



[Home](#) / [Investors](#) / [News Releases](#)

Insmed Receives Positive CHMP Opinion for ARIKAYCE Liposomal 590 mg Nebuliser Dispersion for the Treatment of NTM Lung Infections Caused by MAC in Non-CF Patients with Limited Treatment Options

- If Approved, ARIKAYCE Will Be First and Only Therapy in the European Union for This Difficult-to-Treat Condition -
- Decision from European Commission Expected Second Half of 2020 -

BRIDGEWATER, N.J., July 24, 2020 /PRNewswire/ -- Insmed Incorporated (Nasdaq: INSM), a global biopharmaceutical company on a mission to transform the lives of patients with serious and rare diseases, today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency has adopted a positive opinion recommending ARIKAYCE Liposomal 590 mg Nebuliser Dispersion for the treatment of non-tuberculous mycobacterial (NTM) lung infections caused by *Mycobacterium avium* complex (MAC) in adults with limited treatment options who do not have cystic fibrosis. Consideration should be given to official guidance on the appropriate use of antibacterial agents.

The European Commission (EC) will review the CHMP opinion, with a final decision anticipated in the second half of 2020.

"Today's positive opinion from the CHMP marks an important step in our journey to transform the way MAC lung disease is managed for patients around the world. If approved by the EC, ARIKAYCE would be the first therapy in both the European Union and the United States for patients with this chronic, debilitating condition," said Will Lewis, Chairman and Chief Executive Officer of Insmed. "We look forward to potentially bringing ARIKAYCE to appropriate patients in Europe as quickly as possible."

The CHMP opinion is based on results from the Phase 3 CONVERT study, which demonstrated that once-daily ARIKAYCE, when combined with multi-drug regimen (MDR), improved sputum culture conversion rates in patients with refractory NTM lung disease caused by MAC compared to MDR therapy alone.

"The positive CHMP opinion underscores the potential benefit of ARIKAYCE in the management of MAC lung disease for patients who are particularly difficult to treat and continue to suffer in the absence of an approved therapy in Europe," said Prof. Dr. Christoph Lange, Medical Director of Clinical Infectious Diseases at the Medical Clinic of the Research Center Borstel, Leibniz Lung Center, Germany. "As demonstrated in the Phase 3 CONVERT study, ARIKAYCE has the potential to improve culture-conversion rates in patients with MAC lung disease who were not responsive to standard of care—a critical milestone in the treatment landscape of this disease."

In the United States, ARIKAYCE (under the generic name amikacin liposome inhalation suspension), is the first and only approved treatment for MAC lung disease as part of a combination antibacterial drug regimen for adult patients with limited or no alternative treatment options. Insmed has also submitted a new drug application for ARIKAYCE in Japan for the treatment of patients with NTM lung disease caused by MAC who did not sufficiently respond to prior treatment. New [international treatment guidelines](#) issued in July 2020 recommend the use of ARIKAYCE in combination with a multidrug regimen in patients with MAC lung disease who have failed standard therapy after at least six months of treatment.

ARIKAYCE previously received Orphan Drug Designation in the European Union for the treatment of NTM lung

infections.

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 need.

About ARIKAYCE

In the United States, 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. Current international treatment guidelines recommend the use of ARIKAYCE in combination with a multidrug regimen in patients with MAC lung disease who have failed standard therapy after at least six months of treatment. 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).

ARIKAYCE is not approved in any country other than the United States.

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 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)

CONVERT was a randomized, open-label, global Phase 3 study designed to confirm the sputum culture conversion results seen in Insmed's Phase 2 clinical study of ARIKAYCE in patients with refractory NTM lung disease caused by MAC. CONVERT was conducted in 18 countries at more than 125 sites. In the U.S., the primary efficacy endpoint was the proportion of patients who achieved sputum culture conversion at Month 6 in the ARIKAYCE plus MDR arm compared to the MDR-only arm. Patients who achieved sputum culture conversion by Month 6 continued in the CONVERT study for an additional 12 months of treatment following the first monthly negative sputum culture. The CONVERT study also evaluated the proportion of patients who maintained sputum culture conversion 3 months off all MAC treatment, which was the primary efficacy endpoint in the EU.

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 $\geq 5\%$ 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 overdose, 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 Insmmed

Insmmed Incorporated is a global biopharmaceutical company on a mission to transform the lives of patients with serious and rare diseases. Insmmed's first commercial product, ARIKAYCE® (amikacin liposome inhalation suspension), is the first and only therapy approved in the United States for the treatment of refractory *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 chronic, debilitating condition that can cause severe and permanent lung damage. Insmmed's earlier-stage clinical pipeline includes brensocatib, a novel oral reversible inhibitor of dipeptidyl peptidase 1 with therapeutic potential in non-cystic fibrosis bronchiectasis and other inflammatory diseases, and treprostinil palmitil, an inhaled 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: failure to obtain, or delays in obtaining, regulatory approvals for ARIKAYCE outside the U.S. or for the Company's product candidates in the U.S., Europe, Japan or other markets, including the United Kingdom as a result of its recent exit from the European Union; failure to successfully commercialize or maintain U.S. approval for ARIKAYCE, the Company's only approved product; the risk that brensocatib does not prove effective or safe for patients in the STOP-COVID19 study; business or economic disruptions due to catastrophes or other events, including natural disasters or public health crises; impact of the novel coronavirus (COVID-19) pandemic and efforts to reduce its spread on our business, employees, including key personnel, patients, partners and suppliers; uncertainties 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 full approval of ARIKAYCE from the FDA, including the risk that the Company will not timely and successfully complete the study to validate a PRO tool and complete the confirmatory post-marketing study required for full approval of ARIKAYCE; inability of the Company, PARI or

the Company's other third party manufacturers to comply with regulatory requirements related to ARIKAYCE or the Lamira[®] Nebulizer System; the Company's inability to obtain adequate reimbursement from government or third-party payors for ARIKAYCE or acceptable prices for ARIKAYCE; development of unexpected safety or efficacy concerns related to ARIKAYCE or brensocatib; inaccuracies in the Company's estimates of the size of the potential markets for ARIKAYCE or brensocatib 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; the Company's inability to create an effective direct sales and marketing infrastructure or to partner with third parties that offer such an infrastructure for distribution of ARIKAYCE; failure to obtain regulatory approval to expand ARIKAYCE's indication to a broader patient population; failure to successfully conduct future clinical trials for ARIKAYCE, brensocatib and the Company's other product candidates, including due to the Company's limited experience in conducting preclinical development activities and clinical trials necessary for regulatory approval and the Company's inability to enroll or retain sufficient patients to conduct and complete the trials or generate data necessary for regulatory approval; risks that the Company's clinical studies will be delayed or that serious side effects will be identified during drug development; failure of third parties on which the Company is dependent to manufacture sufficient quantities of ARIKAYCE or the Company's product candidates for commercial or clinical needs, to conduct the Company's clinical trials, or to comply with laws and regulations that impact the Company's business or agreements with the Company; the Company's inability to attract and retain key personnel or to effectively manage the Company's growth; the Company's inability to adapt to its highly competitive and changing environment; the Company's inability to adequately protect its intellectual property rights or prevent disclosure of its trade secrets and other proprietary information and costs associated with litigation or other proceedings related to such matters; restrictions or other obligations imposed on the Company by its agreements related to ARIKAYCE or the Company's product candidates, including its license agreements with PARI and AstraZeneca AB, and failure of the Company to comply with its 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; the Company's limited experience operating internationally; changes in laws and regulations applicable to the Company's business, including any pricing reform, and failure to comply with such laws and regulations; inability to repay the Company's existing indebtedness and uncertainties with respect to the Company's ability to access future capital; and delays in the execution of plans to build out an additional FDA-approved third-party manufacturing facility 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, 2019, our Quarterly Report on Form 10-Q for the quarter ended March 31, 2020 and any subsequent Company filings with the 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.

Contact:

Investors:

Argot Partners
Laura Perry or Heather Savelle
(212) 600-1902
Insmed@argotpartners.com

Media:

Mandy Fahey
Senior Director, Corporate Communications
Insmed
(732) 718-3621
amanda.fahey@insmed.com

SOURCE Insmed Incorporated
