Insmed Announces Positive Topline Results from Phase 3b ENCORE Study of ARIKAYCE® (Amikacin Liposome Inhalation Suspension) in Patients with MAC Lung Disease

—The Study Met Primary and All Multiplicity-Controlled Secondary Culture Conversion Endpoints, Demonstrating Statistically Significant and Clinically Meaningful Improvements in Respiratory Symptom Score and Culture Conversion Rates—

—In the Second Half of 2026, Insmed Plans to File a Supplemental NDA for ARIKAYCE with the FDA and Submit the Data to the PMDA in Japan to Support Potential Label Changes—

—Insmed to Host Investor Conference Call on Monday, March 23, 2026, at 8:00 AM ET—

BRIDGEWATER, N.J., March 23, 2026 /PRNewswire/ -- Insmed Incorporated (Nasdaq: INSM), a people-first global biopharmaceutical company striving to deliver first- and best-in-class therapies to transform the lives of patients facing serious diseases, today announced positive topline results from the Phase 3b ENCORE study. This study evaluated ARIKAYCE® (amikacin liposome inhalation suspension) plus multidrug therapy (azithromycin 250 mg + ethambutol 15 mg/kg) once-daily versus placebo plus multidrug therapy once-daily in diagnosed patients with a new occurrence of *Mycobacterium avium* complex (MAC) lung infection who had not received antibiotics.

Topline efficacy results from the ENCORE study are as follows:

	ARIKAYCE 590 mg plus azithromycin 250 mg + ethambutol 15 mg/kg (N=213)	Placebo plus azithromycin 250 mg + ethambutol 15 mg/kg (N=212)	Treatment difference, *p-value*
Primary Endpoint			
Change from Baseline in Respiratory Symptom Score at Month 13	17.77 points	14.66 points	3.11 points, *p=0.0299**
Multiplicity-Controlled Secondary Endpoints			
Culture Conversion by Month 6	87.8 %	57.0 %	30.8%, *p<0.0001**
Culture Conversion by Month 12	84.7 %	61.3 %	23.3%, *p<0.0001**
Culture Conversion by Month 13	82.4 %	55.6 %	26.8%, *p<0.0001**
Durable Culture Conversion at Month 15	76.2 %	47.6 %	28.6%, *p<0.0001**
Change from Baseline in PROMIS Fatigue T-score at Month 13	-5.07	-4.27	-0.81, *p=0.2900*

*Statistically significant

"These results are an exciting win for patients living with MAC lung disease and a powerful validation of ARIKAYCE's ability to deliver real clinical benefit as part of a multidrug treatment regimen," said Martina Flammer, M.D., MBA, Chief Medical Officer of Insmed. "We are energized by the potential for patients with a new MAC infection to see benefit with ARIKAYCE earlier in their treatment journey and look forward to exploring the expansion of the ARIKAYCE indication in the U.S. and Japan, with the ultimate goal of improving outcomes for an even greater number of patients fighting this difficult disease."

With these results, Insmed has completed the study intended to fulfill the U.S. Food and Drug Administration (FDA) post-marketing requirement, further strengthening the clinical foundation supporting ARIKAYCE. Insmed plans to file a supplemental new drug application (sNDA) for ARIKAYCE in patients with MAC lung disease in the second half of 2026 to support potential label expansion and to obtain traditional approval for the existing refractory indication in the U.S. Additionally, Insmed plans to submit the data to the Pharmaceuticals and Medical Devices Agency (PMDA) in the second half of 2026 to support potential label expansion in Japan. Insmed also plans to present these data at a future medical congress.

"These groundbreaking results show that patients may have significant clinical benefit from including ARIKAYCE as part of their multidrug treatment earlier in their MAC lung disease journey," said David Griffith, M.D., ENCORE Steering Committee Member, Professor of Medicine, National Jewish Health. "The improvements in Respiratory Symptom Score alongside durable culture conversion highlight the potential for this medicine to make a substantial difference in outcomes for patients facing this serious and often progressive infection."

The safety profile was consistent with the known safety profile of ARIKAYCE, and no new safety signals were observed. The most common treatment-emergent adverse events (TEAEs) occurring in 10% or more of patients in a treatment arm and higher in the ARIKAYCE arm compared to the active comparator arm were in line with expectations. Overall TEAEs were as follows:

	ARIKAYCE 590 mg plus azithromycin 250 mg + ethambutol 15 mg/kg (N=213)	Placebo plus azithromycin 250 mg + ethambutol 15 mg/kg (N=212)
Any TEAE, n (%)	209 (98.1)	206 (97.2)
Severe TEAE, n (%)	32 (15.0)	22 (10.4)
Serious TEAE, n (%)	30 (14.1)	24 (11.3)
TEAE Leading to Death, n (%)	1 (0.5)	1 (0.5)
TEAE Leading to ARIKAYCE/Comparator Discontinuation, n (%)	31 (14.6)	18 (8.5)
TEAEs ≥10% and Higher in the ARIKAYCE Arm		
Dysphonia, n (%)	125 (58.7)	18 (8.5)
Cough, n (%)	70 (32.9)	31 (14.6)
Fatigue, n (%)	37 (17.4)	24 (11.3)
Dyspnea, n (%)	35 (16.4)	12 (5.7)
Nausea, n (%)	33 (15.5)	27 (12.7)
Headache, n (%)	27 (12.7)	25 (11.8)

n = number of patients with at least 1 event

Among TEAEs of special interest, only bronchospasm (n=49, 23.0% vs n=25, 11.8%) and hypersensitivity pneumonitis (n=5, 2.3% vs n=0) occurred in notably more patients receiving ARIKAYCE than patients in the comparator arm. Comparable rates between treatment arms were observed for ototoxicity (n=55, 25.8% vs n=48, 22.6%), exacerbation of underlying pulmonary disease (n=23, 10.8% vs n=21, 9.9%), hemoptysis (n=22, 10.3% vs n=22, 10.4%), neuromuscular disorders (n=5, 2.3% vs n=6, 2.8%), and nephrotoxicity (n=1, 0.5% vs n=0). No death was considered related to ARIKAYCE or placebo. The treatment discontinuation rate was 18.3% in the ARIKAYCE arm and 11.8% in the comparator arm. Study completion rates were 90.6% in the ARIKAYCE arm and 93.4% in the comparator arm.

Conference Call
Insmed management will host a conference call for investors beginning at 8:00 AM ET on Monday, March 23, 2026, to discuss the ENCORE results. Shareholders and other interested parties may participate in the conference call by dialing (800) 715-9871 (U.S.) or +1 (646) 307-1963 (International) and referencing access code 2033335. 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 one hour after its completion through March 30, 2026, by dialing (800) 770-2030 (U.S. and Canada) or +1 (609) 800-9909 (International) and referencing access code 2033335. 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 the Phase 3b ENCORE Study
ENCORE was a randomized, double-blind, placebo-controlled, Phase 3b study to evaluate the efficacy and safety of ARIKAYCE plus multidrug therapy in diagnosed patients with a new occurrence of MAC lung infection who have not received antibiotics. Among enrolled patients, 82.4% were experiencing their first MAC infection, while this was the second or third infection for 17.6% of patients. Patients were screened and enrolled at 177 sites globally, and a total of 425 patients were randomized 1:1 to receive once-daily regimens of either ARIKAYCE plus multidrug therapy (azithromycin 250 mg + ethambutol 15 mg/kg; n=213) or placebo (inhaled empty liposome control) plus multidrug therapy (azithromycin 250 mg + ethambutol 15 mg/kg; n=212) for 12 months. Patients then discontinued all study treatments and remained in the trial for three months for the assessment of durability of culture conversion.

The primary endpoint is change from baseline in Respiratory Symptom Score at Month 13 based on eight items from the Quality of Life – Bronchiectasis (QoL-B) Respiratory Domain. The multiplicity-controlled secondary endpoints are the proportion of patients achieving culture conversion by Months 6, 12, and 13, and durable culture conversion at Month 15, and change from baseline in PROMIS Fatigue T-score at Month 13. The Japan-specific primary endpoint is the proportion of patients who achieved both culture conversion by Month 6 and durable culture conversion at Month 15.

About MAC Lung Disease

Mycobacterium avium complex (MAC) lung disease is a rare and serious disease 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.

About ARIKAYCE

ARIKAYCE® is approved in the United States as ARIKAYCE (amikacin liposome inhalation suspension), inEurope as ARIKAYCE Liposomal 590 mg Nebuliser Dispersion, and in Japan as ARIKAYCE inhalation 590 mg (amikacin sulfate inhalation drug product). Current international treatment guidelines recommend the use of ARIKAYCE for appropriate patients. 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, 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 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 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 to improve patient care.

IMPORTANT SAFETY INFORMATION FOR ARIKAYCE IN THE U.S.

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.

Anaphylaxis and Hypersensitivity Reactions: Serious and potentially life-threatening hypersensitivity reactions, including anaphylaxis, have been reported in patients taking ARIKAYCE. Signs and symptoms include acute onset of skin and mucosal tissue hypersensitivity reactions (hives, itching, flushing, swollen lips/tongue/uvula), respiratory difficulty (shortness of breath, wheezing, stridor, cough), gastrointestinal symptoms (nausea, vomiting, diarrhea, crampy abdominal pain), and cardiovascular signs and symptoms of anaphylaxis (tachycardia, low blood pressure, syncope, incontinence, dizziness). Before therapy with ARIKAYCE is instituted, evaluate for previous hypersensitivity reactions to aminoglycosides. If anaphylaxis or a hypersensitivity reaction occurs, discontinue ARIKAYCE and institute appropriate supportive measures.

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.

U.S. 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 people-first global biopharmaceutical company striving to deliver first- and best-in-class therapies to transform the lives of patients facing serious diseases. The Company is advancing a diverse portfolio of approved and mid- to

late-stage investigational medicines as well as cutting-edge drug discovery focused on serving patient communities where the need is greatest. Insmed's most advanced programs are in pulmonary and inflammatory conditions, including two approved therapies to treat chronic, debilitating lung diseases. The Company's early-stage programs encompass a wide range of technologies and modalities, including gene therapy, AI-driven protein engineering, protein manufacturing, RNA end-joining, and synthetic rescue.

Headquartered in Bridgewater, New Jersey, Insmed has offices and research locations throughout the United States, Europe, and Japan. Insmed is proud to be recognized as one of the best employers in the biopharmaceutical industry, including spending five consecutive years as the No. 1 *Science* Top Employer. Visit www.insmed.com to learn more or follow us on LinkedIn, Instagram, YouTube, and X.

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 timings discussed, projected, anticipated or indicated in any forward-looking statements. Such risks, uncertainties and other factors include, among others, the following: risk that topline data from the Company's clinical trials, including the ENCORE trial, that the Company announces or publishes from time to time may change as more patient data become available or may be interpreted differently if additional data are disclosed; failure to continue to successfully commercialize ARIKAYCE in the U.S., Europe or Japan, or to maintain U.S., European or Japanese approval for ARIKAYCE; the Company's inability to obtain full approval of ARIKAYCE from the FDA, or the Company's failure to obtain regulatory approval to expand ARIKAYCE's indication to a broader patient population; failure to obtain, or delays in obtaining, regulatory approvals for ARIKAYCE outside of the U.S., Europe and Japan, including separate regulatory approval for the Lamira® Nebulizer System in each market and for each usage; failure to successfully commercialize ARIKAYCE in a broader patient population, if approved by applicable regulatory authorities; uncertainties or changes in the degree of market acceptance of ARIKAYCE by physicians, patients, third-party payors and others in the healthcare community; the Company's inability to obtain and maintain adequate reimbursement from government or third-party payors for ARIKAYCE in a broader patient population, if approved, or acceptable prices for 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; failure of third parties on which the Company is dependent to manufacture sufficient quantities of ARIKAYCE for commercial needs, or to comply with the Company's agreements or laws and regulations that impact the Company's business; the Company's inability to create or maintain an effective direct sales and marketing infrastructure or to partner with third parties that offer such an infrastructure for distribution of ARIKAYCE; development of unexpected safety or efficacy concerns related to ARIKAYCE; restrictions or other obligations imposed on the Company by agreements related to ARIKAYCE, including the Company's license agreement with PARI, and failure to comply with the Company's 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; and delays in the execution of plans to build out an additional third-party manufacturing facility approved by the appropriate regulatory authorities 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, 2025 and any subsequent Company filings with the Securities and Exchange Commission (SEC).

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 SEC, 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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