Insmed Provides Business Update

-- Company Submits New Drug Application in Japan for ARIKAYCE® (amikacin liposome inhalation suspension) for the Treatment of Patients with NTM Lung Disease Caused by MAC --
-- AstraZeneca Exercises Exclusive Option to Develop INS1007 in Chronic Obstructive Pulmonary Disease or Asthma --
-- COVID-19 Response: Company Directs Employees, Including Commercial Field Force, to Work from Home and Suspends Revenue Guidance --
-- Conference Call at 4:30 p.m. Eastern Time Today --

BRIDGEWATER, N.J., March 16, 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 provided a general business update.

Submission of New Drug Application for ARIKAYCE® (amikacin liposome inhalation suspension) in Japan

Insmed announced today that it has submitted a new drug application (JNDA) to Japan's Ministry of Health, Labour and Welfare (MHLW) for ARIKAYCE for the treatment of patients with non-tuberculous mycobacterial (NTM) lung disease caused by *Mycobacterium avium* complex (MAC) who did not sufficiently respond to prior treatment. Insmed subsequently plans to submit a separate Medical Device Notification (JMDN) to the MHLW for approval of the Lamira® Nebulizer System, the designated device for administration of ARIKAYCE.

"The submission of our JNDA filing for ARIKAYCE marks an important step in our journey to transform the way NTM lung disease caused by MAC is managed for patients in Japan. We look forward to continuing our work with the regulatory authorities during the review period," said Yuji Orihara, General Manager of Japan for Insmed.

AstraZeneca Exercises Option to Develop INS1007 for Treatment of COPD or Asthma

Insmed also announced today that AstraZeneca AB has exercised the first option pursuant to the companies' October 2016 license agreement under which AstraZeneca can advance clinical development of INS1007 in the indication of chronic obstructive pulmonary disease (COPD) or asthma. Under the terms of the agreement, upon exercise of this option, AstraZeneca is solely responsible for all aspects of the development of INS1007 up to and including Phase 2b clinical trials in COPD or asthma.

The agreement also includes a second and final option which, if exercised, would permit AstraZeneca to further develop INS1007 beyond Phase 2b clinical trials upon reaching agreement on commercial terms satisfactory to each party for the further development and commercialization of INS1007 in COPD or asthma. Insmed retains full development and commercialization rights for INS1007 in all other indications and geographies.

"We believe AstraZeneca's decision to exercise its option to develop INS1007 in COPD or asthma validates the potential of INS1007 to offer a promising new approach to modulating neutrophil activity, which could prove beneficial in a broad range of diseases beyond our initial focus in non-cystic fibrosis bronchiectasis," said Will Lewis, Chairman and CEO of Insmed.

In February 2020, Insmed reported positive top-line results from the global, randomized, double-blind placebo-controlled Phase 2 WILLOW study of INS1007 in adults with non-cystic fibrosis bronchiectasis. Insmed plans to advance INS1007 to Phase 3 development for the treatment of bronchiectasis. In addition, as previously communicated, Insmed is exploring several other indications for potential clinical development with INS1007 including, most recently, *in vivo* models of acute respiratory distress syndrome (ARDS) which may be brought on by any number of causes, including in the setting of respiratory failure due to COVID-19.

Business Decisions in Response to COVID-19 and Suspension of Revenue Guidance

Insmed recently implemented a number of corporate initiatives in response to the novel coronavirus (SARS-CoV-

2) global pandemic which manifests as COVID-19. These include a remote working policy for all employees in order to aid the global containment effort and allow infectious disease specialists and pulmonologists to focus exclusively on treating patients and containing the virus. This policy was implemented with the protection of the Company's employees and patients in mind as its patients are particularly vulnerable to infection with potentially serious life-threatening consequences. The policy includes all of the field-based therapeutic specialists and other "customer-facing" employees who support ARIKAYCE prescribers. Insmed's Arikares Trainers will now offer remote training for patients who initiate treatment with ARIKAYCE rather than conducting in-person onboarding.

Importantly, Insmed has observed no disruptions to date in its supply chain for the production of ARIKAYCE. The Company believes it has adequate supply of finished product on hand to support its commercial efforts for at least the next 7 months, with production continuing, and sufficient active pharmaceutical ingredient used in ARIKAYCE to meet anticipated global requirements, including commercial, clinical, and compassionate use, through the end of 2022.

While Insmed has no current supply issues and continues to see use of ARIKAYCE, including new patient adds and continued prescription renewals, the general uncertainty regarding the impact of COVID-19 on the ARIKAYCE patient population and their physicians has led the Company to suspend its previously stated 2020 revenue guidance.

"Patients suffering from refractory NTM lung disease are typically older individuals with underlying lung conditions, and are often treated by pulmonologists and infectious disease specialists. These treating physicians are on the front lines in addressing this global pandemic and must now, understandably, focus their attention on COVID-19. We are active participants in the social distancing policy and recommend its adoption by others to try to help slow the spread of this virus and alleviate the demands on the US hospital system," said Mr. Lewis. "We are committed to the NTM community, and will continue to support them through these trying circumstances."

Conference Call Details

Insmed will host a conference call beginning today at 4:30 p.m. Eastern Time. Shareholders and other interested parties may participate in the conference call by dialing (888) 317-6003 (domestic) or (412) 317-6061 (international) and referencing conference ID number 5399598.

A replay of the conference call will be accessible approximately one hour after its completion through March 30, 2020 by dialing (877) 344-7529 (domestic) or (412) 317-0088 (international) and referencing replay access code 10140406. A webcast of the call will also be archived for 90 days under the Investors section of the Company's website at www.insmed.com.

About MAC Lung Disease

Mycobacterium avium complex (MAC) lung disease is a rare and serious disorder that can significantly increase morbidity and mortality. Patients with MAC lung disease can experience a range of symptoms that often worsen over time, including chronic cough, dyspnea, fatigue, fever, weight loss, and chest pain. In some cases, MAC lung disease can cause severe, even permanent damage to the lungs, and can be fatal.

MAC lung disease is an emerging public health concern worldwide with significant unmet need. Current guideline-based treatment involves the use of multi-drug regimens that are not specifically approved for MAC lung disease. The course of treatment is often two years or more and is inadequate in treating the disease in many patients.

About ARIKAYCE® (amikacin liposome inhalation suspension)

In the United States, ARIKAYCE is the first and only FDA-approved therapy indicated for the treatment of Mycobacterium avium complex (MAC) lung disease as part of a combination antibacterial drug regimen for adult patients with limited or no alternative treatment options. ARIKAYCE is a novel, inhaled, once-daily formulation of amikacin, an established antibiotic that was historically administered intravenously and associated with severe toxicity to hearing, balance, and kidney function. Insmed's proprietary PULMOVANCE™ liposomal technology enables the delivery of amikacin directly to the lungs, where liposomal amikacin is taken up by lung macrophages where the infection resides. This approach prolongs the release of amikacin in the lungs while limiting systemic exposure. ARIKAYCE is administered once daily using the Lamira® Nebulizer System manufactured by PARI Pharma GmbH (PARI).

ARIKAYCE is not approved in any country other than the United States.

About PARI Pharma and the Lamira® Nebulizer System

ARIKAYCE® (amikacin liposome inhalation suspension) is delivered by a novel inhalation device, the Lamira® Nebulizer System, developed by PARI. Lamira® is a quiet, portable nebulizer that enables efficient aerosolization of liquid medications, including liposomal formulations such as ARIKAYCE, via a vibrating, perforated membrane. Based on PARI's 100-year history working with aerosols, PARI is dedicated to advancing inhalation therapies by developing innovative delivery platforms and new pharmaceutical formulations that work together to improve patient care.

About INS1007

INS1007 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. INS1007 may decrease the damaging effects of inflammatory diseases such as bronchiectasis by inhibiting DPP1 and its activation of NSPs.

IMPORTANT SAFETY INFORMATION FOR ARIKAYCE IN THE U.S.

WARNING: RISK OF INCREASED RESPIRATORY ADVERSE REACTIONS

ARIKAYCE has been associated with an increased risk of respiratory adverse reactions, including hypersensitivity pneumonitis, hemoptysis, bronchospasm, and exacerbation of underlying pulmonary disease that have led to hospitalizations in some cases.

Hypersensitivity Pneumonitis has been reported with the use of ARIKAYCE in the clinical trials. Hypersensitivity pneumonitis (reported as allergic alveolitis, pneumonitis, interstitial lung disease, allergic reaction to ARIKAYCE) was reported at a higher frequency in patients treated with ARIKAYCE plus background regimen (3.1%) compared to patients treated with a background regimen alone (0%). Most patients with hypersensitivity pneumonitis discontinued treatment with ARIKAYCE and received treatment with corticosteroids. If hypersensitivity pneumonitis occurs, discontinue ARIKAYCE and manage patients as medically appropriate.

Hemoptysis has been reported with the use of ARIKAYCE in the clinical trials. Hemoptysis was reported at a higher frequency in patients treated with ARIKAYCE plus background regimen (17.9%) compared to patients treated with a background regimen alone (12.5%). If hemoptysis occurs, manage patients as medically appropriate.

Bronchospasm has been reported with the use of ARIKAYCE in the clinical trials. Bronchospasm (reported as asthma, bronchial hyperreactivity, bronchospasm, dyspnea, dyspnea exertional, prolonged expiration, throat tightness, wheezing) was reported at a higher frequency in patients treated with ARIKAYCE plus background regimen (28.7%) compared to patients treated with a background regimen alone (10.7%). If bronchospasm occurs during the use of ARIKAYCE, treat patients as medically appropriate.

Exacerbations of underlying pulmonary disease has been reported with the use of ARIKAYCE in the clinical trials. Exacerbations of underlying pulmonary disease (reported as chronic obstructive pulmonary disease (COPD), infective exacerbation of COPD, infective exacerbation of bronchiectasis) have been reported at a higher frequency in patients treated with ARIKAYCE plus background regimen (14.8%) compared to patients treated with background regimen alone (9.8%). If exacerbations of underlying pulmonary disease occur during the use of ARIKAYCE, treat patients as medically appropriate.

Anaphylaxis and Hypersensitivity Reactions: Serious and potentially life-threatening hypersensitivity reactions, including anaphylaxis, have been reported in patients taking ARIKAYCE. Signs and symptoms include acute onset of skin and mucosal tissue hypersensitivity reactions (hives, itching, flushing, swollen lips/tongue/uvula), respiratory difficulty (shortness of breath, wheezing, stridor, cough), gastrointestinal symptoms (nausea, vomiting, diarrhea, crampy abdominal pain), and cardiovascular signs and symptoms of anaphylaxis (tachycardia, low blood pressure, syncope, incontinence, dizziness). Before therapy with ARIKAYCE is instituted, evaluate for previous hypersensitivity reactions to aminoglycosides. If anaphylaxis or a hypersensitivity reaction occurs, discontinue ARIKAYCE and institute appropriate supportive measures.

Ototoxicity has been reported with the use of ARIKAYCE in the clinical trials. Ototoxicity (including deafness, dizziness, presyncope, tinnitus, and vertigo) were reported with a higher frequency in patients treated with ARIKAYCE plus background regimen (17%) compared to patients treated with background regimen alone (9.8%). This was primarily driven by tinnitus (7.6% in ARIKAYCE plus background regimen vs 0.9% in the

background regimen alone arm) and dizziness (6.3% in ARIKAYCE plus background regimen vs 2.7% in the background regimen alone arm). Closely monitor patients with known or suspected auditory or vestibular dysfunction during treatment with ARIKAYCE. If ototoxicity occurs, manage patients as medically appropriate, including potentially discontinuing ARIKAYCE.

Nephrotoxicity was observed during the clinical trials of ARIKAYCE in patients with MAC lung disease but not at a higher frequency than background regimen alone. Nephrotoxicity has been associated with the aminoglycosides. Close monitoring of patients with known or suspected renal dysfunction may be needed when prescribing ARIKAYCE.

Neuromuscular Blockade: Patients with neuromuscular disorders were not enrolled in ARIKAYCE clinical trials. Patients with known or suspected neuromuscular disorders, such as myasthenia gravis, should be closely monitored since aminoglycosides may aggravate muscle weakness by blocking the release of acetylcholine at neuromuscular junctions.

Embryo-Fetal Toxicity: Aminoglycosides can cause fetal harm when administered to a pregnant woman. Aminoglycosides, including ARIKAYCE, may be associated with total, irreversible, bilateral congenital deafness in pediatric patients exposed *in utero*. Patients who use ARIKAYCE during pregnancy, or become pregnant while taking ARIKAYCE should be apprised of the potential hazard to the fetus.

Contraindications: ARIKAYCE is contraindicated in patients with known hypersensitivity to any aminoglycoside.

Most Common Adverse Reactions: The most common adverse reactions in Trial 1 at an incidence ≥5% for patients using ARIKAYCE plus background regimen compared to patients treated with background regimen alone were dysphonia (47% vs 1%), cough (39% vs 17%), bronchospasm (29% vs 11%), hemoptysis (18% vs 13%), ototoxicity (17% vs 10%), upper airway irritation (17% vs 2%), musculoskeletal pain (17% vs 8%), fatigue and asthenia (16% vs 10%), exacerbation of underlying pulmonary disease (15% vs 10%), diarrhea (13% vs 5%), nausea (12% vs 4%), pneumonia (10% vs 8%), headache (10% vs 5%), pyrexia (7% vs 5%), vomiting (7% vs 4%), rash (6% vs 2%), decreased weight (6% vs 1%), change in sputum (5% vs 1%), and chest discomfort (5% vs 3%).

Drug Interactions: Avoid concomitant use of ARIKAYCE with medications associated with neurotoxicity, nephrotoxicity, and ototoxicity. Some diuretics can enhance aminoglycoside toxicity by altering aminoglycoside concentrations in serum and tissue. Avoid concomitant use of ARIKAYCE with ethacrynic acid, furosemide, urea, or intravenous mannitol.

Overdosage: Adverse reactions specifically associated with overdose of ARIKAYCE have not been identified. Acute toxicity should be treated with immediate withdrawal of ARIKAYCE, and baseline tests of renal function should be undertaken. Hemodialysis may be helpful in removing amikacin from the body. In all cases of suspected overdosage, physicians should contact the Regional Poison Control Center for information about effective treatment.

U.S. INDICATION

LIMITED POPULATION: ARIKAYCE® is indicated in adults, who have limited or no alternative treatment options, for the treatment of *Mycobacterium avium* complex (MAC) lung disease as part of a combination antibacterial drug regimen in patients who do not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy. As only limited clinical safety and effectiveness data for ARIKAYCE are currently available, reserve ARIKAYCE for use in adults who have limited or no alternative treatment options. This drug is indicated for use in a limited and specific population of patients.

This indication is approved under accelerated approval based on achieving sputum culture conversion (defined as 3 consecutive negative monthly sputum cultures) by Month 6. Clinical benefit has not yet been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Limitation of Use: ARIKAYCE has only been studied in patients with refractory MAC lung disease defined as patients who did not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy. The use of ARIKAYCE is not recommended for patients with non-refractory MAC lung disease.

Patients are encouraged to report negative side effects of prescription drugs to the FDA.
Visit **www.fda.gov/medwatch**, or call 1-800-FDA-1088. You can also call the Company at 1-844-4-INSMED.

Please see Full Prescribing Information.

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: business or economic disruptions due to catastrophes or other events, including natural disasters or public health crises, such as the coronavirus; 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 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 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 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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