European Commission Approves Merck’s Enflonsia receives European approval for RSV lower respiratory tract disease in infants during their first RSV season

Merck, known as MSD outside of the United States and Canada, announced that the European Commission (EC) has approved Enflonsia (clesrovimab) for the prevention of respiratory syncytial virus (RSV) lower respiratory tract disease in neonates (newborns) and infants during their first RSV season. Enflonsia is contraindicated for infants with hypersensitivity to the active substance or any of its excipients.

Enflonsia is a preventive, long-acting monoclonal antibody (mAb) designed to provide direct, rapid and durable protection through 5 months, a typical RSV season, with non-weight-based dosing. The EC approval authorizes the marketing of Enflonsia in all 27 European Union (EU) member states, as well as Iceland, Liechtenstein and Norway. The timing for availability of Enflonsia in individual countries will vary by country and depend on multiple factors, including the completion of reimbursement procedures.

“RSV can progress to severe conditions like bronchiolitis and pneumonia in both healthy and at-risk infants and is among the leading causes of infant hospitalization globally,” said Dr. Paolo Manzoni, head of maternal–infant medicine, University of Torino Hospital Degli Infermi, Ponderano, Italy, and an investigator for the SMART clinical trial. “The approval of Enflonsia in Europe represents an important public health achievement. Backed by strong clinical data from the CLEVER and SMART trials showing significant reductions in RSV disease incidence and RSV-associated hospitalizations, paired with dosing convenience, Enflonsia is a valuable new option with potential to help alleviate the burden of RSV on infants, families and health care systems.”

“The European Commission approval of Enflonsia marks a significant milestone in our journey to enable broad access and help reduce the burden of RSV disease on infants around the world,” said Dr. Macaya Douoguih, vice president, therapeutic area head, global clinical development, Merck Research Laboratories. “We are proud to bring Enflonsia to infants in Europe and look forward to equipping families and health care providers with this important new preventive option to help address this widespread and potentially serious disease."

The EC approval is supported by results from the pivotal phase 2b/3 CLEVER trial (MK-1654-004; NCT04767373), which evaluated the safety and efficacy of a single dose of Enflonsia administered to preterm and full-term infants (birth to 1 year of age), as well as interim data from RSV season 1 of the phase 3 SMART trial (MK-1654-007; NCT04938830) evaluating the safety, efficacy and pharmacokinetics of Enflonsia versus palivizumab in infants at increased risk for severe RSV disease. Clinical data from the

CLEVER and SMART trials were published in the New England Journal of Medicine in September 2025.

Enflonsia is approved in the United States, Canada, Switzerland and several other countries for use in infants during their first RSV season, and regulatory filings are underway in additional markets globally.

The CLEVER trial (MK-1654-004; NCT04767373) was a phase 2b/3, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy of Enflonsia in healthy early and moderate preterm infants (=29 to <35 weeks gestational age (GA)) and late preterm and full-term infants (=35 weeks GA) entering their first RSV season. Participants were randomized 2:1 to receive a 105 mg dose of Enflonsia (N=2,412) or saline placebo (N=1,202) by intramuscular (IM) injection.

The primary endpoint was the incidence of RSV-associated medically attended lower respiratory infection (MALRI) characterized as cough or difficulty breathing and requiring =1 indicator of LRI (wheezing, rales/crackles) or severity (chest wall in-drawing/retractions, hypoxemia, tachypnoea, dehydration due to respiratory symptoms) from Day 1 through Day 150 (5 months) after dosing. Medically attended includes all health care professional visits in settings such as outpatient clinic, clinical study site, emergency department, urgent care center and/or hospital. The key secondary endpoint was RSV-associated hospitalization through Day 150 (5 months). RSV associated MALRI through Day 180 (6 months) after dosing was also evaluated as a secondary endpoint. RSV-associated severe MALRI through Day 150 (5 months) and RSV-associated LRI hospitalizations through Day 150 (5 months) were exploratory endpoints. The trial met its primary and key secondary endpoints, as outlined below and reflected in the Summary of Product Characteristics (SmPC).

Enflonsia demonstrated a reduction in incidence of RSV-associated MALRI requiring =1 indicator of LRI or severity compared to placebo through 5 months (primary endpoint) by 60.4% (95% CI: 44.1, 71.9, p<0.001) (incidence rates: Enflonsia, 0.026; placebo, 0.065).

Enflonsia also demonstrated a reduction in RSV-associated hospitalizations through 5 months (key secondary endpoint) by 84.2% (95% CI: 66.6, 92.6, p<0.001) (incidence rates: Enflonsia, 0.004; placebo, 0.024), showing increasing efficacy with increasing disease severity.

Enflonsia was observed to reduce incidence of severe MALRI through 5 months (exploratory endpoint) by 91.7% (95% CI: 62.9, 98.1) (incidence rates: Enflonsia, 0.001; placebo, 0.010).

Enflonsia was observed to reduce RSV-associated LRI hospitalizations through 5 months (exploratory endpoint) by 90.9% (95% CI: 76.2, 96.5).

Enflonsia was observed to reduce incidence of RSV-associated MALRI requiring =1 indicator of LRI or severity compared to placebo through 6 months (secondary endpoint) by 59.5% (95% CI: 43.3, 71.1).

The trial demonstrated that the safety profile of Enflonsia in infants entering their first RSV season was generally comparable to placebo. As reflected in the SmPC, the most frequent adverse reactions were injection-site pain (6.5%), injection-site erythema (4.4%), injection-site swelling (3.2%) and rash (2.3%). Most (>96%) of the adverse reactions were mild or moderate.

The SMART trial (MK-1654-007; NCT04938830) was a Phase 3, randomized, partially-blind, palivizumab-controlled, multicenter study to evaluate the safety, efficacy and pharmacokinetics of Enflonsia in infants and children at increased risk for severe RSV disease over two RSV seasons, including early (<29 weeks GA) or moderate preterm infants (=29 to =35 weeks GA) and infants with chronic lung disease of prematurity or congenital heart disease of any GA.

In RSV season 1, participants were randomized 1:1 to receive either a 105 mg dose of Enflonsia (N=446) or monthly palivizumab (N=450) by IM injection. Data from an interim analysis demonstrated that, among infants at increased risk for severe RSV disease entering their first RSV season, the safety profile of Enflonsia was similar to palivizumab and consistent with the safety profile of Enflonsia in infants in the CLEVER trial.

The efficacy of Enflonsia in infants at increased risk for severe RSV disease was established by extrapolation of efficacy of Enflonsia from the CLEVER trial to the SMART trial based on pharmacokinetic exposure, a secondary endpoint. As reflected in the SmPC, the incidence rates of RSV-associated MALRI requiring =1 indicator of LRI or severity and RSV-associated hospitalization were generally comparable between Enflonsia (3.6%, 95% CI: 2.0, 6.0 and 1.3%, 95% CI: 0.4, 3.0, respectively) and palivizumab (3.0%, 95% CI: 1.6, 5.3 and 1.5%, 95% CI: 0.6, 3.3, respectively) through Day 150 (5 months).

In clinical trials, when Enflonsia was given concomitantly with routine childhood vaccines, the safety profile of the co-administered regimen was similar to the safety profile when Enflonsia and childhood vaccines were administered alone.

Respiratory syncytial virus (RSV) is a contagious virus that causes widespread seasonal infections and can lead to serious respiratory conditions such as bronchiolitis and pneumonia. As a leading cause of hospitalization among infants globally, there is persisting unmet need for RSV preventive options for both healthy and high-risk infants during their first RSV season. RSV season is the time of year when RSV infections are most common, usually occurring autumn through spring of the next year in temperate climates. Timing and severity in a given community or region can vary year to year.

Enflonsia is Merck’s FDA-approved extended half-life monoclonal antibody (mAb) indicated for passive immunization for the prevention of respiratory syncytial virus (RSV) lower respiratory tract disease in newborns and infants who are born during or entering their first RSV season. Enflonsia is administered using the same dose regardless of weight (105 mg/0.7 mL in a prefilled syringe) and is designed to provide direct, rapid and durable protection through 5 months, a typical RSV season. For infants born during the RSV season, Enflonsia is to be administered within the first week of life. For infants born outside of the RSV season, Enflonsia should be administered shortly before the RSV season begins. For infants undergoing cardiac surgery with cardiopulmonary bypass during or entering their first RSV season, an additional 105 mg dose is recommended as soon as the infant is stable after surgery. Enflonsia has a 30-month shelf life.

Merck, known as MSD outside of the United States and Canada, the company unified around its purpose: It use the power of leading-edge science to save and improve lives around the world.

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