

CHMP recommends approval of Beyfortus® (nirsevimab) for prevention of RSV disease in infants

- Recommendation is based on the Beyfortus clinical trial program which demonstrated protection against medically attended lower respiratory tract infection caused by RSV with a single dose during the RSV season
- If approved, Beyfortus would be the first broadly protective option for newborns and infants

Paris, September 16, 2022. The European Medicines Agency’s Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion for Beyfortus® (nirsevimab) for the prevention of respiratory syncytial virus (RSV) lower respiratory tract disease in newborns and infants during their first RSV season. If approved, Beyfortus would be the first and only single-dose passive immunization for the broad infant population, including those born healthy, at term or preterm, or with specific health conditions. Beyfortus is being developed jointly by Sanofi and AstraZeneca.

Jean-François Toussaint

Global Head of Research and Development Vaccines, Sanofi

“Today’s positive CHMP opinion is one of the most significant public health achievements in RSV in decades and has the potential to alleviate the enormous physical and emotional burden that RSV can place on families and healthcare systems. With this endorsement, we are one step closer to achieving our goal of protecting all infants against RSV with a single dose.”

Iskra Reic

Executive Vice President, Vaccines and Immune Therapies, AstraZeneca

“This positive CHMP opinion underscores Beyfortus’ potential as a ground-breaking, first-in-class passive immunization that could transform the medical community’s approach to RSV prevention in infants.”

The CHMP based its positive opinion on results from the Beyfortus clinical development program, including the Phase 3 MELODY, Phase 2/3 MEDLEY, and Phase 2b trials.¹⁻⁸ In the MELODY and Phase 2b trials, Beyfortus met its primary endpoint of reducing the incidence of medically attended lower respiratory tract infections (LRTI) caused by RSV during the RSV season vs. placebo with a single dose.¹⁻⁶ The safety profile of Beyfortus was similar to placebo. Beyfortus also demonstrated a comparable safety and tolerability profile to palivizumab in the Phase 2/3 MEDLEY trial.⁷⁻⁸

RSV is the most common cause of LRTIs and a leading cause of hospitalization in all infants, with most hospitalizations occurring in infants born healthy and at term.⁹⁻¹³ RSV-related direct medical costs, globally — including hospital, outpatient and follow-up care — were estimated at €4.82 billion in 2017.¹⁴ Currently there is no preventative option available for all infants and treatment is limited to symptomatic relief.^{15,16}

About Beyfortus

Beyfortus® (nirsevimab), an investigational long-acting antibody designed for all infants for protection against RSV disease from birth through their first RSV season with a single dose, is being developed jointly by Sanofi and AstraZeneca.

Beyfortus has been developed to offer newborns and infants direct RSV protection via an antibody to help prevent LRTI caused by RSV. Monoclonal antibodies do not require the activation of the immune system to help offer timely, rapid and direct protection against disease.¹⁷

In March 2017, Sanofi and AstraZeneca announced an [agreement](#) to develop and commercialize Beyfortus. Under the terms of the agreement, AstraZeneca leads all development and manufacturing activities and Sanofi will lead commercialization activities and record revenues. Under the terms of the global agreement, Sanofi made an upfront payment of €120m, has paid a development milestone of €30m and will pay up to a further €465m upon achievement of certain development and sales-related milestones. The two companies share all costs and profits. Revenue from the agreement is reported as Collaboration Revenue in the Company's financial statements.

Beyfortus has been granted designations to facilitate expedited development by several major regulatory agencies around the world. These include Breakthrough Therapy Designation by The China Center for Drug Evaluation under the National Medical Products Administration; [Breakthrough Therapy Designation](#) from the US Food and Drug Administration; access granted to the European Medicines Agency (EMA) [PRiority MEDicines](#) scheme; Promising Innovative Medicine designation by the UK Medicines and Healthcare products Regulatory Agency; and named "a medicine for prioritized development" under the Project for Drug Selection to Promote New Drug Development in Pediatrics by the Japan Agency for Medical Research and Development (AMED). The safety and efficacy of Beyfortus was evaluated under an accelerated assessment procedure by the EMA. Beyfortus has not been approved by any regulatory authority.

About the clinical trials

The Phase 2b trial was a randomized, placebo-controlled trial designed to measure the efficacy of Beyfortus[®] (nirsevimab) against medically attended LRTI through 150 days post-dose. Healthy preterm infants of 29–35 weeks' gestation were randomized (2:1) to receive a single 50mg intramuscular injection of Beyfortus or placebo. The primary endpoint was met, reducing the incidence of medically attended LRTI, caused by RSV by 70.1% (95% CI: 52.3, 81.2) compared to placebo. Between November 2016 and December 2017, 1,453 infants were randomized (Beyfortus, n=969; placebo, n=484) at the RSV season start. Studies were conducted in both hemispheres, at 164 sites in 23 countries.^{3,4} Data was published in the *New England Journal of Medicine (NEJM)* in July 2020. The dosing regimen was recommended based on further exploration of the phase 2b data.³ The subsequent Phase 3 study, MELODY, applied the recommended dosing regimen.²

The Phase 3 MELODY trial was a randomized, placebo-controlled trial conducted across 21 countries designed to determine efficacy of Beyfortus against medically attended LRTI due to RSV confirmed by reverse transcriptase polymerase chain reaction testing through 150 days after dosing, versus placebo, in healthy late preterm and term infants (35 weeks gestational age or greater) entering their first RSV season.^{1,2} The primary endpoint was met, reducing the incidence of medically attended LRTI, such as bronchiolitis or pneumonia, caused by RSV by 74.5% (95% CI 49.6, 87.1; P<0.001) compared to placebo. Infants were randomized (2:1) to receive a single 50mg (in infants weighing <5kg) or 100mg (in infants weighing ≥5kg) intramuscular injection of Beyfortus or placebo. Between July 2019 and March 2020, 1,490 infants were randomized to either Beyfortus or placebo at the RSV season start.^{1,2} Data was published on the primary analysis in *NEJM* in March 2022.

Findings from Beyfortus' clinical trial program include a pre-specified pooled analysis of the Phase 3 MELODY trial and the recommended dose from the Phase 2b trial, in which an efficacy (relative risk reduction versus placebo) of 79.5% (95% CI 65.9, 87.7; P<0.0001) was seen against medically attended LRTI, such as bronchiolitis or pneumonia, caused by RSV in infants born at term or preterm entering their first RSV season.⁵ The pooled analysis studied healthy preterm and term infants who received the recommended dose of Beyfortus based on weight compared

to placebo through Day 151 and showed an efficacy of 77.3% (95% CI 50.3, 89.7; P<0.001) against RSV LRTI hospitalizations, as published in *NEJM* in March 2022.^{1,5}

MEDLEY was a Phase 2/3, randomized, double-blind, palivizumab-controlled trial with the primary objective of assessing safety and tolerability for Beyfortus in preterm infants and infants with congenital heart disease (CHD) and/or chronic lung disease of prematurity (CLD) eligible to receive palivizumab.^{7,8} Between July 2019 and May 2021, approximately 918 infants entering their first RSV season were randomized to receive a single 50mg (in infants weighing <5kg) or 100mg (in infants weighing ≥5kg) intramuscular injection of Beyfortus or palivizumab. Safety was assessed by monitoring the occurrence of treatment emergent adverse events (TEAEs) and treatment emergent serious adverse events (TESAEs) through 360 days post-dose.^{7,8} Serum levels of nirsevimab following dosing (on day 151) in this trial were comparable with those observed in the Phase 3 MELODY trial, indicating similar protection in this population to that in the healthy term and late preterm infants is likely.⁷ Data was published in *NEJM* in March 2022.

The results of MELODY, Phase 2/3 MEDLEY and the Phase 2b trials illustrate that Beyfortus helps protect infants during their first RSV season against RSV disease with a single dose.¹⁻⁸ This all-infant population includes preterm, healthy late preterm and term infants, as well as infants with specific conditions.

These trials form the basis of regulatory submissions that began in 2022.

About RSV

RSV is the most common cause of LRTI, including bronchiolitis and pneumonia, in infants.⁹ It is also a leading cause of hospitalization in all infants, with most hospitalizations for RSV occurring in healthy infants born at term.¹⁰⁻¹³ Globally, in 2019, there were approximately 33 million cases of acute lower respiratory infections leading to more than three million hospitalizations, and it was estimated that there were 26,300 in-hospital deaths of children younger than five years.¹⁸ RSV-related direct medical costs, globally — including hospital, outpatient and follow-up care — were estimated at €4.82 billion in 2017.¹⁴

About Sanofi

We are an innovative global healthcare company, driven by one purpose: we chase the miracles of science to improve people's lives. Our team, across some 100 countries, is dedicated to transforming the practice of medicine by working to turn the impossible into the possible. We provide potentially life-changing treatment options and life-saving vaccine protection to millions of people globally, while putting sustainability and social responsibility at the center of our ambitions.

Sanofi is listed on Euronext: SAN and NASDAQ: SNY

Media Relations

Sandrine Guendoul | + 33 6 25 09 14 25 | sandrine.quendoul@sanofi.com

Sally Bain | + 1 617 834 6026 | sally.bain@sanofi.com

Nicolas Obrist | + 33 6 77 21 27 55 | nicolas.obrist@sanofi.com

Kate Conway | + 1 508 364 4931 | kate.conway@sanofi.com

Investor Relations

Eva Schaefer-Jansen | + 33 7 86 80 56 39 | eva.schaefer-jansen@sanofi.com

Arnaud Delépine | + 33 6 73 69 36 93 | arnaud.delepine@sanofi.com

Corentine Driancourt | + 33 6 40 56 92 21 | corentine.driancourt@sanofi.com

Felix Lauscher | + 1 908 612 7239 | felix.lauscher@sanofi.com

Priya Nanduri | + 1 617 764 641 | priya.nanduri@sanofi.com

Nathalie Pham | + 33 7 85 93 30 17 | nathalie.pham@sanofi.com

Sanofi Forward-Looking Statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans" and similar

expressions. Although Sanofi's management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates, the fact that product candidates if approved may not be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities, to complete related transactions and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic and market conditions, cost containment initiatives and subsequent changes thereto, and the impact that COVID-19 will have on us, our customers, suppliers, vendors, and other business partners, and the financial condition of any one of them, as well as on our employees and on the global economy as a whole. Any material effect of COVID-19 on any of the foregoing could also adversely impact us. This situation is changing rapidly and additional impacts may arise of which we are not currently aware and may exacerbate other previously identified risks. The risks and uncertainties also include the uncertainties discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in Sanofi's annual report on Form 20-F for the year ended December 31, 2020. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

References

1. Hammitt LL, MD et al. Nirsevimab for Prevention of RSV in Healthy Late -Preterm and Term Infants. *N Engl J Med.* 2022;386(9): 837-846. doi: 10.1056/NEJMoa2110275.
2. Clinicaltrials.gov. A Study to Evaluate the Safety and Efficacy of MEDI8897 for the Prevention of Medically Attended RSV LRTI in Healthy Late Preterm and Term Infants (MELODY). <https://clinicaltrials.gov/ct2/show/NCT03979313>. Accessed September 2022.
3. Clinicaltrials.gov. A Study to Evaluate the Safety and Efficacy of MEDI8897 for the Prevention of Medically Attended RSV LRTI in Healthy Preterm Infants. (MEDI8897 Ph2b). <https://clinicaltrials.gov/ct2/show/results/NCT02878330>. Accessed September 2022.
4. Griffin P, MD et al. (2020). Single-Dose Nirsevimab for Prevention of RSV in Preterm Infants. *NEJM* 2020; 383: 415-425. DOI: 10.1056/NEJMoa1913556.
5. Simões, E, et al. Pooled efficacy of nirsevimab against RSV lower respiratory tract infection in preterm and term infants. *ESPID 2022 Congress; 2022 May 9-13. Hybrid Congress.*
6. Wilkins, D, et al. Nirsevimab for the prevention of respiratory syncytial virus infection: neutralizing antibody levels following a single dose. *ESPID 2022 Congress; 2022 May 9-13. Hybrid Congress.*
7. Domachowski J, MD et al. Safety of Nirsevimab for RSV in Infants with Heart or Lung Disease or Prematurity. *N Engl J Med.* 2022; 386 (9).
8. Clinicaltrials.gov. A Study to Evaluate the Safety of MEDI8897 for the Prevention of Medically Attended Respiratory Syncytial Virus (RSV) Lower Respiratory Tract Infection (LRTI) in High-risk Children. <https://clinicaltrials.gov/ct2/show/NCT03959488> (MEDLEY). Accessed September 2022.
9. R K. *Respiratory Syncytial Virus Vaccines.* Plotkin SA, Orenstein WA, Offitt PA, Edwards KM, eds Plotkin's Vaccines 7th ed Philadelphia. 2018;7th ed. Philadelphia:943-9.
10. Leader S, Kohlhasse K. Respiratory syncytial virus-coded pediatric hospitalizations, 1997 to 1999. *The Pediatric infectious disease journal.* 2002;21(7):629-32.
11. McLaurin KK, Farr AM, Wade SW, Diakun DR, Stewart DL. Respiratory syncytial virus hospitalization outcomes and costs of full-term and preterm infants. *Journal of Perinatology: official journal of the California Perinatal Association.* 2016;36(11):990-6.
12. Rha B, et al. Respiratory Syncytial Virus-Associated Hospitalizations Among Young Children: 2015-2016. *Pediatrics.* 2020;146:e20193611.
13. Arriola CS, et al. Estimated Burden of Community-Onset Respiratory Syncytial Virus-Associated Hospitalizations Among Children Aged <2 Years in the United States, 2014-15. *J Pediatric Infect Dis Soc.* 2020;9:587-595
14. Zhang S, et al. Cost of Respiratory Syncytial Virus-Associated Acute Lower Respiratory Infection Management in Young Children at the Regional and Global Level: A Systematic Review and Meta-Analysis. *J Infect Dis.* 2020;222(Suppl 7):S680-687.
15. Villafana T, et al. Passive and active immunization against respiratory syncytial virus for the young and old. *Expert Rev Vaccines.* 2017;16:1-39.
16. Respiratory Syncytial Virus Infection (RSV): Infants and Young Children. Centers for Disease Control and Prevention. <https://www.cdc.gov/rsv/high-risk/infants-young-children.html>. Accessed September 2022.
17. Centers for Disease Control and Prevention. Vaccines & Immunizations. August 18, 2017. <https://www.cdc.gov/vaccines/vac-gen/immunity-types.htm>. Accessed September 2022.
18. Li Y, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in children younger than 5 years in 2019: a systematic analysis. *Lancet* 2022;399:92047-64.