Insmed Announces FDA Approval of ARIKAYCE® (amikacin liposome inhalation suspension), the First and Only Therapy Specifically Indicated for the Treatment of Mycobacterium Avium Complex (MAC) Lung Disease in Adult Patients with Limited or No Alternative Treatment Options

Commercial availability expected in early Q4 2018
Conference call scheduled for today at 6:15 PM ET

BRIDGEWATER, N.J., Sept. 28, 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 U.S. Food and Drug Administration (FDA) has granted accelerated approval of ARIKAYCE® (amikacin liposome inhalation suspension) for the treatment of Mycobacterium avium complex (MAC) lung disease as part of a combination antibacterial drug regimen for adult patients who have limited or no alternative treatment options. ARIKAYCE is the first and only therapy approved in the U.S. specifically for patients with MAC lung disease, a chronic and debilitating condition that can significantly increase patient morbidity and mortality.

ARIKAYCE is the first product approved via the Limited Population Pathway for Antibacterial and Antifungal Drugs (LPAD). LPAD, which was enacted as part of the 21st Century Cures Act, serves to advance the development of new antibacterial drugs to treat serious or life-threatening infections in limited populations of patients with unmet needs.

“Today’s approval is a momentous occasion for all of us living with and advocating for people with MAC lung disease,” said Philip Leitman, President of Nontuberculous Mycobacteria Info & Research (NTMir). “ARIKAYCE provides a much-needed treatment for patients with this chronic and life-threatening disease who have not responded to the current standard of care. Many of these patients have been suffering for years and face significant challenges in their day-to-day lives, and we are excited to finally have an approved treatment for them.”

“Patients suffering from MAC lung disease who have not responded to available guideline-based therapies face a restricted quality of life due to this debilitating and progressive illness. As a physician and Principal Investigator in the CONVERT study, I am extremely pleased that there is now a therapy specifically studied in and approved for patients with MAC lung disease who currently have limited or no treatment options,” said David Griffith, M.D., Professor of Medicine, W.A. and E.B. Moncrief Distinguished Professor at The University of Texas Health Science Center. “ARIKAYCE has the potential to address the significant unmet needs in this difficult-to-treat population.”

Physicians can begin prescribing ARIKAYCE immediately and Insmed expects product to be available in select specialty pharmacies in the coming weeks. Insmed is committed to providing access to ARIKAYCE for appropriate patients with MAC lung disease and to supporting these patients throughout their treatment journey. The Company has launched the Arikares Support Program, which provides dedicated coordinators to help patients navigate the reimbursement process and trainers who can familiarize patients with how to use ARIKAYCE. Patients prescribed ARIKAYCE can call 1-833-ARIKARE to enroll in the support program.

“The approval of ARIKAYCE is a significant moment for adult patients suffering from MAC lung disease who have limited or no available treatment options. It also represents an incredible milestone for our company, which has taken this medicine from concept to approval and now will launch the drug across the U.S. Our mission is to address the unmet needs of patients with serious and rare diseases, and we are thrilled to be able to provide the first-ever approved therapy specifically for patients in the U.S. with MAC lung disease,” said Will Lewis, President and Chief Executive Officer of Insmed. “I want to thank the patients and physicians who have made this milestone possible through their participation in the clinical trials, as well as our dedicated Insmed team. We look forward to focusing our efforts on the launch of ARIKAYCE in the U.S.”

The approval of ARIKAYCE under FDA’s LPAD and accelerated approval pathways was based on results from the ongoing Phase 3 CONVERT study, which has demonstrated that ARIKAYCE, when combined with guideline-based therapy (GBT), improved sputum culture conversion rates. The global CONVERT study met its primary endpoint of sputum culture conversion by Month 6 with statistical significance for once-daily ARIKAYCE when added to GBT compared with GBT alone ($p<0.0001$) in patients with refractory nontuberculous mycobacterial (NTM) lung disease caused by MAC. In the study, the addition of ARIKAYCE to GBT eliminated evidence of NTM lung disease caused by MAC in sputum by Month 6 in 29% of patients, compared to 9% of patients on GBT alone.

Patients who are prescribed ARIKAYCE will be provided with a Medication Guide containing important safety information set forth below, including the boxed warning, as well as full Instructions for Use and a step-by-step guide to using the product. Insmed also will send health care providers a letter describing the scope of the limited population approval and the potential risk of respiratory adverse reactions.

As a condition of accelerated approval, Insmed is collaborating with the FDA on the design of an additional clinical study to support full approval. The study design is currently under discussion with FDA and is proposed to be a randomized, double-blind, placebo-controlled clinical trial to assess and describe the clinical benefit of ARIKAYCE in patients with NTM lung disease caused by MAC. The trial will evaluate the effect of ARIKAYCE on a clinically meaningful endpoint, as compared to an appropriate control, in the intended patient population of patients with MAC infection. Insmed will provide additional updates once the study design has been finalized with FDA. Continued approval of ARIKAYCE will be contingent upon verification and description of clinical benefit in this study.

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

Conference Call Information

Insmed will host a conference call today at 6:15 PM Eastern Time to discuss the FDA approval. The call can be accessed by dialing (844) 707-0669 (U.S. and Canada) or (703) 639-1223 (international) and entering the conference ID number 2376004. The call will also be webcast live on the Company's website at www.insmed.com.

A replay of the conference call will be accessible approximately two hours after its completion through October 5, 2018 by dialing (855) 859-2056 (domestic) or (404) 537-3406 (international) and referencing conference ID number 2376004. A webcast of the call will also be archived for 90 days under the Investor Relations 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 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

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.

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.

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