

Nirsevimab significantly protected infants against RSV disease in Phase 3 trial

- * Nirsevimab showed a 74.5% reduction in lower respiratory tract infections caused by RSV requiring medical care in healthy infants^{1,2}
- * Nirsevimab is the first investigational immunization designed to protect all infants across the RSV season with a single dose
- * Pivotal Phase 3 results published in *The New England Journal of Medicine*

Paris, March 3, 2022. [*The New England Journal of Medicine \(NEJM\)*](#) today published detailed results from a Phase 3 trial evaluating nirsevimab, the first investigational long-acting antibody designed to protect all infants across the respiratory syncytial virus (RSV) season with a single dose. The trial involved healthy infants born at term or late preterm (35 weeks gestational age or greater) entering their first RSV season and met the primary endpoint, reducing the incidence of medically attended lower respiratory tract infections (LRTI), such as bronchiolitis or pneumonia, caused by RSV by 74.5% (95% CI 49.6 to 87.1; P<0.001) compared to placebo.^{1,2}

A prespecified pooled analysis of RSV-associated hospitalizations in both the Phase 3 and Phase 2b trials was also conducted. In term and preterm infants (greater than 28 weeks gestational age), the proposed dose of nirsevimab demonstrated efficacy of 77.3% (95% CI 50.3 to 89.7; P<0.001) against RSV-associated hospitalizations.¹⁻³ In the Phase 3 MELODY trial alone, a numerical reduction of the risk of RSV-associated hospitalizations was observed, although not statistically significant (62.1%, 95% CI: -8.6 to 86.8; P=0.07).^{1,2} In the nirsevimab arm, six of 994 infants were hospitalized for RSV LRTI, while eight of 496 infants were hospitalized in the placebo arm.^{1,2} Nirsevimab is being developed by Sanofi and AstraZeneca.

Dr. William Muller

Associate Professor, Pediatrics, Northwestern University Feinberg School of Medicine and Scientific Director, Clinical and Community Trials, Ann & Robert H. Lurie Children's Hospital of Chicago, Illinois

"We know that RSV has seen a resurgence with the easing of COVID-19 public health measures. This shows us a broad immunization approach is needed to help mitigate the substantial global burden RSV places on infants, their families and healthcare services. These exciting data show that nirsevimab has the potential to offer RSV protection for all infants, which would be a paradigm shift in the approach to this disease."

The results of the Phase 3 and Phase 2/3 clinical trials, combined with the Phase 2b trial and conducted in different trial populations, demonstrate nirsevimab's potential to protect all infants across the RSV season with a single dose.¹⁻⁶

Jean-François Toussaint

Global Head of Research and Development Vaccines, Sanofi

"With three pivotal late-stage trials, our research has been focused on delivering a first-in-class RSV prevention for all infants. Our Phase 3 MELODY results in healthy late preterm and term infants represent a major milestone toward that goal. We are pleased nirsevimab has the potential to become the first immunization to protect all infants across the RSV season, with only a single dose."

Potential to provide rapid protection

Nirsevimab is the first investigational long-acting antibody designed to protect all infants during their first RSV season. With nirsevimab, the goal is to provide rapid and direct protection to the infant through a single immunization. It is the first potential immunization to show protection against RSV in infants in a Phase 3 trial.^{1,2} RSV is the most common cause of LRTI, including bronchiolitis and pneumonia, and a leading cause of hospitalizations in all infants.⁷⁻⁹

Mene Pangalos

Executive Vice President, BioPharmaceuticals R&D, AstraZeneca

“Respiratory syncytial virus is a leading cause of lower respiratory tract infections, such as bronchiolitis or pneumonia, as well as hospitalizations in infants. These data show for the first time, the potential to significantly protect all infants through their first RSV season with a single-dose immunization and we look forward to working with health authorities to bring nirsevimab to infants as quickly as possible.”

The safety and tolerability of nirsevimab compared to palivizumab was evaluated in the Phase 2/3 trial, which demonstrated nirsevimab had a similar safety and tolerability profile compared to palivizumab when administered to infants with congenital heart disease, chronic lung disease and prematurity (35 weeks gestational age or fewer) entering their first RSV season.^{5,6} Safety was assessed by monitoring the occurrence of all treatment emergent adverse events (TEAEs) and treatment emergent serious adverse events (TESAEs) through 360 days post-dose. The serum levels of nirsevimab following dosing at Day 151 in this trial were comparable with those observed in the Phase 3 trial, indicating similar protection in this population to that in the healthy term and late preterm infants is likely.^{1,2,5,6} Details from the Phase 2/3 trial were also published in [NEJM](#). The study is ongoing, and topline results were presented at RSVVW'21.

Regulatory submissions have begun in the first half of 2022.

About the Phase 3 trial

MELODY is a randomized, placebo-controlled Phase 3 trial conducted across 21 countries designed to determine the incidence of medically attended LRTI due to RSV confirmed by reverse transcriptase polymerase chain reaction testing through 150 days after dosing, versus placebo, in healthy infants entering their first RSV season.^{1,2} Healthy late preterm and term infants (35 weeks gestational age or greater) were randomized (2:1) to receive a single 50mg (in infants weighing <5kg) or 100mg (in infants weighing ≥5kg) intramuscular injection of nirsevimab or placebo. Between July 2019 and February 2021, 1,490 infants were randomized to either nirsevimab or placebo at the RSV season start.^{1,2} Pooled analyses of the RSV LRTI hospitalization endpoint from both of the MELODY and the Phase 2b trials were prespecified under a multiplicity-protected hierarchical testing strategy. The overall safety profile of nirsevimab in the trial remains consistent with previously reported results. No clinically meaningful differences in safety results between the nirsevimab and placebo groups were seen in MELODY and Phase 2b.¹⁻⁴

The evaluation of the [primary endpoint](#) in the MELODY trial was conducted earlier than anticipated. Global public health measures to control COVID-19 had reduced the circulation of all respiratory viruses, including RSV, at the time of trial enrollment. Sufficient cases had been accrued prior to the pandemic to evaluate nirsevimab's ability to prevent RSV LRTI versus placebo. An additional 1,500 infants have been enrolled in the Northern and Southern Hemispheres to provide additional safety information.^{1,2}

About the Phase 2/3 trial

MEDLEY is a Phase 2/3, randomized, double-blind, palivizumab-controlled trial with the primary objective of assessing safety and tolerability for nirsevimab in preterm infants and infants with congenital heart disease (CHD) and/or chronic lung disease of prematurity (CLD) eligible to receive palivizumab.^{5,6} Between July 2019 and May 2021, approximately 918 infants entering their first RSV season were dosed with either nirsevimab or palivizumab. Safety is assessed by monitoring the occurrence of TEAEs and TSEAEs through 360 days post-dose.^{5,6}

The evaluation of the safety and tolerability of nirsevimab in the MEDLEY trial was carried out earlier than anticipated. A primary analysis was conducted to allow earlier assessment of nirsevimab's safety and tolerability versus palivizumab based on a sufficient number of infants being enrolled and followed through their first RSV season.

The results of MEDLEY, MELODY, and the Phase 2b trial demonstrate that nirsevimab provides protection against RSV in all infants with a single dose.¹⁻⁶ This all-infant population includes preterm, healthy late preterm and term infants, as well as infants with CLD and CHD.

These trials form the basis of regulatory submissions that have begun in first half of 2022.

About RSV

RSV is a common, contagious virus that causes seasonal epidemics of lower respiratory tract infections (LRTI), leading to bronchiolitis and pneumonia in infants.¹⁰⁻¹² It is also a leading cause of hospitalizations in all infants.^{8,9} Globally, in 2015, there were approximately 30 million cases of acute lower respiratory infections leading to more than three million hospitalizations, and it was estimated that there were 60,000 in-hospital deaths of children younger than five years.^{12,13} In recent months, there has been a resurgence of RSV following the easing of COVID-19 public health measures.^{14,15} Most hospitalizations for RSV occur in otherwise healthy infants born at term.^{16,17} Medically attended LRTIs are associated with increased costs to the healthcare system.¹⁸

About nirsevimab

Nirsevimab is an investigational long-acting antibody designed to protect all infants through their first RSV season with a single dose. Due to its extended half-life technology, nirsevimab is being developed as a single dose for all infants experiencing their first RSV season and infants with specific conditions, such as congenital heart disease or chronic lung disease, entering their first and second RSV season.^{2,6,19}

Nirsevimab is an immunization designed to provide direct prophylactic RSV protection to all infants via an antibody to help prevent LRTI caused by RSV. Monoclonal antibodies do not require the activation of the immune system to help offer rapid and direct protection against disease.²⁰

In March 2017, Sanofi and AstraZeneca announced an [agreement](#) to develop and commercialize nirsevimab. 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.

Nirsevimab has been granted regulatory designations to facilitate expedited development by several 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 [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). Nirsevimab is currently under clinical investigation and its safety and efficacy have not been reviewed by any regulatory authority.

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.guendoul@sanofi.com

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

Chrystel Baude | + 33 6 70 98 70 59 | chrystel.baude@sanofi.com

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

Victor Rouault | + 33 6 70 93 71 40 | victor.rouault@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 | 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, 2021. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

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 March 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 March 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. Accessed March 2022.
5. Domachowske 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).
6. *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>. Accessed March 2022.
7. 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.
8. Leader S, Kohlhase K. Respiratory syncytial virus-coded pediatric hospitalizations, 1997 to 1999. *The Pediatric infectious disease journal.* 2002;21(7):629-32.
9. 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.
10. Piedimonte G, Perez MK. Respiratory syncytial virus infection and bronchiolitis. *Pediatr Rev.* 2014;35:519-53.
11. Oymar K, et al. Acute bronchiolitis in infants, a review. *Scand J Trauma Resusc Emerg Med.* 2014;22:23.
12. Shi T, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. *Lancet* 2017; 390: 946–58.
13. Oxford Vaccines Group. What is RSV? <https://vk.ovg.ox.ac.uk/vk/rsv>. Accessed March 2022.
14. Ujiie M, Tsuzuki S, Nakamoto T, et al. Resurgence of Respiratory Syncytial Virus Infections during COVID-19 Pandemic, Tokyo, Japan. *Emerging Infectious Diseases.* 2021;27(11):2969-2970. doi:10.3201/eid2711.211565.
15. CDC Health Alert Network. Increased Interseasonal Respiratory Syncytial Virus (RSV) Activity in Parts of the Southern United States. Centers for Disease Control and Prevention. June 10 2021. <https://emergency.cdc.gov/han/2021/han00443.asp> Accessed March 2022.
16. Rha B et al. Respiratory Syncytial Virus–Associated Hospitalizations Among Young Children: 2015–2016. *Pediatrics.* 2020;146(1):e20193611.
17. Arriola CS, Kim L, Langley G, Anderson EJ, Openo K, Martin AM, et al. Estimated Burden of Community-Onset Respiratory Syncytial Virus-Associated Hospitalizations Among Children Aged <2 Years in the United States, 2014-15. *Journal of the Pediatric Infectious Diseases Society.* 2020;9(5):587-95.
18. Leistner R, et al. “Attributable Costs of Ventilator-Associated Lower Respiratory Tract Infection (LRTI) Acquired on Intensive Care Units: a Retrospectively Matched Cohort Study.” *Antimicrobial Resistance and Infection Control*, vol. 2, no. 1, 4 Apr. 2013, p. 13., doi:10.1186/2047-2994-2-13
19. Zhu Q, et al. A highly potent extended half-life antibody as a potential RSV vaccine surrogate for all infants. *Sci Transl Med.* 2017;9:pil: eaaj1928
20. Centers for Disease Control and Prevention. Vaccines & Immunizations. August 18, 2017. <https://www.cdc.gov/vaccines/vac-gen/immunity-types.htm>. Accessed March 2022.