Insmed Announces Positive Topline Results from Landmark ASPEN Study of Brensocatib in Patients with Bronchiectasis

—Phase 3 Study Achieves Primary Endpoint for Both Dosage Strengths of Brensocatib with Statistically Significant and Clinically Meaningful Reduction in Frequency of Pulmonary Exacerbations Versus Placebo—

—Treatment with Brensocatib Also Achieves Statistical Significance on Multiple Secondary Endpoints for Both Dosage Strengths Versus Placebo—

—Brensocatib Well-Tolerated at Both Dosage Strengths—

—Results from ASPEN Validate DPP1 Inhibition as New Mechanism of Action with Potential to Address Range of Neutrophil-Mediated Diseases—

—Insmed Plans to Advance Quickly Toward U.S. Regulatory Filing, with Anticipated U.S. Launch in Mid-2025, Pending Approval—

—Insmed to Host Investor Call at 8:00 am ET on Tuesday, May 28, 2024—

BRIDGEWATER, N.J., May 28, 2024 /PRNewswire/ -- Insmed Incorporated (Nasdaq: INSM), a global biopharmaceutical company on a mission to transform the lives of patients with serious and rare diseases, today announced positive topline results from the 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. The study met its primary endpoint, with both dosage strengths of brensocatib demonstrating statistically significant reductions in the annualized rate of pulmonary exacerbations (PEs) versus placebo. The study also met several of its prespecified secondary endpoints with statistical significance.

Based on these results, Insmed plans to file a New Drug Application (NDA) with the U.S. Food and Drug Administration (FDA) 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.

Topline efficacy results from the ASPEN study are as follows:

	Brensocatib 10 mg compared to placebo		**Brensocatib 25 mg compared to placebo**	
Primary Endpoint				
Reduction in annualized rate of PEs	21.1 %	p=0.0019*	19.4 %	p=0.0046*
Secondary Endpoints				
Prolongation of time to first PE	18.7 %	p=0.0100*	17.5 %	p=0.0182*
Increase in odds of remaining exacerbation free over 52 weeks	41.2 %	p=0.0059*	40.0 %	p=0.0074*
Change from baseline in post-bronchodilator forced expiratory volume in 1 second (FEV1) at week 52	11 mL	p=0.3841	38 mL	p=0.0054*
Reduction in annualized rate of severe PEs	25.8 %	p=0.1277	26.0 %	p=0.1025
Change from baseline in the Quality of Life – Bronchiectasis (QOL-B) Respiratory Score at week 52	2.0 points	p=0.0594	3.8 points	p=0.0004^

**Statistically significant*

^Nominally significant p-value

"I am thrilled that the ASPEN study has demonstrated a statistically significant and clinically meaningful treatment effect for brensocatib compared with placebo, underscoring the impact this investigational therapy may have on patients with bronchiectasis," said lead study investigator James Chalmers, MBChB, Ph.D., Professor and Consultant Respiratory Physician at the School of Medicine, University of Dundee, UK. "Today, there is no approved treatment for bronchiectasis and there remains an urgent need for a therapy that can reduce exacerbations. As a DPP1 inhibitor, brensocatib would be the first treatment in its class and could offer a completely new approach to managing this difficult-to-treat patient population, heralding a new era in clinical management of bronchiectasis."

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.

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. Additional TEAEs and treatment-emergent adverse events of special interest (TEAESIs) are as follows:

	Brensocatib 10 mg (n=582)	**Brensocatib 25 mg (n=574)**	**Placebo (n=563)**
Any TEAE, n (%)	452 (77.7)	440 (76.7)	448 (79.6)
Severe TEAE, n (%)	74 (12.7)	67 (11.7)	90 (16.0)
Serious TEAE, n (%)	101 (17.4)	97 (16.9)	108 (19.2)
TEAE leading to death, n (%)	3 (0.5)	4 (0.7)	7 (1.2)
TEAE leading to treatment discontinuation, n (%)	25 (4.3)	22 (3.8)	23 (4.1)
TEAESIs, n (%)	42 (7.2)	56 (9.8)	53 (9.4)
Hyperkeratosis, n (%)	8 (1.4)	17 (3.0)	4 (0.7)
Periodontal/gingival event, n (%)	8 (1.4)	12 (2.1)	15 (2.7)
Severe infection, n (%)	4 (0.7)	7 (1.2)	4 (0.7)
Pneumonia, n (%)	23 (4.0)	27 (4.7)	33 (5.9)

"We are incredibly excited about the topline results from the pivotal ASPEN study and what they may mean for patients. These findings not only underscore our belief that brensocatib has the potential to transform the treatment landscape for bronchiectasis, but they also further validate DPP1 inhibition as a mechanism that may hold promise in other neutrophil-mediated diseases," said Martina Flammer, M.D., MBA, Chief Medical Officer of Insmed. "Today's outcome is the result of years of hard work and dedication by many members of the Insmed team, and I'd like to thank them for their efforts. We are especially grateful to the clinical investigators, site staff, patients, and families who made this study possible. We now look forward to further analyzing the data while rapidly advancing toward regulatory filings in our key regions, where we believe approximately 1 million bronchiectasis patients may benefit from an approved treatment."

Brensocatib has received Breakthrough Therapy Designation from the FDA and was granted access to the Priority Medicines (PRIME) scheme by the European Medicines Agency for patients with bronchiectasis. Insmed plans to present detailed results from the ASPEN study at an upcoming medical meeting.

Insmed is also advancing the development of brensocatib in other neutrophil-driven inflammatory diseases with significant health burdens and limited treatment options. A Phase 2 study in patients with chronic rhinosinusitis without nasal polyps (CRSsNP) is currently underway, and Insmed plans to initiate a Phase 2 study in hidradenitis suppurativa (HS) in the second half of 2024.

Insmed looks forward to hosting a commercial webinar on Tuesday, June 4, 2024, at 8:00 am ET, where the Company's commercial leadership will provide details on the market outlook for its three most advanced programs, ARIKAYCE® (amikacin liposome inhalation suspension), brensocatib, and treprostinil palmitil inhalation powder (TPIP).

Conference Call

Insmed management will host a conference call for investors beginning at 8:00 a.m. ET on Tuesday, May 28, to discuss the ASPEN results. Shareholders and other interested parties may participate in the conference call by dialing (800) 715-9871 (U.S.) or (646) 307-1963 (international) and referencing access code 1245105. The call will also be webcast live on the Company's website at www.insmed.com.

A replay of the conference call will be accessible approximately one hour after its completion through June 27, 2024, by dialing (800) 770-2030 (U.S.) or (609) 800-9909 (international) and referencing access code 1245105. A webcast of the call will also be archived for 90 days under the Investor Relations section of the Company's website at www.insmed.com.

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. Bronchiectasis affects approximately 450,000 patients in the U.S., 400,000 patients in Europe, and 150,000 patients in Japan, 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, 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 global biopharmaceutical company on a mission to transform the lives of patients with serious and rare diseases. Insmed's first commercial product is a first-in-disease therapy approved in the United States, Europe, and Japan to treat a chronic, debilitating lung disease. The Company is progressing a robust pipeline of investigational therapies targeting areas of serious unmet need, including neutrophil-mediated inflammatory diseases and rare pulmonary disorders. Insmed is also advancing an early-stage research engine encompassing a wide range of technologies and modalities, including artificial intelligence-driven protein engineering, gene therapy, and protein manufacturing. Insmed is headquartered in Bridgewater, New Jersey, with additional offices and research locations throughout the United States, Europe, and Japan.
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; 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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