

Up to \$50,000,000

Common Stock

We have entered into an Open Market Sale AgreementSM, or the sales agreement, with Jefferies LLC, or Jefferies, dated March 15, 2022, relating to the sale of shares of our common stock. In accordance with the terms of the sales agreement, pursuant to this prospectus, we may offer and sell shares of our common stock, \$0.0001 par value per share, from time to time having an aggregate offering price of up to \$50.0 million through Jefferies, acting as our sales agent.

Our common stock is traded on The Nasdaq Global Market under the symbol "SNSE." On March 11, 2022, the last reported sale price of our common stock was \$2.70 per share.

Sales of our common stock, if any, under this prospectus will be made by any method permitted that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. Jefferies is not required to sell any specific number or dollar amount of securities, but will act as a sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between Jefferies and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Jefferies will be entitled to compensation under the terms of the sales agreement at a fixed commission rate equal to 3.0% of the gross sales price per share sold under the sales agreement. In connection with the sale of common stock on our behalf, Jefferies will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. See section titled "Plan of Distribution" beginning on page S-11 of this prospectus regarding the compensation to be paid to Jefferies. We have also agreed to provide indemnification and contribution to Jefferies against certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act.

We are an "emerging growth company" and "smaller reporting company" under the federal securities laws and, as such, are subject to reduced public company reporting requirements. See "Prospectus Summary—Implications of Being an Emerging Growth Company and Smaller Reporting Company."

Investing in our securities involves a high degree of risk. See "<u>Risk Factors</u>" beginning on page S-5 of this prospectus and under similar headings in the other documents that are incorporated by reference into this prospectus concerning factors you should consider 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 passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

Jefferies

The date of this prospectus is May 9, 2022.

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ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement that we have filed on Form S-3 with the U.S. Securities and Exchange Commission, or the SEC, utilizing a "shelf" registration process. By using a shelf registration statement, we may offer shares of our common stock having an aggregate offering price of up to \$50.0 million shares of our common stock from time to time under this prospectus and on terms to be determined by market conditions at the time of the offering.

Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus, together with the information incorporated by reference as described under the headings "Where You Can Find More Information" and "Incorporation of Certain Information by Reference" in this prospectus, and any free writing prospectus or prospectus supplement that we have authorized for use in connection with this offering. These documents contain important information that you should consider when making your investment decision.

This prospectus describes the terms of this offering of common stock and also adds to and updates information contained in the documents incorporated by reference into this prospectus. To the extent there is a conflict between the information contained in this prospectus, on the one hand, and the information contained in any document incorporated by reference into this prospectus that was filed with the SEC before the date of this prospectus, on the other hand, you should rely on the information in this prospectus. If any statement in one of these documents is inconsistent with a statement in another document having a later date - for example, a document incorporated by reference into this prospectus - the statement in the document having the later date modifies or supersedes the earlier statement.

Neither we nor Jefferies have authorized anyone to provide you with information that is different from that contained in this prospectus or in any free writing prospectus we may authorize to be delivered or made available to you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are not, and Jefferies is not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus, the documents incorporated by reference in this prospectus, and in any free writing prospectus or prospectus supplement that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus, the documents incorporated by reference in this prospectus, and any free writing prospectus or prospectus supplement that we have authorized for use in connection or prospectus supplement that we have authorized for use in connection or prospectus supplement that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents incorporated by reference in this prospectus, and any free writing prospectus or prospectus supplement that we have authorized for use in connection with this offering, in their entirety before making an investment decision.

As used in this prospectus, unless the context otherwise requires, references to "we," "us," "our," "the company," "Sensei" and "Sensei Biotherapeutics" refer to Sensei Biotherapeutics, Inc., together with its consolidated subsidiaries. We own various U.S. federal trademark applications and unregistered trademarks, including our company name. All other trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the symbols \mathbb{B} and \mathbb{M} , but such references should not be construed as any indication that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

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SUMMARY

This following summary highlights information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus, including the information incorporated by reference in this prospectus, and the information included in any free writing prospectus that we have authorized for use in connection with this offering, including the information under the heading "Risk Factors" in this prospectus on page S-5 and in the documents incorporated by reference into this prospectus.

Overview

We are a biopharmaceutical company engaged in the discovery, development, and delivery of next-generation immunotherapies with an initial focus on treatments for cancer. Our focus is to leverage well characterized biological targets to generate novel product candidates that incorporate next generation technologies or approaches. We have built a robust set of R&D capabilities and infrastructure to support the discovery and advancement of our product candidates. Our goal is to efficiently develop these product candidates by incorporating state-of-the-art biomarker approaches and mechanistic understanding into clinical trial designs targeted to well-defined patient populations.

We have developed two platforms that are designed to address resistance to immunotherapy. Our TMAb (Tumor Microenvironment Activated Biologics) platform generates next-generation antibodies that block key immune checkpoints selectively within the tumor microenvironment. Our ImmunoPhage platform is a pioneering approach to cancer therapy that utilizes and combines aspects of vaccine, gene therapy, and personalized medicine approaches. Both platforms are designed to work independently or have the potential to be combined for to create powerful rational drug combinations.

Our Pipeline

We believe there are multiple opportunities and significant potential for patients within our product pipeline. Each program is derived from either our TMAb or ImmunoPhage platform and targets validated immune checkpoints or tumor antigens.

	Program (Target)	Indication	Discovery	IND-enabling	Phase 1 / 2 Clinical
T ak	SNS-101 (VISTA)	Solid Tumors			
	SNS-102 (VSIG4)	Solid Tumors			
	SNS-103 (ENTPDase1/CD39)	Solid Tumors			
ImmunoPhage	SNS-401-NG (Mutiple Tumor Antigens)	Merkel Cell Carcinoma			
		Head and Neck Cancer			
		Lung Cancer		1	
		Melanoma			
		Breast Cancer		0	

Corporate Information

We were originally incorporated as Panacea Pharmaceuticals, Inc., or Panacea, under the laws of the state of Maryland in 1999. In December 2017, in order to reincorporate in the state of Delaware, we entered into an Agreement and Plan of Merger, or Merger Agreement, by and among us, Panacea and our wholly owned subsidiary, PPI Acquisition I Corp., a Delaware corporation, or Merger Sub. Pursuant to the Merger Agreement, Merger Sub merged with and into Panacea and Panacea became our wholly-owned subsidiary. In connection with our reincorporation in Delaware, we changed our name to Sensei Biotherapeutics, Inc.

Our principal executive offices are located at 451 D Street, Suite 710, Boston, MA 02210. Our telephone number is (240) 243-8000. Our website address is www.senseibio.com. Information contained on, or that can be accessed through, our website is not incorporated by reference into this prospectus. We have included our website in this prospectus solely as an inactive textual reference.

Implications of Being an Emerging Growth Company and a Smaller Reporting Company

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For so long as we remain an emerging growth company, we may take advantage of relief from certain reporting requirements and other burdens that are otherwise applicable generally to public companies. These provisions include:

- reduced obligations with respect to financial data, including only being required to present two years of audited financial statements, in addition to any required unaudited interim financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- an exception from compliance with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended;
- reduced disclosure about our executive compensation arrangements in our periodic reports, proxy statements and registration statements;
- exemptions from the requirements of holding non-binding advisory votes on executive compensation or golden parachute arrangements; and
- an exemption from compliance with the requirements of the Public Company Accounting Oversight Board regarding the communication of critical audit matters in the auditor's report on financial statements.

We may take advantage of these provisions until we no longer qualify as an emerging growth company. We will cease to qualify as an emerging growth company on the date that is the earliest of: (i) December 31, 2026, (ii) the last day of the fiscal year in which we have more than \$1.07 billion in total annual gross revenues, (iii) the date on which we are deemed to be a "large accelerated filer" under the rules of the U.S. Securities and Exchange Commission, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th, or (iv) the date on which we have issued more than \$1.0 billion of non-convertible debt over the prior three-year period. We may choose to take advantage of some but not all of these reduced reporting burdens. We have taken advantage of certain reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different than you might obtain from other public companies in which you hold equity interests.

In addition, under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to take advantage of the extended transition period to comply with new or revised accounting standards and to adopt certain of the reduced disclosure requirements available to emerging growth companies. As a result of the accounting standards election, we will not be subject to the same implementation timing for new or revised accounting standards as

other public companies that are not emerging growth companies, which may make comparison of our financials to those of other public companies more difficult. As a result of these elections, the information that we provide in this prospectus may be different than the information you may receive from other public companies in which you hold equity interests. In addition, it is possible that some investors will find our common stock less attractive as a result of these elections, which may result in a less active trading market for our common stock and higher volatility in our share price.

We are also a "smaller reporting company," meaning that the market value of our shares held by non-affiliates is less than \$700 million and our annual revenue was less than \$100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company after this offering if either (i) the market value of our shares held by non-affiliates is less than \$250 million or (ii) our annual revenue was less than \$100 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

THE OFFERING				
Common stock offered by us	Shares of our common stock having an aggregate offering price of up to \$50,000,000.			
Common stock to be outstanding after this offering	49,127,547 shares, assuming sales of 18,518,518 shares of our common stock in this offering at an offering price of \$2.70 per share, the last reported sale price of our common stock on The Nasdaq Global Market on March 11, 2022. The actual number of shares issued will vary depending on the sales price under this offering.			
Manner of offering	"At the market offering" that may be made from time to time through Jefferies. See "Plan of Distribution" on page S-10.			
Use of proceeds	We currently intend to use the net proceeds from this offering primarily to fund the research and development of our product candidates and for working capital and general corporate purposes. We may also use a portion of the net proceeds to invest in or acquire businesses or technologies that we believe are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus. See "Use of Proceeds."			
Risk factors	You should read the "Risk Factors" section of this prospectus and in the documents incorporated by reference herein for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.			
Nasdaq Global Market symbol	"SNSE"			

The number of shares of our common stock that will be outstanding after this offering is based on 30,609,029 shares of our common stock outstanding as of December 31, 2021, and excludes:

- 3,026,464 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2021, at a weighted-average exercise price of \$10.84 per share;
- 469,266 shares of common stock issuable upon the exercise of warrants outstanding as of December 31, 2021, at a weighted-average exercise price of \$9.46 per share;
- 1,964,702 shares of our common stock reserved for future issuance under our 2021 Equity Incentive Plan; and
- 321,633 shares of our common stock reserved for future issuance under our 2021 Employee Stock Purchase Plan.

Unless otherwise indicated, all information in this prospectus assumes no exercise of the outstanding options and no vesting of restricted stock units, and reflects an assumed public offering price of \$2.70 per share, the last reported sale price of our common stock on The Nasdaq Global Market on March 11, 2022.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before you decide to invest in our common stock, you should carefully consider the risks and uncertainties described below together with all other information contained in this prospectus and in our filings with the SEC that we have incorporated by reference into this prospectus. See the sections of this prospectus entitled "Where You Can Find More Information" and "Incorporation of Certain Information by Reference." If any of the following risks actually occurs, our business, prospects, operating results and financial condition could suffer materially. In such event, the trading price of our common stock could decline and you might lose all or part of your investment.

Additional Risks Related to This Offering

We have broad discretion over the use of our cash, cash equivalents and marketable securities, including the net proceeds we receive in this offering, and may not use them effectively.

We currently intend to use the net proceeds from this offering primarily to fund the research and development of our product candidates and for working capital and general corporate purposes. Our management has broad discretion to use our cash and cash equivalents, including the net proceeds we receive in this offering, to fund our operations and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have an adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use to fund operations, we may invest our cash, cash equivalents and marketable securities in a manner that does not produce income or that losses value. See "Use of Proceeds."

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

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Because the sales of the shares offered hereby will be made directly into the market, the prices at which we sell these shares will vary and these variations may be significant. Purchasers of the shares we sell, as well as our existing stockholders, will experience significant dilution if we sell shares at prices significantly below the price at which they invested.

Investors in this offering may experience future dilution.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into, or exchangeable for, our common stock at prices that may not be the same as the price per share in this offering. We cannot assure you that we will be able to sell shares of our common stock or other related securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering. If the price per share at which we sell additional shares of our common stock or related securities in future transactions is less than the price per share in this offering, investors who purchase our common stock in this offering will suffer dilution in their investment.

In addition, we have a significant number of stock options and unvested restricted stock units for shares of our common stock outstanding. To the extent that outstanding stock options or warrants have been or may be exercised or we have issued shares of our common stock upon the vesting of restricted stock units, investors purchasing our common stock in this offering may experience further dilution in the future. Furthermore, a significant portion of our total outstanding shares are eligible to be sold into the market, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

The actual number of shares of common stock we will issue under the sales agreement, at any one time or in total, is uncertain.

Subject to certain limitations in the sales agreement and compliance with applicable law, we have the discretion to deliver a placement notice to Jefferies at any time throughout the term of the sales agreement. The per share price of the shares of common stock that are sold by Jefferies after delivering a placement notice will fluctuate based on the market price of our common stock during the sales period and limits we set with Jefferies. Because the price per share of each share of common stock sold will fluctuate based on the market price of our common stock during the sales period, it is not possible at this stage to predict the number of shares of common stock that will be ultimately issued.

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

Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold, and there is no minimum or maximum sales price. Investors may experience a decline in the value of their shares as a result of share sales made at prices lower than the prices they paid.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference herein contain forward-looking statements. These are based on our management's current beliefs, expectations and assumptions about future events, conditions and results and on information currently available to us. Discussions containing these forward-looking statements may be found, among other places, in the sections entitled "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" contained in the documents incorporated by reference herein.

Any statements in this prospectus, or incorporated herein, about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and are forward-looking statements. Within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act, these forward-looking statements include statements regarding:

- the ability of our preclinical studies and future clinical trials to demonstrate acceptable safety and efficacy of our product candidates;
- business disruptions affecting the initiation, patient enrollment, development and operation of our clinical trials, including a public health emergency, such as the global outbreak of the COVID-19 coronavirus;
- the timing, progress and results of preclinical studies and clinical trials for our current and future product candidates, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available, and our research and development programs;
- the timing, scope and likelihood of regulatory filings and approvals, including IND submissions for our product candidates;
- our ability to develop and advance our current product candidates and programs into, and successfully complete, clinical trials;
- our manufacturing, commercialization, and marketing capabilities and strategy;
- the need to hire additional personnel and our ability to attract and retain such personnel;
- the size of the market opportunity for our product candidates, including our estimates of the number of patients who suffer from the diseases we are targeting;
- our expectations regarding the approval and use of our product candidates as first, second or subsequent lines of therapy or in combination with other drugs;
- our competitive position and the success of competing therapies that are or may become available;
- the characteristics and therapeutic effects of our product candidates;
- our ability to obtain and maintain regulatory approval of our product candidates;
- our plans relating to the further development of our product candidates, including additional indications we may pursue;
- our intellectual property position, including the scope of protection we are able to establish and maintain for intellectual property rights covering product candidates we may develop, including the validity of intellectual property rights held by third parties, and our ability not to infringe, misappropriate or otherwise violate any third-party intellectual property rights;
- our continued reliance on third parties to conduct additional clinical trials of our product candidates;
- our ability to obtain, and negotiate favorable terms of, any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our product candidates;



- the pricing and reimbursement of our product candidates we may develop, if approved;
- the rate and degree of market acceptance and clinical utility of our product candidates we may develop;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our financial performance and our ability to effectively manage our anticipated growth;
- the period over which we estimate our existing cash and cash equivalents will be sufficient to fund our future operating expenses and capital expenditure requirements;
- the impact of laws and regulations;
- our expectations regarding the period during which we will qualify as an emerging growth company under the JOBS Act; and
- our anticipated use of our existing resources and the proceeds of any sales of common stock pursuant to this prospectus.

In some cases, you can identify forward-looking statements by the words "may," "might," "can," "will," "to be," "could," "would," "should," "expect," "intend," "plan," "objective," "anticipate," "believe," "estimate," "predict," "project," "potential," "likely," "continue" and "ongoing," or the negative of these terms, or other comparable terminology intended to identify statements about the future, although not all forward-looking statements contain these words. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements.

You should refer to the "Risk Factors" section contained in this prospectus and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus, for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Given these risks, uncertainties and other factors, many of which are beyond our control, we cannot assure you that the forward-looking statements in this prospectus will prove to be accurate, and you should not place undue reliance on these forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to revise any forward-looking statements to reflect events or developments occurring after the date of this prospectus, even if new information becomes available in the future.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$50.0 million from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that we will sell any shares under or fully utilize the sales agreement as a source of financing.

We currently intend to use the net proceeds from this offering primarily to fund the research and development of our product candidates and for working capital and general corporate purposes. We may also use a portion of the net proceeds to invest in or acquire businesses or technologies that we believe are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus. Pending these uses, we intend to invest the net proceeds in investment-grade, interest-bearing securities.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Jefferies, under which we may offer and sell up to \$50.0 million of our shares of common stock from time to time through Jefferies acting as agent. 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 our shares of 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 second 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 equal to 3.0% of the aggregate gross proceeds we receive from each sale of our shares of common stock. 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 the fees and disbursements of its counsel, payable upon execution of the sales agreement, in an amount not to exceed \$75,000, in addition to certain ongoing disbursements of its legal counsel payable in the amount of \$15,000 in connection with each diligence bring-down thereafter. 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, will be approximately \$300,000. 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 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, the 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 will be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have agreed to indemnify Jefferies against certain civil liabilities, including liabilities under the Securities 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 upon the earlier of (i) the sale of all shares of common stock subject to the sales agreement and (ii) the termination of the sales agreement as permitted therein. We and Jefferies may each terminate the sales agreement at any time upon ten trading days' prior notice.

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 is filed as an exhibit to the registration statement of which this prospectus supplement forms a part.

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

LEGAL MATTERS

The validity of the securities offered by this prospectus will be passed upon by Cooley LLP, Palo Alto, California. Goodwin Procter LLP is counsel to Jefferies LLC in connection with this offering.

EXPERTS

The financial statements of Sensei Biotherapeutics, Inc. incorporated by reference in this Prospectus have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report. Such financial statements are incorporated by reference in reliance upon the report of such firm given, upon their authority as experts in accounting and auditing.

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 with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. You should rely only on the information contained in this prospectus or incorporated by reference in this prospectus. We have not authorized anyone else to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus, regardless of the time of delivery of this prospectus or any sale of the securities offered by this prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website at *www.sec.gov* that contains reports, proxy and information statements, and other information regarding issuers, such as us, that file electronically with the SEC.

Copies of certain information filed by us with the SEC are also available on our website at *www.senseibio.com*. Information contained in or accessible through our website does not constitute a part of this prospectus and is not incorporated by reference in this prospectus. We have included our website address as an inactive textual reference only.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The SEC file number for the documents incorporated by reference in this prospectus is 001-39980. The documents incorporated by reference into this prospectus contain important information that you should read about us.

The following documents are incorporated by reference into this document:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, filed with the SEC on March 15, 2022;
- our Current Reports on Form 8-K filed with the SEC on March 9, 2022, to the extent the information in such reports is filed and not furnished; and
- the description of our common stock set forth in the amendment to the registration statement on Form 8-A registering our common stock under Section 12 of the Exchange Act, which was filed with the SEC on February 2, 2021, including any amendments or reports filed for purposes of updating such description. For a description of our capital stock, please also see the Description of Securities included as Exhibit 4.3 to our Annual Report on Form 10-K for the year ended December 31, 2021, filed with the SEC on March 15, 2022, which is incorporated by reference herein.

We also incorporate by reference into this prospectus all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (i) after the date of the initial filing of the registration statement of which this prospectus forms a part and prior to effectiveness of the registration statement, or (ii) after the date of this prospectus but prior to the termination of the offering. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits that are specifically incorporated by reference into such documents. You should direct any requests for documents to Sensei Biotherapeutics, Inc., Attn: Corporate Secretary, 451 D Street, Suite 710, Boston, Massachusetts 02210, and our telephone number is (240) 243-8000.

Any statement contained in this prospectus or contained in a document incorporated or deemed to be incorporated by reference into this prospectus will be deemed to be modified or superseded to the extent that a statement contained in this prospectus or any subsequently filed supplement to this prospectus, or document deemed to be incorporated by reference into this prospectus, modifies or supersedes such statement.



Up to \$50,000,000

Common Stock

PROSPECTUS

Jefferies

May 9, 2022