New England Journal of Medicine Publishes Positive Results from Insmed's Pivotal Phase 3 ASPEN Study of Brensocatib in Patients with Bronchiectasis

—Largest Global Clinical Trial Ever Conducted in Bronchiectasis Demonstrates Statistically Significant and Clinically Meaningful Reduction in Frequency of Pulmonary Exacerbations Versus Placebo—

—Brensocatib 25 mg is the First Investigational Therapy for Bronchiectasis to Show a Statistically Significant Reduction in the Rate of Lung Function Decline—

—Brensocatib is Currently Under Priority Review with the U.S. Food and Drug Administration—

BRIDGEWATER, N.J., April 23, 2025 /PRNewswire/ -- Insmed Incorporated (Nasdaq: INSM), a people-first global biopharmaceutical company striving to deliver first- and best-in-class therapies to transform the lives of patients facing serious diseases, today announced that positive results from the pivotal phase 3 ASPEN study of brensocatib in patients with non-cystic fibrosis bronchiectasis were published in the *New England Journal of Medicine* (NEJM). The landmark ASPEN study is the largest clinical trial ever conducted in bronchiectasis, a serious, chronic, and progressive inflammatory pulmonary disease that today has no approved therapies.

"Bronchiectasis is a debilitating disease characterized by pulmonary exacerbations, which contribute to lung function decline and severely impact quality of life," said lead author James Chalmers, MBChB, PhD, Professor and Consultant Respiratory Physician at the School of Medicine, University of Dundee, UK. "With limited treatment options and no approved therapies, the burden of exacerbations remains high, with many patients experiencing multiple episodes each year. For the first time, the ASPEN data published in *NEJM* demonstrates that a treatment which targets inflammation can reduce exacerbations and slow the rate of lung function decline. This is an exciting development and represents a potentially transformative breakthrough for people living with bronchiectasis, offering new hope for patients with this challenging condition if brensocatib is approved."

As previously reported, the ASPEN study met its primary endpoint, with both brensocatib doses achieving statistical and clinical significance for the reduction in the annualized rate of pulmonary exacerbations versus placebo over the 52-week treatment period. The annualized rate of exacerbations was 1.02 for brensocatib 10 mg, 1.04 for brensocatib 25 mg, and 1.29 for placebo. These rates were significantly lower in the brensocatib 10 mg and 25 mg groups versus placebo with rate ratios of 0.79 (adjusted P=0.004) and 0.81 (adjusted P=0.005), respectively.

Both dosage strengths of brensocatib also met several exacerbation-related secondary endpoints, including significantly prolonging the time to first exacerbation and significantly increasing the proportion of patients remaining exacerbation-free over the treatment period. Patients treated with brensocatib 25 mg also showed significantly lower lung function decline at week 52 as measured by post-bronchodilator forced expiratory volume over one second (FEV1).

Brensocatib was well-tolerated in the study. Treatment-emergent adverse events (TEAEs) occurring in at least 5.0% of patients treated with either dose of brensocatib and more frequently than in placebo were COVID-19 (15.8%, 20.9%, 15.8%), nasopharyngitis (7.7%, 6.3%, 7.6%), cough (7.0%, 6.1%, 6.4%), and headache (6.7%, 8.5%, and 6.9%) for brensocatib 10 mg, brensocatib 25 mg, and placebo, respectively.

"Currently, people with bronchiectasis have no approved treatments to address the frequent, damaging exacerbations that are the hallmark of this disease," said Martina Flammer, M.D., MBA, Chief Medical Officer of Insmed. "Brensocatib has the potential to be the first approved therapy to fill this critical unmet need in the care of patients with bronchiectasis, as well as the first approved dipeptidyl peptidase 1 (DPP1) inhibitor—a new mechanism of action with the potential to address a range of neutrophil-mediated inflammatory diseases. The ASPEN trial represents a transformative step forward for the millions of people globally diagnosed with bronchiectasis."

Brensocatib is currently under Priority Review with the U.S. Food and Drug Administration, with a target action date of August 12, 2025, under the Prescription Drug User Fee Act (PDUFA).

About ASPEN

The total number of active sites in ASPEN was 391 sites in 35 countries. Adult patients (ages 18 to 85 years) were randomized 1:1:1 and adolescent patients (ages 12 to <18 years) were randomized 2:2:1 for treatment with brensocatib 10 mg, brensocatib 25 mg, or placebo once daily for 52 weeks, followed by 4 weeks off treatment. The primary efficacy analysis included data from 1,680 adult patients and 41 adolescent patients.

About Bronchiectasis

Bronchiectasis is a serious, chronic lung disease in which the bronchi become permanently dilated due to a cycle of infection, inflammation, and lung tissue damage. The condition is marked by frequent pulmonary exacerbations requiring antibiotic therapy and/or hospitalizations. Symptoms include chronic cough, excessive sputum production, shortness of breath, and repeated respiratory infections, which can worsen the underlying condition. Today, approximately 500,000 patients in the U.S., 600,000 patients in the EU5 (France, Germany, Italy, Spain, and UK), and 150,000 patients in Japan have been diagnosed with bronchiectasis, and there are currently no approved therapies specifically targeting bronchiectasis in these regions.

About Brensocatib

Brensocatib is a small molecule, oral, reversible inhibitor of dipeptidyl peptidase 1 (DPP1) being developed by Insmed for the treatment of patients with bronchiectasis, chronic rhinosinusitis without nasal polyps, hidradenitis suppurativa, and other neutrophil-mediated diseases. DPP1 is an enzyme responsible for activating neutrophil serine proteases (NSPs), such as neutrophil elastase, in neutrophils when they are formed in the bone marrow. Neutrophils are the most common type of white blood cell and play an essential role in pathogen destruction and inflammatory mediation. In chronic inflammatory lung diseases, neutrophils accumulate in the airways and result in excessive active NSPs that cause lung destruction and inflammation. Brensocatib may decrease the damaging effects of inflammatory diseases such as bronchiectasis by inhibiting DPP1 and its activation of NSPs. Brensocatib is an investigational drug product that has not been approved for any indication in any jurisdiction.

About Insmed

Insmed Incorporated is a people-first global biopharmaceutical company striving to deliver first- and best-in-class therapies to transform the lives of patients facing serious diseases. The Company is advancing a diverse portfolio of approved and mid- to late-stage investigational medicines as well as cutting-edge drug discovery focused on serving patient communities where the need is greatest. Insmed's most advanced programs are in pulmonary and inflammatory conditions, including a therapy approved in the United States, Europe, and Japan to treat a chronic, debilitating lung disease. The Company's early-stage programs encompass a wide range of technologies and modalities, including gene therapy, AI-driven protein engineering, protein manufacturing, RNA end-joining, and synthetic rescue.

Headquartered in Bridgewater, New Jersey, Insmed has offices and research locations throughout the United States, Europe, and Japan. Insmed is proud to be recognized as one of the best employers in the biopharmaceutical industry, including spending four consecutive years as the No. 1 *Science* Top Employer. Visit **www.Insmed.com** to learn more.

Forward-looking Statements

This press release contains 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, 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) may identify forward-looking statements.

The forward-looking statements in this press release are based upon the Company's current expectations and beliefs, and involve known and unknown risks, uncertainties and other factors, which may cause the Company's actual results, performance and achievements and the timing of certain events to differ materially from the results, performance, achievements or timings discussed, projected, anticipated or indicated in any forward-looking statements. Such risks, uncertainties and other factors include, among others, the following: failure to obtain, or delays in obtaining, regulatory approvals for brensocatib in the U.S., Europe or Japan; failure to successfully commercialize brensocatib, if approved by applicable regulatory authorities, or to maintain applicable regulatory approvals for brensocatib, if approved; uncertainties in the degree of market acceptance of brensocatib, if approved, 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 brensocatib, if approved, or acceptable prices for brensocatib, if approved; inaccuracies in our estimates of the size of the potential markets for brensocatib 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 brensocatib 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; 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 brensocatib, if approved; development of unexpected safety or efficacy concerns related to brensocatib; 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; the 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; 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; restrictions or other obligations imposed on us by agreements related to brensocatib, including our license agreement with AstraZeneca AB, and failure to comply with our obligations under such agreements; 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; business or economic disruptions due to catastrophes or other events, including natural disasters or public health crises; and inability to repay our existing indebtedness and uncertainties with respect to our ability to access future capital.

The Company may not actually achieve the results, plans, intentions or expectations indicated by the Company's 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. For additional information about the risks and uncertainties that may affect the Company's business, please see the factors discussed in Item 1A, "Risk Factors," in the Company's Annual Report on Form 10-K for the year ended December 31, 2024 and any subsequent Company filings with the Securities and Exchange Commission (SEC).

The Company cautions readers not to place undue reliance on any such forward-looking statements, which speak only as of the date of this press release. The Company disclaims 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 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 the forward-looking statements.

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