Insmed Presents New Data at IDWeek 2018 and CHEST Annual Meeting Enhancing the Understanding of MAC Lung Disease and Treatment with ARIKAYCE® (amikacin liposome inhalation suspension)

BRIDGEWATER, N.J., Oct. 11, 2018 (GLOBE NEWSWIRE) -- Insmed Incorporated (Nasdaq:INSM), a global biopharmaceutical company focused on the unmet needs of patients with rare diseases, today announced that the Company presented data at IDWeek 2018 and at the CHEST Annual Meeting that provide additional insight into *Mycobacterium avium* complex (MAC) lung disease, a chronic and debilitating condition that can significantly increase patient morbidity and mortality. The Company also presented additional data from clinical trials of ARIKAYCE® (amikacin liposome inhalation suspension), the first and only therapy approved in the U.S. for the treatment of MAC lung disease as part of a combination antibacterial drug regimen for adult patients who have limited or no alternative treatment options. ARIKAYCE received accelerated approval from the U.S. Food and Drug Administration (FDA) on September 28, 2018.

“The data presented at IDWeek and CHEST add to the growing body of research surrounding MAC lung disease and reaffirm our understanding that this is a serious disease associated with significantly increased mortality,” said Paul Streck, M.D., Chief Medical Officer of Insmed. “We are very pleased that with the recent FDA approval of ARIKAYCE, patients with MAC lung disease who are refractory to the current standard of care now have an approved treatment available. We are committed to gleaning additional data from the ongoing CONVERT clinical trial program as well as conducting a clinical study to support full approval of ARIKAYCE.”

The following data were presented at IDWeek 2018, October 3-7 in San Francisco:

All-cause Mortality Increased with Nontuberculous Mycobacterial Lung Disease in US Medicare Beneficiaries

In this oral presentation on October 4, researchers shared results from a database analysis assessing the rate and risk factors of all-cause mortality in Medicare beneficiaries with nontuberculous mycobacterial (NTM) lung disease. Researchers reported that within Medicare Part A and B programs between 2008 and 2015, all-cause mortality was two times higher among patients with NTM lung disease compared with age- and sex-matched controls. When adjusted for comorbidities, patients with NTM lung disease had a 1.3 times higher death rate than controls.

Incidence and Prevalence of Nontuberculous Mycobacterial Lung Disease in US Medicare Beneficiaries, 2008-2015

In this poster presentation on October 4, researchers reported results from an investigation to evaluate the incidence and prevalence of NTM lung disease among Medicare Part A and B beneficiaries. The study demonstrated that incidence increased from 2008 through 2013 and leveled off in more recent years, while prevalence continued to rise through 2015. Incidence and prevalence were higher in females than in males, and higher in Asian than in other races/ethnicities.

Amikacin Liposome Inhalation Suspension (ALIS) Add-on Therapy for Refractory Mycobacterium avium Complex (MAC) Lung Disease: Effect of In Vitro Amikacin Susceptibility on Sputum Culture Conversion

In a poster presentation on October 4, researchers reported the results of a post-hoc analysis of the Phase 3 CONVERT (INS-212) study to evaluate the impact of amikacin susceptibility on culture conversion outcomes in the study. CONVERT is an ongoing randomized, open-label comparison of ARIKAYCE plus guideline-based therapy (GBT) with GBT alone in patients with treatment-refractory MAC lung disease.

Researchers reported that at baseline, amikacin minimum inhibitory concentrations (MIC), the lowest concentration of amikacin that inhibits MAC growth, were similar across treatment arms and across evaluated geographic regions. The percentage of patients achieving culture conversion was similar for patients who had MAC isolates with amikacin MIC values ranging from 8 µg/mL to 64 µg/mL. Additionally, conversion rates were similar for patients with *M. avium* and *M. intracellulare*, and across geographic regions studied in CONVERT. MAC isolates with postbaseline amikacin MIC > 64 µg/mL were found in 7.7% of patients and were associated with low culture conversion rates; no patients with concurrent macrolide resistance achieved culture conversion.

The following data were presented at the CHEST Annual Meeting, October 6-10 in San Antonio:

Relationship Between In Vitro Clarithromycin Susceptibility and Sputum Culture Conversion with Add-on Amikacin Liposome Inhalation Suspension (ALIS) for Treatment of Refractory Mycobacterium avium Complex (MAC) Lung Disease

In this oral presentation on October 8, researchers reported results from a post-hoc analysis of MAC species epidemiology, macrolide susceptibility, and relationship to culture conversion in the CONVERT study. Results demonstrated regional differences in MAC species and macrolide susceptibility at baseline, with higher prevalence of *M. avium* and higher rates of macrolide resistance in Japan compared with other regions assessed. Researchers also reported that culture conversion was numerically higher in the ARIKAYCE plus GBT group compared with the GBT-alone group across MAC species and geographic regions. Overall, culture conversion was numerically lower among patients with macrolide resistance.

“The susceptibility analyses presented at IDWeek and CHEST provide important insight into how susceptibility testing can help guide treatment decisions for patients with MAC lung disease,” said David Griffith, M.D., Professor of Medicine, W.A. and E.B. Moncrief Distinguished Professor at The University of Texas Health Science Center. “Importantly, the general trends of both analyses suggest that patients treated with ARIKAYCE plus GBT had better culture-conversion outcomes than patients treated with GBT alone regardless of geography or MAC species, and across a wide range of amikacin MICs. Not surprisingly, we observed lower culture conversion rates overall among patients with amikacin MIC > 64 µg/mL or macrolide MIC ≥ 32 µg/mL.”

Extension Study of Amikacin Liposome Inhalation Suspension (ALIS) for Treatment-Refractory Lung Disease Caused by Mycobacterium avium Complex (MAC): Interim Analysis

In a poster presentation on October 10, researchers reported interim results from the ongoing open-label single-arm extension of the Phase 3 CONVERT study (INS-312) evaluating the long-term safety and tolerability of once-daily ARIKAYCE in patients who did not achieve culture conversion by Month 6 in CONVERT. As of the July 2017 data cutoff for this analysis, results were consistent with the safety and tolerability of ARIKAYCE plus GBT observed in the CONVERT trial. Treatment-emergent adverse events were reported by 72.9% of patients who had previously received ARIKAYCE plus GBT in CONVERT and by 93.2% of patients who had ARIKAYCE added to

GBT in INS-312. There were no new safety signals.

Additionally, 27.4% of patients (17/62) who initiated add-on ARIKAYCE in the extension study achieved culture conversion, which is consistent with the 29.0% rate of culture conversion achieved by patients receiving ARIKAYCE plus GBT in the CONVERT study. Continuation of ARIKAYCE was associated with culture conversion in 6.1% of patients (3/49) who had received ARIKAYCE plus GBT in CONVERT but had not achieved culture conversion during that study.

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

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 needs. 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 it 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.

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 CONVERT (INS-212) and INS-312

CONVERT is a randomized, open-label, global Phase 3 trial designed to confirm the sputum culture conversion results seen in Insmed's Phase 2 clinical trial of ARIKAYCE in patients with refractory NTM lung disease caused by MAC. 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 are continuing in the CONVERT study for an additional 12 months of treatment following the first monthly negative sputum culture. Patients who did not culture convert may have been eligible to enroll in our INS-312 study. INS-312 is a single-arm open-label extension study for patients who completed six months of treatment in the INS-212 study but did not demonstrate culture conversion by Month 6. Under the study protocol, non-converting patients in the ARIKAYCE plus GBT arm of the INS-212 study will receive an additional 12 months of ARIKAYCE plus GBT. Patients who crossed over from the GBT-only arm of the INS-212 study will receive 12 months of treatment of ARIKAYCE plus GBT.

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 nanoparticle 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.

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 exacer

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 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.

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: risks that the remainder of the data from the treatment and off-treatment phases of INS-212 will not be consistent with the six-month results of the study; uncertainties in the research and development of the Company's existing product candidates, including due to delays in data readouts, such as the full data from the INS-212 study, patient enrollment and retention or failure of the Company's preclinical studies or clinical trials to satisfy pre-established endpoints, including secondary endpoints in the INS-212 study and endpoints in the INS-212 extension study (the INS-312 study); risks that subsequent data from the INS-312 study will not be consistent with the interim results; imposition of significant post-approval regulatory requirements on our product candidates, including a requirement for a post-approval confirmatory clinical study, or failure to maintain or obtain full regulatory approval for the Company's product candidates, if received, due to a failure to satisfy post-approval regulatory requirements, such as the submission of sufficient data from a confirmatory clinical study; safety and efficacy concerns related to the Company's product candidates; uncertainties in the rate and degree of market acceptance of product candidates, if approved; inability to create an effective direct sales and marketing infrastructure or to partner with third parties that offer such an infrastructure for distribution of the Company's product candidates, if approved; failure to obtain, or delays in obtaining, regulatory approval from the U.S. Food and Drug Administration, Japan's Ministry of Health, Labour and Welfare, Japan's Pharmaceuticals and Medical Devices Agency, the European Medicines Agency, and other regulatory authorities for the Company's product candidates or their delivery devices, including due to insufficient clinical data, selection of endpoints that are not satisfactory to regulators or complexity in the review process for combination products; lack of experience in conducting and managing preclinical development activities and clinical trials necessary for regulatory approval, including the regulatory filing and review process; inaccuracies in the Company's estimates of the size of the potential markets for the Company's product candidates or limitations by regulators on the proposed treatment population for the Company's product candidates; failure of third parties on which the Company is dependent to conduct the Company's clinical trials, to manufacture sufficient quantities of the Company's product candidates for clinical or commercial needs, including the Company's raw materials suppliers, or to comply with the Company's agreements or laws and regulations that impact the Company's business; inaccurate estimates regarding the Company's future capital requirements, including those necessary to fund the Company's ongoing clinical development, regulatory and commercialization efforts as well as milestone payments or royalties owed to third parties; failure to develop, or to license for development, additional product candidates, including a failure to attract experienced third-party collaborators; uncertainties in the timing, scope and rate of reimbursement for the Company's product candidates; 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 or to obtain additional capital when needed on desirable terms or at all; failure to obtain, protect and enforce the Company's patents and other intellectual property and costs associated with litigation or other proceedings related to such matters; restrictions imposed on the Company by license agreements that are critical for the Company's product development, including the Company's license agreements with PARI Pharma GmbH and AstraZeneca AB, and failure to comply with the Company's obligations under such agreements; competitive developments affecting the Company's product candidates and potential exclusivity related thereto; the cost and potential reputational damage resulting from litigation to which the Company is or may become a party; loss of key personnel; and lack of experience operating internationally.

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, 2017 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:

Blaine Davis
Insmed Incorporated
(908) 947-2841
blaine.davis@insmed.com