Brensocatib (Formerly INS1007) to be Studied in Patients with Severe COVID-19 in Investigator-Initiated Trial

--Insmed to support STOP-COVID19 Study, Expected to Begin in the UK in May 2020--

BRIDGEWATER, N.J., April 23, 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 that it will provide funding and clinical drug supply for the STOP-COVID19 (**S**uperiority **T**rial **o**f **P**rotease inhibition in **COVID-19**) trial, an investigator-initiated study of brensocatib (formerly known as INS1007) in up to 300 hospitalized patients with COVID-19 sponsored by the University of Dundee. The study, which has been prioritized and designated an Urgent Public Health trial by the UK's National Institute for Health Research, is expected to begin enrollment in May 2020.

Brensocatib is a novel oral, reversible inhibitor of dipeptidyl peptidase 1 (DPP1) currently being developed by Insmed for the treatment of bronchiectasis and other inflammatory diseases. DPP1 is an enzyme that catalyzes the activation of neutrophil serine proteases (NSPs) 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. By inhibiting the activation of NSPs, brensocatib may offer applicability in a range of neutrophil-mediated diseases. Neutrophil influx into the lungs is a defining characteristic of acute respiratory distress syndrome (ARDS), a severe outcome of COVID-19 that is associated with high mortality. Reduction of neutrophil proteases may reduce the progression of lung injury and the need for ventilation in these patients.

"The global COVID-19 pandemic has generated an extraordinary response from the biopharmaceutical industry to bring to bear all potential means of fighting this disease and preventing its most severe outcomes, including the need for ventilation and ICU stays," said Martina Flammer, M.D., Chief Medical Officer of Insmed. "At the start of the outbreak, Insmed began pursuing an *in vivo* mouse model to better understand the potential of brensocatib in preventing ARDS. As we rapidly advance this early-stage research simultaneously, we are very pleased to support Professor James Chalmers and the University of Dundee in leading a controlled clinical trial that will help us evaluate the potential impact of brensocatib on hospitalized patients suffering from severe COVID-19."

The STOP-COVID19 trial is a prospective, randomized, double-blind, placebo-controlled trial of brensocatib in patients with severe COVID-19. The multicenter study is expected to enroll up to 300 patients at 10 sites in the UK who present to the hospital with confirmed COVID-19 and are at risk of needing increased levels of supplemental oxygen and/or ventilation. Patients will be randomized 1:1 to receive either brensocatib 25 mg once daily or matching placebo on top of standard of care. The primary endpoint is clinical improvement on a seven-point ordinal scale as defined by the World Health Organization. Patients will be treated for 28 days, with a sample-size reassessment performed once 100 patients have been enrolled and treated.

"The medical community has never faced a more urgent need for treatment than the unprecedented situation we face today with COVID-19," said lead study investigator James Chalmers, MBChB, Ph.D., Professor and Consultant Respiratory Physician at the School of Medicine, University of Dundee, UK. "The mechanism of action of brensocatib that we observed in a Phase 2 study in patients with non-cystic fibrosis bronchiectasis provides a strong rationale for evaluating this novel treatment candidate in other neutrophil-driven inflammatory conditions. It is my hope that this novel approach will have applicability in patients at risk of ARDS—a devastating outcome of COVID-19 for which there are currently no approved therapies."

In February 2020, Insmed reported positive top-line results from the global randomized, double-blind placebo-controlled Phase 2 WILLOW study evaluating the efficacy, safety, and pharmacokinetics of brensocatib in adults with non-cystic fibrosis bronchiectasis. In this study of more than 250 patients, brensocatib was generally well-tolerated. The study met both its primary and key secondary endpoint.

Insmed will continue to develop brensocatib in patients with bronchiectasis and expects to begin enrollment in a Phase 3 program in the second half of 2020 following anticipated discussions later this year with health authorities on the design of the program.

About Brensocatib (Formerly INS1007)

Brensocatib is a small molecule, oral, reversible inhibitor of dipeptidyl peptidase I (DPP1) being developed by Insmed for the

treatment of patients with bronchiectasis. 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.

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 brensocatib, 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 brensocatib does not prove effective or safe for patients in the STOP-COVID19 study; business or economic disruptions due to catastrophes or other events, including natural disasters or public health crises; impact of the novel coronavirus (COVID-19) pandemic and efforts to reduce its spread on our business, employees, including key personnel, patients, partners and suppliers; the risk that the full data set from the WILLOW study, our six-month Phase 2 trial of brensocatib in patients with NCBFE or data generated in further clinical trials of brensocatib will not be consistent with the top-line results of the study; 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 a PRO tool and complete 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 brensocatib; inaccuracies in the Company's estimates of the size of the potential markets for ARIKAYCE or 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; 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, brensocatib 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 the United Kingdom as a result of its 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 FDA-approved 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, 2019 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.

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