News Releases

FDA Advisory Committee Votes 12-2 in Favor of the Safety and Effectiveness of Insmed's ALIS for the Treatment of NTM Lung Disease Caused by MAC for Adult Patients with Limited or No Treatment Options

Advisory committee supports surrogate endpoint of sputum culture conversion

ALIS currently under FDA Priority Review; PDUFA action date set for September 28, 2018

BRIDGEWATER, N.J., Aug. 07, 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's (FDA) Antimicrobial Drugs Advisory Committee voted 12 to 2 in favor of the safety and effectiveness of ALIS (amikacin liposome inhalation suspension) for adults with nontuberculous mycobacterial (NTM) lung disease caused by Mycobacterium avium complex (MAC) who have limited or no treatment options. The committee also voted in favor of the surrogate endpoint of sputum culture conversion used in the Phase 3 CONVERT study being reasonably likely to predict clinical benefit. If approved, ALIS will be the first and only therapy in the U.S. specifically indicated for the treatment of patients with NTM lung disease caused by MAC.

"We are very pleased by the outcome of today's advisory committee meeting, which recognized the role ALIS may be able to play in addressing the significant unmet medical need among patients suffering from NTM lung disease caused by MAC, a chronic, debilitating and potentially fatal infection," said Will Lewis, President and Chief Executive Officer of Insmed.

The advisory committee's recommendation was based on briefing materials developed from Insmed's new drug application (NDA) for ALIS, which was submitted under accelerated approval provisions and includes data from the Phase 3 CONVERT study. The study met its primary endpoint of culture conversion by Month 6 with statistical significance for once-daily ALIS when added to guideline-based therapy (GBT) compared with GBT alone in patients with refractory NTM lung disease due to MAC.

"The patients included in our Phase 3 clinical trial represent the most difficult-to-treat segment of the NTM lung disease population, having already failed treatment with current guideline-based therapy. The committee's favorable recommendation brings us one step closer to providing the first and only FDA-approved treatment for these patients. We look forward to working closely with the FDA as it completes its review of our application," said Paul Streck, M.D., Chief Medical Officer of Insmed.

In a separate vote, the committee voted against the safety and effectiveness of ALIS in the broadest population of adult patients with NTM lung disease caused by MAC.

The FDA is not bound by the committee's recommendation but takes its input into consideration when evaluating whether to approve Insmed's NDA for ALIS, which is currently under Priority Review by the FDA with an action date of September 28, 2018 under the Prescription Drug User Fee Act (PDUFA). The FDA has previously designated ALIS an orphan drug, a breakthrough therapy, and a Qualified Infectious Disease Product (QIDP) under the Generating Antibiotic Incentives Now (GAIN) Act.

About NTM Lung Disease

NTM lung disease is a rare and serious disorder associated with increased rates of morbidity and mortality. There is an increasing prevalence of lung disease caused by NTM and Insmedbelieves it is an emerging public health concern worldwide. Patients with NTM lung disease may experience a multitude of symptoms such as fever, weight loss, cough, lack of appetite, night sweats, blood in the sputum, and fatigue. Patients with NTM lung disease frequently require lengthy hospital stays to manage their condition. Insmed is not aware of any approved inhaled therapies specifically indicated for refractory NTM lung disease caused by MAC in North America, Japan or Europe. Current guideline-based approaches involve use of multi-drug regimens not approved for the treatment of NTM lung disease, and treatment can be as long as two years or more.

The prevalence of human disease attributable to NTM has increased over the past two decades. In a decade long study (1997 to 2007), researchers found that the prevalence of NTM lung disease in the U.S. was increasing at approximately 8% per year and that NTM patients on Medicare over the age of 65 were 40% more likely to die over the period of the study than those who did not have the disease. In the U.S., Insmed estimates there will be between 75,000 and 105,000 patients with diagnosed NTM lung disease in 2018, of which the Company expects 40,000 to 50,000 will be treated for NTM lung disease caused by MAC. Insmed expects that between 10,000 and 15,000 of these patients will be refractory to treatment.
In Japan, Insmedestimates there will be between 125,000 and 145,000 patients with diagnosed NTM lung disease in 2018, with approximately 60,000 to 70,000 of those patients being treated for NTM lung disease caused by MAC and 15,000 to 18,000 of these treated patients being refractory to treatment. Insmed also estimates there will be approximately 14,000 patients with diagnosed NTM lung disease in the EU5 (comprised of France, Germany, Italy, Spain and the United Kingdom) in 2018, of which the Company estimates approximately 4,400 will be treated for NTM lung disease caused by MAC and approximately 1,400 of these treated patients will be refractory to treatment.

About ALIS

ALIS is a novel, inhaled, once-daily formulation of amikacin that is in late-stage clinical development and under regulatory review by the FDA for adult patients with NTM lung disease caused by MAC. Amikacin solution for parenteral administration is an established drug that has activity against a variety of NTM; however, its use is limited by the need to administer it intravenously and by toxicity to hearing, balance, and kidney function. Insmed's advanced pulmonary liposome technology uses charge neutral liposomes to deliver amikacin directly to the lung where it is taken up by the lung macrophages where the NTM infection resides. This prolongs the release of amikacin in the lungs while minimizing systemic exposure, thereby offering the potential for decreased systemic toxicities. ALIS's ability to deliver high levels of amikacin directly to the lung distinguishes it from intravenous amikacin. ALIS is administered once daily using an optimized, investigational eFlow® Nebulizer System manufactured by PARI Pharma GmbH (PARI), a portable aerosol delivery system.

About CONVERT (INS-212) and INS-312

CONVERT is a randomized, open-label, global Phase 3 trial designed to confirm the culture conversion results seen in Insmed's Phase 2 clinical trial of ALIS 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 culture conversion at Month 6 in the ALIS plus GBT arm compared to the GBT-only arm. Patients who achieved 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 ALIS plus GBT arm of the INS-212 study will receive an additional 12 months of ALIS plus GBT. Patients who crossed over from the GBT-only arm of the INS-212 study will receive 12 months of treatment of ALIS plus GBT.

About Insmed

Insmed Incorporated is a global biopharmaceutical company focused on the unmet needs of patients with rare diseases. The Company’s lead product candidate is ALIS, which is in late-state development and under regulatory review by the FDA for adult patients with NTM lung disease caused by MAC, which is a rare and often chronic infection that is capable of causing 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.

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; 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, such as the eFlow Nebulizer System, including due to insufficient clinical data, selection of endpoints that are not satisfactory to regulators, extensions of action dates under PDUFA or complexity in the review process for combination products; imposition of significant post-approval regulatory requirements on our product candidates or failure to maintain 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 confirmatory clinical studies; safety and efficacy concerns related to the Company's product candidates; lack of experience in conducting and managing preclinical development activities and clinical trials necessary for regulatory approval, including the regulatory filing and review process; 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; 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 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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