Press Release

FDA accepts nirsevimab application as first protective option against RSV disease for all infants

- Nirsevimab would be the first broadly protective option against RSV disease designed for all infants, if approved
- Nirsevimab delivered consistent protection of approximately 80% against medically attended RSV disease across several trials in healthy term and preterm infants and has been approved under accelerated review in the EU and the UK

Paris, January 5, 2023. The U.S. Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER) has accepted the Biologics License Application (BLA) for nirsevimab for the prevention of respiratory syncytial virus (RSV) lower respiratory tract disease in newborns and infants entering or during their first RSV season and for children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season.

Nirsevimab is being developed jointly by Sanofi and AstraZeneca and, if approved, would be the first protective option for the broad infant population, including those born healthy, at term or preterm, or with specific health conditions. The FDA has indicated they will work to expedite their review. The Prescription Drug User Fee Act date, the FDA target action date for their decision, is in the third quarter of 2023.

Thomas Triomphe
Executive Vice President, Vaccines, Sanofi
"This is a landmark file acceptance in the US as it brings us one step closer to offering the first and only broadly protective option against RSV disease designed for all infants. Given the unprecedented number of otherwise healthy infants who have been hospitalized with RSV this year in the US and the recurrent pattern of RSV epidemics year after year, it is our intention to make nirsevimab available, if approved in time, for the 2023/2024 season to help alleviate the burden of RSV on families and the healthcare system."

RSV is a very contagious virus that can lead to serious respiratory illness, according to the Centers for Disease Control and Prevention (CDC).[10] In the US, RSV is the leading cause of hospitalisation for babies under one.[11] Any infant can be hospitalized in their first RSV season: about 75% of infants hospitalized for RSV in the U.S. are born at term, with no underlying conditions.[12-14] The current 2022/23 RSV season has placed a particularly high burden on infants and families in the United Stated with the American Academy of Pediatrics (AAP) requesting the White House declare an emergency to support the national response to the alarming surge of pediatric hospitalizations due to RSV and influenza.

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
"A substantial burden of disease from RSV affects infants, families, and healthcare providers every year. Effective interventions to prevent RSV are a critical need. This year in the US, we've seen first-hand how frightening the impact of this respiratory disease is on our patients and how stressful it is on the healthcare system, highlighting the urgency of addressing this problem."

The submission was based on results from the Phase 3 MELODY, Phase 2/3 MEDLEY and Phase

2b trials.[1-8] Results across the MELODY and Phase 2b trials showed that nirsevimab demonstrated consistent protection of approximately 80%, against medically attended RSV disease with a single dose.[1-5]

In these trials, nirsevimab helped protect an all-infant population (including healthy term, late preterm, and preterm infants, as well as infants with specific health conditions) against RSV disease requiring medical care, including physician office, urgent care, emergency room visits and hospitalizations, through the duration of the RSV season.[1-8] The safety profile of nirsevimab was similar to placebo. Nirsevimab also demonstrated a comparable safety and tolerability profile to palivizumab in the Phase 2/3 MEDLEY trial.[7-9]

About nirsevimab

In the U.S., nirsevimab is an investigational single-dose long-acting antibody designed to help protect all infants from birth through their first RSV season and for children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season.

Nirsevimab has been developed to offer newborns and infants direct RSV protection via an antibody to help prevent lower respiratory tract infection (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.[15]

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 leads commercialization activities and records 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.

Nirsevimab has been granted 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 FDA; 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). Nirsevimab was approved by the European Commission in October 2022, and by the UK Medicines and Healthcare products Regulatory Agency (MHRA) in November 2022.[16,17]

About the clinical trials

The Phase 2b trial was a randomized, placebo-controlled trial designed to measure the efficacy of nirsevimab against medically attended LRTI through 150 days post-dose. Healthy preterm infants of 29–<35 weeks' gestation (n= 1,453) were randomized (2:1) to receive a single 50mg intramuscular injection of nirsevimab (n= 969) or placebo (n= 484) at the RSV season start.[3,4] The primary endpoint was met, significantly reducing the incidence of medically attended LRTI caused by RSV by 70.1% (95% CI: 52.3, 81.2) compared to placebo.[3,4] The proposed dosing regimen was recommended based on further exploration of the Phase 2b data.[3] When considering the dosing regimen recommended for approval in this study, nirsevimab reduced the incidence of medically attended LRTI caused by RSV by 86.2% (95% CI: 68.0, 94.0) in gestational age ≥29 to <35 weeks.[3,4] The subsequent Phase 3 study, MELODY, applied the recommended dosing regimen.[1,2]

The Phase 3 MELODY (primary cohort) trial was a randomized, placebo-controlled trial conducted across 21 countries designed to determine efficacy of nirsevimab 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, significantly reducing the incidence of medically attended LRTI, such as bronchiolitis or pneumonia, caused by RSV compared to placebo.[1,2] Infants 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.[1,2]

Following the analysis of the initial 1,490 infants within the MELODY primary cohort additional infants continued to be enrolled. A total of 3,012 healthy late preterm and term infants (35 weeks gestational age or greater) entering their first RSV season were randomized to receive nirsevimab (n=2,009) or placebo (n=1,003). In the exploratory analysis, a single 50mg (in infants weighing <5kg) or 100mg (in infants weighing ≥5kg) intramuscular injection of nirsevimab reduced the incidence of medically attended LRTI caused by RSV through 150 days after dosing by 76.4% (95%: CI 62.3, 85.2) compared to placebo, with an acceptable safety profile. Further, nirsevimab demonstrated a 76.8% (95%: CI 49.4, 89.4) reduction in the risk of RSV LRTI with hospitalization through 150 days after dosing compared to placebo.

MEDLEY was 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.[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 nirsevimab or palivizumab. Safety was assessed by monitoring the occurrence of treatment emergent adverse events (TEAEs) and treatment emergent severe 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]

The safety profile of nirsevimab was similar to palivizumab in the MEDLEY Phase 2/3 and consistent with the safety profile in term and preterm infants studied in the MELODY Phase 3 trial compared to placebo.[1-4,7,8] The most commonly reported adverse reactions were: rash 14 days post-dose, (the majority of which were mild to moderate); pyrexia (fever) within 7 days post-dose; non-serious injection site reactions within 7 days post-dose.[16]

Findings from the nirsevimab clinical trial program included a pre-specified pooled analysis of the Phase 3 MELODY trial (primary cohort) and the recommended dose from the Phase 2b trial, in which a relative risk reduction of 79.5% versus placebo (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] This analysis also showed a relative risk reduction of 77.3% (95% CI 50.3, 89.7; P<0.001) against RSV LRTI hospitalizations.[5]

About RSV

RSV is a very contagious virus that can lead to serious respiratory illness for infants, according to the Centers for Disease Control and Prevention (CDC).[10] In the U.S., RSV is the leading cause of hospitalization in infants under 12 months.[11] Approximately 75% of infants hospitalized for RSV are born at term with no underlying conditions.[12-14] RSV symptoms can include runny nose, coughing, sneezing, fever, decrease in appetite, and wheezing.[10] Each year RSV infection leads to approximately 500,000 emergency department visits by children under 5 years of age, which represents 1 in 4 of all RSV-related doctor visits, according to the CDC.[18]

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
Evan Berland | + 1 215 432 0234 | evan.berland@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 6418 | priya.nanduri@sanofi.com
Nathalie Pham | + 33 7 85 93 30 17 | nathalie.pham@sanofi.com

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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.

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