Insmed Announces Positive Top-Line Results from Phase 2 WILLOW Study of INS1007 in Patients with Non-Cystic Fibrosis Bronchiectasis

-- Study Achieves Primary Endpoint with Statistically Significant Improvement in Time to First Exacerbation for Both Dosage Strengths of INS1007 Versus Placebo --
-- Treatment with INS1007 also Achieves Key Secondary Endpoint of Reduction of Frequency of Pulmonary Exacerbation --
-- INS1007 Was Generally Well-Tolerated at Both Dosage Strengths --
-- Company Plans to Advance INS1007 to Phase 3 Development --

BRIDGEWATER, N.J., Feb. 3, 2020 /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 top-line results from its global, randomized, double-blind placebo-controlled Phase 2 WILLOW study evaluating the efficacy, safety, and pharmacokinetics of INS1007 administered once daily in adults with non-cystic fibrosis bronchiectasis (NCFBE). INS1007 is a novel, oral, selective, reversible inhibitor of dipeptidyl peptidase 1 (DPP1).

The WILLOW study met its primary endpoint of time to first pulmonary exacerbation over the 24-week treatment period for both the 10 mg and 25 mg dosage groups of INS1007 compared to placebo (p=0.027, p=0.044, respectively). In addition, treatment with INS1007 resulted in a reduction in the frequency of pulmonary exacerbations, a key secondary endpoint, versus placebo. Specifically, patients treated with INS1007 experienced a 36% reduction in the 10 mg arm (p=0.041) and a 25% reduction in the 25 mg arm (p=0.167) versus placebo. Change in concentration of active neutrophil elastase (NE) in sputum versus placebo from baseline to the end of the treatment period was also statistically significant (p=0.034 for 10 mg, p=0.021 for 25 mg).

"These results are incredibly encouraging and highlight the potentially important role INS1007 may play in the management of 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, many bronchiectasis patients suffer from persistent symptoms and frequent exacerbations, with no pharmaceutical therapies available that are approved to help them manage this disease. There is an urgent need for approved, effective therapies that can break the vicious cycle of inflammation, lung damage, and infection for these patients."

INS1007 was generally well-tolerated in the study. Rates of adverse events (AEs) leading to discontinuation in patients treated with placebo, INS1007 10 mg, and INS1007 25 mg were 10.6%, 7.4%, and 6.7%, respectively. The most common AEs in patients treated with INS1007 were cough, headache, sputum increase, dyspnea, fatigue, and upper respiratory tract infection. Rates of adverse events of special interest (AESIs) in patients treated with placebo, INS1007 10 mg, and INS1007 25 mg, respectively, were as follows: rates of periodontal disease were 2.4%, 7.4%, and 10.1%; rates of hyperkeratosis were 0%, 3.7%, and 1.1%; and rates of infections that were considered AESIs were 18.8%, 16.0%, and 16.9%.

"This molecule represents a novel, potentially first-in-class mechanism that utilizes an anti-inflammatory approach to treat the debilitating cycle of inflammation, infection, and lung damage associated with NCFBE," said Martina Flammer, M.D., MBA, Chief Medical Officer of Insmed. "Importantly, in addition to achieving the primary and a key secondary endpoint, we saw significant reductions in sputum neutrophil elastase, an important biomarker that reflects the mechanism of action of INS1007. These data provide a strong rationale for continued development in this disease and potentially other neutrophil-driven inflammatory conditions. We look forward to further analyzing the data and discussing next steps with regulatory authorities."

"The entire Insmed team is elated by the positive results observed in this study. This is a day of incredible promise for the hundreds of thousands of patients around the world who currently suffer from NCFBE. We believe these results further validate both our business and clinical development capabilities," stated Will Lewis, Chairman and CEO of Insmed. "With INS1007, Insmed has a unique and significant opportunity with a potential first-in-class therapy for NCFBE. There are currently no approved therapies specifically targeting this severe and chronic pulmonary disease in the United States, Europe, or Japan."

Insmed plans to present detailed study results at an upcoming medical meeting. The top-line results will be further discussed on Insmed's upcoming fourth quarter and year-end 2019 earnings call.

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 INS1007 administered once daily for 24 weeks in patients with non-cystic fibrosis bronchiectasis (NCFBE). WILLOW was conducted at 116 sites and enrolled 256 adult patients diagnosed with NCFBE 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 INS1007 or matching placebo. The primary efficacy endpoint was the time to first pulmonary exacerbation over the 24-week treatment period in the INS1007 arms compared to the placebo arm.

About INS1007

INS1007 is an investigational, first-in-class, oral, selective, reversible inhibitor of dipeptidyl peptidase I (DPP1) being developed by Insmed for the treatment of patients with non-cystic fibrosis bronchiectasis (NCFBE). 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. INS1007 may decrease the damaging effects of inflammatory diseases such as NCFBE by inhibiting DPP1 and its activation of NSPs.

About Non-Cystic Fibrosis Bronchiectasis

NCFBE is a severe, chronic pulmonary disorder 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. NCFBE affects approximately 340,000 to 520,000 patients in U.S. Today, there are no approved therapies specifically targeting NCFBE in the U.S., Europe, or Japan for the treatment of patients with NCFBE.

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, ARIKAYCE® (amikacin liposome inhalation suspension), is the first and only therapy approved in the United States for the treatment of refractory *Mycobacterium avium* complex (MAC) lung disease as part of a combination antibacterial drug regimen for adult patients with limited or no alternative treatment options. MAC lung disease is a chronic, debilitating condition that can cause severe and permanent lung damage. Insmed's earlier-stage clinical pipeline includes INS1007, a novel oral reversible inhibitor of dipeptidyl peptidase 1 with therapeutic potential in non-cystic fibrosis bronchiectasis and other inflammatory diseases, and INS1009, an inhaled formulation of a treprostinil prodrug that may offer a differentiated product profile for rare pulmonary disorders, including pulmonary arterial hypertension. For more information, visit www.insmed.com.

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 timing 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 WILLOW or data generated in further clinical trials of INS1007 will not be consistent with the top-line results of WILLOW; failure to successfully commercialize or maintain U.S. approval for ARIKAYCE, the Company's only approved product; uncertainties in the degree of market acceptance of ARIKAYCE by physicians, patients, third-party payors and others in the healthcare community; the Company's inability to obtain full approval of ARIKAYCE from the FDA, including the risk that the Company will not timely and successfully complete the study to validate the PRO tool and the confirmatory post-marketing study required for full approval of ARIKAYCE; inability of the Company, PARI or the Company's other third party manufacturers to comply with regulatory requirements related to ARIKAYCE or the Lamira® Nebulizer System; the Company's 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 or INS1007; inaccuracies in the Company's estimates of the size of the potential markets for ARIKAYCE or INS1007 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 create an effective direct sales and marketing infrastructure or to partner with third parties that offer such an infrastructure for distribution of ARIKAYCE; failure to

obtain regulatory approval to expand ARIKAYCE's indication to a broader patient population; failure to successfully conduct future clinical trials for ARIKAYCE, INS1007 and the Company's other product candidates, including due to the Company's limited experience in conducting preclinical development activities and clinical trials necessary for regulatory approval and the Company's inability to enroll or retain sufficient patients to conduct and complete the trials or generate data necessary for regulatory approval; risks that the Company's 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. or for the Company's product candidates in the U.S., Europe, Japan or other markets, including theUnited Kingdom as a result of the United Kingdom's recent exit from the European Union; failure of third parties on which the Company is dependent to manufacture sufficient quantities of ARIKAYCE or the Company's product candidates for commercial or clinical needs, to conduct the Company's clinical trials, or to comply with laws and regulations that impact the Company's business or agreements with the Company; the Company's inability to attract and retain key personnel or to effectively manage the Company's growth; the Company's inability to adapt to its highly competitive and changing environment; the Company's inability to adequately protect its intellectual property rights or prevent disclosure of its trade secrets and other proprietary information and costs associated with litigation or other proceedings related to such matters; restrictions or other obligations imposed on the Company by its agreements related to ARIKAYCE or the Company's product candidates, including its license agreements with PARI and AstraZeneca AB, and failure of the Company to comply with its obligations under such agreements; the cost and potential reputational damage resulting from litigation to which the Company is or may become a party, including product liability claims; the Company's limited experience operating internationally; changes in laws and regulations applicable to the Company's business, including any pricing reform, and failure to comply with such laws and regulations; inability to repay the Company's existing indebtedness and uncertainties with respect to the Company's ability to access future capital; and delays in the execution of plans to build out an additional third-party manufacturing facility and unexpected expenses associated with those plans.

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, 2018 and any subsequent Company filings with the Securities and Exchange Commission.

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 Securities and Exchange Commission, 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.

Contact:

Investors:

Argot Partners
Laura Perry or Heather Savelle
(212) 600-1902
insmed@argotpartners.com

Media:

Mandy Fahey
Senior Director, Corporate Communications
Insmed
(732) 487-7468
amanda.fahey@insmed.com

SOURCE Insmed Incorporated