European Commission Approves BRINSUPRI™ (brensocatib) as the First and Only Treatment Approved for Non-Cystic Fibrosis Bronchiectasis in the European Union

— Non-Cystic Fibrosis Bronchiectasis (NCFB) Is a Serious, Progressive Lung Disease That Can Lead to Permanent Lung Damage —

— BRINSUPRI Is a First-in-Disease, First-in-Class DPP1 Inhibitor Targeting Neutrophilic Inflammation —

— BRINSUPRI Was Reviewed Under EMA's Accelerated Assessment Pathway as It Is Considered of Major Interest for Public Health —

BRIDGEWATER, N.J., Nov. 18, 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 the European Commission has approved BRINSUPRI (brensocatib 25 mg tablets) for the treatment of non-cystic fibrosis bronchiectasis (NCFB) in patients 12 years of age and older with two or more exacerbations in the prior 12 months. BRINSUPRI is a first-in-class therapy, offering the first and only approved treatment indicated for NCFB in the European Union (EU). BRINSUPRI was reviewed under accelerated assessment by the EMA as it is deemed to be of major interest for public health.

NCFB is a chronic and progressive disease that can lead to permanent lung damage and lung function decline. Unlike other respiratory diseases that are characterized by airway narrowing, bronchiectasis causes airways to permanently widen, making it harder to clear mucus and bacteria, leading to persistent inflammation and infection. A hallmark of bronchiectasis is frequent exacerbations, or flares, when symptoms—such as coughing, increased mucus, shortness of breath and fatigue—worsen. An estimated 600,000 people in the EU are diagnosed with NCFB, with approximately two million additional people potentially undiagnosed.

"Living with non-cystic fibrosis bronchiectasis profoundly alters daily life, taking a toll on both physical health and emotional well-being," said ASPEN lead study investigator James Chalmers, MBChB, Ph.D., Professor and Consultant Respiratory Physician at the School of Medicine, University of Dundee, UK. "The European Commission's approval represents a major milestone for patients and clinicians in Europe, offering a much-needed treatment that can help reduce exacerbations, potentially slow disease progression, and reshape the treatment landscape for this debilitating disease."

This approval is based on a comprehensive scientific evaluation of the marketing authorization application, including data from the Phase 3 ASPEN and Phase 2 WILLOW studies, which were both published in the *New England Journal of Medicine*. In ASPEN, patients taking BRINSUPRI 25 mg had a 19.4% reduction in annual rate of exacerbations, as compared to placebo. BRINSUPRI 25 mg 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 who received BRINSUPRI 25 mg experienced statistically significant less decline in lung function, as measured by forced expiratory volume in one second (FEV_1) after using a bronchodilator, at week 52. The safety of BRINSUPRI was also evaluated in both studies. The most frequently reported adverse reactions are headache (9.2%), hyperkeratosis (5.9%), dermatitis (4.2%), rash (4.1%), upper respiratory tract infections (3.9%), and dry skin (3.0%).

"At Insmed, our mission has always been to bring new therapies to underserved patient communities. With BRINSUPRI, we now have the first treatment for non-cystic fibrosis bronchiectasis approved in the European Union—a historically overlooked population with long-standing unmet medical needs," said Martina Flammer, M.D., MBA, Chief Medical Officer of Insmed. "The accelerated approval reflects the strength of the data and the potential to become the new standard of care for treating patients with non-cystic fibrosis bronchiectasis who had at least two prior exacerbations. We are grateful to the patients, clinicians and partners who made this milestone possible."

The EC approval follows a positive opinion from the Committee for Medicinal Products for Human Use of the European Medicines Agency (EMA) on 16 October 2025. Insmed will engage with authorities across the EU to secure access to BRINSUPRI for eligible patients beginning in early 2026.

Applications for brensocatib are currently under review with the Medicines and Healthcare products Regulatory Agency in the U.K. and the Pharmaceuticals and Medical Devices Agency in Japan.

About BRINSUPRI (brensocatib)

BRINSUPRI (brensocatib) is a small molecule, once-daily, oral, reversible inhibitor of dipeptidyl peptidase 1 (DPP1). BRINSUPRI (brensocatib 10 mg and 25 mg tablets) is indicated in the United States for the treatment of non-cystic fibrosis bronchiectasis (NCFB) in adult and pediatric patients 12 years of age or older. In the European Union, BRINSUPRI (brensocatib 25 mg tablets) is approved for the treatment of NCFB in patients 12 years of age and older with two or more exacerbations in the prior 12 months.

Brensocatib is designed to inhibit the activation of enzymes (neutrophil serine proteases) in neutrophils that are key drivers of chronic airway inflammation in NCFB. Brensocatib is also being evaluated for its potential role in other neutrophil-mediated diseases.

About ASPEN

ASPEN was a global, randomized, double-blind, placebo-controlled Phase 3 study to assess the efficacy, safety, and tolerability of brensocatib in patients with non-cystic fibrosis bronchiectasis (NCFB). As part of the ASPEN study's conduct, more than 460 trial sites were engaged in nearly 40 countries. After excluding sites that did not enrol any patients and all sites in Ukraine, 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 WILLOW

WILLOW was a randomized, double-blind, placebo-controlled, parallel-group, multi-center, multi-national, Phase 2 study to assess the efficacy, safety and tolerability, and pharmacokinetics of brensocatib administered once daily for 24 weeks in patients with non-cystic fibrosis bronchiectasis (NCFB). WILLOW was conducted at 116 sites and enrolled 256 adult patients diagnosed with NCFB who had at least two documented pulmonary exacerbations in the 12 months prior to screening. Patients were randomized 1:1:1 to receive either 10 mg or 25 mg of brensocatib or matching placebo. The primary efficacy endpoint was the time to first pulmonary exacerbation over the 24-week treatment period in the brensocatib arms compared to the placebo arm.

About Bronchiectasis

NCFB is a chronic, progressive, and inflammatory lung disease that causes the airways to become permanently widened due to a cycle of infection, inflammation, lung tissue damage, and mucociliary dysfunction. Patients with NCFB often experience repeated exacerbations, requiring antibiotic therapy and/or hospitalizations. Symptoms include chronic cough, excessive sputum production, shortness of breath, fatigue, and repeated respiratory infections, which can worsen the underlying disease. An estimated 600,000 people in the EU are diagnosed with NCFB, with approximately two million additional people potentially undiagnosed.

BRINSUPRI™ (brensocatib) U.S. INDICATION AND IMPORTANT SAFETY INFORMATION

Indication in the U.S.

BRINSUPRI is indicated for the treatment of non-cystic fibrosis bronchiectasis (NCFB) in adult and pediatric patients 12 years of age and older.

Important Safety Information in the U.S.

WARNINGS AND PRECAUTIONS
Dermatologic Adverse Reactions
Treatment with BRINSUPRI is associated with an increase in dermatologic adverse reactions, including rash, dry skin, and hyperkeratosis. Monitor patients for development of new rashes or skin conditions and refer patients to a dermatologist for evaluation of new dermatologic findings.

Gingival and Periodontal Adverse Reactions
Treatment with BRINSUPRI is associated with an increase in gingival and periodontal adverse reactions. Refer patients to dental care services for regular dental checkups while taking BRINSUPRI. Advise patients to perform routine dental hygiene.

Live Attenuated Vaccines
It is unknown whether administration of live attenuated vaccines during BRINSUPRI treatment will affect the safety or effectiveness of these vaccines. The use of live attenuated vaccines should be avoided in patients receiving BRINSUPRI.

ADVERSE REACTIONS
The most common adverse reactions ≥2% in the ASPEN trial included upper respiratory tract infection, headache, rash, dry skin, hyperkeratosis, and hypertension. The safety profile for adult patients with NCFB in WILLOW was generally similar to ASPEN, except for a higher incidence of gingival and periodontal adverse reactions.

Less Common Adverse Reactions

Liver Function Test Elevations
In ASPEN, there was an increase from baseline in average ALT, AST, and alkaline phosphatase levels at all time points from Week 4 through Week 56 in both BRINSUPRI 10 mg and 25 mg arms compared to placebo. The incidence of ALT >3X upper limit of normal (ULN) was 0%, 1.2%, and 0.9%; the incidence of AST >3X ULN was 0.2%, 0.3%, and 0.5%; and the incidence of alkaline phosphatase >1.5X ULN was 2.5%, 4.1%, and 4.0% in patients treated with placebo and BRINSUPRI 10 mg and 25 mg, respectively.

Skin Cancers
In ASPEN, the incidence of skin cancers among patients treated with BRINSUPRI 10 mg and 25 mg was 0.5% and 1.9%, respectively, compared to 1.1% in placebo-treated patients.

Alopecia
In ASPEN, the incidence of alopecia among patients treated with BRINSUPRI 10 mg and 25 mg was 1.5% and 1.6% respectively, compared to 0.4% in placebo-treated patients.

USE IN SPECIFIC POPULATIONS
Pregnancy: There are no clinical data on the use of BRINSUPRI in pregnant women.

Lactation: There is no information regarding the presence of BRINSUPRI and/or its metabolite(s) in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for BRINSUPRI and any potential adverse effects on the breastfed child from BRINSUPRI or from the underlying maternal condition.

Pediatric use: The safety and effectiveness of BRINSUPRI for the treatment of NCFB have been established in pediatric patients aged 12 years and older. Common adverse reactions in pediatric patients aged 12 years and older enrolled in ASPEN were consistent with those in adults. The safety and effectiveness of BRINSUPRI have not been established in pediatric patients younger than 12 years of age.

Please see full US Prescribing Information.

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 two approved therapies to treat chronic, debilitating lung diseases. 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 throughoutthe United States, Europe, and Japan. Insmed is proud to be recognized as one of the best employers in the biopharmaceutical industry, including spending five consecutive years as the No. 1 *Science* Top Employer. Visit **www.insmed.com** to learn more or follow us on **LinkedIn**, **Instagram**, **YouTube**, and **X**.

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 successfully commercialize BRINSUPRI in the U.S. or European Union (EU) or

to maintain U.S. or EU approval for BRINSUPRI; failure to obtain, or delays in obtaining, regulatory approvals for BRINSUPRI in the United Kingdom or Japan, including the risk that any regulatory approvals, if granted, may be subject to significant limitations on use or subject to withdrawal or other adverse actions by the applicable regulatory authority; uncertainties in the degree of market acceptance of BRINSUPRI by physicians, patients, third-party payors and others in the healthcare community; inaccuracies in the Company's estimates of the size of the potential markets for BRINSUPRI or in data the Company has used to identify physicians; expected rates of patient uptake, duration of expected treatment, or expected patient adherence or discontinuation rates; the Company's inability to obtain adequate reimbursement from government or third-party payors for BRINSUPRI or acceptable prices for BRINSUPRI; development of unexpected safety or efficacy concerns related to BRINSUPRI, including the risk that data generated in further clinical trials of brensocatib may not be consistent with the results of the ASPEN study, which may result in changes to the product label and may adversely affect sales, or result in withdrawal of BRINSUPRI from the market; failure by us to comply with agreements related to brensocatib, including our license agreement with AstraZeneca AB; failure to successfully conduct future clinical trials for brensocatib, including due to the Company's potential inability to enroll or retain sufficient patients to conduct and complete the trials or generate data necessary for regulatory approval, among other things; failure to obtain regulatory approval for potential future brensocatib indications; and 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 or agreements with the Company.

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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