New Phase 3 Data Show Sustainability and Durability of Culture Conversion with ARIKAYCE® (amikacin liposome inhalation suspension) in Patients with Refractory MAC Lung Disease

--ARIKAYCE Plus Guideline-Based Therapy (GBT) Associated with Significantly Higher Rates of Sustained Culture Conversion on Therapy and Durable Culture Conversion Three Months Post-Treatment Compared with GBT Alone--
--New Data from Insmed-Supported Investigator-Initiated Open-Label Trial of ARIKAYCE in NTM Lung Disease Caused by M. Abscessus Show 37% Culture Conversion without Reversion by Month 12--
--Data Presented at ATS International Conference--

BRIDGEWATER, N.J., May 20, 2019 /PRNewswire/ -- Insmed Incorporated (NASDAQ: INSM), a global biopharmaceutical company on a mission to transform the lives of patients with serious and rare diseases, today presented new data from the ongoing Phase 3 CONVERT study of ARIKAYCE® (amikacin liposome inhalation suspension) in patients with refractory *Mycobacterium avium* complex (MAC) lung disease, demonstrating that the addition of ARIKAYCE to guideline-based therapy (GBT) was associated with sustained culture conversion through the end of treatment as well as durable culture conversion three months post-treatment compared with GBT alone. These data were presented during a late-breaking session at the American Thoracic Society (ATS) International Conference in Dallas. Researchers at ATS also presented new ARIKAYCE pharmacokinetic (PK) data as well as new data from an investigator-initiated study of ARIKAYCE in the treatment of NTM lung disease caused by *M. abscessus*.

"We are pleased to be sharing sustainability and durability data from our pivotal ARIKAYCE trial, which provide important insight into the potential long-term experience of patients on the first approved therapy in the U.S. for refractory MAC lung disease," said Will Lewis, Chairman and Chief Executive Officer of Insmed. "Overall, the breadth of data on NTM lung disease presented at ATS reflects the growing urgency around this chronic, debilitating disease and underscores Insmed's ongoing commitment to helping to transform its treatment landscape."

ARIKAYCE received accelerated approval from the U.S. Food and Drug Administration (FDA) in September of 2018 as the first and only therapy approved for the treatment of patients with refractory MAC lung disease as part of a combination antibacterial drug regimen for adult patients who have limited or no alternative treatment options.

Sustainability and Durability of Culture Conversion in Patients Receiving ARIKAYCE for Treatment-Refractory MAC Lung Disease in the CONVERT Study

In a late-breaking oral session today, researchers reported longer-term results from the pivotal Phase 3 CONVERT study of ARIKAYCE. As previously reported, the addition of ARIKAYCE to GBT eliminated evidence of MAC infection in sputum by Month 6 in 29.0% of patients, compared to 8.9% of patients on GBT alone ($p<0.0001$). The new data presented today showed that among patients who achieved culture conversion by Month 6, 80.0% (52/65) of those receiving ARIKAYCE plus GBT sustained culture conversion for up to 12 months of treatment after the first dose that defined culture conversion compared to 30.0% (3/10) of patients receiving GBT alone ($p=0.0014$). Three months after the completion of treatment, 63.1% (41/65) of patients

receiving ARIKAYCE plus GBT maintained durable culture conversion, compared to 0.0% (0/10) of patients receiving GBT alone (p=0.0002). These durability data were consistent with interim durability data from the CONVERT study announced in January 2018.

No new safety signals were associated with continued ARIKAYCE use in the study. Treatment-emergent adverse events (TEAEs) were reported by 98.2% of patients who received ARIKAYCE plus GBT and by 91.1% of patients who received GBT alone. The most common TEAEs were dysphonia (46.6% for patients receiving ARIKAYCE plus GBT vs. 1.8% for GBT alone), cough (38.1% vs. 15.2%), dyspnea (21.5% vs. 8.9%), and hemoptysis (18.4% vs. 14.3%). Serious TEAEs occurred in 20.2% of patients who received ARIKAYCE plus GBT and in 20.5% of patients who received GBT alone.

"These longer-term findings from the CONVERT study suggest that the culture conversion achieved by many patients during the first six months of taking ARIKAYCE combined with guideline-based therapy could be maintained throughout the course of therapy," said David Griffith, M.D., Professor of Medicine, W.A. and E.B. Moncrief Distinguished Professor at The University of Texas Health Science Center and principal investigator of the CONVERT study. "Importantly, the data also suggest that many patients who complete the full course of therapy may be able to maintain durable culture conversion three months off all treatment, which would be an important advance in the treatment of refractory MAC lung disease. These insights from the CONVERT study are critical as we build our understanding and experience with ARIKAYCE."

ARIKAYCE is administered once daily using the Lamira® Nebulizer System (PARI Pharma GmbH).

PK Evaluation of ARIKAYCE in Patients with Treatment-Refractory NTM Lung Disease

In an oral session today, researchers presented pooled PK data from two randomized, multicenter, prospective studies of ARIKAYCE in patients with treatment-refractory NTM lung disease (the Phase 3 CONVERT study [N=39] and the 112 study, a double-blind, placebo-controlled Phase 2 study [N=14]). In this pooled analysis, daily dosing of ARIKAYCE for approximately 6 months did not result in significant systemic accumulation of amikacin, with <10% of ARIKAYCE reaching systemic circulation. Systemic exposure was similar in Japanese and Caucasian patients. Researchers concluded that systemic exposure of amikacin in serum and urine was notably lower than what has been reported with parenteral administration of amikacin.

Open-Label Trial of ARIKAYCE in *M. Abscessus* Lung Disease

In a separate oral session today, researchers presented interim data from an Insmed-supported investigator-initiated study of once-daily ARIKAYCE in a prospective cohort of patients (N=33) with NTM lung disease caused by *Mycobacterium abscessus*—the second most common NTM pathogen. The study included both cystic fibrosis (CF) and non-CF patients. In this open-label trial, 37% (11/30) of patients receiving ARIKAYCE for at least four months met the primary endpoint of achieving sputum culture conversion without reversion by Month 12. The most common adverse events among the safety population (N=33) were dysphonia (42%), dyspnea (27%), fatigue (27%), nausea (27%) and pulmonary exacerbation of CF (24%) or pulmonary exacerbation of bronchiectasis (21%).

Preclinical Pipeline Data

Investigators will also showcase new preclinical data for Insmed's INS1009 pipeline candidate during two poster sessions (poster #P1120 and poster #P1129) on Tuesday, May 21, 2019.

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)

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).

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 the CONVERT Study

CONVERT is a randomized, open-label, global Phase 3 study designed to confirm the sputum culture conversion results seen in Insmed's Phase 2 clinical study of ARIKAYCE in patients with refractory MAC lung disease. CONVERT is being conducted in 18 countries at more than 125 sites. The primary efficacy endpoint is the proportion of patients who achieved sputum culture conversion at Month 6 in the ARIKAYCE plus GBT arm compared to the GBT-only arm. Patients who achieved sputum culture conversion by Month 6 continued in the CONVERT study for an additional 12 months of treatment following the first monthly negative sputum culture. The CONVERT study is ongoing.

IMPORTANT SAFETY INFORMATION

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.

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.

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 is ARIKAYCE® (amikacin liposome inhalation suspension), which is approved in the United States 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. MAC lung disease is a rare and often chronic infection that can cause irreversible lung damage and can be fatal. 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: 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 payers 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 successfully complete the confirmatory post-marketing study required for full approval; 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 payers for ARIKAYCE or acceptable prices for ARIKAYCE; development of unexpected safety or efficacy concerns related to ARIKAYCE; inaccuracies in the Company's estimates of the size of the potential markets for ARIKAYCE 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 and the Company's 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 regulatory approvals for ARIKAYCE outside the U.S. or for the Company's product candidates in the U.S., Europe, Japan or other markets; 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 its drug 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; limited experience operating internationally; changes in laws and regulations applicable to the Company's business 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 and move into the leased space at the Company's new headquarters and 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.

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