New Subgroup Analyses from Landmark Phase 3 ASPEN Study of Brensocatib in Patients with Bronchiectasis Demonstrate Consistency with Positive Overall Trial Population Results

—Data Presented at the CHEST 2024 Annual Meeting—

BRIDGEWATER, N.J., Oct. 8, 2024 /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 presented positive late-breaking subgroup data from the Phase 3 ASPEN study, 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. Posters with the details from these subgroup analyses can be found HERE. These data were presented at the CHEST 2024 Annual Meeting, held October 6-9 in Boston, along with several other presentations from across Insmed's respiratory portfolio.

"The positive results from the landmark Phase 3 ASPEN study have generated tremendous excitement among physicians and patients alike, providing hope for a much-needed approved treatment for bronchiectasis. Given the heterogeneity of this disease, it is striking that these new sub-analyses show a consistent positive impact on the rate of exacerbations across the majority of prespecified subgroups," said lead study investigator James Chalmers, MBChB, Ph.D., Professor and Consultant Respiratory Physician at the School of Medicine, University of Dundee, UK. "It is particularly exciting to see that, consistent with the overall trial analysis, brensocatib 25 mg was able to slow lung function decline as measured by FEV1 for all prespecified subgroups, further underscoring the potential impact this investigational treatment candidate may have on a diverse range of patients if approved."

Consistent with positive results for the overall ASPEN population, the annualized rate of pulmonary exacerbations favored brensocatib at both the 10 mg and 25 mg doses over placebo for almost all subgroups. In a separate analysis, least squares mean difference for brensocatib 25 mg demonstrated a reduced decline in post-bronchodilator FEV1 at Week 52 versus placebo for all prespecified subgroups. Results for patients treated with brensocatib 10 mg among subgroups were aligned with the overall trial population results.

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.

"We are incredibly excited to present subgroup findings from the ASPEN study at CHEST 2024, building on the positive results we have already shared with the bronchiectasis community," said Martina Flammer, M.D., MBA, Chief Medical Officer of Insmed. "The consistency of efficacy observed across most subgroups, particularly at the higher dose, further supports our belief that brensocatib has the potential to transform the treatment landscape for patients with bronchiectasis. We eagerly look forward to filing a new drug application for brensocatib in the U.S., followed by Europe and Japan, in hopes of delivering the first approved therapy for patients affected by this serious and difficult-to-treat disease."

Insmed plans to file a New Drug Application with the U.S. Food and Drug Administration for brensocatib in patients with bronchiectasis in the fourth quarter of 2024. Pending regulatory approvals, Insmed anticipates a U.S. launch for brensocatib in mid-2025 followed by launches in Europe and Japan in the first half of 2026. If approved, brensocatib would be the first approved treatment for 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 diseases.

About ASPEN

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 enroll 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 Brensocatib
Brensocatib is a small molecule, oral, reversible inhibitor DPP1 being developed by Insmed for the treatment of patients with bronchiectasis, CRSsNP, 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 research 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 three 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: the risk that the full data set from the ASPEN study or data generated in further clinical trials of brensocatib will not be consistent with the topline results of the ASPEN study or any additional results of theASPEN study; 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, in the U.S., Europe or Japan, or to maintain U.S., European or Japanese approval for brensocatib once approved; uncertainties in the degree of market acceptance of brensocatib 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 brensocatib 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; inability of the Company, Esteve Pharmaceuticals, S.A., Thermo Fisher Scientific, Inc. or the Company's other third-party manufacturers to comply with regulatory requirements related to brensocatib; the Company's inability to obtain adequate reimbursement from government or third-party payors for brensocatib or acceptable prices for brensocatib; development of unexpected safety or efficacy concerns related to brensocatib; failure to obtain regulatory approval for potential future brensocatib indications; 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; 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; risks that the Company's clinical studies will be delayed or that serious side effects will be identified during drug development; 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 strength and enforceability of the Company's intellectual property rights or the rights of third parties; the cost and potential reputational damage resulting from litigation to which the Company may become a party, including product liability claims; changes in laws and regulations applicable to the Company's business 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 the Company's existing indebtedness and uncertainties with respect to the Company's need and 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, 2023 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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