented in connection with this offering by Cooley LLP, New York, New York.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2025, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and other 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. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge through the internet. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. You may also access these filings through our website at www.zenasbio.com. The information contained on our website is not a part of this prospectus.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" into this prospectus certain information we file with it, which means that we can disclose important information about us by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus, and information in documents that we file later with the SEC will automatically update and supersede information in this prospectus. We incorporate by reference into this prospectus the documents listed below and any future filings, including all filings made after the date of the filing of the registration statement of which this prospectus is part and prior to the effectiveness of such registration statement, made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, except for information "furnished" under Items 2.02, 7.01 or 9.01 on Form 8-K or other information "furnished" to the SEC which is not deemed filed and not incorporated in this prospectus, until the termination of the offering of securities described in the applicable prospectus supplement. We hereby incorporate by reference the following documents:

- our Annual Report on Form 10-K for the year ended December 31, 2025, as filed with the SEC on March 16, 2026;
- our Quarterly Reports on Form 10-Q for the quarter ended March 31, 2026, as filed with the SEC on May 13, 2026, for the quarter ended June 30, 2026, as filed with the SEC on August 13, 2026, and for the quarter ended September 30, 2026, as filed with the SEC on November 5, 2026;
- our Current Reports on Form 8-K filed with the SEC on January 5, 2026, February 13, 2026, March 31, 2026, May 13, 2026 and August 13, 2026;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2025 from our Definitive Proxy Statement on Schedule 14A for the 2026 Annual Meeting of Stockholders, as filed with the SEC on March 16, 2026; and
- the description of our common stock, which is contained in the Registration Statement on Form 8-A, dated September 10, 2024, as supplemented by the description of our common stock and preferred stock contained in Exhibit 4.3 to our Annual Report on Form 10-K for the fiscal year ended December 31, 2024, filed with the SEC on March 11, 2025.

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed modified, superseded or replaced for purposes of this prospectus to the extent that a statement contained in this prospectus modifies, supersedes or replaces such statement.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address:

Attention: Investor Relations
Zenas BioPharma, Inc.
852 Winter Street, Suite 250
Waltham, Massachusetts 02451
(857) 271-2954
email address: IR@zenasbio.com

Copies of these filings are also available, without charge, on the SEC's website at www.sec.gov and on our website at www.zenasbio.com as soon as reasonably practicable after they are filed electronically with the SEC. The information contained on our website is not a part of this prospectus.

PROSPECTUS



Common Stock
Preferred Stock
Warrants
Debt Securities

We may offer and sell from time to time, in one or more series or issuances and in an amount and on terms that we will determine at the time of the respective offering, any combination of an indeterminate number of the securities described in this prospectus.

We will provide specific terms of any offering in a supplement to this prospectus. We may amend or supplement this prospectus from time to time by filing amendments or supplements as required. Any prospectus supplement may also add, update, or change information contained in this prospectus. You should carefully read this prospectus and any amendments or prospectus supplements as well as the documents incorporated or deemed to be incorporated by reference in this prospectus before you purchase any of the securities offered hereby.

These securities may be offered and sold in the same offering or in separate offerings; to or through underwriters, dealers, and agents; or directly to purchasers. The names of any underwriters, dealers, or agents involved in the sale of our securities and their compensation will be described in the applicable prospectus supplement.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "ZBIO." On October 7, 2025, the last reported sale price of our common stock, par value $0.0001 per share, was $20.85 per share.

Investing in our securities involves a high degree of risk. Before making an investment decision, please read the information under the heading. See "Risk Factors" on page 5 of this prospectus, in any applicable prospectus supplement, and under similar headings in the other documents that are incorporated by reference into this prospectus.

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

Prospectus dated October 8, 2025

TABLE OF CONTENTS

	Page
ABOUT THIS PROSPECTUS	1
ABOUT THE COMPANY	3
RISK FACTORS	5
FORWARD-LOOKING STATEMENTS	6
USE OF PROCEEDS	8
PLAN OF DISTRIBUTION	9
DESCRIPTION OF COMMON STOCK	11
DESCRIPTION OF PREFERRED STOCK	12
DESCRIPTION OF WARRANTS	13
DESCRIPTION OF DEBT SECURITIES	14
WHERE YOU CAN FIND MORE INFORMATION	22
INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE	23
LEGAL MATTERS	24
EXPERTS	24

ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement on Form S-3 that we filed with the Securities and Exchange Commission (the "SEC") as a "well-known seasoned issuer" as defined in Rule 405 under the Securities Act of 1933, as amended (the "Securities Act"), using a "shelf" registration process. Under this shelf registration process, we may from time to time offer to sell any combination of the securities described in this prospectus in one or more offerings. Each time we sell securities under this prospectus, we will provide a prospectus supplement and, if necessary, a free writing prospectus, that will contain specific information about the terms of that offering. The prospectus supplement and, if necessary, a free writing prospectus, may also add to, update or change information contained in this prospectus. Accordingly, to the extent inconsistent, the information in this prospectus will be deemed to be modified or superseded by any inconsistent information contained in a prospectus supplement or a free writing prospectus. You should read this prospectus and the applicable prospectus supplement and any free writing prospectus carefully, including all documents incorporated herein and therein by reference, together with the additional information described below under "Where You Can Find More Information" before making an investment in our securities.

This prospectus does not include all of the information that is in the registration statement. We omitted certain parts of the registration statement from this prospectus as permitted by the SEC. We refer you to the registration statement and its exhibits for additional information about us and the securities that may be sold under this prospectus.

We have not authorized any dealer, agent or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and any accompanying prospectus supplement or any free writing prospectus provided in connection with an offering. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or an accompanying prospectus supplement. This prospectus and the accompanying prospectus supplement, if any, do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and the accompanying prospectus supplement constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus and any accompanying prospectus supplement, if any, is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus and any accompanying prospectus supplement is delivered or securities are sold on a later date. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under "Where You Can Find More Information."

References in this prospectus to "Zenas," the "Company," "we," "us," "our" or similar terms refer to Zenas BioPharma, Inc. and our subsidiaries on a consolidated basis, as appropriate, unless we state otherwise or the context otherwise requires. The phrase "this prospectus" refers to this prospectus and any applicable prospectus supplement, unless the context otherwise requires.

Trademarks and Tradenames

The Zenas BioPharma word mark, logo mark, and the "lightning bolt" design are trademarks of Zenas BioPharma, Inc. or its affiliated companies. This prospectus and any applicable prospectus supplement and documents incorporated by reference herein and therein contain references to our trademarks and to trademarks belonging to other entities. Each of the other trademarks, trade names and service marks included in this prospectus belongs to its respective holder. Solely for convenience, trademarks, trade names and service marks referred to in this prospectus, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks, trade names and service marks. We do not intend our use or display of other entities' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

ABOUT THE COMPANY

We are a clinical-stage global biopharmaceutical company committed to being a leader in the development and commercialization of transformative immunology-based therapies for patients in need. With the evolving understanding of the pathogenesis of autoimmune diseases, along with the expansion of promising immunology-based pharmacologic targets, we are building an immunology and inflammation ("I&I") focused biopharmaceutical company. Our core business strategy combines disciplined product candidate acquisition with strategic deployment of internal expertise and effective use of external resources. We leverage our experienced executive management team and our established networks throughout the biopharmaceutical industry to identify, acquire and develop product candidates that we believe can provide superior clinical benefits to patients living with autoimmune diseases.

Our lead I&I product candidate, obexelimab, is a bifunctional monoclonal antibody designed to bind both CD19 and FcγRIIb, which are broadly present across B cell lineage, in order to inhibit the activity of cells that are implicated in many autoimmune diseases without depleting them. Based on existing clinical data generated to date, we believe that targeting B cell lineage via CD19 and FcγRIIb can inhibit B cells and has been shown to be well-tolerated.

We are developing obexelimab as a potential I&I franchise for patients in several autoimmune diseases, representing substantial commercial opportunities individually and in the aggregate. The first three indications we are pursuing include IgG4-RD through an ongoing registration-directed Phase 3 trial (the "INDIGO" trial), and systemic lupus erythematosus (the "SunStone" trial) and relapsing multiple sclerosis (the "MoonStone" trial) through ongoing Phase 2, double-blind, randomized, placebo-controlled trials. In the fourth quarter of 2024, we completed the target enrollment of the INDIGO trial and expect to report topline results from the INDIGO trial around year-end 2025. If the topline results are positive, we expect to file a Biologics License Application with the U.S. Food and Drug Administration in the first half of 2026, followed by a Marketing Authorization Application with the European Medicines Agency, and, if approved, commence the commercial launch initially in the United States and then in Europe. In the second quarter of 2025, we completed enrollment of the MoonStone trial and expect to report results from the MoonStone trial, including the 12-week primary endpoint results, early in the fourth quarter of 2025. In early 2026, we expect to decide whether and how to advance obexelimab for RMS based on a variety of factors, including our analysis of MoonStone trial data, including the 12 and 24-week data, the evolving landscape for the development of new therapies for RMS, including available therapies and regulatory endpoints, and allocation of capital. We expect to complete enrollment in the SunStone trial by around year-end 2025 and to report topline results from the SunStone trial in mid-2026. Based on the outcome of the SunStone trial, and considering other factors, we may initiate a Phase 3 program in patients with SLE in the first half of 2027.

On October 7, 2025, we entered into a License Agreement with InnoCare Pharma Inc. pursuant to which we were granted exclusive rights to develop, manufacture, and commercialize orelabrutinib, a Bruton's Tyrosine Kinase inhibitor, for multiple sclerosis worldwide, and in all non-oncology indications worldwide excluding mainland China, Hong Kong, Macau and Taiwan ("Greater China") and Brunei, Burma, Cambodia, Timor-Leste, Indonesia, Laos, Malaysia, Philippines, Singapore, Thailand and Vietnam ("Southeast Asia"), as well as two early-development product candidates: ZB021, an IL-17AA/AF inhibitor, in all fields of use worldwide excluding Greater China and Southeast Asia, and ZB022, a TYK2-JH2 inhibitor, in all fields of use worldwide.

Orelabrutinib, also known as ZB020, is a highly selective and central nervous system ("CNS")-penetrant, oral small molecule BTK inhibitor. Orelabrutinib is designed to bind irreversibly to BTK with minimal off-target effects, compared to certain other BTK inhibitors, which may potentially reduce certain side effects. We believe orelabrutinib is designed to efficiently cross the blood-brain barrier, reaching therapeutic levels within the CNS to directly target inflammation in diseases like MS. In September 2025, the Phase 3 clinical trial of orelabrutinib in patients with Primary Progressive Multiple Sclerosis ("PPMS") was initiated. In the first quarter of 2026, we plan to initiate a Phase 3 clinical trial evaluating orelabrutinib in patients with Secondary Progressive Multiple Sclerosis ("SPMS").

ZB021 is an oral IL-17AA/AF inhibitor designed to block both IL-17AA homodimer and IL-17AF heterodimer signaling, and ZB022 is an oral, brain-penetrant TYK2-JH2 inhibitor. Subject to the results of

Investigational New Drug ("IND")-enabling studies, we expect to submit an IND application for each of ZB021 and ZB022, and if cleared, initiate a Phase 1 clinical study in 2026 for each, with the potential for initial data in 2027.

Our principal executive offices are located at 852 Winter Street, Suite 250, Waltham, MA 02451, and our telephone number is (857) 271-2954. Our website address is: www.zenasbio.com. We have included our website address as a factual reference and do not intend it to be an active link to our website. The information that can be accessed through our website is not part of this prospectus, and investors should not rely on any such information in deciding whether to purchase our securities.

RISK FACTORS

Investing in our securities involves a high degree of risk. See "Item 1A — Risk Factors" in our most recent Annual Report on Form 10-K incorporated by reference in this prospectus and in any subsequent Quarterly Reports on Form 10-Q, as may be updated by subsequent annual, quarterly and other reports that are incorporated by reference into this prospectus and the "Risk Factors" section in the applicable prospectus supplement for a discussion of the factors you should carefully consider before deciding to purchase our securities. Before making a decision about investing in our securities, you should carefully consider these risks as well as other information we include or incorporate by reference into this prospectus and the applicable prospectus supplement. The risks and uncertainties we have described are not the only ones facing our Company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business operations, operating results and financial condition. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities. The discussion of risks includes or refers to forward-looking statements; you should read the explanation of the qualifications and limitations on such forward-looking statements discussed elsewhere in this prospectus.

FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement and the other documents we have filed with the SEC that are incorporated herein by reference, contain forward-looking statements.

All statements other than statements of historical facts contained incorporated by reference into this prospectus are forward-looking statements. In some cases, forward-looking statements can be identified by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential," or "continue" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. Forward-looking statements include, but are not limited to, statements concerning:

- the commercial opportunities stemming from the development of our product candidates for multiple immunology and inflammation diseases;
- our ability to develop and, if approved, ultimately commercialize our product candidates and, with partners, our other programs;
- our ability to obtain or maintain orphan drug designation for certain of our product candidates;
- the initiation, timing, progress, results, and cost of our development programs, and our current and future preclinical and clinical studies, including statements regarding the timing of initiation and completion of our clinical trials, and the period during which the results of the trials will become available;
- the success, cost and timing of our clinical development of our product candidates;
- our ability to establish clinical differentiation of our product candidates;
- our ability to develop product candidates that have broad therapeutic potential;
- our ability to utilize our business development strategy and expertise to build a balanced portfolio;
- our ability to identify collaborations and strategic partnerships to maximize the value of our portfolio;
- our ability to build our operational and commercial capabilities for supplying and marketing our products, if approved, in key markets;
- market conditions in the biopharmaceutical sector and issuance of securities analysts' reports or recommendations;
- the trading volume of our common stock;
- an inability to obtain additional funding;
- our ability to initiate, recruit and enroll patients in and conduct our clinical trials at the pace that we project;
- our ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations or warnings in the label of any of our product candidates, if approved;
- our reliance on third parties to manufacture drug substance and drug product for use in our clinical trials;
- our ability to retain and recruit key personnel;
- our ability to obtain and maintain adequate intellectual property rights;
- our expectations regarding government and third-party payor coverage and reimbursement;
- the impact of current and future healthcare reforms, including those affecting the delivery of or payment for healthcare products and services;
- our expectations regarding federal, state and foreign regulatory requirements;
- our estimates of our expenses, ongoing losses, capital requirements and our needs for or ability to obtain additional financing;

- our existing cash and the sufficiency of our existing cash and proceeds from future capital-raising efforts, if any, to fund our future operating expenses and capital expenditure requirements;
- the potential benefits of strategic collaboration agreements;
- our ability to enter into strategic collaborations or arrangements, including potential business development opportunities and potential licensing partnerships, and our ability to attract collaborators with development, regulatory and commercialization expertise;
- sales of our stock by us, our insiders or our stockholders;
- our expectations regarding the time during which we will be an emerging growth company and smaller reporting company under the Jumpstart Our Business Startups Act of 2012, as amended;
- general economic, industry, geopolitical and market conditions, such as military conflict or war, inflation and financial institution instability, tariffs and other trade measures, or pandemic or epidemic disease outbreaks, many of which are beyond our control;
- additions or departures of senior management, directors or key personnel;
- our financial performance;
- developments and projections relating to our competitors or our industry; and
- other risks and uncertainties, including those included under the section heading "Risk Factors" contained in this prospectus.

The forward-looking statements in this prospectus may prove incorrect. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of known and unknown risks, uncertainties and assumptions, including those described under the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" contained in our Annual Report on Form 10-K for the year ended December 31, 2024, as filed with the SEC on March 11, 2025, any subsequent Quarterly Report on Form 10-Q, and as described or may be described in any subsequent Annual Report on Form 10-K, each incorporated by reference in this prospectus and any other documents we file with the SEC that are deemed incorporated by reference into this prospectus. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and should not be unduly relied upon. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, these forward-looking statements should not be relied upon as guarantees of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual future results, levels of activity, performance and events and circumstances could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risks and uncertainties may emerge from time to time, and management cannot predict all risks and uncertainties. Except as required by applicable law, we do not undertake to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

USE OF PROCEEDS

Except as otherwise provided in the applicable prospectus supplement, in connection with an offering of securities pursuant to this prospectus, we currently intend to use any net proceeds we receive from the sale of any securities offered by us under this prospectus primarily for general corporate purposes. General corporate purposes may include, without limitation, research and development expenditures, preclinical and clinical development and commercialization of our product candidates, the acquisition or in-licensing of products or product candidates, business or technologies, collaborations, working capital and capital expenditures. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds. Additional information on the use of net proceeds we receive from the sale of securities covered by this prospectus may be set forth in the prospectus supplement relating to the specific offering.

PLAN OF DISTRIBUTION

We are registering securities to be sold by us under a "shelf" registration process.

If we offer any securities under this prospectus, we will amend or supplement this prospectus by means of an accompanying prospectus supplement setting forth the specific terms and conditions and other information about that offering as is required or necessary.

We may sell the securities in any of the following ways (or in any combination thereof) from time to time:

- to or through one or more underwriters;
- through dealers, who may act as agents or principal (including a block trade in which a broker or dealer so engaged will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction);
- through one or more agents;
- through registered direct offerings;
- as part of a collaboration with a third party;
- as part of an acquisition or merger with a third party;
- through at-the-market issuances within the meaning of Rule 415(a)(4) of the Securities Act, to or through a market maker or into an existing trading market, or an exchange or otherwise;
- in privately negotiated transactions; or
- directly to purchasers or to a single purchaser.

The distribution of the securities by us may be effected from time to time in one or more transactions:

- at a fixed price, or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement will describe the terms of the offering of the securities, including the following, as applicable:

- the terms of the securities being offered, including the public offering price of the securities and the proceeds to us;
- the name or names of any underwriters, dealers or agents and the amounts of securities underwritten or purchased by each of them;
- any underwriting discounts and commissions or agency fees and other items constituting underwriters' or agents' compensation;
- any options under which underwriters may purchase additional securities from us;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any securities exchanges on which the securities may be listed.

Only the agents or underwriters named in each prospectus supplement are agents or underwriters in connection with the securities being offered thereby.

We may authorize underwriters, dealers or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and

delivery on a specified date in the future. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in each applicable prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will be subject only to those conditions set forth in each applicable prospectus supplement, and each prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

We may indemnify agents, underwriters, dealers, their affiliates, or other third parties who participate in the distribution of securities against certain liabilities, including liabilities under the Securities Act, and agree to contribute to payments which these agents, underwriters, dealers, or other third parties may be required to make. Agents, underwriters, dealers and such other third parties may be customers of, engage in transactions with, or perform services for us in the ordinary course of business. We may also use underwriters or such other third parties with whom we have a material relationship. We will describe the nature of any such relationship in the applicable prospectus supplement.

One or more firms, referred to as "remarketing firms," may also offer or sell the securities, if a prospectus supplement so indicates, in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own accounts or as our agents. These remarketing firms will offer or sell the securities in accordance with the terms of the securities. Each prospectus supplement will identify and describe any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm's compensation. Remarketing firms may be deemed to be underwriters in connection with the securities they remarket. Remarketing firms may be entitled under agreements that may be entered into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may engage in transactions with or perform services for us in the ordinary course of business.

Certain underwriters may use this prospectus and any accompanying prospectus supplement for offers and sales related to market-making transactions in the securities. These underwriters may act as principal or agent in these transactions, and the sales will be made at prices related to prevailing market prices at the time of sale. Any underwriters involved in the sale of the securities may qualify as "underwriters" within the meaning of Section 2(a)(11) of the Securities Act. In addition, the underwriters' commissions, discounts or concessions may qualify as underwriters' compensation under the Securities Act and the rules of the Financial Industry Regulatory Authority.

Our common stock is listed on The Nasdaq Global Select Market. Underwriters may make a market in our common stock, but will not be obligated to do so and may discontinue any market making at any time without notice. We can make no assurance as to the development, maintenance or liquidity of any trading market for the securities.

Certain persons participating in an offering may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with rules and regulations under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a short covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

We are subject to the applicable provisions of the Exchange Act and the rules and regulations under the Exchange Act, including Regulation M, which may limit the timing of purchases and sales of any of the securities offered in this prospectus by any other person. The anti-manipulation rules under the Exchange Act may apply to sales of securities in the market and to the actions of the Company.

To the extent required, this prospectus may be amended and/or supplemented from time to time to describe a specific plan of distribution.

DESCRIPTION OF COMMON STOCK

The description of our common stock is incorporated by reference to Exhibit 4.3 of our Annual Report on Form 10-K for the year ended December 31, 2024, as filed with the SEC on March 11, 2025, including any amendments or reports filed for the purpose of updating such description.

DESCRIPTION OF PREFERRED STOCK

Under the terms of our second restated certificate of incorporation (our "Restated Charter"), our board of directors is authorized to issue up to 25,000,000 shares of preferred stock, par value $0.0001 per share, in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock. It is not possible to state the actual effect of the issuance of any shares of preferred stock upon the rights of the holders of common stock until the board of directors determines the specific rights of the holders of preferred stock. However, effects of the issuance of preferred stock include restricting dividends on common stock, diluting the voting power of common stock, impairing the liquidation rights of common stock, and making it more difficult for a third party to acquire us, which could have the effect of discouraging a third party from acquiring, or deterring a third party from paying a premium to acquire, a majority of our outstanding voting stock.

If we offer any additional specific class or series of preferred stock under this prospectus, we will describe the terms of the preferred stock in the prospectus supplement for such offering and will file a copy of the certificate establishing the terms of the preferred stock with the SEC. To the extent required, this description will include:

- the title and stated value;
- the number of shares offered, the liquidation preference per share and the purchase price;
- the dividend rate(s), period(s) and/or payment date(s), or method(s) of calculation for such dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption, if applicable;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price (or how it will be calculated) and conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price (or how it will be calculated) and exchange period;
- voting rights, if any, of the preferred stock;
- a discussion of any material U.S. federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the affairs of the Company; and
- any material limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the Company.

The preferred stock offered by this prospectus, when issued, will not have, or be subject to, any preemptive or similar rights.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase shares of our common stock, preferred stock and/or debt securities in one or more series together with other securities or separately, as described in each applicable prospectus supplement. Below is a description of certain general terms and provisions of the warrants that we may offer. Particular terms of the warrants will be described in the applicable warrant agreements and the applicable prospectus supplement for the warrants.

The applicable prospectus supplement will contain, where applicable, the following terms of and other information relating to the warrants:

- the specific designation and aggregate number of, and the price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the designation, amount and terms of the securities purchasable upon exercise of the warrants;
- if applicable, the exercise price for shares of our common stock and the number of shares of common stock to be received upon exercise of the warrants;
- if applicable, the exercise price for shares of our preferred stock, the number of shares of preferred stock to be received upon exercise, and a description of that class or series of our preferred stock;
- if applicable, the exercise price for our debt securities, the amount of our debt securities to be received upon exercise, and a description of that series of debt securities;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if the warrants may not be continuously exercised throughout that period, the specific date or dates on which the warrants may be exercised;
- whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- if applicable, the date from and after which the warrants and the common stock, preferred stock and/or debt securities will be separately transferable;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the anti-dilution provisions of the warrants, if any;
- any redemption or call provisions;
- whether the warrants are to be sold separately or with other securities as parts of units; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

DESCRIPTION OF DEBT SECURITIES

We may issue the debt securities offered by this prospectus and any accompanying prospectus supplement under an indenture to be entered into between us and the trustee identified in the applicable prospectus supplement. The terms of the debt securities will include those stated in the indenture and those made part of the indenture by reference to the Trust Indenture Act of 1939, as in effect on the date of the indenture. We have filed a copy of the form of indenture as an exhibit to the registration statement in which this prospectus is included. The indenture will be subject to and governed by the terms of the Trust Indenture Act of 1939.

We may offer debt securities as described in this prospectus that, unless otherwise specified in the applicable prospectus supplement, will represent direct, unsecured obligations of the Company and will rank equally with all of our other unsecured indebtedness.

The applicable prospectus supplement will describe the terms and features of any debt securities which we may offer, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The following description and any description of debt securities in the applicable prospectus supplement may not be complete and is subject to, and are qualified in their entirety by reference to, the indenture, any supplemental indentures or forms of debt securities, in each case that we will file with the SEC in connection with a public offering of debt securities.

General

We may issue the debt securities in one or more series with the same or various maturities, at par, at a premium, or at a discount. We will describe the particular terms of each series of debt securities in the applicable prospectus supplement relating to that series, which we will file with the SEC.

The prospectus supplement will set forth, to the extent required, the following terms of the debt securities in respect of which the prospectus supplement is delivered:

- the title of the series (which shall distinguish the debt securities of that particular series from the debt securities of any other series);
- any limit upon the aggregate principal amount of the debt securities of the series which may be authenticated and delivered under the indenture;
- the price or prices (expressed as a percentage of the principal amount thereof) at which the series of debt securities will be issued;
- the date or dates on which principal of the securities of the series is payable;
- the rate or rates (which may be fixed or variable) per annum or, if applicable, the method used to determine such rate or rates (including, but not limited to, any commodity, commodity index, stock exchange index or financial index) at which the debt securities of the series shall bear interest, if any, the date or dates from which such interest, if any, shall accrue, the date or dates on which such interest, if any, shall commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where the principal, interest and premium, if any, on the debt securities of the series are payable, or the method of such payment, if by wire transfer, mail or other means;
- if applicable, the period or periods within which, the price or prices at which and the terms and conditions upon which the debt securities of the series may be redeemed, in whole or in part, at our option;
- our obligation, if any, to redeem or purchase the debt securities of the series pursuant to any sinking fund or analogous provisions or at the option of a holder thereof, and the period or periods within which, the price or prices at which and the terms and conditions upon which debt securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;
- the dates, if any, on which and the price or prices at which the debt securities of the series will be repurchased by us at the option of the holders thereof, and other detailed terms and provisions of such repurchase obligations;

- if other than denominations of $1,000 and any integral multiple thereof, the denominations in which the debt securities of the series shall be issuable;
- the forms of the debt securities of the series in bearer (if to be issued outside of the United States of America) or fully registered form (and, if in fully registered form whether the debt securities will be issuable as global securities);
- if other than the principal amount thereof, the portion of the principal amount of the debt securities of the series that shall be payable upon declaration of acceleration of the maturity thereof;
- the currency of denomination of the debt securities of the series, which may be dollars or any foreign currency, and the agency or organization, if any, responsible for overseeing such composite currency;
- the designation of the currency, currencies or currency units in which payment of the principal of, and interest and premium, if any, on the debt securities of the series will be made;
- if payments of principal of, or interest or premium, if any, on the debt securities of the series are to be made in one or more currencies or currency units other than the that or those in which such securities are denominated are, the manner in which the exchange rate with respect to such payments will be determined;
- the manner in which the amounts of payment of principal of, or interest and premium, if any, on the debt securities of the series will be determined if such amounts may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index;
- the provisions, if any, relating to any collateral provided for the debt securities of the series;
- any addition to or change in the covenants in the indenture which applies to the debt securities of the series;
- any addition to or change in the events of default which applies to any debt securities of the series, and any change in the right of the trustee or the requisite holders of such debt securities to declare the principal amount thereof due and payable;
- the terms and conditions, if any, for conversion of the debt securities into or exchange of the debt securities for shares of common stock or preferred stock of the Company that apply to debt securities of the series;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to debt securities of such series;
- the terms and conditions, if any, upon which the debt securities shall be subordinated in right of payment to other indebtedness of the Company;
- if applicable, that the debt securities of the series, in whole or any specified part, shall be defeasible; and
- any other terms of the debt securities of the series (which terms shall not be inconsistent with the provisions of the indenture, except as permitted by the indenture, but which may modify or delete any provision of the indenture insofar as it applies to such series).

We may issue discount debt securities that provide for an amount less than the stated principal amount to be due and payable upon acceleration of the maturity of such debt securities in accordance with the terms of the indenture. We may also issue debt securities in bearer form, with or without coupons. If we issue discount debt securities or debt securities in bearer form, we will describe material U.S. federal income tax considerations and other material special considerations which apply to these debt securities in the applicable prospectus supplement.

We may issue debt securities denominated in or payable in a foreign currency or currencies or a foreign currency unit or units. If we do, we will describe the restrictions, elections, and general tax considerations relating to the debt securities and the foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Exchange and/or Conversion Rights

We may issue debt securities which can be exchanged for or converted into shares of our common stock or preferred stock. If we do, we will describe the terms of exchange or conversion in the applicable prospectus supplement relating to these debt securities.

Transfer and Exchange

We may issue debt securities that will be represented by either:

- "book-entry," which means that there will be one or more global securities registered in the name of a depositary or a nominee of a depositary; or
- "certificated securities," which means that they will be represented by a certificate issued in definitive registered form.

We will specify in the prospectus supplement applicable to a particular offering whether the debt securities offered will be book-entry or certificated securities.

Certificated Debt Securities

If we issue certificated debt securities, a holder may transfer or exchange such debt securities at the trustee's office or at the paying agent's office or agency in accordance with the terms of the indenture. A holder will not be charged a service charge for any transfer or exchange of certificated debt securities but may be required to pay an amount sufficient to cover any tax or other governmental charge payable in connection with such transfer or exchange.

A holder may effect the transfer of certificated debt securities and of the right to receive the principal of, premium, and/or interest, if any, on the certificated debt securities only by surrendering the certificate representing the certificated debt securities and having us or the trustee issue a new certificate to the new holder.

Global Securities

If we decide to issue debt securities in the form of one or more global securities, then we will register the global securities in the name of the depositary for the global securities or the nominee of the depositary, and the global securities will be delivered by the trustee to the depositary for credit to the accounts of the holders of beneficial interests in the debt securities.

The prospectus supplement will describe the specific terms of the depositary arrangement for debt securities of a series that are issued in global form. None of our Company, the trustee, any payment agent or the security registrar will have any responsibility or liability for any aspect of the records relating to or payments made on account of beneficial ownership interests in a global debt security or for maintaining, supervising or reviewing any records relating to these beneficial ownership interests.

No Protection in the Event of Change of Control

Unless we indicate otherwise in a prospectus supplement with respect to a particular series of debt securities, the debt securities will not contain any provisions that may afford holders of debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control).

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities.

Consolidation, Merger and Sale of Assets

Unless we indicate otherwise in a prospectus supplement, we will not in any transaction or series of transactions, merge or consolidate with or into, or sell, assign, convey or transfer, lease or otherwise dispose of all or substantially all of our properties and assets, unless:

- either (A) if the transaction or series of transactions is a merger or consolidation, the Company shall be the surviving person of such merger or consolidation, or (B) the person formed by such consolidation or into which the Company is merged or to which the properties and assets of the Company are transferred shall be a corporation or entity treated as a corporation for U.S. federal income tax purposes organized and existing under the laws of the United States of America, any state thereof or the District of Columbia, or a corporation or comparable legal entity treated as a corporation for U.S. federal income tax purposes organized under the laws of a foreign jurisdiction and shall expressly assume by a supplemental indenture executed and delivered to the trustee, in form reasonably satisfactory to the trustee, all of the obligations of the Company (including, without limitation, the obligation to pay the principal of, and premium and interest, if any, on, the securities and the performance of the other covenants) under the indenture as supplemented, and in each case, the indenture shall remain in full force and effect; and
- immediately before and immediately after giving effect to such transaction or series of transactions on a pro forma basis (including, without limitation, any indebtedness incurred or anticipated to be incurred in connection with or in respect of such transaction or series of transactions), no default or event of default shall have occurred and be continuing.

Events of Default

Unless otherwise specified in the applicable prospectus supplement, the following events will be events of default under the indenture with respect to debt securities of any series:

- we default in the payment of any principal of, or premium, if any, on, the debt securities when it becomes due and payable at maturity, upon acceleration, redemption or otherwise;
- we default in the payment of any interest on any debt security of a series when the same becomes due and payable, and the default continues for a period of 30 days;
- we default in observance or performance of any other covenant in the debt securities of a series or the indenture for 60 days after written notice from the trustee or the holders of not less than 25% in the aggregate principal amount of the debt securities of such series then outstanding which notice must specify the default, demand that it be remedied and state that the notice is a "Notice of Default";
- certain events involving bankruptcy, insolvency or reorganization of Zenas or any of our significant subsidiaries; and
- any other event of default provided for in such series of debt securities as may be specified in the applicable prospectus supplement.

Holders of a majority in principal amount of the debt securities of any series then outstanding have the right to waive any existing default or event of default with respect to such series or compliance with any provision of the indenture (with respect to such series) or the debt securities of such series with written notice to the trustee. Upon any such waiver, such default with respect to such series shall cease to exist, and any event of default with respect to such series arising therefrom shall be deemed to have been cured for every purpose of the indenture; but no such waiver shall extend to any subsequent or other default or event of default or impair any right consequent thereto. If an event of default (other than an event of default resulting from certain events of bankruptcy, insolvency or reorganization with respect to the Company) occurs, and is continuing, then the trustee, by written notice, or the holders of not less than 25% in aggregate principal amount of the outstanding debt securities of that series may declare that the entire principal amount, plus the premium, if any, of all the debt securities of that series then outstanding plus accrued and unpaid interest to the date of acceleration are immediately due and payable. At any time after the acceleration, but before a judgment or decree based on such acceleration is obtained by the trustee, the holders of a majority in aggregate principal amount of outstanding debt securities of such series may rescind and annul such acceleration if:

- all existing events of default (other than nonpayment of accelerated principal, premium or interest) have been cured or waived;
- all lawful interest on overdue installments of interest and overdue principal have been paid; and

- the rescission would not conflict with any judgment or decree.

In addition, if the acceleration occurs at any time when we have outstanding indebtedness which is senior to the debt securities, the payment of the principal amount of outstanding debt securities may be subordinated in right of payment to the prior payment of any amounts due under the senior indebtedness, in which case the holders of debt securities will be entitled to payment under the terms prescribed in the instruments evidencing the senior indebtedness and the indenture.

If an event of default resulting from certain events of bankruptcy, insolvency or reorganization with respect to the Company occurs, such principal, premium, if any, and interest amount with respect to all the debt securities of that series shall be due and payable immediately without any declaration or other act on the part of the trustee or the holders of the debt securities of that series.

The holders of a majority in principal amount of the outstanding debt securities of a series will have the right to waive any existing default or compliance with any provision of the indenture or the debt securities of that series and to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, subject to certain limitations specified in the indenture.

No holder of any debt security of a series will have any right to institute any proceeding with respect to the indenture or for any remedy under the indenture, unless:

- the holder gives to the trustee written notice of a continuing event of default with respect to the debt securities of that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of the affected series make a written request to the trustee;
- the holder or holders offer to the trustee indemnity satisfactory to the trustee against any loss, liability or expense to be incurred in compliance with such request;
- the trustee does not comply with the request within 60 days after such request; and
- the holders of a majority in aggregate principal amount of the outstanding debt securities of the affected series do not give the trustee a direction inconsistent with such request during such 60-day period.

Modification and Waiver

From time to time, we and the trustee may, without the consent of holders of the debt securities of one or more series, amend the indenture or the debt securities of one or more series, or supplement the indenture, for certain specified purposes, including:

- to provide that the surviving entity following a change of control of Zenas permitted under the indenture will assume all of our obligations under the indenture and debt securities;
- to provide for certificated debt securities in addition to uncertificated debt securities;
- to comply with any requirements of the SEC under the Trust Indenture Act of 1939;
- to cure any mistake, ambiguity, defect or inconsistency, or make any other change that does not materially and adversely affect the rights of any holder;
- to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture; and
- to evidence and provide for the acceptance of the appointment of a successor trustee under the indenture with respect to one or more series and to add to or change any of the provisions of the indenture as shall be necessary to provide for or facilitate the administration of the trusts by more than one trustee.

From time to time we and the trustee may, with the consent of holders of not less than a majority of the aggregate principal amount of an outstanding series of debt securities, amend or supplement the indenture or the debt securities series, or waive compliance in a particular instance by us with any provision

of the indenture or the debt securities. We may not, however, without the consent of each holder affected by such action, modify or supplement the indenture or the debt securities or waive compliance with any provision of the indenture or the debt securities in order to:

- reduce the amount of debt securities whose holders must consent to an amendment, supplement, or waiver to the indenture or such debt security;
- reduce the rate of or change the time for payment of interest on any of the debt securities;
- reduce the principal of or change the stated maturity of the debt securities, or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation;
- make any debt security payable in money other than that stated in the debt security;
- change the amount or time of any payment required by the debt securities or reduce the premium payable upon any redemption of the debt securities, or change the time before which no such redemption may be made;
- waive a default or event of default in the payment of the principal of, or interest or premium, if any, on any debt securities (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in principal amount of the outstanding debt securities of such series and a waiver of the payment default that resulted from such acceleration);
- waive a redemption payment with respect to any debt securities or change any provision with respect to redemption of debt securities;
- take any other action otherwise prohibited by the indenture to be taken without the consent of each holder affected by the action; or
- make any changes to the above provisions or the acceleration provisions of the indenture, except to increase any percentage of debt securities the holders of which must consent to any matter.

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

The indenture permits us, at any time, to elect to discharge our obligations with respect to one or more series of debt securities by following certain procedures described in the indenture. These procedures will allow us either:

- to defease and be discharged from any and all of our obligations with respect to any debt securities except for the following obligations (which discharge is referred to as "legal defeasance"):
  (1) to replace temporary or mutilated, destroyed, lost or stolen debt securities;
  (2) the rights, powers, trusts, duties and immunities of the trustee; or
  (3) to maintain an office or agency in respect of the debt securities and to hold monies for payment in trust; or
- to be released from our obligations with respect to the debt securities under certain covenants contained in the indenture, as well as any additional covenants which may be contained in an applicable supplemental indenture (which release is referred to as "covenant defeasance").

In order to exercise either defeasance option, we must irrevocably deposit with the trustee or other qualifying trustee, in trust for that purpose:

- money;
- U.S. Government Obligations (as described below) or Foreign Government Obligations (as described below) which through the scheduled payment of principal and interest in accordance with their terms will provide, not later than the due date of any payment, money; or
- a combination of money and/or U.S. Government Obligations and/or Foreign Government Obligations sufficient in the written opinion of a nationally-recognized firm of independent accountants to provide money;

which in each case specified above, provides an amount sufficient to pay the principal of, premium, if any, and interest, if any, on the debt securities of the series, on the scheduled due dates or on a selected date of redemption in accordance with the terms of the indenture.

In addition, defeasance may be effected only if, among other things:

- in the case of either legal or covenant defeasance, we deliver to the trustee an opinion of counsel, as specified in the indenture;
- in the case of legal defeasance, we deliver to the trustee an opinion of counsel stating that we have received from, or there has been published by, the Internal Revenue Service a ruling to the effect that, or there has been a change in any applicable federal income tax law with the effect that or there has been a change in any applicable U.S. Federal income tax law with the effect that, and such opinion shall confirm that, the holders of the outstanding debt securities of such series or persons will not recognize income, gain or loss for U.S. federal income tax purposes solely as a result of such legal defeasance and will be subject to U.S. federal income tax on the same amounts, in the same manner, including as a result of prepayment, and at the same times as would have been the case if legal defeasance had not occurred;
- in the case of covenant defeasance, we deliver to the trustee an opinion of counsel to the effect that the holders of the outstanding debt securities will not recognize income, gain or loss for U.S. federal income tax purposes as a result of covenant defeasance and will be subject to U.S. federal income tax on the same amounts, in the same manner and at the same times as would have been the case if covenant defeasance had not occurred; and
- certain other conditions described in the indenture are satisfied.

If we fail to comply with our remaining obligations under the indenture and any applicable supplemental indenture after a covenant defeasance of the indenture and any applicable supplemental indenture, and the debt securities are declared due and payable because of the occurrence of any undefeased event of default, the amount of money and/or U.S. Government Obligations and/or Foreign Government Obligations on deposit with the trustee could be insufficient to pay amounts due under the debt securities of the affected series at the time of acceleration. We will, however, remain liable in respect of these payments.

The term “U.S. Government Obligations” as used in the above discussion means direct non-callable obligations of or non-callable obligations guaranteed by the United States of America for the payment of which obligation or guarantee the full faith and credit of the United States of America is pledged.

The term “Foreign Government Obligations” as used in the above discussion means, with respect to Securities that are denominated in a foreign currency (i) direct obligations of the government that issued or caused to be issued such currency for the payment of which obligations its full faith and credit is pledged or (ii) obligations of a person controlled or supervised by or acting as an agency or instrumentality of such government the timely payment of which is unconditionally guaranteed as a full faith and credit obligation by such government, which in either case under clauses (i) and (ii), are not callable or redeemable at the option of the issuer thereof.

Regarding the Trustee

We will identify the trustee with respect to any series of debt securities in the prospectus supplement relating to the applicable debt securities. You should note that if the trustee becomes a creditor of Zenas, the indenture and the Trust Indenture Act of 1939 limit the rights of the trustee to obtain payment of claims in certain cases, or to realize on certain property received in respect of any such claim, as security or otherwise. The trustee and its affiliates may engage in, and will be permitted to continue to engage in, other transactions with us and our affiliates. If, however, the trustee acquires any “conflicting interest” within the meaning of the Trust Indenture Act of 1939, it must eliminate such conflict or resign.

The holders of a majority in principal amount of the then outstanding debt securities of any series may direct the time, method and place of conducting any proceeding for exercising any remedy available to the trustee. If an event of default occurs and is continuing, the trustee, in the exercise of its rights and powers, must use the degree of care and skill of a prudent person under the same circumstances in the conduct of

his or her own affairs. Subject to that provision, the trustee will be under no obligation to exercise any of its rights or powers under the indenture at the request of any of the holders of the debt securities, unless they have offered to the trustee indemnity or security against the costs, expenses and liabilities which may be incurred therein or thereby.

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the securities, will be governed by the laws of the State of New York.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement we filed with the SEC. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including us. The address of the SEC website is www.sec.gov.

We maintain a website at www.zenasbio.com. Information contained in, or accessible through, our website is not a part of, and is not incorporated into, this prospectus, and you should not consider it part of this prospectus.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" into this prospectus certain information we file with it, which means that we can disclose important information about us by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus, and information in documents that we file later with the SEC will automatically update and supersede information in this prospectus. We incorporate by reference into this prospectus the documents listed below and any future filings, including all filings made after the date of the filing of the registration statement of which this prospectus is part and prior to the effectiveness of such registration statement, made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, except for information "furnished" under Items 2.02, 7.01 or 9.01 on Form 8-K or other information "furnished" to the SEC which is not deemed filed and not incorporated in this prospectus, until the termination of the offering of securities described in the applicable prospectus supplement. We hereby incorporate by reference the following documents:

- our Annual Report on Form 10-K for the year ended December 31, 2024, as filed with the SEC on March 11, 2025;
- our Quarterly Reports on Form 10-Q for the quarter ended March 31, 2025, as filed with the SEC on May 15, 2025, and for the quarter ended June 30, 2025, as filed with the SEC on August 12, 2025;
- our Current Reports on Form 8-K filed with the SEC on June 12, 2025, September 2, 2025 and October 8, 2025;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2024 from our Definitive Proxy Statement on Schedule 14A for the 2025 Annual Meeting of Stockholders, as filed with the SEC on April 28, 2025; and
- the description of our common stock, which is in our Registration Statement on Form 8-A, dated September 10, 2024, as supplemented by the description of our common stock and preferred stock contained in Exhibit 4.3 to our Annual Report on Form 10-K for the fiscal year ended December 31, 2024, filed with the SEC on March 11, 2025.

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed modified, superseded or replaced for purposes of this prospectus to the extent that a statement contained in this prospectus modifies, supersedes or replaces such statement.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address:

Attention: Investor Relations
Zenas BioPharma, Inc.
852 Winter Street, Suite 250
Waltham, Massachusetts 02451
(857) 271-2954
email address: IR@zenasbio.com

Copies of these filings are also available, without charge, on the SEC's website at www.sec.gov and on our website at https://investors.zenasbio.com as soon as reasonably practicable after they are filed electronically with the SEC. The information contained on our website is not a part of this prospectus.

LEGAL MATTERS

The validity of the issuance of the securities offered pursuant to this prospectus will be passed upon for us by Ropes & Gray LLP, Boston, Massachusetts. The validity of any securities will be passed upon for any underwriters or agents by counsel that we will name in the applicable prospectus supplement.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2024, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.



Up to $200,000,000

Common Stock

PROSPECTUS SUPPLEMENT

Jefferies

November 6, 2026

Calculation of Filing Fee Tables

S-3

Zenas BioPharma, 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													
Fees to be Paid	1	Equity	Common Stock, par value $0.0001 per share	Other			$ 200,000,000.00	0.000087	$ 17,400.00				
Fees Previously Paid													
Carry Forward Securities													
Carry Forward Securities													
				Total Offering Amounts:			$ 200,000,000.00		$ 17,400.00				
				Total Fees Previously Paid:					$ 0.00				
				Total Fee Offsets:					$ 6,465.21				
				Net Fee Due:					$ 10,934.79				

Offering Note

1

The registration fee is calculated in accordance with Rule 457(o) under the Securities Act of 1933, as amended (the "Securities Act"), based on the proposed maximum aggregate offering price, and Rule 457(r) under the Securities Act. In accordance with Rules 456(b) and 457(r) under the Securities Act, the registrant initially deferred payment of all of the registration fee for its Registration Statement on Form S-3ASR (Registration No. 333-290777) (the "Registration Statement"), which was filed with the Securities and Exchange Commission on October 8, 2025. Pursuant to Rule 457(p) under the Securities Act, the registrant hereby applies $6,465.21 of the registration fee previously paid in connection with the Prior Prospectus Supplement (as defined below) to offset the registration fees that are payable in connection with the registration of securities under this prospectus supplement.

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	1	Zenas BioPharma, Inc.	S-3	333-290777	10/08/2025		$ 6,465.21	Equity	Common Stock, par value $0.0001 per share		$ 46,815,389.00	
Fee Offset Sources		Zenas BioPharma, Inc.	S-3	333-290777		10/08/2025						$ 6,465.21

Rule 457(p) Statement of Withdrawal, Termination, or Completion:

1

On October 8, 2025, the registrant filed the Registration Statement, which includes a sales agreement prospectus supplement covering the offering, issuance and sale by the registrant of up to an aggregate of $200,000,000 of its common stock pursuant to its "at-the-market" offering program (the "Prior Prospectus Supplement"). The registrant incurred a filing fee in the amount of $27,620.00 in connection with the Prior Prospectus Supplement, which fee was calculated pursuant to Rule 457(o) under the Securities Act (at the fee rate in effect on the filing date of the

Prior Prospectus Supplement of $138.10 per million dollars of the maximum aggregate offering price). As of the date of filing of this prospectus supplement, $46,815,389.00 of shares of the registrant's common stock (the "Unsold Securities") remained unsold under the Prior Prospectus Supplement. Pursuant to Rule 457(p) under the Securities Act, filing fees in the amount of $6,465.21 relating to the Unsold Securities are being carried forward, and the offering pursuant to the Prior Prospectus Supplement is deemed terminated.

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

Narrative Disclosure

The maximum aggregate offering price of the securities to which the prospectus relates is $200,000,000.00. The prospectus is a final prospectus for the related offering.