Insmed Announces Publication of Phase 2 Study of ARIKAYCE in Treatment-Refractory Nontuberculous Mycobacterial Lung Disease

Data in American Journal of Respiratory and Critical Care Medicine demonstrate ARIKAYCE's potential to achieve early and sustained negative sputum cultures

BRIDGEWATER, N.J., Oct. 18, 2016 (GLOBE NEWSWIRE) -- Insmed Incorporated (Nasdaq:INSM), a global biopharmaceutical company focused on the unmet needs of patients with rare diseases, today announced the online publication of data from its phase 2 study of ARIKAYCE™ (liposomal amikacin for inhalation or LAI) in the American Journal of Respiratory and Critical Care Medicine. ARIKAYCE is a novel formulation of amikacin administered once-daily using an optimized eFlow® Electronic Nebulizer (PARI Pharma GmbH). ARIKAYCE is being studied in treatment-refractory nontuberculous mycobacterial (NTM) lung disease.

The phase 2 study evaluated ARIKAYCE in patients with nontuberculous mycobacterial lung infections who had been unable to achieve culture conversion to negative despite receiving a multi-drug guideline-based regimen for six or more months. Although the primary endpoint was not reached, data from the study suggest that the addition of ARIKAYCE to the guideline-based multi-drug regimen can achieve early and sustained negative sputum cultures. In addition, culture conversion resulting from ARIKAYCE plus multi-drug treatment was associated with improvements in the six-minute walk test. ARIKAYCE is currently being evaluated in a global phase 3 randomized open-label clinical study designed to evaluate the culture conversion results observed in the phase 2 clinical study. The phase 3 study, which is known as the CONVERT study, is enrolling adult non-cystic fibrosis patients with an NTM lung infection caused by Mycobacterium avium complex (MAC).

"Pulmonary nontuberculous mycobacterial disease is a chronic, progressive infection associated with irreversible lung damage and mortality," said Eugene Sullivan, MD, chief medical officer of Insmed. "Current treatment options are not approved for pulmonary NTM and are limited to lengthy multi-drug regimens that are associated with intolerance, treatment failures, and problematic multi-drug interactions. The novel drug formulation of liposomal amikacin for inhalation delivers high levels of a potent aminoglycoside directly to the lung macrophages where the infection resides. There is an important unmet need among patients with refractory NTM lung disease and data from this phase 2 study suggest that liposomal amikacin could be a treatment option."

Insmed's clinical development program in refractory NTM lung disease represents the largest and most comprehensive program conducted to date. Insmed has received multiple designations for ARIKAYCE from the U.S. Food and Drug Administration (FDA) for the treatment of NTM, including: orphan, breakthrough therapy, Qualified Infectious Disease Product (QIDP), and Fast Track status. Products in development under QIDP status gain certain incentives if they are approved by the FDA, which include a five-year extension of data exclusivity provisions and priority review of its NDA. Fast Track status is intended to facilitate development and expedite review of drugs to treat serious and life-threatening conditions.

Study Design

The phase 2 study was a randomized, double-blind, placebo-controlled study that evaluated the efficacy and safety of ARIKAYCE in adults with NTM lung disease due to MAC or Mycobacterium abscessus (M. abscessus) that was refractory to guideline-based therapy. Eligibility for the study required patients to have been on the American Thoracic Society/Infectious Disease Society of America (ATS/IDSA) guideline therapy for at least

six months prior to screening and to have had persistently positive mycobacterial cultures. The study included an 84-day double-blind phase in which subjects were randomized 1:1 either to ARIKAYCE once-daily plus a multi-drug regimen or to placebo once-daily plus a multi-drug regimen. After completing the 84-day double-blind phase, subjects had the option of continuing in an 84-day open-label phase during which all subjects received ARIKAYCE plus a multi-drug regimen. The study also included 28-day and 12-month off-ARIKAYCE follow-up assessments.

Study Results

Eighty-nine subjects were randomized and dosed in the study. Of the 80 subjects who completed the 84-day double-blind phase, 78 subjects entered the open-label phase during which all patients received ARIKAYCE plus a multi-drug regimen for 84 days. Seventy-six (76) percent (59/78) of subjects who entered the open-label phase of the study completed the open-label study.

The primary efficacy endpoint of the study was the change from baseline (day 1) to the end of the double-blind phase of the trial (day 84) in a semi-quantitative measurement of mycobacterial density on a seven-point scale. The primary endpoint did not reach statistical significance; however, a positive numerical trend in favor of ARIKAYCE was observed (p=0.072). The p-value for the key secondary endpoint of culture conversion to negative at Day 84 was 0.003, in favor of ARIKAYCE. A shorter time to first negative sputum culture was also observed with ARIKAYCE relative to placebo during the double-blind phase (p=0.013).

The microbiologic outcomes from the study were also explored post hoc using a more stringent definition of culture conversion, which is defined as at least three consecutive monthly sputum samples that test negative for NTM. This definition of culture conversion is in the guidelines and used in clinical practice.

Twenty-three subjects achieved at least three consecutive negative monthly sputum samples by the 28-day follow-up assessment, of which four started to convert at baseline prior to administration of study drug. For the 19 patients who achieved culture conversion, 17 achieved culture conversion after receiving ARIKAYCE, 10 who were randomized to ARIKAYCE in the double-blind phase and seven after entering the open-label phase. Two patients achieved culture conversion while receiving placebo in the double-blind phase.

The majority of patients who achieved culture conversion (three consecutive negative monthly sputum samples) during the double-blind phase continued to have negative cultures through the open-label and follow-up phases.

At the end of the double-blind phase, the ARIKAYCE group improved from baseline in mean distance walked in the six-minute walk test. At the end of the open-label phase, patients in the ARIKAYCE group continued to improve in the mean distance walked in the six-minute walk test while the patients who previously received placebo in the double-blind phase and subsequently received ARIKAYCE in the open-label phase demonstrated a reduced rate of decline from baseline.

The majority (90 percent) of patients in both treatment groups experienced at least one treatment-emergent adverse event with most events either mild or moderate in severity. During the double-blind phase a greater percentage of patients treated with ARIKAYCE experienced dysphonia, bronchiectasis exacerbation, cough, oropharyngeal pain, fatigue, chest discomfort, wheezing, and infective pulmonary exacerbation of cystic fibrosis. No clinically relevant changes were detected in laboratory values and vital signs.

About Nontuberculous Mycobacteria Lung Disease

NTM is a rare and serious disorder associated with increased morbidity and mortality. There is an increasing rate of lung disease caused by NTM and this 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. There are no products specifically indicated for the treatment of NTM lung disease in the US, Europe and Canada. Current guideline-based approaches involve multi-drug regimens that may cause severe side effects 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 in the US is increasing at approximately 8% per year and that NTM patients on Medicare over the age of 65 are 40% more likely to die over the period of the study than those who did not have the disease. A 2015 publication from co-authors from several US government departments projected 181,037 national annual cases in 2014 costing the US healthcare system approximately $1.7 billion.

For more information about NTM lung disease, visit NTMfacts.com.

About ARIKAYCE

ARIKAYCE, or liposomal amikacin for inhalation, is a novel, once daily formulation of amikacin that is in late-stage clinical development for patients with NTM lung disease. Amikacin solution for parenteral administration is an established drug that is effective 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. ARIKAYCE's ability to deliver high levels of amikacin directly to the lung distinguishes it from intravenous amikacin. ARIKAYCE is administered once daily using an optimized, investigational eFlow® Nebulizer System manufactured by PARI Pharma GmbH, a novel, highly efficient and portable aerosol delivery system.

About PARI Pharma and the eFlow® Electronic Nebulizer

Arikayce is delivered by a novel, inhalation device, the eFlow® Electronic Nebulizer, developed by PARI Pharma GmbH. eFlow 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 Pharma is dedicated to advancing inhalation therapies by developing innovative platforms and new pharmaceutical formulations that work together to improve patient care.

About Insmed

Insmed Incorporated is a global biopharmaceutical company focused on the unmet needs of patients with rare diseases. The company is advancing a global phase 3 clinical study of ARIKAYCE (liposomal amikacin for inhalation) in nontuberculous mycobacteria (NTM) lung disease, a rare and often chronic infection that is capable of causing irreversible lung damage and can be fatal. There are currently no products indicated for the treatment of NTM lung disease in the United States or European Union (EU). Insmed's earlier-stage clinical pipeline includes INS1007, a novel oral inhibitor of dipeptidyl peptidase I with therapeutic potential in non-cystic fibrosis bronchiectasis, and INS1009, a nebulized prodrug formulation of treprostinil that may offer a differentiated product profile for rare pulmonary disorders such as pulmonary arterial hypertension (PAH), idiopathic pulmonary fibrosis (IPF), sarcoidosis, and severe refractory asthma. To complement its internal research, Insmed actively seeks in-licensing opportunities for a broad range of rare diseases. For more information, visit www.insmed.com.

Forward-looking statements

This press release contains forward looking statements. "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) identify forward-looking statements.

Forward-looking statements are based upon the company's current expectations and beliefs, and involve known and unknown risks, uncertainties and other factors, which may cause 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 factors include, among others, the factors discussed in Item 1A "Risk Factors" in the company's Annual Report on Form 10-K for the year ended December 31, 2015 and subsequent quarterly reports on Form 10-Q, and the following: the ability to complete development of, receive, and maintain regulatory approval for, and successfully commercialize ARIKAYCE, INS1007 (formerly known as AZD7986), and INS1009; the number of patients enrolled and the timing of patient enrollment in the company's global phase 3 clinical study of ARIKAYCE; estimates of expenses and future revenues and profitability; status, timing, and the results of preclinical studies and clinical trials and preclinical and clinical data described herein; the sufficiency of preclinical and clinical data in obtaining regulatory approval for the company's product candidates; the timing of responses to information and data requests from the US Food and Drug Administration, the European Medicines Agency, and other regulatory authorities; expectation as to the timing of regulatory review and approval; estimates regarding capital requirements and the needs for additional financing, including for payment milestones and royalty obligations under the license agreement; estimates of the size of the potential markets for product candidates; selection and licensing of product candidates; ability to attract third parties with acceptable development, regulatory and commercialization expertise; the benefits to be derived from corporate license agreements and other third party efforts, including those relating to the development and commercialization of product candidates; the degree of protection afforded to the company by its intellectual property portfolio; the safety and efficacy of

product candidates; sources of revenues and anticipated revenues, including contributions from license agreements and other third party efforts for the development and commercialization of products; ability to create an effective direct sales and marketing infrastructure for products the company elects to market and sell directly; the rate and degree of market acceptance of product candidates; the impact of any litigation the company is a party to, including, without limitation, the class action lawsuit recently filed against the company; the timing, scope and rate of reimbursement for product candidates; the success of other competing therapies that may become available; and the availability of adequate supply and manufacturing capacity and quality for product candidates.

The company cautions readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they are made. Insmed 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.
