

**180-DAY  
FINAL PUBLICATION**

# **180-day efficacy of Beyfortus<sup>®</sup> against hospitalization for RSV-LRTIs in infants (HARMONIE study)**

Sponsored by SANOFI and AstraZeneca and published in  
*The Lancet Child & Adolescent Health*

Beyfortus is the **first long-acting antibody** indicated for the **prevention of RSV lower respiratory tract disease** in<sup>1</sup>:

- Neonates and infants born during or entering their first RSV season
- Children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season

**RSV-LRTI**, respiratory syncytial virus lower respiratory tract infection.

## **IMPORTANT SAFETY INFORMATION**

### **Contraindication**

Beyfortus is contraindicated in infants and children with a history of serious hypersensitivity reactions, including anaphylaxis, to nirsevimab-alip or to any of the excipients.

**Please see additional Important Safety Information throughout this summary and accompanying full Prescribing Information.**

 **Beyfortus<sup>®</sup>**  
(nirsevimab-alip) | 50 mg  
100 mg  
Injection

# Beyfortus® (nirsevimab-alip) Pivotal Trial Data<sup>1-5</sup>

In 2 randomized, placebo-controlled pivotal trials, Beyfortus demonstrated efficacy against MA RSV-LRTI and RSV hospitalization<sup>1-4\*†</sup>

In Trial 04, Beyfortus exhibited a reduction in MA RSV-LRTI and RSV hospitalization compared to placebo: healthy term and late preterm infants (≥35 wGA)<sup>1-4</sup>

## Trial 04 Primary Cohort<sup>‡§||</sup>

50 mg IM dose if <5 kg weight, 100 mg IM dose if ≥5 kg weight<sup>1</sup>

**Primary endpoint:** incidence of MA RSV-LRTI through 150 days post 1 dose<sup>1</sup>

**↓74.9%**  
RRR

(95% CI: 50.6, 87.3;  $P < 0.001$ )  
Beyfortus: 1.2% (12/994)  
Placebo: 5.0% (25/496)

**Secondary endpoint:** incidence of RSV hospitalization through 150 days post 1 dose<sup>1,2</sup>

**↓60.2%**  
RRR

(95% CI: -14.6, 86.2;  $P = 0.09$ )  
Beyfortus: 0.6% (6/994)  
Placebo: 1.6% (8/496)

## Trial 04 Full Study Cohort<sup>§</sup>

50 mg IM dose if <5 kg weight, 100 mg IM dose if ≥5 kg weight<sup>1</sup>

**Exploratory post hoc analysis of secondary endpoint:** incidence of RSV hospitalization through 150 days post 1 dose<sup>2-4</sup>

**↓76.8%**  
RRR

(95% CI: 49.4, 89.4)  
Beyfortus: 0.4% (9/2,009)  
Placebo: 2.0% (20/1,003)

CI, confidence interval; IM, intramuscular; MA, medically attended; RRR, relative risk reduction; wGA, weeks gestational age.

Signs of LRTI involvement included rhonchi, rales, crackles, or wheezing and at least one sign of worsening clinical severity, including at least one of the following: increased respiratory rate, hypoxemia, acute hypoxic or ventilatory failure, new onset apnea, nasal flaring, retractions, grunting, or dehydration due to respiratory distress.<sup>1</sup>

\*Results of Trials 04 and 03 for infants entering their first RSV season.<sup>1</sup>

†RSV hospitalization was defined as hospitalization for LRTI with a positive RSV test.<sup>1</sup>

‡Primary Cohort: 1,490 healthy term and late preterm infants (≥35 wGA) in Trial 04.<sup>1</sup>

§During Trial 04, the COVID-19 pandemic interrupted trial enrollment. The efficacy analysis is based on the Primary Cohort, which included those participants enrolled prior to the pause due to COVID-19. Trial 04 continued monitoring the Primary Cohort and included an additional 1,522 subjects enrolled after the pause to comprise the full study cohort. The full study cohort included 3,012 infants randomized to receive Beyfortus or placebo in the post hoc analysis.<sup>4</sup>

||Efficacy for MA RSV-LRTI based on RRR against placebo adjusted for age at randomization.<sup>1</sup>

## IMPORTANT SAFETY INFORMATION (cont'd)

### Warnings and Precautions

- **Hypersensitivity Reactions Including Anaphylaxis:** Serious hypersensitivity reactions have been reported following Beyfortus administration. These reactions included urticaria, dyspnea, cyanosis, and/or hypotonia. Anaphylaxis has been observed with human immunoglobulin G1 (IgG1) monoclonal antibodies. If signs and symptoms of anaphylaxis or other clinically significant hypersensitivity reactions occur, initiate appropriate treatment.

2 Please see additional Important Safety Information throughout this summary and accompanying full [Prescribing Information](#).

In Trial 03, Beyfortus® exhibited a reduction in MA RSV-LRTI and RSV hospitalization compared to placebo: healthy preterm infants (≥29 to <35 wGA)<sup>1,5</sup>

## Trial 03\*†

50 mg IM dose regardless of weight<sup>1</sup>

**Primary endpoint:** incidence of MA RSV-LRTI through 150 days post 1 dose<sup>1</sup>

**↓70.1%**  
RRR

(95% CI: 52.3, 81.2;  $P < 0.001$ )  
Beyfortus: 2.6% (25/969)  
Placebo: 9.5% (46/484)

**Secondary endpoint:** incidence of RSV hospitalization through 150 days post 1 dose<sup>1,5</sup>

**↓78.4%**  
RRR

(95% CI: 51.9, 90.3;  $P < 0.001$ )  
Beyfortus: 0.8% (8/969)  
Placebo: 4.1% (20/484)

## Trial 03 Post Hoc Analysis<sup>‡</sup>

Subgroup of infants <5 kg receiving 50 mg IM dose<sup>1</sup>

**Exploratory post hoc analysis of primary endpoint:** incidence of MA RSV-LRTI through 150 days post 1 dose<sup>1,2</sup>

**↓86.2%**  
RRR

(95% CI: 68.0, 94.0)  
Beyfortus: 1.2% (7/570)  
Placebo: 9.0% (26/290)

This subgroup included 860 infants weighing <5 kg who were randomized to receive 50 mg IM dose of Beyfortus (coinciding with the approved weight-based dose) or placebo.

The most common adverse reactions reported at an incidence higher than placebo in the Safety Population (Trial 04 and Trial 03) were rash (0.9%) and injection site reactions (0.3%)<sup>1§</sup>

Trial 04 and Trial 03 were pooled to evaluate the safety of Beyfortus (N=2,570) compared to placebo (N=1,284).<sup>1</sup>

- Adverse reactions were reported in 1.2% of infants who received Beyfortus; most (97%) of adverse reactions were mild to moderate in severity

\*1,453 preterm infants (≥29 to <35 wGA) in Trial 03.<sup>1</sup>

†Efficacy for MA RSV-LRTI based on RRR against placebo adjusted for age at randomization and hemisphere.<sup>1</sup>

‡860 infants from the full study cohort of 1,453 healthy preterm infants in Trial 03 were analyzed in a post hoc analysis. For infants in their first RSV season, the recommended dose is 50 mg for infants <5 kg or 100 mg for infants ≥5 kg via IM injection.<sup>1,2</sup>

§The Safety Population includes all infants who received the recommended dose of Beyfortus in Trials 04 and 03: Primary and Safety cohorts from Trial 04; infants who weighed <5 kg and who received the recommended dose of Beyfortus (single 50 mg IM dose) in Trial 03.<sup>1</sup>

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Injection 3

# HARMONIE Phase 3b Study<sup>6,7</sup>

## HARMONIE assessed the reduction of RSV hospitalization with Beyfortus® in healthy term and preterm infants (aged ≤12 months and born at ≥29 wGA) through 180 days<sup>6\*</sup>

The Phase 3b HARMONIE study was a pragmatic, open-label, randomized, parallel, 2-arm trial that studied Beyfortus vs no intervention in healthy term and preterm infants aged ≤12 months (≥29 wGA) entering their first RSV season in France, Germany, or the United Kingdom. The RSV season ended on February 28, 2023, in each country.<sup>6†</sup>

### HARMONIE Efficacy Results<sup>6</sup>

**Efficacy endpoint:** overall incidence of RSV hospitalization through 180 days after randomization<sup>†‡§||</sup>

50 mg IM dose if <5 kg weight, 100 mg IM dose if ≥5 kg weight

**↓82.7%**  
RRR

(95% CI: 67.8, 91.5)

Beyfortus: 0.3% (12/4,038)

No intervention: 1.7% (68/4,019)

The 180-day (6-month) efficacy data against RSV hospitalization reported in this study extends beyond the 150-day (5-month) data reported in Beyfortus pivotal trials. In most of the continental United States, the typical RSV season lasts 5 months.<sup>6</sup>

### The findings in this report are subject to limitations<sup>6</sup>:

- The follow-up does not include a second RSV season where most of the loss of efficacy would be expected to occur
- The possibility of bias exists because the study is unblinded; however, extensive efforts have been made to reduce the risk of bias, including the use of endpoints that are robust to the open-label nature of the study
- The HARMONIE study was conducted in the epidemiological setting typical for European countries, with a period of high RSV circulation followed by low circulation after February. The lower number of cases due to low viral circulation in the latter part of the follow-up makes it more difficult to definitively assess sustained protection

### This study is not included in the Beyfortus Prescribing Information.

\*RSV hospitalization was defined as hospitalization for RSV-associated LRTI with hospital admission and an RSV-positive test result.<sup>6</sup>

†Infants could be born before or during the RSV season, which began on September 11, 2022 (week 37) in France; on October 9, 2022 (week 41) in Germany; and on September 4, 2022 (week 36) in the United Kingdom. The RSV season ended on February 28, 2023, in each country.<sup>6</sup>

‡Overall incidence of hospitalization for RSV-LRTI was defined as admission to the hospital on the basis of the treating physician's decision and confirmation of RSV by means of a positive result of a test performed in accordance with routine practice, during the RSV season in France, Germany, and the United Kingdom.<sup>6</sup>

§8,057 infants were randomized 1:1 to receive either a single IM injection of Beyfortus or the standard care (no intervention) (Beyfortus [n=4,038] or no intervention [n=4,019]) before or during the 2022-2023 RSV season. The characteristics of infants at randomization were similar in the 2 groups and 85.2% of infants were ≥37 wGA at birth.<sup>6</sup>

||The 2-sided 95% CI for the efficacy is calculated by an exact method assuming a binomial distribution of the number of hospitalizations due to RSV-associated LRTI through 180 days after randomization in the Beyfortus group conditional on the total number in both groups (described by Breslow and Day) accounting for the follow-up time after randomization.<sup>6</sup>

### IMPORTANT SAFETY INFORMATION (cont'd)

#### Warnings and Precautions (cont'd)

- **Use in Individuals with Clinically Significant Bleeding Disorders:** As with other IM injections, Beyfortus should be given with caution to infants and children with thrombocytopenia, any coagulation disorder or to individuals on anticoagulation therapy.

Most common adverse reactions with Beyfortus were rash (0.9%) and injection site reactions (0.3%).

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## HARMONIE Safety Results<sup>6,7</sup>:

Treatment-emergent adverse events (TEAEs) in safety analysis population: healthy infants aged ≤12 months, during 12 months following randomization.<sup>6,7</sup>

Adverse events (AEs)*	Beyfortus®, % (n=4,016)	No intervention, % (n=4,018)
Any TEAE	80.0	79.4
Immediate TEAE: ≤30 minutes post dosing/randomization	0.7	0
Any study treatment-related TEAE <sup>†</sup>	2.5	0
TEAE of special interest	0.3	<0.1
Any serious TEAE	6.5	5.5
Any serious study treatment-related TEAE	<0.1	0
Medically attended TEAE	77.3	77.2

### Most AEs in the 2 trial groups were grade 1 or 2 in severity.<sup>6</sup>

FDA, US Food and Drug Administration.

\*Assessment of AE severity was based on the AE severity grading scales adapted from FDA Guidance for Industry: Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials, September 2007.<sup>7</sup>

†The relationship between a TEAE and treatment was assessed as related or not related. A treatment-related TEAE was defined as a TEAE considered by the investigator as related to or with an unknown or missing relationship to treatment for participants who received Beyfortus on Day 1. An unknown or missing relationship between a TEAE and treatment for participants who received no intervention was considered not related (Medical Dictionary for Regulatory Activities Version 25.0).<sup>7</sup>

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Injection

# Beyfortus<sup>®</sup> | 50 mg (nirsevimab-alip) | 100 mg Injection

Contact your Sanofi representative to access real-world evidence studies, or visit [Beyfortus.com](https://www.beyfortus.com) for more information



Scan to read the study in  
[\*The Lancet Child & Adolescent Health\*](#)

## INDICATION

Beyfortus is indicated for the prevention of respiratory syncytial virus (RSV) lower respiratory tract disease in:

- Neonates and infants born during or entering their first RSV season.
- Children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season.

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Beyfortus is contraindicated in infants and children with a history of serious hypersensitivity reactions, including anaphylaxis, to nirsevimab-alip or to any of the excipients.

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- **Use in Individuals with Clinically Significant Bleeding Disorders:** As with other IM injections, Beyfortus should be given with caution to infants and children with thrombocytopenia, any coagulation disorder or to individuals on anticoagulation therapy.

Most common adverse reactions with Beyfortus were rash (0.9%) and injection site reactions (0.3%).

Please see accompanying full [Prescribing Information](#).

**References:** **1.** Beyfortus (nirsevimab-alip). Prescribing Information. Sanofi. **2.** Data on File. Sanofi. **3.** Muller WJ, Madhi SA, Nuñez BS, et al. Nirsevimab for prevention of RSV in term and late-preterm infants. *N Engl J Med.* 2023;388(16):1533-1534. **4.** Muller WJ, Madhi SA, Nuñez BS, et al. Nirsevimab for prevention of RSV in term and late-preterm infants. *N Engl J Med.* 2023;388(16)(suppl):1533-1534. **5.** Griffin MP, Yuan Y, Takas T, et al. Single-dose nirsevimab for prevention of RSV in preterm infants. *N Engl J Med.* 2020;383(5):415-425. **6.** Munro APS, Drysdale SB, Cathie K, et al. 180-day efficacy of nirsevimab against hospitalisation for respiratory syncytial virus lower respiratory tract infections in infants (HARMONIE): a randomised, controlled, phase 3b trial. *Lancet Child Adolesc Health.* 2025;9(6):404-412. **7.** Munro APS, Drysdale SB, Cathie K, et al. 180-day efficacy of nirsevimab against hospitalisation for respiratory syncytial virus lower respiratory tract infections in infants (HARMONIE): a randomised, controlled, phase 3b trial. *Lancet Child Adolesc Health.* 2025;9(6)(suppl):404-412.

**sanofi**

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