Supplement dated April 27, 2023

To Prospectus dated July 1, 2022



Up to \$50,000,000 of Shares

Common Stock

This prospectus supplement, or Prospectus Supplement, supplements certain information contained in the sales agreement prospectus dated July 1, 2022, or the Sales Agreement Prospectus, relating to the offer and sale of shares of our common stock having an aggregate offering price of up to \$50,000,000 from time to time through or directly to BofA Securities, Inc. and Stifel, Nicolaus & Company, Incorporated, acting as sales agents, in sales deemed to be "at the market offerings" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. This Prospectus Supplement should be read in conjunction with the Sales Agreement Prospectus and the base prospectus dated July 1, 2022, or the Prospectus. Capitalized terms used and not defined herein shall have the meanings ascribed to such terms in the Sales Agreement Prospectus.

We have entered into an amended Sales Agreement with BofA Securities, Inc., Stifel, Nicolaus & Company, Incorporated, and BTIG, LLC, collectively referred to as Sales Agents and each individually a Sales Agent, pursuant to which we may offer and sell our common stock, par value \$0.0001 per share, from time to time through the Sales Agents in sales deemed to be "at the market offerings" as defined in Rule 415 promulgated under the Securities Act. This Prospectus Supplement is being filed to reflect the amendment of the sales agreement by and between us and BofA Securities, Inc. and Stifel, Nicolaus & Company, Incorporated, to include BTIG, LLC, as an additional Sales Agent. Accordingly, each reference to the term "Sales Agents" in the Sales Agreement Prospectus are hereby amended to refer to "Sales Agents" and include BTIG, LLC.

As of April 26, 2023, we have sold 422,160 shares of our common stock having an aggregate offering price of approximately \$4,246,131 under the sales agreement with BofA Securities, Inc. and Stifel, Nicolaus & Company, Incorporated, pursuant to the Sales Agreement Prospectus. As of the date of this Prospectus Supplement, shares of common stock having an aggregate offering price of approximately \$45,753,869 are available for sale under the Sales Agreement Prospectus and this Prospectus Supplement. On April 26, 2023, the last reported sale price of our common stock on Nasdaq Capital Market was \$3.76 per share.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" beginning on page S-4 of the Sales Agreement Prospectus, on page 5 of the accompanying Prospectus and discussed in our most recent Annual Report on Form 10-K and other reports and information that we file from time to time with the Securities and Exchange Commission, or the SEC, which are incorporated by reference into this Prospectus Supplement and the accompanying Sales Agreement Prospectus.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS SUPPLEMENT OR THE ACCOMPANYING SALES AGREEMENT PROSPECTUS OR PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

BofA Securities Stifel BTIG

The date of this prospectus is April 27, 2023.

PLAN OF DISTRIBUTION

We have entered into an amendment, dated as of April 27, 2023 ("Amendment No. 1"), to the Sales Agreement, dated as of July 1, 2022 (the "Sales Agreement" and, as amended by Amendment No. 1, the "Amended Sales Agreement") with BofA Securities, Inc., Stifel, Nicolaus & Company, Incorporated and BTIG, LLC (collectively, "Sales Agents" and, each individually, a "Sales Agent"). Amendment No. 1 is filed as an exhibit to our Current Report on Form 8-K filed with the SEC on April 27, 2023, which is incorporated by reference in this Prospectus Supplement. Pursuant to the Amended Sales Agreement, we may, over a period of time and from time to time, offer and sell shares of our common stock having an aggregate sales price of up to \$50.0 million through the Sales Agents or to the Sales Agents. As of April 26, 2023, we have sold 422,160 shares of our common stock having an aggregate offering price of approximately \$4,246,131 under the Sales Agreement, pursuant to the Sales Agreement Prospectus. As of the date of this Prospectus Supplement, shares of common stock having an aggregate offering price of approximately \$45,753,869 are available for sale under the Sales Agreement Prospectus and this Prospectus Supplement. The sales, if any, of our common stock made under the Amended Sales Agreement, and to which this prospectus relates, will be made in "at-the-market" offerings as defined in Rule 415 under the Securities Act, including sales made directly on The Nasdaq Global Select Market, the existing trading market for our common stock, or sales made to or through a market maker or through an electronic communications network. In addition, our common stock may be offered and sold by such other methods, including privately negotiated transactions, as we and the Sales Agents agree to in writing. The sales may be made at market prices prevailing at the time of the sale, at prices related to prevailing market prices or at negotiated prices.

We also may sell shares of our common stock to the Sales Agents, as principal for their own respective accounts, at a price per share agreed upon at the time of sale. If we sell shares of our common stock to the Sales Agents, as principal, we will enter into a separate terms agreement with the Sales Agents, and we will describe the agreement in a separate prospectus supplement or pricing supplement.

From time to time during the term of the Amended Sales Agreement, we may deliver a placement notice to a Sales Agent specifying the length of the selling period, the amount of shares of common stock to be sold and the minimum price below which sales may not be made.

The Sales Agents have agreed that, upon receipt of a placement notice from us that is accepted by such Sales Agent, and is subject to the terms and conditions of the Amended Sales Agreement, the applicable Sales Agent will use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares of our common stock on such terms. We or the applicable Sales Agent may suspend the offering of the shares of common stock at any time upon proper notice to the other party, upon which the selling period will immediately terminate. Settlement for sales of the shares of our common stock is expected to occur on the second business day, that is also a trading day, following the date on which any sales were made, or on some other date that is agreed upon by us and the applicable Sales Agent in connection with a particular transaction. The obligation of the Sales Agents under the Amended Sales Agreement to sell common shares pursuant to any placement notice is subject to a number of conditions, which the Sales Agents reserve the right to waive in their sole discretion.

If acting as a sales agent, the applicable Sales Agent will provide to us written confirmation following the close of trading on The Nasdaq Global Select Market on each trading day on which shares are sold under the Amended Sales Agreement. Each confirmation will include the number of shares sold on that day, the aggregate gross sales proceeds of the shares, the net proceeds to us (after deduction of any transaction fees, transfer taxes or similar taxes or fees imposed by any governmental entity or self-regulatory organization in respect of such sales) and the aggregate compensation payable by us to the applicable Sales Agent with respect to such sales. We will report, on a quarterly basis, the number of shares sold by or through the Sales Agents during such quarterly fiscal period, the net proceeds received by the Company and the aggregate compensation paid by the Company to the Sales Agents with respect to such sales.

We will pay the Sales Agents an aggregate commission of up to 3.0% of the gross sales price per share for any shares sold through it as an agent under the Amended Sales Agreement. We have agreed to reimburse the Sales Agents for certain fees and expenses in connection with this offering, including the fees and disbursements of counsel to the Sales Agents. We estimate that the total expenses of this offering payable by us, excluding commissions and reimbursements payable to the Sales Agents under the Amended Sales Agreement, will be approximately \$460,000.

In connection with the sale of our common stock on our behalf, either Sales Agent may be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation paid to the Sales Agents may be deemed to be underwriting commissions or discounts. We have agreed in the Amended Sales Agreement to provide indemnification and contribution to the Sales Agents against certain civil liabilities, including liabilities under the Securities Act.

Sales of the common stock as contemplated by this prospectus will be settled through the facilities of the Depository Trust Company or by such other means as we and the Sales Agents may agree upon. The offering of the common stock pursuant to the Amended Sales Agreement will terminate upon the earliest of (1) the sale of the maximum aggregate amount of our common stock subject to the Amended Sales Agreement, (2) the expiration date of the registration statement of which this prospectus is a part, and (3) the termination of the Amended Sales Agreement by any party at any time upon three days' notice, or by the Sales Agents, upon notice to us, in certain circumstances, including certain bankruptcy events relating to us or any material subsidiary, our failure to maintain a listing of our common stock on The Nasdaq Global Select Market or the occurrence of a material adverse effect on our Company, as defined in the Amended Sales Agreement.

The Sales Agents and their affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. The Sales Agents and their affiliates have provided, and may in the future provide, a variety of these services to us and to persons and entities with relationships with us, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the Sales Agents and their affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own accounts and for the accounts of their customers, and such investment and trading activities may involve or relate to our assets, securities and/or instruments (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with us. The Sales Agents and their affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

Selling Restrictions

Other than in the United States, no action has been taken by us or the Sales Agents that would permit a public offering of the shares of common stock offered by this prospectus in any jurisdiction where action for that purpose is required. The shares offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such shares be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any shares of common stock offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

You should be aware that the laws and practices of certain countries require investors to pay stamp taxes and other charges in connection with purchases of securities.

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each a "Relevant State"), no shares of our common stock have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in

that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation), except that offers of shares may be made to the public in that Relevant State at any time under the following exemptions under the Prospectus Regulation:

- a. to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
- b. to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of representatives for any such offer; or
- c. in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of shares shall require the Issuer or the Sales Agents to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

Each person in a Relevant State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with us and the Sales Agents that it is a qualified investor within the meaning of the Prospectus Regulation.

In the case of any shares being offered to a financial intermediary as that term is used in Article 5(1) of the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer to the public other than their offer or resale in a Relevant State to qualified investors, in circumstances in which the prior consent of the Sales Agent has been obtained to each such proposed offer or resale.

We, the Sales Agents and our respective affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares, and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129.

The above selling restriction is in addition to any other selling restrictions set out below.

Notice to Prospective Investors in the United Kingdom

In relation to the United Kingdom ("UK"), no shares have been offered or will be offered pursuant to the offering to the public in the UK prior to the publication of a prospectus in relation to the shares which has been approved by the Financial Conduct Authority in the UK in accordance with the UK Prospectus Regulation and the FSMA, except that offers of shares may be made to the public in the UK at any time under the following exemptions under the UK Prospectus Regulation and the FSMA:

- a. to any legal entity which is a qualified investor as defined under the UK Prospectus Regulation;
- b. to fewer than 150 natural or legal persons (other than qualified investors as defined under the UK Prospectus Regulation), subject to obtaining the prior consent of representatives for any such offer; or
- c. at any time in other circumstances falling within section 86 of the FSMA,

provided that no such offer of shares shall require the Issuer or the Sales Agents to publish a prospectus pursuant to Section 85 of the FSMA or Article 3 of the UK Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation.

Each person in the UK who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with us and the Sales Agents that it is a qualified investor within the meaning of the UK Prospectus Regulation.

In the case of any shares being offered to a financial intermediary as that term is used in Article 5(1) of the UK Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer to the public other than their offer or resale in the UK to qualified investors, in circumstances in which the prior consent of the Sales Agents has been obtained to each such proposed offer or resale.

We, the Sales Agents and our respective affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

For the purposes of this provision, the expression an "offer to the public" in relation to any in the UK means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares, the expression "UK Prospectus Regulation" means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018, and the expression "FSMA" means the Financial Services and Markets Act 2000.

This document is for distribution only to persons who (i) have professional experience in matters relating to investments and who qualify as investment professionals within the meaning of Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (as amended, the "Financial Promotion Order"), (ii) are persons falling within Article 49(2)(a) to (d) ("high net worth companies, unincorporated associations etc.") of the Financial Promotion Order, (iii) are outside the United Kingdom, or (iv) are persons to whom an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000, as amended ("FSMA")) in connection with the issue or sale of any securities may otherwise lawfully be communicated or caused to be communicated (all such persons together being referred to as "relevant persons"). This document is directed only at relevant persons and must not be acted on or relied on by persons who are not relevant persons. Any investment or investment activity to which this document relates is available only to relevant persons and will be engaged in only with relevant persons.

Notice to Prospective Investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange ("SIX") or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, Acumen Pharmaceuticals, Inc., the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes ("CISA"). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to Prospective Investors in the Dubai International Financial Centre

This prospectus relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority ("DFSA"). This prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth herein and has no responsibility for the prospectus. The shares to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus you should consult an authorized financial advisor.

Notice to Prospective Investors in Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission ("ASIC"), in relation to the offering. This prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001 (the "Corporations Act"), and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons (the "Exempt Investors") who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Notice to Prospective Investors in Hong Kong

The securities have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the securities has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to Prospective Investors in Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, "Japanese Person" shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, the securities were not offered or sold or caused to be made the subject of an invitation for subscription or purchase and will not be offered or sold or caused to be made the subject of an invitation for subscription or purchase, and this prospectus or any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the securities, has not been circulated or distributed, nor will it be circulated or distributed, whether directly or indirectly, to any person in Singapore other than (i) to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time (the "SFA")) pursuant to Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the securities pursuant to an offer made under Section 275 of the SFA except:

- (a) to an institutional investor or to a relevant person, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- (b) where no consideration is or will be given for the transfer;
- (c) where the transfer is by operation of law; or
- (d) as specified in Section 276(7) of the SFA.

Notice to Prospective Investors in Canada

The securities may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the securities must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 *Underwriting Conflicts* (**NI 33-105**), the Sales Agents are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

LEGAL MATTERS

The validity of the securities offered by this prospectus will be passed upon by Ropes & Gray LLP. Latham & Watkins LLP has acted as counsel for the sales agents in connection with certain legal matters related to this offering.