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Filed Pursuant to Rule 424(b)(5) Registration Number 333-272088

PROSPECTUS SUPPLEMENT

(To Prospectus dated May 19, 2023)

7,812,500 Shares



Common Stock

We are offering 7,812,500 shares of our common stock.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "INSM". The last reported sale price of our common stock on the Nasdaq Global Select Market on June 11, 2025 was \$97.98 per share.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described under the heading "Risk Factors" beginning on page $S-\underline{8}$ of this prospectus supplement and the documents incorporated by reference into this prospectus supplement.

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

	Per Share	Total
Public offering price	\$96.00	\$750,000,000
Underwriting discounts and commissions(1)	\$ 4.32	\$ 33,750,000
Proceeds, before expenses, to us	\$91.68	\$716,250,000

⁽¹⁾ We have agreed to reimburse the underwriters for certain expenses in connection with this offering. See "Underwriting."

The underwriters expect to deliver the shares against payment therefor in New York, New York on or about June 13, 2025.

Joint Book-Running Managers

Goldman Sachs & Co. LLC Leerink Partners BofA Securities Jefferies J.P. Morgan

Lead Manager

Stifel

The underwriters also may purchase up to an additional 1,171,875 shares of our common stock at the public offering price, less the underwriting discounts and commissions payable by us, within 30 days from the date of this prospectus supplement.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering of common stock and updates the information contained in the accompanying prospectus and the documents incorporated by reference herein and therein. The second part is the accompanying prospectus, which provides more general information about securities that we and our selling shareholders may offer from time to time, some of which does not apply to this offering. This prospectus supplement and the accompanying prospectus relate to a registration statement that we filed with the U.S. Securities and Exchange Commission ("SEC") using a shelf registration process (File No. 333-272088). To the extent the information contained in this prospectus supplement differs or varies from the information contained in the accompanying prospectus or documents previously filed with the SEC that are incorporated by reference herein, the information in this prospectus supplement will supersede such information. For a more detailed understanding of an investment in our common stock, you should read both this prospectus supplement and the accompanying prospectus, together with the information incorporated by reference herein and therein and additional information described under the heading "Incorporation of Certain Documents by Reference" in this prospectus supplement.

Neither the Company nor any underwriter has authorized anyone to provide you with information that is different from or in addition to the information contained in this prospectus supplement and the accompanying prospectus and in any related free writing prospectus filed by us with the SEC. Accordingly, neither the Company nor any underwriter takes any responsibility for, or can provide any assurance as to the reliability of, any information that others may give. Neither the Company nor any underwriter is making offers to sell or seeking offers to buy shares of our common stock in any jurisdiction where the offer or sale is not permitted. You should assume that the information contained in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein and therein and any related free writing prospectus is accurate only as of the respective dates of such documents, regardless of the time of delivery of this prospectus supplement or any sale of the common stock offered hereby. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise indicates, references in this prospectus supplement and the accompanying prospectus to "Insmed", the "Company", "we", "us" and "our" refer to Insmed Incorporated, a Virginia corporation, together with its consolidated subsidiaries. Insmed, PULMOVANCE and ARIKAYCE are trademarks of Insmed Incorporated. Our logos and trademarks are the property of Insmed. All other brand names or trademarks appearing in this prospectus supplement and the accompanying prospectus are the property of their respective holders. Use or display by us of other parties' trademarks or trade dress in this prospectus supplement and the accompanying prospectus is not intended to, and does not, imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owners.

FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the other documents that are incorporated herein or therein by reference contain forward-looking statements that involve substantial risks and uncertainties. "Forward-looking statements", as that term is defined in the Private Securities Litigation Reform Act of 1995, Section 27A of the Securities Act of 1933, as amended (the "Securities Act") and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act") are statements that are not historical facts and involve a number of risks and uncertainties. Words such as "may", "will", "should", "could", "would", "expects", "plans", "anticipates", "believes", "estimates", "projects", "predicts", "intends", "potential", "continues", and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) identify forward-looking statements.

Forward-looking statements are based on our current expectations and beliefs, and involve known and unknown risks, uncertainties and other factors, which may cause our actual results, performance and achievements and the timing of certain events to differ materially from the results, performance, achievements or timing discussed, projected, anticipated or indicated in any forward-looking statements. Such risks, uncertainties and other factors include, among others, the following:

- failure to continue to successfully commercialize ARIKAYCE, our only approved product, in the United States ("U.S."), Europe or Japan (amikacin liposome inhalation suspension, Liposomal 590 mg Nebuliser Dispersion, and amikacin sulfate inhalation drug product, respectively), or to maintain U.S., European or Japanese approval for ARIKAYCE;
- our inability to obtain full approval of ARIKAYCE from the U.S. Food and Drug Administration ("FDA"), including the risk that we will not successfully or in a timely manner complete the confirmatory post-marketing clinical trial required for full approval of ARIKAYCE, or our failure to obtain regulatory approval to expand ARIKAYCE's indication to a broader patient population;
- failure to obtain, or delays in obtaining, regulatory approvals for brensocatib, treprostinil palmitil
 inhalation powder ("TPIP") or our other product candidates in the U.S., Europe or Japan or for
 ARIKAYCE outside the U.S., Europe or Japan, including separate regulatory approval for the Lamira®
 Nebulizer System in each market and for each usage;
- failure to successfully commercialize brensocatib, TPIP or our other product candidates, if approved by applicable regulatory authorities, or to maintain applicable regulatory approvals for brensocatib, TPIP or our other product candidates, if approved;
- uncertainties or changes in the degree of market acceptance of ARIKAYCE or, if approved, brensocatib, TPIP, or our other product candidates, by physicians, patients, third-party payors and others in the healthcare community;
- our inability to obtain and maintain adequate reimbursement from government or third-party payors for ARIKAYCE or, if approved, brensocatib, TPIP, or our other product candidates, or acceptable prices for ARIKAYCE or, if approved, brensocatib, TPIP, or our other product candidates;
- inaccuracies in our estimates of the size of the potential markets for ARIKAYCE, brensocatib, TPIP, or our
 other product candidates or in data we have used to identify physicians, expected rates of patient uptake,
 duration of expected treatment, or expected patient adherence or discontinuation rates;
- failure of third parties on which the Company is dependent to manufacture sufficient quantities of ARIKAYCE, brensocatib, or TPIP for commercial or clinical needs, to conduct the Company's clinical trials, or to comply with the Company's agreements or laws and regulations that impact the Company's business;
- the risks and uncertainties associated with, and the perceived benefits of, our senior secured loan with
 certain funds managed by Pharmakon Advisors, LP and our royalty financing with OrbiMed Royalty &
 Credit Opportunities IV, LP, including our ability to maintain compliance with the covenants in the
 agreements for the senior secured loan and royalty financing and the impact of the restrictions on our
 operations under these agreements;

- our inability to create or maintain an effective direct sales and marketing infrastructure or to partner with third parties that offer such an infrastructure for distribution of ARIKAYCE or any of our product candidates that are approved in the future;
- failure to successfully conduct future clinical trials for ARIKAYCE, brensocatib, TPIP, or our other
 product candidates and our potential inability to enroll or retain sufficient patients to conduct and complete
 the trials or generate data necessary for regulatory approval of our product candidates or to permit the use
 of ARIKAYCE in the broader population of patients with Mycobacterium avium complex ("MAC") lung
 disease, among other things;
- development of unexpected safety or efficacy concerns related to ARIKAYCE, brensocatib, TPIP, or our other product candidates;
- risks that our clinical studies will be delayed, that serious side effects will be identified during drug development, or that any protocol amendments submitted will be rejected;
- failure to successfully predict the time and cost of development, regulatory approval and commercialization for novel gene therapy products;
- the risk that the full data set from the TPIP study in pulmonary arterial hypertension ("PAH") or data generated in further clinical trials of TPIP will not be consistent with the topline results of the TPIP PAH study;
- risk that interim, topline or preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available or may be interpreted differently if additional data are disclosed, or that blinded data will not be predictive of unblinded data;
- risk that our competitors may obtain orphan drug exclusivity for a product that is essentially the same as a
 product we are developing for a particular indication;
- our inability to attract and retain key personnel or to effectively manage our growth;
- our inability to successfully integrate our acquisitions and appropriately manage the amount of management's time and attention devoted to integration activities;
- risks that our acquired technologies, products and product candidates will not be commercially successful;
- inability to adapt to our highly competitive and changing environment;
- inability to access, upgrade or expand our technology systems or difficulties in updating our existing technology or developing or implementing new technology;
- risk that we are unable to maintain our significant customers;
- risk that government healthcare reform materially increases our costs and damages our financial condition;
- business or economic disruptions due to catastrophes or other events, including natural disasters or public health crises;
- risk that our current and potential future use of artificial intelligence and machine learning may not be successful:
- deterioration in general economic conditions in the U.S., Europe, Japan and globally, including the effect
 of prolonged periods of inflation, affecting us, our suppliers, third-party service providers and potential
 partners;
- the risk that we could become involved in costly intellectual property disputes, be unable to adequately
 protect our intellectual property rights or prevent disclosure of our trade secrets and other proprietary
 information, and incur costs associated with litigation or other proceedings related to such matters;
- restrictions or other obligations imposed on us by agreements related to ARIKAYCE, brensocatib or our
 other product candidates, including our license agreements with PARI Pharma GmbH and AstraZeneca
 AB, and failure to comply with our obligations under such agreements;

- the cost and potential reputational damage resulting from litigation to which we are or may become a
 party, including product liability claims;
- · risk that our operations are subject to a material disruption in the event of a cybersecurity attack or issue;
- our limited experience operating internationally;
- changes in laws and regulations applicable to our business, including any pricing reform and laws that
 impact our ability to utilize certain third parties in the research, development or manufacture of our
 product candidates, and failure to comply with such laws and regulations;
- our history of operating losses, and the possibility that we never achieve or maintain profitability;
- goodwill impairment charges affecting our results of operations and financial condition;
- inability to repay our existing indebtedness and uncertainties with respect to our ability to access future capital; and
- delays in the execution of plans to build out an additional third-party manufacturing facility approved by the appropriate regulatory authorities and unexpected expenses associated with those plans.

We may not actually achieve the results, plans, intentions or expectations indicated by our forward-looking statements because, by their nature, forward-looking statements involve risks and uncertainties because they relate to events and depend on circumstances that may or may not occur in the future. These risks and uncertainties include, but are not limited to, those described above, in the "Risk Factors" section of this prospectus supplement and the documents incorporated by reference into this prospectus supplement.

We caution readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they were made. We disclaim any obligation, except as specifically required by law, and the rules of the SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in such forward-looking statements.

You should read this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein with the understanding that our actual future results may be materially different from those expressed in forward-looking statements.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information included or incorporated by reference in this prospectus supplement and the accompanying prospectus and does not contain all of the information that may be important to you. You should carefully review this entire prospectus supplement and the accompanying prospectus, including the risk factors and financial statements and related notes thereto included or incorporated by reference herein and therein, before making a decision to purchase our common stock.

Overview

We are a people-first global biopharmaceutical company striving to deliver first- and best-in-class therapies to transform the lives of patients facing serious diseases. Our first commercial product, ARIKAYCE, is approved in the U.S. as ARIKAYCE (amikacin liposome inhalation suspension), in Europe as ARIKAYCE Liposomal 590 mg Nebuliser Dispersion and in Japan as ARIKAYCE inhalation 590 mg (amikacin sulfate inhalation drug product). ARIKAYCE received accelerated approval in the U.S. in September 2018 for the treatment of MAC lung disease as part of a combination antibacterial drug regimen for adult patients with limited or no alternative treatment options in a refractory setting. In October 2020, the European Commission approved ARIKAYCE for the treatment of nontuberculous mycobacterial ("NTM") lung infections caused by MAC in adults with limited treatment options who do not have cystic fibrosis. In March 2021, Japan's Ministry of Health, Labour and Welfare approved ARIKAYCE for the treatment of patients with NTM lung disease caused by MAC who did not sufficiently respond to prior treatment with a multidrug regimen. NTM lung disease caused by MAC (which we refer to as MAC lung disease) is a rare and often chronic infection that can cause irreversible lung damage and can be fatal.

Our pipeline includes clinical-stage programs, brensocatib, TPIP, and INS1201, as well as pre-clinical research programs. Brensocatib is a small molecule, oral, reversible inhibitor of dipeptidyl peptidase 1, which we are developing for the treatment of patients with bronchiectasis and other neutrophil-mediated diseases, including chronic rhinosinusitis without nasal polyps and hidradenitis suppurativa. TPIP is an inhaled formulation of the treprostinil prodrug treprostinil palmitil which may offer a differentiated product profile for pulmonary hypertension associated with interstitial lung disease ("PH-ILD") and PAH. INS1201 is an intrathecally delivered gene therapy for patients with Duchenne muscular dystrophy. Our pre-clinical research programs encompass a wide range of technologies and modalities, including gene therapy, artificial intelligence-driven protein engineering, protein manufacturing, RNA end-joining, and synthetic rescue.

Recent Developments

On June 10, 2025, we announced positive topline results from our Phase 2b TPIP PAH study, a randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of TPIP administered once-daily in patients with PAH (World Health Organization Group 1). The study met its primary endpoint and all secondary efficacy endpoints. For the primary endpoint, the placebo-adjusted reduction from baseline in pulmonary vascular resistance was 35% with Least Squares ("LS") mean ratio of 0.65 (95% Confidence Interval ("CI"): 0.54, 0.79; p<0.001). For the secondary efficacy endpoints, the placebo-adjusted improvement in six-minute walk distance was 35.5 meters (95% CI: 11.2, 60.7; p=0.003) and the placebo-adjusted reduction from baseline in N-terminal pro b-type natriuretic peptide ("NT-proBNP") concentrations, a biomarker for cardiac stress, was 60% with LS mean ratio of 0.40 (95% CI: 0.27, 0.59; p<0.001). Efficacy of TPIP was evaluated approximately 24 hours after therapy was administered.

Based on these results, we will engage with the FDA regarding the Phase 3 trial design for PAH. We plan to initiate a Phase 3 trial in patients with PH-ILD before the end of 2025 and a Phase 3 trial in patients with PAH in early 2026.

The TPIP PAH study was conducted at 44 sites globally, and a total of 102 patients were randomized 2:1 to receive either TPIP (n=69) or placebo (n=33) for 16 weeks. Demographics and baseline characteristics were similar in both study arms. Patients started at a dose of 80 μg once daily (TPIP or matching placebo) and were titrated up to their maximum tolerated dose, or to the a maximum allowable dose of 640 μg, once daily over a three-week period, with the possibility of a final dose increase occurring at Week 5. Of the patients treated with TPIP, 84% titrated to at least 480 μg once daily (n=58) and 75% titrated to the maximum allowed dose of 640 μg once daily (n=52). Overall, 90% of patients receiving TPIP (n=62) and all patients receiving placebo completed the study.

Once-daily TPIP therapy was well-tolerated in the study. Treatment-emergent adverse events ("TEAEs") occurred in 88.4% of patients who received TPIP versus 75.8% of patients who received placebo; serious TEAEs were observed in 7.2% of patients who received TPIP versus 3.0% of patients who received placebo, and severe TEAEs were observed in 5.8% of patients who received TPIP versus 3.0% of patients who received placebo. TEAEs leading to treatment discontinuation were experienced by 5.8% of patients taking TPIP; there were none in the placebo arm. There were no deaths in the study. The most common TEAEs occurring in at least 5.0% of patients in any study arm, and more frequently with TPIP than with placebo, were cough (40.6%, 21.2%), headache (31.9%, 15.2%), fatigue (10.1%, 3.0%), chest discomfort (8.7%, 0.0%), flushing (8.7%, 3.0%), upper respiratory tract infection (7.2%, 3.0%), and non-cardiac chest pain (5.8%, 3.0%) for TPIP and placebo, respectively.

All patients who completed the Phase 2b study were eligible to enroll in the long-term open-label extension, which will evaluate TPIP up to a maximum allowable dose of 1,280 µg once daily. Of the patients who completed the Phase 2b study (n=95), 95% enrolled in the open-label extension. We plan to present detailed results from the Phase 2b study of TPIP in PAH and the open-label extension at future medical meetings. Topline results from the Phase 2a study of TPIP in patients with PH-ILD were previously reported in May 2024.

Corporate Information

We were incorporated in the Commonwealth of Virginia on November 29, 1999. Our principal executive offices are located at 700 US Highway 202/206, Bridgewater, NJ 08807, and our telephone number is (908) 977-9900. Our website address is www.insmed.com. The information on our website is not incorporated by reference into this prospectus supplement or the accompanying prospectus and should not be considered to be part of either document.

Risk factors

THE OFFERING

Common stock offered by us 7,812,500 shares.

Option to purchase additional shares We have granted the underwriters an option for a period

of 30 days from the date of this prospectus supplement to purchase up to an additional 1,171,875 shares of our

common stock.

Common stock to be outstanding after this offering 189,712,574 shares (or 190,884,449 shares if the

underwriters' option to purchase additional shares is

exercised in full).

Use of proceeds We intend to use the net proceeds we receive from this

offering to fund continued research and development of brensocatib as well as pre-commercial and, if approved, commercialization activities related to brensocatib, activities related to the further commercialization and development of ARIKAYCE, further research and development of TPIP, INS1201, and our pre-clinical research product candidates, and for other general corporate purposes, including business expansion activities. See "Use of Proceeds" on page S-10 of this prospectus supplement for additional information

prospectus supplement for additional information.

An investment in our common stock involves a high degree of risk. See "Risk Factors" beginning on page S-8 of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement for a discussion of factors to consider before deciding to

invest in our common stock.

Nasdaq Global Select Market symbol

Our common stock is listed on the Nasdaq Global Select

Market under the symbol "INSM".

Except as otherwise indicated herein, the number of shares of our common stock to be outstanding immediately after this offering is based on 181,900,074 shares of our common stock outstanding as of March 31, 2025. The number of shares of our common stock to be outstanding immediately after this offering excludes:

- 21,227,364 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2025 at a weighted average exercise price of \$25.74 per share;
- 3,646,828 shares of our common stock issuable pursuant to unvested restricted stock units ("RSUs") outstanding as of March 31, 2025 at a weighted average grant price of \$32.79;
- 8,870 shares of our common stock issuable pursuant to unvested performance-based restricted stock units ("PSUs") outstanding as of March 31, 2025 at a weighted average grant price of \$26.43;
- 3,387,045 shares of our common stock reserved for issuance under our Amended and Restated 2019 Incentive Plan, as amended, plus any shares subject to outstanding awards as of March 31, 2025 under our 2017 Incentive Plan, 2015 Incentive Plan and 2013 Incentive Plan that subsequently are cancelled, terminated unearned, expired, forfeited, lapsed for any reason or are settled in cash without the delivery of shares;
- 1,000,000 shares of our common stock reserved for issuance under our 2025 Inducement Plan;
- 17,922,626 shares of our common stock that were issued upon conversion of our 0.75% convertible senior notes due 2028 (the "2028 Notes") after March 31, 2025;
- 4,530,488 shares of our common stock reserved for issuance under our Employee Stock Purchase Plan;
 and
- 5,963,446 shares of our common stock reserved for issuance as acquisition consideration in connection with our acquisitions of Motus Biosciences, Inc. and AlgaeneX, Inc.

Unless otherwise stated, all information in this prospectus supplement excludes the shares referenced in the bullets immediately above and assumes no exercise by the underwriters of their option to purchase additional shares.

RISK FACTORS

An investment in our common stock involves significant risks. Before making an investment in our common stock, you should carefully read all of the information contained in this prospectus supplement, the accompanying prospectus and in the documents incorporated by reference herein and therein. For a discussion of risks that you should carefully consider before deciding to purchase any of our common stock, please review the risk factors disclosed below, together with the other information in this prospectus supplement, the accompanying prospectus, and the information and documents incorporated by reference herein and therein. Any of these risks, as well as additional risks not currently known to us or that we currently deem immaterial, may adversely affect our business, financial condition, results of operations, and prospects, resulting in a decline in the trading price of our common stock and loss of all or part of your investment.

Our management will have broad discretion over the actual amount and timing of the expenditures of the proceeds we receive in this offering and might not apply these proceeds in ways that enhance our financial condition or operating results or increase the value of your investment.

We intend to use the net proceeds we receive from this offering to fund continued research and development of brensocatib as well as pre-commercial and, if approved, commercialization activities related to brensocatib, activities related to the further commercialization and development of ARIKAYCE, further research and development of TPIP, INS1201, and our pre-clinical research product candidates, and for other general corporate purposes, including business expansion activities. This expected use of our net proceeds from this offering represents our intentions based upon our current plans and business conditions. The amount and timing of our actual expenditures may vary significantly depending on numerous factors, the most significant of which are expenses related to our commercialization efforts for ARIKAYCE and brensocatib, if approved, expenses related to future ARIKAYCE, brensocatib and TPIP clinical trials, as well as any strategic transactions that we may enter into with third parties, and any unforeseen cash needs. Because of the number and variability of factors that will determine our use of the proceeds from this offering, their ultimate use may vary substantially from their currently intended use. As a result, our management will retain broad discretion over the allocation of the net proceeds we receive from this offering and could spend the proceeds in ways that do not necessarily improve our financial condition or operating results or enhance the value of our common stock and your investment therein. Additionally, until the net proceeds we receive are used, they may be placed in investments that do not produce income or that lose value. See "Use of Proceeds" for additional information.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

The price per share of common stock in this offering is substantially higher than the net tangible book deficit per share of our common stock as of March 31, 2025. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book deficit per share of common stock. After giving effect to the sale of 7,812,500 shares of our common stock in this offering at a price of \$96.00 per share and based on our net tangible book deficit as of March 31, 2025 of \$(0.52) per share, if you purchase shares of common stock in this offering you will suffer substantial and immediate dilution of \$92.72 per share. Further dilution of your investment will result from, among other things, future equity issuances by us, the future exercise of stock options, vesting of RSUs and PSUs, and issuance of shares in connection with our acquisitions. See "Dilution" for a more detailed description of the dilution investors purchasing shares of our common stock in the offering will incur.

A significant portion of our total outstanding shares may be sold into the market at any time, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. Such sales, or the perception in the market that the holders of a large number of shares intend to sell, could reduce the market price of our common stock significantly. In connection with this offering, we and our executive officers and directors have entered into lock-up agreements with Goldman Sachs & Co. LLC and Leerink Partners LLC, as representatives of the underwriters, that prohibit us and our executive officers and directors, subject to certain exceptions or receipt of the prior written consent of Goldman Sachs & Co. LLC and Leerink Partners LLC, from disposing or pledging, or hedging against, our common stock or securities convertible into or exchangeable for shares of our common stock for periods of up to 60 days after the date of

this prospectus supplement. However, all of the shares sold in this offering and the remaining shares of our common stock outstanding immediately prior to this offering will not be subject to lock-up agreements with Goldman Sachs & Co. LLC and Leerink Partners LLC and, except to the extent such shares are held by our affiliates, will be freely tradeable without restriction. In addition, Goldman Sachs & Co. LLC and Leerink Partners LLC may, in their discretion, release the lock-up restrictions described above at any time without notice.

Proposed legislation could result in higher rates of tax imposed on non-U.S. holders (as defined herein) that are resident in countries imposing "unfair foreign taxes."

Legislation is being considered by the United States Congress that could affect the rates of United States federal income taxes imposed on non-U.S. holders of our common stock. In particular, one proposal is being considered that could substantially increase certain United States tax rates applicable to payments made to residents of countries that impose "unfair foreign taxes." For that purpose, under the currently proposed version of Section 899 of the United States Internal Revenue Code of 1986, as amended (the "Code"), digital services taxes imposed by countries aiming to tax the revenues of large technology companies derived from consumers within their borders, undertaxed profits rule taxes designed to ensure that multinational enterprises pay a minimum level of tax globally, and diverted profits taxes targeting multinational companies that divert profits away from countries where the economic activities occur are deemed to be unfair foreign taxes. It is uncertain whether this legislation will be enacted in its current form or in modified form, or will ultimately not be enacted. Non-U.S. holders should consult their tax advisors regarding the legislative proposals under consideration.

USE OF PROCEEDS

We estimate that the net proceeds we will receive from this offering will be approximately \$715.7 million, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate the net proceeds we receive from this offering will be approximately \$823.1 million, after deduction underwriting discounts and commissions and estimated offering expenses.

We currently plan to use the net proceeds we receive from this offering to fund continued research and development of brensocatib as well as pre-commercial and, if approved, commercialization activities related to brensocatib, activities related to the further commercialization and development of ARIKAYCE, further research and development of TPIP, INS1201, and our pre-clinical research product candidates, and for other general corporate purposes, including business expansion activities.

This expected use of our net proceeds from this offering represents our intentions based upon our current plans and business conditions. The amount and timing of our actual expenditures may vary significantly depending on numerous factors, the most significant of which are expenses related to our commercialization efforts for ARIKAYCE and brensocatib, if approved, expenses related to future ARIKAYCE, brensocatib and TPIP clinical trials, as well as any strategic transactions that we may enter into with third parties, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds we receive from this offering. We have no current understandings, agreements or commitments for any material acquisitions or licenses of any compounds, product candidates, technology or businesses.

Pending our use of the net proceeds we receive from this offering, we intend to invest such net proceeds in a variety of capital preservation investments, including short-term, investment grade, interest bearing instruments and U.S. government securities.

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 price per share you pay in this offering and the net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book deficit as of March 31, 2025 was \$(94.3) million, or \$(0.52) per share of our common stock, based upon 181,900,074 shares outstanding on March 31, 2025. Net tangible book value (deficit) per share is equal to our total tangible assets, less our total liabilities, divided by the total number of shares outstanding as of March 31, 2025. After giving effect to the sale of 7,812,500 shares of our common stock offered by us at a price of \$96.00 per share, less underwriting discounts and commissions and estimated offering expenses payable by us, our as-adjusted net tangible book value would have been \$621.3 million, or \$3.28 per share of common stock based upon 189,712,574 shares outstanding. This represents an immediate increase in net tangible book value of \$3.80 per share to our existing shareholders and an immediate dilution in net tangible book value of \$92.72 per share to investors purchasing shares of our common stock in this offering. The following table illustrates this calculation on a per share basis:

	\$96.00
\$(0.52)	
3.80	
	3.28
	\$92.72

If the underwriters exercise in full their option to purchase additional shares of common stock, less the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value at March 31, 2025, after giving effect to this offering, would be approximately \$728.7 million, or approximately \$3.82 per share, representing an increase in net tangible book value of \$4.34 per share to existing shareholders and immediate dilution in net tangible book value of \$92.18 per share to investors purchasing shares of our common stock in this offering.

The foregoing table and calculations are based on upon 181,900,074 shares of our common stock outstanding as of March 31, 2025, and exclude:

- 21,227,364 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2025 at a weighted average exercise price of \$25.74 per share;
- 3,646,828 shares of our common stock issuable pursuant to unvested RSUs outstanding as of March 31, 2025 at a weighted average grant price of \$32.79;
- 8,870 shares of our common stock issuable pursuant to unvested PSUs outstanding as of March 31, 2025 at a weighted average grant price of \$26.43;
- 3,387,045 shares of our common stock reserved for issuance under our Amended and Restated 2019 Incentive Plan, as amended, plus any shares subject to outstanding awards as of March 31, 2025 under our 2017 Incentive Plan, 2015 Incentive Plan and 2013 Incentive Plan that subsequently are cancelled, terminated unearned, expired, forfeited, lapsed for any reason or are settled in cash without the delivery of shares;
- 1,000,000 shares of our common stock reserved for issuance under our 2025 Inducement Plan;
- 17,922,626 shares of our common stock that were issued upon conversion of the 2028 Notes after March 31, 2025;
- 4,530,488 shares of our common stock reserved for issuance under our Employee Stock Purchase Plan;
 and
- 5,963,446 shares of our common stock reserved for issuance as acquisition consideration in connection with our acquisitions of Motus Biosciences, Inc. and AlgaeneX, Inc.

Investors purchasing shares of our common stock in this offering will experience further dilution upon, among other things, the future exercise of stock options, vesting of RSUs and PSUs, and issuance of shares in connection with our acquisitions. Furthermore, subject to the terms of our lock-up agreement with Goldman Sachs & Co. LLC and Leerink Partners LLC, as described in "Underwriting", we may choose to raise additional capital through the sale of additional securities due to market conditions or strategic considerations even if we believe we have sufficient funds on hand for our current or future operating plans. To the extent that we raise additional capital in this manner, the issuance of such securities would likely result in further dilution to investors purchasing shares of our common stock in this offering.

UNDERWRITING

The Company and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Goldman Sachs & Co. LLC and Leerink Partners LLC are the representatives of the underwriters.

Underwriters	Number of Shares
Goldman Sachs & Co. LLC	2,734,375
Leerink Partners LLC	1,953,125
BofA Securities, Inc.	937,500
Jefferies LLC	937,500
J.P. Morgan Securities LLC	937,500
Stifel, Nicolaus & Company, Incorporated	312,500
Total	7,812,500

The underwriters are committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

The underwriters have an option to buy up to an additional 1,171,875 shares of common stock from the Company to cover sales by the underwriters of a greater number of shares than the total number set forth in the table above. They may exercise that option for 30 days from the date of this prospectus supplement. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by the Company. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase up to an additional 1,171,875 shares of common stock.

Paid by the Company	No Exercise	Full Exercise	
Per Share	\$4.32	\$4.32	
Total	\$33,750,000	\$38,812,500	

Shares sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to \$2.592 per share from the initial public offering price. After the initial offering of the shares, the representatives may change the offering price and the other selling terms. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

Our directors and executive officers (each such person, a "lock-up party") have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each lock-up party, with limited exceptions, for a period of 60 days after the date of this prospectus supplement (such period, the "restricted period"), may not, without the prior written consent of Goldman Sachs & Co. LLC and Leerink Partners LLC, (i) offer, sell, contract to sell, pledge, grant any option, right or warrant to purchase, purchase any option or contract to sell, lend or otherwise transfer or dispose of any shares of common stock, or any options or warrants to purchase any shares of common stock, or any securities convertible into, exchangeable for or that represent the right to receive common stock (such shares of common stock, options, rights, warrants or other securities, collectively, "Lock-Up Securities"), including without limitation any such Lock-Up Securities now owned or hereafter acquired by the lockup party, (ii) engage in any hedging or other transaction or arrangement (including, without limitation, any short sale or the purchase or sale of, or entry into, any put or call option, or combination thereof, forward, swap or any other derivative transaction or instrument, however described or defined), which is designed to or which reasonably could be expected to lead to or result in a sale, loan, pledge or other disposition (whether by the lock-up party or someone other than the lock-up party) or transfer of any of the economic consequences of ownership, in whole or in part, directly or indirectly, of any Lock-Up Securities, whether any such transaction or arrangement (or instrument provided for thereunder) would be settled by delivery of common stock or other securities, in cash or otherwise, (iii) make any demand for or

exercise any right with respect to the registration of any Lock-Up Securities or (iv) otherwise publicly announce any intention to engage in or cause any action, activity, transaction or arrangement described in clause (i), (ii) or (iii) above. Other than (i) pursuant to a written plan meeting the requirements of Rule 10b5-1 under the Exchange Act (a "10b5-1 trading plan") existing on the date hereof or (ii) any "sell to cover arrangement" for the payment of taxes, including estimated taxes, and remittance payments due as a result of the vesting, settlement or exercise of restricted stock units, options, warrants or other rights to purchase shares of common stock that are scheduled to expire or automatically vest during the restricted period, in all such cases pursuant to equity awards granted under a stock incentive plan or other equity award plan, or pursuant to the terms of convertible securities, each as described herein, the lock-up party represents and warrants that the lock-up party is not, and has not caused or directed any of its affiliates to be or become, currently a party to any agreement or arrangement that provides for, is designed to or reasonably could be expected to lead to or result in any transfer during the restricted period.

The restrictions described in the immediately preceding paragraph and contained in the lock-up agreements between the underwriters and each lock-up party do not apply, subject in certain cases to various conditions, to certain transactions, including transfers of the Lock-Up Securities (a) as one or more bona fide gifts or by will, other testamentary document or intestate succession; (b) as distributions to limited partners, members, stockholders or wholly-owned subsidiaries of the lock-up party; (c) pursuant to any order or settlement agreement not involving any public sale of shares of common stock or other securities and approved by any court of competent jurisdiction; (d) to any member of the immediate family of the lock-up party or to any trust for the direct or indirect benefit of the lockup party or the immediate family of the lock-up party or, if the lock-up party is a trust, to a trustor or beneficiary of the trust or the estate of a beneficiary of such trust; (e) to any corporation, partnership, limited liability company or similar entity of which all of the beneficial ownership interests are held by the lock-up party or the immediate family of the lock-up party; provided that in the case of any transfer or distribution pursuant to clauses (a)-(e), (i) each donee, distributee or transferee shall sign and deliver to the representatives of the underwriters a lock-up agreement, (ii) no public announcement or filing by any party (the lock-up party, donor, donee, distributor, distributee, transferor or transferee) under the Exchange Act, including, without limitation, any Section 16(a) filing, shall be voluntarily made in connection with such transfer or distribution, provided that, if any such filing, report or announcement shall be legally required during the restricted period, such filing, report or announcement shall clearly indicate in the footnotes thereto (1) the circumstances of such transfer or distribution and (2) in the case of a transfer or distribution pursuant to clause (d), that the donee, devisee, transferee or distributee has agreed to be bound by a lock-up agreement and (iii) any such transfer or distribution shall not involve a disposition for value; (f) in connection with the exercise of options or other stock-based awards to purchase common stock or vesting of restricted stock units or other stock-based awards outstanding or granted under equity incentive plans or pursuant to inducement awards, provided that the underlying common stock continues to be subject to the lock-up agreements; (g) for the repurchase by the Company or forfeiture of securities to the Company in connection with termination of the lock-up party's employment with the Company; (h) to the Company in connection with the vesting, settlement or exercise of restricted stock units, options, warrants or other rights to purchase shares of common stock (including, in each case, by way of "net" or "cashless" exercise) that are scheduled to expire or automatically vest during the restricted period, including any transfer to the Company for the payment of tax withholdings or remittance payments due as a result of the vesting, settlement or exercise of such restricted stock units, options, warrants or other rights, or in connection with the conversion of convertible securities, in all such cases pursuant to equity awards granted under a stock incentive plan or other equity award plan, or pursuant to the terms of convertible securities, provided that (x) any securities received upon such vesting, settlement, exercise or conversion shall be subject to the terms of the lock-up agreements and (y) any such settled or withheld shares are surrendered to the Company in the net exercise; (i) under a "sell to cover arrangement" for the payment of taxes, including estimated taxes, and remittance payments due as a result of the vesting, settlement or exercise of restricted stock units, options, warrants or other rights to purchase shares of common stock that are scheduled to expire or automatically vest during the restricted period, in all such cases pursuant to equity awards granted under a stock incentive plan or other equity award plan, or pursuant to the terms of convertible securities; provided, in each case (a) through (i), that the lock-up party shall provide the representatives of the underwriters two days' advance notice of such transfers, distributions, exercises, repurchases, forfeitures, settlements or withholdings, as applicable; (j) pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction made to all holders of the Company's capital stock involving a Change of Control of the Company (for purposes hereof, "Change of Control" shall mean the transfer (whether by tender offer, merger,

consolidation or other similar transaction), in one transaction or a series of related transactions, to a person or group of affiliated persons, of shares of capital stock if, after such transfer, such person or group of affiliated persons would hold at least a majority of the outstanding voting securities of the Company (or the surviving entity)), provided that in the event that such tender offer, merger, consolidation or other similar transaction is not completed during the restricted period, the Lock-Up Securities shall remain subject to the provisions of the corresponding lock-up agreement; and (k) (1) in connection with entering into a 10b5-1 trading plan relating to the transfer, sale or other disposition of the Lock-up Securities, if then permitted by the Company, provided that none of the securities subject to such plan may be transferred, sold or otherwise disposed of until after the expiration of the restricted period and no public announcement, report or filing under the Exchange Act, or any other public filing, report or announcement, shall be voluntarily made regarding the establishment of such plan during the restricted period, and provided further that the lock-up party shall provide the representatives of the underwriters two days' advance notice of such plan establishment, and (2) pursuant to a 10b5-1 trading plan entered into prior to the date of the lock-up agreements, provided that to the extent a public announcement or filing under the Exchange Act is required for such transfer, such announcement or filing shall include a statement to the effect that the transfer was made pursuant to a 10b5-1 trading plan.

Goldman Sachs & Co. LLC and Leerink Partners LLC, in their sole discretion, may release the securities subject to any of the lock-up agreements with the underwriters described above, in whole or in part at any time.

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A "covered short position" is a short position that is not greater than the amount of additional shares for which the underwriters' option described above may be exercised. The underwriters may cover any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to cover the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase additional shares pursuant to the option described above. "Naked" short sales are any short sales that create a short position greater than the amount of additional shares for which the option described above may be exercised. The underwriters must cover any such naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the Company's stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. The underwriters are not required to engage in these activities and may end any of these activities at any time. These transactions may be effected on Nasdaq, in the over-the-counter market or otherwise.

We estimate that the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately \$600,000. We also have agreed to reimburse the underwriters for up to \$10,000 for their Financial Industry Regulatory Authority, Inc. ("FINRA") counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

The underwriters and their respective 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. Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

In the ordinary course of their various business activities, the underwriters and their respective 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 account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities and/or instruments of the issuer (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with the issuer. The underwriters and their respective 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.

European Economic Area

In relation to each Member State of the European Economic Area (each, a "Relevant Member State"), an offer to the public of any shares of our common stock in this offering may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any shares of our common stock in this offering may be made at any time under the following exemptions under the EU Prospectus Regulation:

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

provided that no such offer of shares of our common stock in this offering shall result in a requirement for the Company or any of the Joint Book-Running Managers to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or a supplemental prospectus pursuant to Article 23 of the Prospectus Regulation and each person who initially acquires any shares of our common stock in this offering or to whom any offer is made will be deemed to have represented, warranted and agreed to and with each of the Joint Book-Running Managers and the Company that it is a qualified investor within the meaning of Article 2 of the EU Prospectus Regulation.

In the case of any shares of our common stock in this offering being offered to a financial intermediary as that term is used in Article 1(4) of the EU Prospectus Regulation, each financial intermediary will also be deemed to have represented, warranted and agreed that the shares of our common stock in this offering 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 of any shares of our common stock in this offering to the public, other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the Joint Book-Running Managers has been obtained to each such proposed offer or resale.

The Company, the Joint Book-Running Managers and their affiliates will rely upon the truth and accuracy of the foregoing representations, warranties and agreements. Notwithstanding the above, a person who is not a "qualified investor" and who has notified the Joint Book-Running Managers of such fact in writing may, with the prior consent of the Joint Book-Running Managers, be permitted to acquire shares of our common stock in this offering.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares of our common stock in this offering in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock in this offering to

be offered so as to enable an investor to decide to purchase or subscribe for any shares of our common stock in this offering, and the expression "EU Prospectus Regulation" means Regulation (EU) 2017/1129.

United Kingdom

An offer to the public of any shares of our common stock in this offering may not be made in the United Kingdom, except that an offer to the public in the United Kingdom of any shares of our common stock in this offering may be made at any time under the following exemptions under the UK Prospectus Regulation:

- a) to any legal entity which is a "qualified investor" as defined under the UK Prospectus Regulation;
- 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 the Joint Book-Running Managers for any such offer; or
- in any other circumstances falling within section 86 of the Financial Services and Markets Act 2000 (as amended, "FSMA"),

provided that no such offer of shares of our common stock in this offering shall result in a requirement for the Company or any Joint Book-Running Managers to publish a prospectus pursuant to section 85 of the FSMA or a supplemental prospectus pursuant to Article 23 of the UK Prospectus Regulation and each person who initially acquires any shares of our common stock in this offering or to whom any offer is made will be deemed to have represented, warranted and agreed to and with each of the Joint Book-Running Managers and the Company that it is a qualified investor within the meaning of Article 2 of the UK Prospectus Regulation.

In the case of any shares of our common stock in this offering being offered to a financial intermediary as that term is used in Article 1(4) of the UK Prospectus Regulation, each financial intermediary will also be deemed to have represented, warranted and agreed that the shares of our common stock acquired by it in this offering 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 of any shares of our common stock in this offering to the public, other than their offer or resale in the United Kingdom to qualified investors as so defined or in circumstances in which the prior consent of the Joint Book-Running Managers has been obtained to each such proposed offer or resale.

The Company, the Joint Book-Running Managers and their affiliates will rely upon the truth and accuracy of the foregoing representations, warranties and agreements. Notwithstanding the above, a person who is not a "qualified investor" and who has notified the Joint Book-Running Managers of such fact in writing may, with the prior consent of the Joint Book-Running Managers, be permitted to acquire shares of our common stock in this offering.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares of our common stock in this offering in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock in this offering to be offered so as to enable an investor to decide to purchase or subscribe for any shares of our common stock in this offering.

This prospectus is only being distributed to and is only directed at: (A) persons who are outside the United Kingdom; or (B) qualified investors who are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the "Order"), or (ii) high net worth companies, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). The shares of our common stock in this offering are only available to, and any invitation, offer or agreement to subscribe, purchase or otherwise acquire the shares of our common stock in this offering will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this prospectus or any of its contents.

Canada

The securities may be sold in Canada 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 form, 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 offering memorandum (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 of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Hong Kong

The shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of Hong Kong) ("Companies (Winding Up and Miscellaneous Provisions) Ordinance") or which do not constitute an invitation to the public within the meaning of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) ("Securities and Futures Ordinance"), or (ii) to "professional investors" as defined in the Securities and Futures Ordinance and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance, and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case 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 in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" in Hong Kong as defined in the Securities and Futures Ordinance and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined under Section 4A of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA")) under 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, in each case subject to conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is 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, the securities (as defined in Section 239(1) of the SFA) of that corporation shall not be transferable for six months after that corporation has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer in that corporation's securities pursuant

to Section 275(1A) of the SFA, (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore ("Regulation 32")

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a trust (where the trustee is not an accredited investor (as defined in Section 4A of the SFA)) whose sole purpose is to hold investments and each beneficiary of the trust is an accredited investor, the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferable for six months after that trust has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer that is made on terms that such rights or interest are acquired at a consideration of not less than S\$200,000 (or its equivalent in a foreign currency) for each transaction (whether such amount is to be paid for in cash or by exchange of securities or other assets), (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32.

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended) (the "FIEA"). The securities may not be offered or sold, directly or indirectly, in Japan or to or for the benefit of any resident of Japan (including any person resident in Japan or any corporation or other entity organized under the laws of Japan) or to others for reoffering or resale, directly or indirectly, in Japan or to or for the benefit of any resident of Japan, except pursuant to an exemption from the registration requirements of the FIEA and otherwise in compliance with any relevant laws and regulations of Japan.

Brazil

THE OFFER AND SALE OF THE SECURITIES HAVE NOT BEEN AND WILL NOT BE REGISTERED WITH THE BRAZILIAN SECURITIES COMMISSION (COMISSÃO DE VALORES MOBILIÁRIOS, OR "CVM") AND, THEREFORE, WILL NOT BE CARRIED OUT BY ANY MEANS THAT WOULD CONSTITUTE A PUBLIC OFFERING IN BRAZIL UNDER CVM RESOLUTION NO 160, DATED 13 JULY 2022, AS AMENDED OR UNAUTHORIZED DISTRIBUTION UNDER BRAZILIAN LAWS AND REGULATIONS. THE SECURITIES MAY ONLY BE OFFERED TO BRAZILIAN PROFESSIONAL INVESTORS (AS DEFINED BY APPLICABLE CVM REGULATION), WHO MAY ONLY ACQUIRE THE SECURITIES THROUGH A NON-BRAZILIAN ACCOUNT, WITH SETTLEMENT OUTSIDE BRAZIL IN NON-BRAZILIAN CURRENCY. THE TRADING OF THESE SECURITIES ON REGULATED SECURITIES MARKETS IN BRAZIL IS PROHIBITED.

MATERIAL UNITED STATES FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF SHARES OF OUR COMMON STOCK

The following discussion describes certain material United States federal income and estate tax considerations relating to the purchase, ownership, and disposition of shares of our common stock by a non-U.S. holder (as defined below) that acquires our common stock in this offering and holds it as a capital asset. This discussion is based on the tax laws of the United States, including the Code, Treasury regulations promulgated or proposed thereunder, and administrative and judicial interpretations thereof, all as in effect on the date of this prospectus supplement. These tax laws are subject to change, possibly with retroactive effect, and subject to differing interpretations that could affect the tax consequences described herein. This section does not address the treatment of a non-U.S. holder under the laws of any state, local or foreign taxing jurisdiction.

For purposes of this discussion, a "non-U.S. holder" is a beneficial owner of our common stock that, for United States federal income tax purposes, is:

- a non-resident alien individual;
- a foreign corporation (or other entity taxable as a foreign corporation);
- an estate the income of which is not subject to United States federal income taxation regardless of its source; or
- a trust that does not have in effect a valid election under the Treasury regulations to be treated as a United States person and either (1) no court within the United States is able to exercise primary supervision over the trust's administration or (2) no United States person has the authority to control all substantial decisions of that trust.

This discussion does not address all aspects of United States federal income and estate taxation that may be applicable to non-U.S. holders in light of their particular circumstances or status, including, for example, financial institutions, banks, investment funds, broker-dealers or traders in securities, insurance companies, persons subject to the alternative minimum tax, partnerships or other pass-through entities, corporations that accumulate earnings to avoid United States federal income tax, certain United States expatriates, tax-exempt organizations, pension plans, persons that have elected to mark securities to market or that hold shares of our common stock as part of a straddle, hedge or other integrated investment, and foreign governments or agencies. In addition, this discussion does not address any pending or proposed legislation, which, if enacted, may affect the United Sates federal income tax consequences discussed below. See "Risk Factors—Proposed legislation could result in higher rates of tax imposed on non-U.S. holders (as defined herein) that are resident in countries imposing 'unfair foreign taxes.""

If a partnership (including any entity or arrangement treated as a partnership for United States federal income tax purposes) purchases, owns, or disposes of our common stock, the tax treatment of a person treated as a partner in the partnership for United States federal income tax purposes generally will depend on the status of the partner and the activities of the partnership. Partnerships (and other entities or arrangements so treated for United States federal income tax purposes) and their partners should consult their own tax advisors.

This discussion addresses only non-U.S. holders and does not discuss any tax considerations other than United States federal income tax and certain United States federal estate tax considerations. Prospective investors are urged to consult their own tax advisors regarding the United States federal, state, and local, and foreign tax consequences of the purchase, ownership, and disposition of our common stock, including the effect of any applicable income or estate tax treaty, any changes in applicable tax laws, and any pending or proposed legislation or regulations.

Dividends

We have never declared or paid cash dividends on our common stock. We anticipate that we will retain all earnings, if any, to support our operations and to finance the growth and development of our business for the foreseeable future.

If we do make a distribution of cash or property with respect to our common stock, any such distribution generally will constitute a dividend for United States federal income tax purposes to the extent of our current or accumulated earnings and profits, as determined under United States federal income tax principles. Subject to the discussion below under "FATCA Withholding" and "Information Reporting and Backup Withholding," any such

dividend paid to a non-U.S. holder generally will be subject to withholding tax at a 30% rate or at a lower rate under an applicable income tax treaty between the United States and the non-U.S. holder's country of residence. In order to receive a reduced treaty withholding tax rate, a non-U.S. holder must furnish to us or our paying agent a properly executed Internal Revenue Service ("IRS") Form W-8BEN or Form W-8BEN-E (or other applicable form) prior to payment of the dividend, certifying under penalties of perjury that the non-U.S. holder is entitled to a reduction in withholding under an applicable income tax treaty. A non-U.S. holder that holds our common stock through a financial institution or other agent will be required to provide appropriate documentation to the financial institution or other agent, which then will be required to provide certification to us or our paying agent either directly or through other intermediaries. A non-U.S. holder that is eligible for a reduced rate of withholding tax pursuant to an income tax treaty may obtain a refund of any excess amounts withheld by timely filing a refund claim with the IRS.

A non-U.S. holder is exempt from the withholding tax described above if the dividend is "effectively connected" with the conduct of a trade or business in the United States of the non-U.S. holder (and, if an applicable income tax treaty so provides, attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States) and the non-U.S. holder furnishes to us or our paying agent an IRS Form W-8ECI (or applicable successor form), certifying under penalties of perjury that the dividend is effectively connected with the non-U.S. holder's conduct of a trade or business in the United States (and, if an applicable income tax treaty so provides, attributable to a permanent establishment or fixed base maintained in the United States). "Effectively connected" dividends will generally be subject to United States federal income tax at the rates that also apply to U.S. persons. A corporate non-U.S. holder may, under certain circumstances, be subject to an additional branch profits tax at a 30% rate (or at a lower rate under an applicable income tax treaty) with respect to its "effectively connected" dividends.

Any distribution (or portion thereof) in excess of our current or accumulated earnings and profits will be treated, first, as a tax-free return of the non-U.S. holder's capital, up to the holder's adjusted tax basis in shares of our common stock, and thereafter, as capital gain subject to the tax treatment described below in "Gain on Sale, Exchange or Other Taxable Disposition."

Gain on Sale, Exchange or Other Taxable Disposition

Subject to the discussion below under "FATCA Withholding" and "Information Reporting and Backup Withholding," a non-U.S. holder generally will not be subject to United States federal income tax or withholding tax on gain realized upon a sale, exchange or other taxable disposition of shares of our common stock (including a redemption, but only if the redemption would be treated as a sale or exchange rather than a distribution for United States federal income tax purposes) unless:

- the gain is "effectively connected" with the conduct of a trade or business of the non-U.S. holder in the United States (and, if required by an applicable income tax treaty, attributable to a permanent establishment or fixed base maintained in the United States), in which case the non-U.S. holder generally will be subject to United States federal income tax on a net income basis with respect to such gain in the same manner as if such holder were a resident of the United States and, if the non-U.S. holder is a corporation for United States federal income tax purposes, may be subject to an additional "branch profits tax" at a 30% rate (or at a lower rate under an applicable income tax treaty);
- the non-U.S. holder is an individual who is present in the United States for 183 or more days in the taxable
 year of the disposition and meets certain other conditions, in which case the non-U.S. holder generally will
 be subject to United States federal income tax at a 30% rate (or at a lower rate under an applicable income
 tax treaty) on the gain derived from the sale, which gain may be offset by U.S.-source capital losses for the
 year; or
- we are or have been a "United States real property holding corporation" ("USRPHC") at any time within
 the shorter of the five-year period preceding the disposition and the non-U.S. holder's holding period for
 our common stock (the "relevant period") and the non-U.S. holder (i) disposes of our common stock
 during a calendar year when our common stock is no longer regularly traded on an established securities
 market or (ii) owned (directly, indirectly, and constructively) more than 5% of our

common stock at any time during the relevant period, in which case such a non-U.S. holder will be subject to tax on the gain on the disposition of shares of our common stock generally as if the gain were effectively connected with the conduct of a trade or business in the United States, except that the "branch profits tax" will not apply.

We believe we currently are not, and we do not anticipate becoming, a USRPHC for United States federal income tax purposes. Generally, a corporation is a USRPHC only if the fair market value of its United States real property interests (as defined in the Code) equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests and its other assets used or held for use in a trade or business.

FATCA Withholding

Sections 1471 through 1474 of the Code and the regulations issued thereunder (commonly referred to as the Foreign Account Tax Compliance Act ("FATCA")) impose a 30% withholding tax on dividends paid on our common stock to, and (subject to the proposed Treasury regulations discussed below) the gross proceeds derived from the sale or other disposition of our common stock by, a foreign entity if the foreign entity is:

- a "foreign financial institution" (as defined under FATCA) that does not furnish proper documentation, typically on IRS Form W-8BEN-E, evidencing either (i) an exemption from FATCA withholding or (ii) its compliance (or deemed compliance) with specified due diligence, reporting, withholding and certification obligations under FATCA or (iii) residence in a jurisdiction that has entered into an intergovernmental agreement with the United States relating to FATCA and compliance with the diligence and reporting requirements of the intergovernmental agreement and local implementing rules; or
- a "non-financial foreign entity" (as defined under FATCA) that does not provide sufficient documentation, typically on IRS Form W-8BEN-E, evidencing either (i) an exemption from FATCA or (ii) adequate information regarding substantial United States beneficial owners of such entity (if any).

Withholding under FATCA generally applies to payments of dividends on our common stock and to payments of gross proceeds from a sale or other disposition of our common stock. Withholding agents may, however, rely on proposed Treasury Regulations that would no longer require FATCA withholding on payments of gross proceeds. A withholding agent such as a broker, and not Insmed Incorporated, will determine whether or not to implement gross proceeds FATCA withholding.

Non-U.S. holders of our common stock should consult their own tax advisors regarding these requirements and whether they may be relevant to their ownership and disposition of our common stock.

Under certain circumstances, a non-U.S. holder will be eligible for refunds or credits of withholding taxes imposed under FATCA by filing a United States federal income tax return. Prospective investors should consult their tax advisors regarding the effect of FATCA on their ownership and disposition of our common stock.

Information Reporting and Backup Withholding

Except as described below, a non-U.S. holder generally will be exempt from backup withholding and information reporting requirements with respect to dividend payments and the payment of the proceeds from the sale of shares of our common stock effected at a United States office of a broker, as long as the payor or broker does not have actual knowledge or reason to know that the holder is a United States person, and the holder has furnished to the payor or broker:

- a valid IRS Form W-8BEN or Form W-8BEN-E on which the non-U.S. holder certifies, under penalties of perjury, that it is a non-United States person; or
- other documentation upon which it may rely to treat the payments as made to a non-United States person
 in accordance with Treasury regulations, or the non-U.S. holder otherwise establishes an exemption.

However, we must report annually to the IRS and to non-U.S. holders the amount of dividends paid to non-U.S. holders and the tax withheld with respect to such dividends, regardless of whether withholding was required. Copies of the information returns reporting such dividends and withholding may also be made available to the tax authorities in the country in which the respective non-U.S. holder resides under the provisions of an applicable income tax treaty or exchange of information agreement.

Payment of the proceeds from the sale of our common stock effected at a foreign office of a broker generally will not be subject to information reporting or backup withholding. However, a sale of our common stock by a non-U.S. holder that is effected at a foreign office of a broker will be subject to information reporting and backup withholding, at a rate of 24% under current law, if:

- the proceeds are transferred to an account maintained by the non-U.S. holder in the United States;
- the payment of proceeds or the confirmation of the sale is mailed to the non-U.S. holder at a United States address; or
- the sale has some other specified connection with the United States as provided in the Treasury regulations,

unless the broker does not have actual knowledge or reason to know that the holder is a United States person and the documentation requirements described above are met or the non-U.S. holder otherwise establishes an exemption.

In addition, a sale of shares of our common stock will be subject to information reporting if it is effected at a foreign office of a broker that is:

- a United States person;
- a "controlled foreign corporation" for United States federal income tax purposes;
- a foreign person 50% or more of whose gross income is effectively connected with the conduct of a United States trade or business for a specified three-year period; or
- a foreign partnership, if at any time during its tax year (a) one or more of its partners are "U.S. persons", as defined in the Treasury regulations, who in the aggregate hold more than 50% of the income or capital interest in the partnership, or (b) such foreign partnership is engaged in the conduct of a trade or business in the United States,

unless the broker does not have actual knowledge or reason to know that the holder is a United States person and the documentation requirements described above are met or an exemption is otherwise established. Backup withholding will apply if the sale is subject to information reporting and the broker has actual knowledge that the holder is a United States person.

Backup withholding is not an additional tax. A non-U.S. holder generally may obtain a refund of any amounts withheld under the backup withholding rules that exceed the non-U.S. holder's income tax liability by filing a refund claim with the IRS.

Federal Estate Taxes

The estates of nonresident alien decedents generally are subject to United States federal estate tax on property with a United States situs. Because we are a United States corporation, our common stock will be United States situs property and therefore will be included in the taxable estate of a nonresident alien decedent at the time of the decedent's death, unless an applicable estate tax treaty between the United States and the decedent's country of residence provides otherwise. An estate tax credit is available to reduce the net tax liability of a nonresident alien's estate, but the estate tax credit for a nonresident alien is generally much smaller than the applicable credit for computing the estate tax of a United States resident. Nonresident aliens should consult their personal tax advisors regarding the United States federal estate tax consequences of owning our common stock.

LEGAL MATTERS

Certain legal matters in connection with this offering will be passed upon for us by Covington & Burling LLP, Washington, D.C. The validity of the common stock being offered hereby will be passed upon for us by Hunton Andrews Kurth LLP, Richmond, Virginia. Ropes & Gray LLP, Boston, Massachusetts, is counsel to the underwriters in connection with this offering.

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, and the effectiveness of our internal control over financial reporting as of December 31, 2024, as set forth in their reports, which are incorporated by reference in this prospectus supplement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

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INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring to those publicly available documents. The information that we incorporate by reference is considered to be part of this prospectus supplement. We incorporate by reference the documents listed below (File No. 000-30739) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) between the date of this prospectus supplement and the date this offering is terminated:

- Annual Report on Form 10-K for the year ended December 31, 2024, filed with the SEC on <u>February 20</u>, 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, as filed with the SEC on April 4, 2025;
- Quarterly Report on Form 10-Q for the quarter ended March 31, 2025, filed with the SEC on May 8, 2025;
- Current Reports on Form 8-K, filed with the SEC on February 6, 2025 (solely with respect to Item 8.01), February 20, 2025 (solely with respect to Item 5.02), February 24, 2025 (solely with respect to Item 8.01), April 17, 2025, April 24, 2025 (as amended on April 24, 2025), May 16, 2025, June 6, 2025 and June 10, 2025 (solely with respect to Item 8.01); and
- Description of our common stock contained in our registration statement on <u>Form 8-A</u>, dated June 1, 2000, as updated by the Description of Securities Registered Under Section 12 of the Exchange Act, filed as <u>Exhibit 4.5</u> to our Annual Report on Form 10-K for the year ended December 31, 2024, and including any amendment or report subsequently filed for the purpose of updating such description.

You may access our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, proxy statement, and other information, if any, we file with or furnish to the SEC free of charge at the SEC's website (www.sec.gov) or our website (www.insmed.com) as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not part of this prospectus supplement.

You may also request a copy of our SEC filings at no cost, by telephoning or writing us at the following telephone number or address:

Insmed Incorporated
700 US Highway 202/206
Bridgewater, New Jersey 08807
Attention: Michael A. Smith, Chief Legal Officer and Corporate Secretary
(908) 977-9900

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PROSPECTUS



Common Stock Debt Securities

We or any selling securityholder may from time to time offer to sell the securities identified above in amounts, at prices and on terms determined at the time of the offering and described in one or more supplements to this prospectus. Each time we or any selling securityholders sell securities pursuant to this prospectus, the specific terms and any other information relating to a specific offering and, if applicable, the selling securityholders, will be set forth in a prospectus supplement.

Our securities may be offered and sold in the same offering or in separate offerings to or through one or more underwriters, dealers, and agents, directly to purchasers, or through a combination of these methods. The names and compensation of any underwriter, dealer or agent involved in the sale of our securities will be described in the applicable prospectus supplement. See "Plan of Distribution" on page 20 of this prospectus for additional information.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "INSM." The last reported sale price for our common stock on The Nasdaq Global Select Market on May 18, 2023 was \$18.82.

Our principal executive offices are located at 700 US Highway 202/206, Bridgewater, NJ 08807, and our telephone number is (908) 977-9900.

Investing in our securities involves a high degree of risk. You should carefully consider the risk factors incorporated in this prospectus by reference and described under the heading "Risk Factors" on page $\underline{3}$ of this prospectus.

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

The date of this prospectus is May 19, 2023.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the SEC, utilizing a "shelf" registration process as a "well-known seasoned issuer," as defined in Rule 405 under the Securities Act of 1933 (the "Securities Act"). Under this shelf registration process, we and any selling securityholders may offer and sell from time to time in one or more offerings the securities described in this prospectus.

This prospectus provides you with a general description of our securities. Each time we or any selling securityholders sell securities pursuant to this prospectus, we and the selling securityholders will provide a prospectus supplement, which will be delivered with this prospectus, that will contain specific information about the offering and the terms of the particular securities offered. The prospectus supplement, or information incorporated by reference in this prospectus or any prospectus supplement that is of a more recent date, may also add to, update or change information contained in this prospectus. To the extent that any statement that we or any selling securityholders make in a prospectus supplement or incorporate by reference from a future SEC filing is inconsistent with statements made in this prospectus, the statements made in this prospectus will be deemed modified or superseded by those made in the prospectus supplement or such incorporated document. This prospectus may not be used to consummate a sale of our securities unless it is accompanied by a prospectus supplement. We and the selling securityholders may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to an offering of our securities. You should carefully read this prospectus, any applicable prospectus supplement and any relevant free writing prospectus, together with the information incorporated herein by reference, prior to making any decision regarding an investment in our securities.

We have not, and no selling securityholder has, authorized anyone to provide you with different or additional information from that contained in this prospectus. We take no responsibility for, and can provide no assurance as to the reliability of, any information that others may give. We are not, and no selling securityholder is, making offers to sell or seeking offers to buy our securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information contained in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of the respective dates of such documents. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise indicates, references in this prospectus to "Insmed", the "Company", "we", "us" and "our" refer to Insmed Incorporated, a Virginia corporation, together with its consolidated subsidiaries. Insmed, PULMOVANCE, ARIKARES and ARIKAYCE are trademarks of Insmed Incorporated. Our logos and trademarks are the property of Insmed. All other brand names or trademarks appearing in this prospectus are the property of their respective holders. Use or display by us of other parties' trademarks or trade dress in this prospectus is not intended to, and does not, imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owners.

INSMED INCORPORATED

We are a global biopharmaceutical company on a mission to transform the lives of patients with serious and rare diseases. We were incorporated in the Commonwealth of Virginia on November 29, 1999. On December 1, 2010, we completed a business combination with Transave, Inc., a privately held New Jersey based company focused on the development of differentiated and innovative inhaled pharmaceuticals for the site specific treatment of serious lung diseases.

Our first commercial product, ARIKAYCE, is approved in the United States (the "U.S.") as ARIKAYCE® (amikacin liposome inhalation suspension), in Europe as ARIKAYCE Liposomal 590 mg Nebuliser Dispersion and in Japan as ARIKAYCE inhalation 590mg (amikacin sulfate inhalation drug product). ARIKAYCE received accelerated approval in the U.S. in September 2018 for the treatment of *Mycobacterium avium* complex ("MAC") lung disease as part of a combination antibacterial drug regimen for adult patients with limited or no alternative treatment options in a refractory setting. In October 2020, the European Commission approved ARIKAYCE for the treatment of nontuberculous mycobacterial ("NTM") lung infections caused by MAC in adults with limited treatment options who do not have cystic fibrosis ("CF"). In March 2021, Japan's Ministry of Health, Labour and Welfare approved ARIKAYCE for the treatment of patients with NTM lung disease caused by MAC who did not sufficiently respond to prior treatment with a multidrug regimen.

Our clinical-stage pipeline includes brensocatib, treprostinil palmitil inhalation powder ("TPIP") and early-stage research programs. Brensocatib is a small molecule, oral, reversible inhibitor of dipeptidyl peptidase 1, which we are developing for the treatment of patients with bronchiectasis, CF and other neutrophil-mediated diseases, including chronic rhinosinusitis without nasal polyps. TPIP is an inhaled formulation of the treprostinil prodrug trespostinil palmitil which may offer a differentiated product profile for pulmonary hypertension associated with interstitial lung disease and pulmonary arterial hypertension. Our early-stage research programs encompass a wide range of technologies and modalities, including artificial intelligence-driven protein engineering, gene therapy, and protein manufacturing.

Our principal executive offices are located at 700 US Highway 202/206, Bridgewater, NJ 08807, and our telephone number is (908) 977-9900. Our Internet address is www.insmed.com. The information on our web site is not incorporated by reference into this prospectus or any applicable prospectus supplement and should not be considered to be part of this prospectus or any applicable supplement.

RISK FACTORS

An investment in our securities involves risks. Prior to making a decision about investing in our securities, you should carefully consider the specific risks discussed under "Risk Factors" in our Annual Report on Form 10-K for our most recent fiscal year, as updated by our Quarterly Reports on Form 10-Q and other SEC filings subsequent thereto, pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and in any applicable prospectus supplement. The risks and uncertainties described in any applicable prospectus supplement and in our SEC filings are not the only ones we face. Each of these risks could materially and adversely affect our business, financial condition, results of operations and prospects, resulting in a complete or partial loss of your investment.

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains, and the information incorporated by reference herein and any applicable prospectus supplement may contain, forward-looking statements that involve substantial risks and uncertainties. "Forward-looking statements," as that term is defined in the Private Securities Litigation Reform Act of 1995, Section 27A of the Securities Act and Section 21E of the Exchange Act, are statements that are not historical facts and involve a number of risks and uncertainties. Words herein such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "intends," "potential," "continues," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) identify forward-looking statements.

Forward-looking statements are based on our current expectations and beliefs, and involve known and unknown risks, uncertainties and other factors, which may cause our actual results, performance and achievements and the timing of certain events to differ materially from the results, performance, achievements or timing discussed, projected, anticipated or indicated in any forward-looking statements. Such risks, uncertainties and other factors include, among others, the following:

- failure to successfully commercialize ARIKAYCE, our only approved product, in the U.S., Europe or Japan (amikacin liposome inhalation suspension, Liposomal 590 mg Nebuliser Dispersion, and amikacin sulfate inhalation drug product, respectively), or to maintain U.S., European or Japanese approval for ARIKAYCE;
- uncertainties in the degree of market acceptance of ARIKAYCE by physicians, patients, third-party payors and others in the healthcare community;
- our inability to obtain full approval of ARIKAYCE from the U.S. Food and Drug Administration, including the risk that we will not successfully or in a timely manner complete the study to validate a patient reported outcome tool and the confirmatory post-marketing clinical trial required for full approval of ARIKAYCE;
- inability of us, PARI Pharma GmbH or our other third-party manufacturers to comply with regulatory requirements related to ARIKAYCE or the Lamira® Nebulizer System ("Lamira");
- our inability to obtain adequate reimbursement from government or third-party payors for ARIKAYCE or acceptable prices for ARIKAYCE;
- development of unexpected safety or efficacy concerns related to ARIKAYCE, brensocatib, or our other product candidates;
- inaccuracies in our estimates of the size of the potential markets for ARIKAYCE, brensocatib, TPIP or our other product candidates or in data we have used to identify physicians, expected rates of patient uptake, duration of expected treatment, or expected patient adherence or discontinuation rates;
- the risks and uncertainties associated with, and the perceived benefits of, our secured senior loan with
 certain funds managed by Pharmakon Advisors, LP and our royalty financing with OrbiMed Royalty &
 Credit Opportunities IV, LP, including our ability to maintain compliance with the covenants in the
 agreements for the senior secured loan and royalty financing and the impact of the restrictions on our
 operations under these agreements;
- our inability to create an effective direct sales and marketing infrastructure or to partner with third parties
 that offer such an infrastructure for distribution of ARIKAYCE or any of our product candidates that are
 approved in the future;
- failure to obtain regulatory approval to expand ARIKAYCE's indication to a broader patient population;
- risk that brensocatib or TPIP does not prove to be effective or safe for patients in ongoing and future clinical studies, including, for brensocatib, the ASPEN study;
- risk that our competitors may obtain orphan drug exclusivity for a product that is essentially the same as a product we are developing for a particular indication;
- failure to successfully predict the time and cost of development, regulatory approval and commercialization for novel gene therapy products;

- failure to successfully conduct future clinical trials for ARIKAYCE, brensocatib, TPIP and our other
 product candidates due to our limited experience in conducting preclinical development activities and
 clinical trials necessary for regulatory approval and our potential inability to enroll or retain sufficient
 patients to conduct and complete the trials or generate data necessary for regulatory approval, among other
 things;
- risks that our clinical studies will be delayed or that serious side effects will be identified during drug development;
- failure to obtain, or delays in obtaining, regulatory approvals for ARIKAYCE outside the U.S., Europe or Japan, or for our product candidates in the US, Europe, Japan or other markets, including separate regulatory approval for Lamira in each market and for each usage;
- failure of third parties on which we are dependent to manufacture sufficient quantities of ARIKAYCE or
 our product candidates for commercial or clinical needs, to conduct our clinical trials, or to comply with
 our agreements or laws and regulations that impact our business or agreements with us;
- our inability to attract and retain key personnel or to effectively manage our growth;
- our inability to successfully integrate our recent acquisitions and appropriately manage the amount of management's time and attention devoted to integration activities;
- risks that our acquired technologies, products and product candidates are not commercially successful;
- our inability to adapt to our highly competitive and changing environment;
- risk that we are unable to maintain our significant customers;
- risk that government healthcare reform materially increases our costs and damages our financial condition;
- business or economic disruptions due to catastrophes or other events, including natural disasters or public health crises;
- impact of the COVID-19 pandemic and efforts to reduce its spread on our business, employees, including key personnel, patients, partners and suppliers;
- deterioration in general economic conditions in the U.S., Europe, Japan and globally, including the effect
 of prolonged periods of inflation, affecting us, our suppliers, third-party service providers and potential
 partners;
- our inability to adequately protect our intellectual property rights or prevent disclosure of our trade secrets
 and other proprietary information and costs associated with litigation or other proceedings related to such
 matters:
- restrictions or other obligations imposed on us by agreements related to ARIKAYCE or our product candidates, including our license agreements with PARI Pharma GmbH and AstraZeneca AB, and failure to comply with our obligations under such agreements;
- the cost and potential reputational damage resulting from litigation to which we are or may become a
 party, including product liability claims;
- risk that our operations are subject to a material disruption in the event of a cybersecurity attack or issue;
- our limited experience operating internationally;
- changes in laws and regulations applicable to our business, including any pricing reform, and failure to comply with such laws and regulations;
- our history of operating losses, and the possibility that we never achieve or maintain profitability;
- goodwill impairment charges affecting our results of operations and financial condition;
- inability to repay our existing indebtedness and uncertainties with respect to our ability to access future capital; and
- delays in the execution of plans to build out an additional third-party manufacturing facility approved by the appropriate regulatory authorities and unexpected expenses associated with those plans.

We caution readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they are made. Any forward-looking statement is based on information current as of the date of this prospectus and speaks only as of the date on which such statement is made. Actual events or results may differ materially from the results, plans, intentions or expectations anticipated in these forward-looking statements as a result of a variety of factors, many of which are beyond our control. More information on factors that could cause actual results to differ materially from those anticipated is included from time to time in our reports filed with the Securities and Exchange Commission (the "SEC"), including, but not limited to, those described in the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in our Annual Report on Form 10-K for our most recent fiscal year, as updated from time to time in our Quarterly Reports on Form 10-Q and other SEC filings subsequent thereto, including any applicable prospectus supplement. We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in such forward-looking statements.

You should read this prospectus, the registration statement of which this prospectus forms a part, any applicable prospectus supplement, and the documents incorporated by reference herein and therein, in their entirety and with the understanding that our actual future results may be materially different from those expressed in forward-looking statements.

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of our securities offered under this prospectus. Unless we indicate otherwise in the applicable prospectus supplement, we anticipate that any net proceeds will be used for working capital and general corporate purposes. We will not receive proceeds from sales of securities by selling securityholders except as otherwise stated in an applicable prospectus supplement.

DESCRIPTION OF COMMON STOCK

The following is a summary of the material terms of our common stock, which is based upon, and is qualified in its entirety by reference to, our Articles of Incorporation, as amended (the "Articles of Incorporation"), our Amended and Restated Bylaws (the "Bylaws") and applicable provisions of the Virginia Stock Corporation Act ("VSCA"). This summary may not contain all the information that is important to you; you can obtain additional information regarding our Articles of Incorporation and Bylaws by referring to such documents, copies of which are included as exhibits to the registration statement of which this prospectus forms a part.

General

Under our Articles of Incorporation, we have authority to issue 500,000,000 shares of common stock, par value \$0.01 per share. As of March 14, 2023, there were 136,428,466 shares of common stock issued and outstanding. All shares of common stock will, when issued pursuant to this prospectus, be duly authorized, fully paid and nonassessable.

Dividend Rights

Subject to the rights of the holders of any of our preferred stock then outstanding, the holders of our common stock are entitled to receive ratably such dividends, if any, as may be declared from time to time by our board of directors out of legally available funds. As of the date of this prospectus, we have not declared or paid any dividends on our shares of common stock, and there were no shares of preferred stock outstanding, although our board of directors is authorized to issue preferred stock with rights senior to those of the common stock without any further vote or action by the holders of our common stock.

Rights Upon Liquidation

In the event we are liquidated, dissolved or our affairs are wound up, after we pay or make adequate provision for all of our known debts and liabilities, each holder of common stock will receive distributions pro rata out of assets that we can legally use to pay distributions, subject to the rights of the holders of any of our preferred stock then outstanding.

Voting Rights

Holders of our common stock are entitled to one vote per share and will have the exclusive power to vote on all matters presented to our shareholders, including the election of directors, except as otherwise provided by the VSCA and subject to the rights of the holders of any of our preferred stock then outstanding. An election of directors by our shareholders will be determined by a plurality of the votes cast by the shareholders entitled to vote on the election, although we have a director resignation policy applicable to director nominees in uncontested elections. Our Articles of Incorporation do not provide for cumulative voting. In accordance with our Articles of Incorporation, our board is divided into three classes serving staggered three-year terms, with one class being elected each year at our annual meeting of shareholders.

Subject to certain exceptions set forth in the VSCA, matters other than the election of directors generally will be approved if the votes cast by our shareholders favoring the action exceed the votes cast opposing the action. Subject to the rights of the holders of any of our preferred stock then outstanding, however, the affirmative vote of at least 75% of the voting power of the outstanding shares of our capital stock entitled to vote generally in the election of directors, voting together as a single group, will be required to take the following actions:

- · remove a director, which may only be done for cause; and
- alter, amend, repeal, or adopt any provision inconsistent with, the provisions of (1) our Articles of
 Incorporation that provide for a classified board, director removal only for cause, filling of newly created
 or vacant directorships, or bylaw amendments or (2) our Bylaws.

Other Rights

Holders of our common stock will have no preference, appraisal or exchange rights, except for any appraisal rights provided by the VSCA. Furthermore, holders of our common stock have no conversion, sinking fund or redemption rights, or preemptive rights to subscribe for any of our securities.

Potential Anti-Takeover Effects of Certain Provisions of Virginia Law and Our Organizational Documents

Certain provisions of the VSCA, our Articles of Incorporation and our Bylaws could hamper a third-party's acquisition of, or discourage a third-party from attempting to acquire control of, us or limit the price that investors might be willing to pay for shares of our common stock. These provisions or arrangements include:

- The ability to issue preferred stock with rights senior to those of our common stock without any further
 vote or action by the holders of our common stock. The issuance of preferred stock could decrease the
 amount of earnings and assets available for distribution to the holders of our common stock or could
 adversely affect the rights and powers, including voting rights, of the holders of our common stock. In
 certain circumstances, such issuance could have the effect of decreasing the market price of our common
 stock.
- The existence of a staggered board of directors in which there are three classes of directors serving staggered three-year terms, thus expanding the time required to change the composition of a majority of directors.
- The requirement that shareholders provide advance notice when nominating director candidates to serve on our board of directors.
- The inability of shareholders to convene a shareholders' meeting without the chair of the board, the president or a majority of the board of directors first calling the meeting.
- The prohibition against entering into a business combination with the beneficial owner of 10% or more of
 our outstanding voting stock for a period of three years after the 10% or greater owner first reached that
 level of stock ownership, unless certain criteria are met.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Broadridge Corporate Issuer Solutions, LLC. Its address is 1717 Arch Street, Suite 1300, Philadelphia, PA 19103.

Listing

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

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DESCRIPTION OF DEBT SECURITIES

We may issue, separately or together with, or upon conversion, exercise or exchange of other securities, debt securities, including debentures, notes, bonds and other evidences of indebtedness as set forth in the applicable prospectus supplement. The debt securities will be our direct obligations, either secured or unsecured, and may include convertible debt securities. The debt securities may be our senior, senior subordinated or subordinated obligations. The debt securities will be issued under an indenture between us and Computershare Trust Company, N.A. (as successor to Wells Fargo Bank, National Association), as trustee, which we may amend or supplement from time to time. This prospectus, together with the applicable prospectus supplement, will describe the terms of a particular series of debt securities that we may offer from time to time. The indenture has been qualified under the Trust Indenture Act of 1939, as amended (the "Trust Indenture Act").

The following summary of the material provisions of the indenture and the debt securities does not purport to be complete and is subject to, and is qualified in its entirety by reference to, the provisions of the indenture and certificate evidencing the applicable debt securities. Therefore, you should carefully consider the indenture that is filed as an exhibit to the registration statement that includes this prospectus. Other specific terms of the indenture and debt securities will be described in the applicable prospectus supplement. If any particular terms of the indenture or debt securities described in a prospectus supplement differ from any of the terms described below, then the terms described below will be deemed to have been superseded by that prospectus supplement. In this description of the debt securities, the words "we," "us" or "our" refer only to Insmed Incorporated and not to our subsidiaries, unless we otherwise expressly state or the context otherwise requires.

General

Debt securities may be issued in one or more series without limitation as to aggregate principal amount. We may specify a maximum aggregate principal amount for the debt securities of any series. We are not limited as to the amount of debt securities that we may issue under the indenture. The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer's certificate or by a supplemental indenture. The prospectus supplement relating to a particular series of debt securities will set forth the material terms of the debt securities being offered, including:

- the title of the debt securities;
- the offering price;
- the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;
- any limit on the aggregate principal amount that may be issued;
- the person to whom any interest on a debt security will be payable, if other than the person in whose name that debt security is registered at the close of business on the record date for such interest;
- the date or dates on which the principal of any debt securities is payable;
- the interest rate or rates (which may be fixed or variable) at which the debt securities will bear interest, if
 any, the date or dates from which any such interest will accrue, the interest payment dates on which any
 such interest will be payable and the record date for any such interest payable on any interest payment date
 (or the method of determining the dates or rates);
- the place or places where the principal of and any premium and interest on the debt securities will be payable;
- the period or periods within which, the price or prices at which and the terms and conditions upon which
 the debt securities may be redeemed, in whole or in part, at our option and, if other than by a resolution of
 the board of directors, the manner in which any election by us to redeem the debt securities will be
 evidenced;
- the obligation, if any, of ours to redeem or repurchase the debt securities pursuant to any sinking fund or
 analogous provisions or at the option of a holder and the period or periods within which, the price or
 prices at which and the terms and conditions upon which the debt securities will be redeemed or
 repurchase, in whole or in part, pursuant to such obligation;

- if other than in denominations of \$1,000 or any integral multiple thereof, the denominations in which the
 debt securities will be issuable;
- if the amount of principal of or any premium or interest on the debt securities may be determined with reference to an index or pursuant to a formula, the manner in which such amounts will be determined;
- if other than U.S. currency, the currency, currencies or currency units in which the principal of or any
 premium or interest on the debt securities will be payable and the manner of determining the equivalent
 thereof in U.S. currency for any purpose, and whether we or a holder may elect payment to be made in a
 different currency;
- if the principal of or any premium or interest on the debt securities is to be payable, at our election or the election of a holder, in one or more currencies or currency units other than that or those in which such debt securities are stated to be payable, the currency, currencies or currency units that the principal of or any premium or interest on such debt securities as to which such election is made will be payable, the periods within which and the terms and conditions upon which such election is to be made and the amount so payable (or the manner in which such amount will be determined);
- if other than the entire principal amount thereof, the portion of the principal amount of the debt securities that will be payable upon declaration of acceleration of maturity thereof;
- if the principal amount payable at stated maturity of the debt securities will not be determinable as of any
 one or more dates prior to stated maturity, the amount which will be deemed to be the principal amount of
 such debt securities as of any such date for any purpose, including the principal amount thereof that will
 be due and payable upon maturity other than the state maturity or that will be deemed to be outstanding as
 of any date prior to the stated maturity (or, in each case, the manner that such amount deemed to be the
 principal amount will be determined);
- if applicable, whether the debt securities will be subject to the defeasance provisions described below under "Satisfaction and Discharge; Defeasance" or such other defeasance provisions specified in the applicable prospectus supplement for the debt securities and, if other than by a resolution of the board of directors, the manner in which any election by us to defease such debt securities will be evidenced;
- if applicable, the terms of any right or obligation to convert or exchange debt securities, including, if
 applicable, the conversion or exchange rate or price, the conversion or exchange period, provisions as to
 whether conversion or exchange will be mandatory, at the option of a holder or at our option, the events
 requiring an adjustment of the conversion price or exchange price and provisions affecting conversion or
 exchange if such debt securities are redeemed;
- whether or not the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;
- the forms of the debt securities and whether the debt securities will be issuable in whole or in part in the form of one or more global securities, and if so, the respective depositaries for such global securities, the form of any legend or legends that will be borne by any such global securities in addition to or in lieu of that set forth in the indenture and any circumstances in addition to or in lieu of those set forth in the indenture in which any such global security may be exchanged in whole or in part for debt securities registered, and any transfer of such global security in whole or in part may be registered, in the name or names of the persons other than the depositary for such global security or a nominee thereof;
- any deletion of, addition to or change in the events of default which applies to the debt securities 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 pursuant to the indenture;
- any deletion of, addition to or change in the covenants set forth in the indenture which apply to the debt securities;
- any authenticating agents, paying agents, security registrars or such other agents necessary in connection
 with the issuance of the debt securities, including exchange rate agents and calculations agents;

- if applicable, any terms of any security provided for the debt securities, including any provisions regarding
 the circumstances under which collateral may be released or substituted;
- if applicable, the terms of any guaranties for the debt securities and any circumstances under which there
 may be additional obligors on the debt securities; and
- any other terms of such debt securities.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies, or if the principal of or premium, if any, or interest on any series of debt securities is payable in a foreign currency or currencies, we will include in the applicable prospectus supplement information on the restrictions, elections, material federal income tax considerations, specific terms and other information with respect to that issue of debt securities and the foreign currency or currencies.

Unless otherwise specified in the applicable prospectus supplement, the debt securities will be registered debt securities. Debt securities may be sold at a substantial discount below their stated principal amount, bearing no interest or interest at a rate which at the time of issuance is below market rates. The U.S. federal income tax considerations applicable to debt securities sold at a discount will be described in the applicable prospectus supplement.

Exchange and Transfer

Debt securities may be transferred or exchanged at the office of the security registrar or at the office of any transfer agent designated by us for this purpose.

We will not impose a service charge for any transfer or exchange, but we may require holders to pay any tax or other governmental charges associated with any transfer or exchange.

In the event of any partial redemption of debt securities of any series, we will not be required to:

- issue, register the transfer of or exchange any debt security of that series during a period beginning at the
 opening of business 15 days before the day of sending a notice of redemption and ending at the close of
 business on the day of sending such notice; or
- register the transfer of or exchange any debt security of that series selected for redemption, in whole or in part, except the unredeemed portion being redeemed in part.

Initially, we will appoint the trustee as the security registrar. Any transfer agent, in addition to the security registrar initially designated by us, will be named in the applicable prospectus supplement. We may designate additional transfer agents or change transfer agents or change the office of the transfer agent. However, we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

Global Securities

The debt securities of any series may be represented, in whole or in part, by one or more global securities. Each global security will:

- · be registered in the name of a depositary, or its nominee, that we will identify in a prospectus supplement;
- be delivered to the depositary or nominee or custodian;
- · bear any required legends; and
- constitute a single debt security.

No global security may be exchanged in whole or in part for debt securities registered in the name of any person other than the depositary or any nominee unless:

- the depositary has notified us that it is unwilling or unable to continue as depositary or has ceased to be qualified to act as depositary;
- an event of default has occurred and is continuing with respect to the debt securities of the applicable series; or
- any other circumstance described in the applicable prospectus supplement has occurred permitting or requiring the issuance of any such security.

Conversion or Exchange

If any debt securities being offered are convertible into or exchangeable for our common stock or other securities, the relevant prospectus supplement will set forth the terms of conversion or exchange. Those terms will include, as applicable, the conversion or exchange price or rate, the conversion or exchange period, provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option, the number of shares of common stock or other securities, or the method of determining the number of shares of common stock or other securities, to be received by the holder upon conversion or exchange, the events requiring an adjustment of the conversion price or exchange price and provisions affecting conversion or exchange if such series of debt securities are redeemed. These provisions may allow or require the number of shares of our common stock or other securities to be received by the holders of such series of debt securities to be adjusted.

Payment and Paying Agents

Unless otherwise indicated in the prospectus supplement applicable to a series of debt securities, the provisions described in this paragraph will apply to the debt securities. Payment of interest on a debt security on any interest payment date will be made to the person in whose name the debt security is registered at the close of business on the regular record date. Payment on debt securities of a particular series will be payable at the office of a paying agent or paying agents designated by us. However, at our option, we may pay interest by mailing a check or by wire transfer to the record holder. The trustee will be designated as our initial paying agent.

We may also name any other paying agents in the prospectus supplement applicable to a series of debt securities. We may designate additional paying agents, change paying agents or change the office of any paying agent. However, we will be required to maintain a paying agent in each place of payment for the debt securities of a particular series.

All moneys paid by us to a paying agent for payment on any debt security that remain unclaimed for a period ending the earlier of:

- 10 business days prior to the date the money would be turned over to the applicable state; and
- at the end of two years after such payment was due, will be repaid to us thereafter. The holder may look
 only to us for such payment.

No Protection in the Event of a Change of Control

Unless otherwise indicated 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 the 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 prospectus supplement any financial or restrictive covenants applicable to any issue of a particular series of debt securities.

Consolidation, Merger and Sale of Assets

Unless otherwise indicated in a prospectus supplement with respect to a particular series of debt securities, we may not consolidate with or merge into any other person, in a transaction in which we are not the surviving corporation, or sell, convey, transfer or lease all or substantially all our properties and assets to, any entity, unless:

- the successor entity, if any, is a corporation, limited liability company, partnership, trust or other business
 entity existing under the laws of the United States, any State within the United States or the District of
 Columbia;
- the successor entity assumes our obligations under the debt securities and the applicable indenture;
- immediately after giving effect to the transaction, no default or event of default shall have occurred and be continuing; and
- certain other conditions specified in the indenture are met regarding our delivery of our officer's certificate
 and opinion of counsel to trustee.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into, sell or transfer all or part of its properties to us.

Events of Default

Unless we indicate otherwise in a prospectus supplement with respect to a particular series of debt securities, the following will be events of default for any series of debt securities under the indenture:

- (1) we fail to pay any interest on any debt security of that series when it becomes due and we subsequently fail to pay such interest for 30 days;
- (2) we fail to pay principal of or any premium on any debt security of that series when due;
- (3) we fail to perform, or breach, any other covenant or warranty in the applicable indenture and such failure continues for 90 days after we are given the notice required in the indenture; and
- (4) certain bankruptcy, insolvency or reorganization events with respect to us.

Additional or different events of default applicable to a series of debt securities may be described in the prospectus supplement for that series. An event of default for one series of debt securities is not necessarily an event of default for any other series of debt securities.

Within 90 days after the occurrence of any default under the indenture with respect to the debt securities of any series that is known to a responsible officer of the trustee, the trustee will give the holders of the debt securities of such series notice of such default as and to the extent provided by the Trust Indenture Act.

The trustee may withhold notice to the holders of any default, except defaults in the payment of principal, premium, if any, interest, any sinking fund installment on, or with respect to any conversion right of, the debt securities of such series. However, the trustee must consider it to be in the interests of the holders of the debt securities of such series to withhold this notice.

Unless we indicate otherwise in a prospectus supplement, if an event of default, other than an event of default described in clause (4) above, shall occur and be continuing with respect to any series of debt securities, either the trustee or the holders of at least 25% in aggregate principal amount of the outstanding securities of that series may declare the principal amount and premium, if any, of the debt securities of that series, or if any debt securities of that series are original issue discount securities, such other amount as may be specified in the applicable prospectus supplement, in each case together with accrued and unpaid interest, if any, thereon, to be due and payable immediately.

If an event of default described in clause (4) above shall occur, the principal amount and premium, if any, of all the debt securities of that series, or if any debt securities of that series are original issue discount securities, such other amount as may be specified in the applicable prospectus supplement, in each case together with accrued and unpaid interest, if any, thereon, will automatically become immediately due and payable without any declaration or other action on the part of the trustee or any holder.

After acceleration, the holders of a majority in aggregate principal amount of the outstanding securities of that series may, under certain circumstances, rescind and annul such acceleration if all events of default, other than the non-payment of accelerated principal, or other specified amounts or interest, have been cured or waived.

Other than the duty to act as a prudent person during an event of default, the trustee will not be obligated to exercise any of its rights or powers at the request of the holders unless the holders shall have offered to the trustee indemnity reasonably satisfactory to it. Generally, the holders of a majority in aggregate principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee.

A holder of debt securities of any series will not have any right to institute any proceeding under the indenture, or for the appointment of a receiver or a trustee, or for any other remedy under the indenture, unless:

- (1) the holder has previously given to the trustee written notice of a continuing event of default with respect to the debt securities of that series;
- (2) the holders of at least a majority in aggregate principal amount of the outstanding debt securities of

- that series have made a written request to the trustee and have offered to the trustee security or indemnity reasonably satisfactory to the trustee to institute the proceeding; and
- (3) the trustee has failed to institute the proceeding and has not received direction inconsistent with the original request from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series within 60 days after the original request.

Holders may, however, sue to enforce the payment of principal, premium or interest on any debt security on or after the due date or to enforce the right, if any, to convert any debt security (if the debt security is convertible) without following the procedures listed in clauses (1) through (3) immediately above.

To the extent any debt securities are outstanding, we will furnish the trustee an annual statement as to whether or not we are in default in the performance of the conditions and covenants under the indenture and, if so, specifying all known defaults.

Modification and Waiver

Unless we indicate otherwise in a prospectus supplement, we and the applicable trustee may make modifications and amendments to an indenture with the consent of the holders of a majority in aggregate principal amount of the outstanding securities of each series affected by the modification or amendment.

We may also make modifications and amendments to the indenture for the benefit of holders without their consent, for certain purposes including, but not limited to:

- providing for our successor to assume the covenants under the indenture;
- adding covenants and/or events of default;
- making certain changes to facilitate the issuance of the debt securities;
- securing the debt securities, including provisions relating to the release or substitution of collateral;
- providing for guaranties of, or additional obligors on, the debt securities;
- providing for a successor trustee or additional trustees;
- curing any ambiguities, defects or inconsistencies;
- conforming the terms to the description of the terms of the securities in an offering memorandum, prospectus supplement or other offering document;
- any other changes that do not adversely affect the rights or interest of any holder;
- complying with the requirements of the SEC in order to effect or maintain the qualification of the Indenture under the Trust Indenture Act; and
- complying with the applicable procedures of the applicable depositary.

However, neither we nor the trustee may make any modification or amendment without the consent of the holder of each outstanding debt security affected by the modification or amendment if such modification or amendment would:

- · change the stated maturity of any debt security;
- reduce the principal, premium, if any, or interest on any debt security or any amount payable upon redemption or repurchase, whether at our option or the option of any holder, or reduce the amount of any sinking fund payments;
- reduce the principal of an original issue discount security or any other debt security payable on acceleration of maturity;
- change the currency in which any debt security is payable;
- impair the right to enforce any payment after the stated maturity or redemption date of such debt security;
- reduce the percentage in principal amount of outstanding securities of any series required for the consent of holders for any supplemental indenture or for any waiver provided for in the indenture;

- adversely affect the right to convert any debt security if the debt security is a convertible debt security; or
- change the provisions in the indenture that relate to modifying or amending the indenture, except to
 increase any such percentage or to provide that certain other provisions of the indenture cannot be
 modified or waived without the consent of the holder of each outstanding debt security affected thereby.

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. The holders of not less than a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except:

- a default in the payment of the principal of or any premium or interest on any debt security of that series as and when the same will become due and payable by the terms thereof, otherwise than by acceleration; or
- in respect of a covenant or provision of the Indenture which cannot be modified or amended without the
 consent of the holder of each outstanding security of such series affected by such default.

Satisfaction and Discharge; Defeasance

We may be discharged from our obligations under the debt securities of any series that have matured or will mature or be redeemed within one year, subject to limited exceptions, if we deposit enough money with the trustee to pay all of the principal, interest and any premium due to the stated maturity date or redemption date of the debt securities.

The indenture contains a provision that permits us to elect either or both of the following:

- We may elect to be discharged from all of our obligations, subject to limited exceptions, with respect to
 any series of debt securities then outstanding. If we make this election, the holders of the debt securities of
 the series will not be entitled to the benefits of the indenture, except for the rights of holders to receive
 payments on debt securities or the registration of transfer and exchange of debt securities and replacement
 of lost, stolen or mutilated debt securities.
- We may elect to be released from our obligations under some or all of any financial or restrictive
 covenants applicable to the series of debt securities to which the election relates and from the
 consequences of an event of default resulting from a breach of those covenants.

To make either of the above elections, we must irrevocably deposit in trust with the trustee enough money to pay in full the principal, interest and premium on the debt securities and satisfy certain other conditions described in the indenture. This amount may be deposited in cash and/or U.S. government obligations or, in the case of debt securities denominated in a currency other than U.S. dollars, cash in the currency in which such series of securities is denominated and/or foreign government obligations. As one of the conditions to either of the above elections, for debt securities denominated in U.S. dollars, we must deliver to the trustee an opinion of counsel that the holders of the debt securities will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the action.

"Foreign government obligations" means, with respect to debt securities of any series that are denominated in a currency other than United States dollars:

- direct obligations of the government that issued or caused to be issued the currency in which such
 securities are denominated and for the payment of which obligations its full faith and credit is pledged, or,
 with respect to debt securities of any series which are denominated in euros, direct obligations of certain
 members of the European Union for the payment of which obligations the full faith and credit of such
 members is pledged, which in each case are not callable or redeemable at the option of the issuer thereof;
- obligations of a person controlled or supervised by or acting as an agency or instrumentality of a
 government described in the bullet above, the timely payment of which is unconditionally guaranteed as a
 full faith and credit obligation by such government, which are not callable or redeemable at the option of
 the issuer thereof; or

any depository receipt issued by a bank as custodian with respect to any obligation specified in the
first two bullet points and held by such bank for the account of the holder of such deposit any receipt, or
with respect to any such obligation which is so specified and held.

"U.S. government obligations" means:

- (1) any security which is:
 - a direct obligation of the United States of America for the payment of which the full faith and credit of the United States of America is pledged, which is not callable or redeemable at the option of the issuer thereof or
 - an obligation of a person controlled or supervised by or acting as an agency or instrumentality of
 the United States of America the payment of which is unconditionally guaranteed as a full faith
 and credit obligation by the United States of America, which is not callable or redeemable at the
 option of the issuer thereof; and
- (2) any depository receipt issued by a bank as custodian with respect to any U.S. government obligation specified in the two bullet points above and held by such bank for the account of the holder of such deposit any receipt, or with respect to any specific payment of principal of or interest on any U.S. government obligation which is so specified and held, provided that (except as required by law) such custodian is not authorized to make any deduction from the amount payable to the holder of such depositary receipt from any amount received by the custodian in respect of the U.S. government obligation or the specific payment of principal or interest evidenced by such depositary receipt.

Notices

Notices to holders will be delivered in person, mailed by first-class mail (registered or certified, return receipt requested), sent by facsimile transmission, email or overnight air courier guaranteeing next day delivery. If any debt securities are in the form of global securities, notices will be sent in accordance with the applicable rules and procedures of the depositary.

Governing Law; Wavier of Jury Trial; Jurisdiction

The indenture and the debt securities will be governed by, and construed under, the laws of the State of New York.

The indenture will provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably waive, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to the indenture, the debt securities or the transactions contemplated thereby.

The indenture will provide that any legal suit, action or proceeding arising out of or based upon the indenture, the securities or the transactions contemplated thereby may be instituted in the Federal courts of the United States of America located in the City of New York or the courts of the State of New York in each case located in the City of New York, and we, the trustee and the holder of the debt securities irrevocably submit to the non-exclusive jurisdiction of such courts in any such suit, action or proceeding. The indenture will further provide that service of any process, summons, notice or document by any method permitted under the indenture (to the extent allowed under any applicable statute or rule of court) to such party's address set forth in the indenture will be effective service of process for any suit, action or other proceeding brought in any such court. The indenture will further provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the courts specified above and irrevocably and unconditionally waive and agree not to plead or claim any such suit, action or other proceeding has been brought in an inconvenient forum.

No Personal Liability of Directors, Officers, Employees and Shareholders

No incorporator, shareholder, employee, agent, officer, director or subsidiary of ours will have any liability for any obligations of ours, or because of the creation of any indebtedness, under the debt securities, the

indenture, or in any board resolution, officer's certificate or supplemental indenture. The indenture provides that all such liability is expressly waived and released as a condition of, and as a consideration for, the execution of such indenture and the issuance of the debt securities.

Regarding the Trustee

The accompanying prospectus supplement will specify the trustee for the particular series of debt securities to be issued under the indenture.

The indenture will limit the right of the trustee, should it become our creditor, to obtain payment of claims or secure its claims.

The trustee is permitted to engage in certain other transactions with us. However, if the trustee acquires any conflicting interest, and there is a default under the debt securities of any series for which it is trustee, the trustee must eliminate the conflict or resign.

SELLING SECURITYHOLDERS

Selling securityholders are persons or entities that, directly or indirectly, have acquired or will from time to time acquire from us, our securities in various private transactions. Such selling securityholders may be parties to registration rights agreements with us, or we otherwise may have agreed or will agree to register their securities for resale. The initial purchasers of our securities, as well as their transferees, pledgees, donees or successors, all of whom we refer to as "selling securityholders," may from time to time offer and sell the securities pursuant to this prospectus and any applicable prospectus supplement.

The applicable prospectus supplement will set forth the name of each selling securityholder and the number of and type of securities beneficially owned by such selling securityholder that are covered by such prospectus supplement. The applicable prospectus supplement also will disclose whether any of the selling securityholders have held any position or office with, have been employed by or otherwise have had a material relationship with us during the three years prior to the date of the prospectus supplement.

PLAN OF DISTRIBUTION

We and any selling securityholders may sell the securities registered pursuant to this prospectus in the following ways:

- · to or through underwriters;
- · to or through dealers;
- through agents;
- directly to purchasers;
- in at-the-market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act to or through an underwriter or underwriters acting as principal or agent;
- through a combination of any of the foregoing methods; or
- through any other method described in the applicable prospectus supplement.

We and any selling securityholders reserve the right to sell directly to or exchange our securities directly with investors on our own behalf in those jurisdictions where we are authorized to do so.

We and any selling securityholders may distribute such securities 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.

We and any selling securityholders, or the purchasers of the securities for whom the underwriters may act as agents, may compensate underwriters in the form of underwriting discounts or commissions in connection with the sale of the securities. Underwriters may sell our securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for whom they may act as agents. Unless otherwise indicated in the applicable prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase our securities as a principal and may then resell such securities at varying prices to be determined by the dealer.

We and any selling securityholders will name any underwriter, dealer or agent involved in the offer and sale of securities in the applicable prospectus supplement. In addition, we and any selling securityholders will describe in the applicable prospectus supplement the public offering or purchase price and the proceeds we and any selling securityholders will receive from the sale of our securities, any compensation we and any selling securityholders will pay to underwriters, dealers or agents in connection with such offering of our securities, any discounts, concessions or commissions allowed or re-allowed by underwriters to participating dealers, and any exchanges on which our securities will be listed. Dealers and agents participating in the distribution of the securities may be deemed to be underwriters, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We and any selling securityholders may enter into agreements to indemnify underwriters, dealers and agents against certain civil liabilities, including liabilities under the Securities Act, and to reimburse these persons for certain expenses. We and any selling securityholders may also agree to contribute to payments that the underwriters, dealers or agents or any of their controlling persons may be required to make in respect of such liabilities. We and any selling security holders may grant underwriters who participate in the distribution of the securities being registered pursuant to this prospectus an option to purchase additional securities in connection with a subsequent distribution. Certain underwriters, dealers or agents and their associates may engage in transactions with and perform services for us in the ordinary course of our business.

To facilitate the offering of our securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of our securities. Such transactions may include over-allotments or short sales of our securities, which involve the sale by persons participating in the offering of more securities than we and any selling securityholders sold to them. In these circumstances, these persons

would cover such over-allotments or short positions by making purchases in the open market or by exercising their option to purchase additional securities, if any. In addition, these persons may stabilize or maintain the price of our securities by bidding for or purchasing such securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if the securities sold by them are repurchased in connection with stabilization transactions. Should these transactions be undertaken, they may be discontinued at any time.

LEGAL MATTERS

Unless the applicable prospectus supplement indicates otherwise, the legality of the securities being offered by this prospectus will be passed upon for us by Covington & Burling LLP, Washington, D.C. and/or Hunton Andrews Kurth LLP, Richmond, Virginia.

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, 2022, and the effectiveness of our internal control over financial reporting as of December 31, 2022, as set forth in their reports, which are 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 reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public from the SEC's website at www.sec.gov. We maintain a website at www.insmed.com. The information on our website is not incorporated by reference into this prospectus or any applicable prospectus supplement and should not be considered to be part of this prospectus or any applicable supplement. We have filed with the SEC a registration statement under the Securities Act with respect to the securities registered pursuant hereto. This prospectus omits some information contained in the registration statement in accordance with SEC rules and regulations. For further information with respect to us and the securities registered pursuant to this prospectus, you should review the registration statement, the applicable prospectus supplement, the information incorporated herein and therein, and the exhibits included herein and therein.

INCORPORATION BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring to those publicly available documents. The information that we incorporate by reference is considered to be part of this prospectus. We incorporate by reference the documents listed below (File No. 000-30739) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) between the date of this registration statement and, in the case of any particular offering of our securities, the date such offering is terminated:

- Annual Report on Form 10-K for the year ended December 31, 2022, filed with the SEC on <u>February 23</u>, 2023;
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2022 from our definitive proxy statement on Schedule 14A, as filed with the SEC on March 31, 2023;
- Quarterly Report on Form 10-Q for the quarter ended March 31, 2023, filed with the SEC on May 4, 2023;
- Current Report on Form 8-K, filed with the SEC on May 11, 2023; and
- Description of our common stock contained in our registration statement on <u>Form 8-A, dated June 1, 2000</u>, as updated by the <u>Description of Securities Registered Under Section 12 of the Exchange Act</u>, filed as Exhibit 4.5 to the Annual Report on Form 10-K for the year ended December 31, 2020, and including any amendment or report subsequently filed for the purpose of updating such description.

Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and information that we subsequently file with the SEC will automatically update and supersede the information herein to the extent inconsistent herewith. This means that it is important to review all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference has been modified or superseded.

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

Insmed Incorporated
700 US Highway 202/206
Bridgewater, New Jersey 08807
Attention: Michael A. Smith, General Counsel
(908) 977-9900

7,812,500 Shares



Common Stock

PROSPECTUS SUPPLEMENT

Joint Book-Running Managers

Goldman Sachs & Co. LLC

Leerink Partners

BofA Securities

Jefferies

J.P. Morgan

Lead Manager

Stifel

June 11, 2025