Category

Best Biotechnology Product

General Information

Company Name *

AstraZeneca and Sanofi

Product/Solution Name *

Beyfortus (nirsevimab-alip)

Compound/Tech Name*

nirsevimab

Trade Name *

Beyfortus

Corporate Name *

Beyfortus

Date of Approval *

2023-07-17

Indications *

Beyfortus® (nirsevimab-alip) is a long-acting antibody approved in the United States (US) for the prevention of respiratory syncytial virus (RSV) lower respiratory tract disease (LRTD) in newborns and infants born during or entering 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.

Beyfortus is the first monoclonal antibody approved for the prevention of RSV LRTD in a broad infant population, from preterm or immunocompromised infants to those born full-term and healthy. The single dose can be administered directly to infants as an intramuscular injection, providing fast-acting protection with demonstrated efficacy and safety for the nation's youngest, most vulnerable population.

Beyfortus is currently approved in more than 40 markets and was granted regulatory designations to facilitate expedited development by several major regulatory agencies around the world, including Breakthrough Therapy Designation from the US Food and Drug Administration (FDA).

Beyfortus received FDA approval in July 2023 following a unanimous vote by the Antimicrobial Drugs Advisory Committee (AMDAC). Furthermore, Beyfortus is the first monoclonal antibody to be

recommended by the US Advisory Committee on Immunization Practices (ACIP) for broad infant use and was included in the Vaccines for Children program supporting equitable access in the US.

Early data from the US Centers for Disease Control and Prevention (CDC) show that in the 2023-2024 RSV season, Beyfortus was associated with a 90% reduction against RSV-associated hospitalization among infants in their first RSV season, building on the strong evidence generated from its clinical program's pivotal studies.(1) Preclinical, clinical, and real-world evidence supporting Beyfortus has been published in more than 30 publications across high-impact journals including The New England Journal of Medicine.

Beyfortus is developed and commercialized in partnership by AstraZeneca and Sanofi.

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Therapeutic Areas *

Respiratory syncytial virus
Infectious diseases
Pediatric immunization

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Attached Files:

- Beyfortus Prescribing Information.pdf
- Beyfortus Brochure.pdf

Background information and need for drug / device
(please be as specific as possible in your description; limit 500 words)

Each year, there are up to 80,000 RSV-related infant hospitalizations in the US.(2) That is 80,000 babies fighting to breathe with hundreds of thousands more seeking medical attention without hospitalization.

RSV is one of the most common respiratory viruses among infants and young children.(3,4) While the majority of cases don't progress beyond mild, cold-like symptoms, RSV can quickly become severe and progress to a lower respiratory tract infection, such as bronchiolitis and pneumonia.(3,4) In fact, RSV is the leading cause of hospitalization in infants under 12 months, averaging 16 times higher than the annual rate for influenza in the US.(5,6) The burden of disease is significant, with an estimated 590,000 medically attended RSV lower respiratory tract infections in the US each year.(7) Approximately 75% of infants hospitalized for RSV are born at term and have no underlying conditions, demonstrating the widespread impact and unpredictability of the virus across a broad population.(8-10)

Despite being described as a 'hidden virus,' RSV causes annual seasonal epidemics worldwide.(11-13) Two out of three infants are infected with RSV during their first year of life and almost all children are infected by their second birthday.(4,14) In the US alone, infant RSV treatment costs $709.6 million annually.(15)

Even with more than 60 years of research, the scientific community has struggled to develop new preventive options in the RSV field.(16) Until recently, RSV prevention was limited to high-risk infants with pre-existing conditions-leaving most infants unprotected from this virus.(16,17) The 2022-2023 RSV season, in particular, took a record toll, likely due to a reduction in preventive public health measures as COVID-19 precautions eased.(18,19)

Following those unprecedented levels of illness and hospitalizations, the development of Beyfortus represents a significant breakthrough and innovation to protect infants from RSV.

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Attached Files:

- AstraZenecacom_The Price of RSV.pdf
- AstraZenecacom_Advancing the Science of RSV.pdf
- Beyfortuscom_What is RSV.pdf

History of the development of the solution/product *
(please be as specific as possible in your description; 500 words)

The story of Beyfortus began in the mid-2000s with the identification and optimization of nirsevimab, an antibody that binds with high affinity to the prefusion conformation of the RSV fusion (F) protein. Nirsevimab was substantially more potent and more effective at binding the F protein than previously studied antibodies. Additionally, nirsevimab employs AstraZeneca's proprietary YTE technology, which enhances binding of IgG1 and prolongs serum half-life, more than tripling the longevity of nirsevimab and enabling once-per-season dosing.(20)

Extensive discovery and preclinical efforts set the stage for Beyfortus' robust clinical development program that spanned three pivotal late-stage clinical trials over nearly a decade. Clinical trials consistently showed that a single dose of Beyfortus protected infants for at least five months, the duration of a typical RSV season, and demonstrated approximately 70-80% efficacy against medically attended RSV lower respiratory tract infection (MA RSV LRTI).(21-24) The clinical program included:
- Trial 03, a Phase IIb randomized, double-blind, placebo-controlled, multicenter clinical trial that included 1,453 preterm infants entering their first RSV season. Among infants treated with Beyfortus, 25 (2.6%) experienced MA RSV LRTI compared with 46 (9.5%) infants who received placebo. Beyfortus reduced the risk of MA RSV LRTI by approximately 70% relative to placebo.(21,23)
- MELODY (Trial 04), a Phase III randomized, double-blind, placebo-controlled, multicenter clinical trial that included 3,012 term and late preterm infants. Among the primary cohort infants (1490) treated with Beyfortus, 12 (1.2%) experienced MA RSV LRTI compared with 25 (5.0%) infants who received placebo. Beyfortus reduced the risk of MA RSV LRTI by approximately 75% relative to placebo.(21,22,25)
- MEDLEY (Trial 05), a Phase II/III randomized, double-blind, active (palivizumab)-controlled, multicenter trial that supported the use of Beyfortus in children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season. In addition to safety, the pharmacokinetic data provided evidence for the use of Beyfortus to prevent MA RSV LRTI in this population.(24-26)

The development team worked closely with regulatory stakeholders to define endpoints that were representative of the burden of disease, and ensured the key measure of efficacy included all healthcare provider visits.

The robust clinical study program was designed to include a diverse infant population, including studies in immunocompromised and high-risk populations, as well as Native American populations, who are disproportionately impacted by higher rates of RSV.

Researchers worked closely with regulatory bodies to design optimal, yet flexible programs regarding dose optimization and quality of evidence, to help build the pathway for broad access and widespread approval as quickly as possible. Despite significant roadblocks during the peak of the pandemic, the research team acted quickly, working closely with regulatory agencies to optimize program delivery and implement health tools such as telehealth for remote patient monitoring, home health visits, and online apps to stay on track and ensure robust oversight of enrollees.

Beyfortus is paving the way for other long-acting antibody drugs as a new standard of prevention and for passive immunization as an approach across therapeutic areas, potentially enabling future protection strategies.

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- Domachowske_N Engl J Med_2022.pdf
- Griffin_N Engl J Med_2020.pdf
- Hammitt_N Engl J Med_2022.pdf
- Muller_N Engl J Med_2023.pdf
- Zhu_J Infect Dis_2018.pdf
- Zhu_Sci Transl Med_2017.pdf
- Wilkins_Nat Med_2023.pdf
- Simoes_Lancet Child Adolesc Health_2023.pdf

Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition *

The innovation behind Beyfortus was driven by AstraZeneca's YTE technology, which together with nirsevimab's high potency, led to significant clinical efficacy and seasonal dosing. Notably, in HARMONIE, a close to real-world setting Phase IIIb trial, Beyfortus reduced the risk of RSV LRTI hospitalization by 83%.(27)

In the first RSV season following Beyfortus' commercial launch, more than 2 million doses were supplied globally, marking the fastest pediatric immunization uptake on record-and tracking to be the largest biologic by volume in the first two years since launch. Beyfortus showed impressive impact this respiratory virus season with initial real-world reports demonstrating 90% efficacy in the US, with similar evidence reported globally.(1,28,29)

To get there, AstraZeneca and Sanofi worked closely with the CDC to establish a pathway for broad access for a monoclonal antibody. Beyfortus-the first passive immunization on the CDC's vaccine schedule and first monoclonal antibody implemented "at scale"-dramatically changed the RSV landscape for babies regardless of health status. ACIP's unanimous recommendation means Beyfortus is available with no out-of-pocket cost to families-enabling true practice-changing care.

As "the year of RSV prevention," 2023 included the approval of Beyfortus and one maternal RSV vaccine for infants. Late that year, Galicia, a region in northwestern Spain, enacted a universal immunization program using Beyfortus, where early results have shown RSV LRTI hospitalizations were reduced by 89%.(30) Prof. Federico Martinón-Torres, MD, PhD, a trial investigator and head of pediatrics at Hospital Clínico Universitario de Santiago de Compostela, said, "The infant wards and ICUs were almost empty this past winter virus season. Unlike prior years, there were very few young infants with bronchiolitis in the hospital."

Imagine, a world where pediatric RSV-associated hospitalization is confined to history-driven by paradigm-shifting innovations that protect the resiliency of our healthcare systems and improve the lives of millions.

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Attached Files:

- Ernst_Euro Surveill_2024.pdf
- Drysdale_N Engl J Med_2023.pdf
- Ezpeleta_Vaccines_2024.pdf
- Immunisation Foundation of Australia_LinkedIn Post.pdf
- Moline_MMWR Morb Mortal Wkly Rep_2024.pdf
- Paireau_Influenza Resp Viruses_2024.pdf
- Assad_ESPID_2024.pdf
- Coma_Lancet Preprint_2024.pdf
- LopezLacort_Euro Surveill_2024.pdf
- AresGomez_Lancet Infect Dis_2024.pdf
- Haute Autorite de sante_2023.pdf

Please provide appropriate references (PubMed, Abstract, Website) *

1. Moline HL, Tannis A, Toepfer AP, et al. Early Estimate of Nirsevimab Effectiveness for Prevention of Respiratory Syncytial Virus-Associated Hospitalization Among Infants Entering Their First Respiratory Syncytial Virus Season - New Vaccine Surveillance Network, October 2023-February 2024. MMWR Morb Mortal Wkly Rep 2024;73:209-214. doi: http://dx.doi.org/10.15585/mmwr.mm7309a4
2. McLaughlin JM, Khan F, Schmitt HJ, Agosti Y, Jodar L, Simões EAF, Swerdlow DL. Respiratory Syncytial Virus-Associated Hospitalization Rates among US Infants: A Systematic Review and Meta-Analysis. J Infect Dis. 2022 Mar 15;225(6):1100-1111. doi: 10.1093/infdis/jiaa752. PMID: 33346360; PMCID: PMC8921994.
3. Respiratory Syncytial Virus (RSV). Centers for Disease Control and Prevention. https://www.cdc.gov/rsv/index.html. Accessed May 2022.

4. 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 May 2022.
5. Leader S, Kohlhase K. Recent trends in severe respiratory syncytial virus (RSV) among US infants, 1997 to 2000. J Pediatr. 2003;143(5 Suppl):S127-S132. doi:10.1067/s0022-3476(03)00510-9.
6. Zhou H, et al. Hospitalizations associated with influenza and respiratory syncytial virus in the United States, 1993-2008. Clin Infect Dis. 2012;54 :1427-1436.
7. Rainisch G, et al. Estimating the impact of multiple immunization products on medically- attended respiratory syncytial virus (RSV) infections in infants. Vaccine. 2020;38(2):251-257.
8. Arriola CS, Kim L, Langley G, Anderson EJ, Openo K, Martin AM, Lynfield R, Bye E, Como-Sabetti K, Reingold A, Chai S, Daily P, Thomas A, Crawford C, Reed C, Garg S, Chaves SS. 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 Nov 10;9(5):587-595. doi: 10.1093/jpids/piz087. PMID: 31868913; PMCID: PMC7107566.
9. Hall CB, Weinberg GA, Blumkin AK, Edwards KM, Staat MA, Schultz AF, Poehling KA, Szilagyi PG, Griffin MR, Williams JV, Zhu Y, Grijalva CG, Prill MM, Iwane MK. Respiratory syncytial virus-associated hospitalizations among children less than 24 months of age. Pediatrics. 2013 Aug;132(2):e341-8. doi: 10.1542/peds.2013-0303. Epub 2013 Jul 22. PMID: 23878043.
10. Gantenberg JR, van Aalst R, Zimmerman N, Limone B, Chaves SS, La Via WV, Nelson CB, Rizzo C, Savitz DA, Zullo AR. Medically Attended Illness due to Respiratory Syncytial Virus Infection Among Infants Born in the United States Between 2016 and 2020. J Infect Dis. 2022 Aug 15;226(Suppl 2):S164-S174. doi: 10.1093/infdis/jiac185. PMID: 35968869; PMCID: PMC9377038.
11. Piedimonte G, Perez MK. Respiratory syncytial virus infection and bronchiolitis. Pediatr Rev. 2014;35:519-53.
12. Oymar K, et al. Acute bronchiolitis in infants, a review. Scand J Trauma Resusc Emerg Med. 2014;22:23.
13. 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.
14. Walsh, EE. Respiratory Syncytial Virus infection: an illness for all ages. Clin Chest Med. 2017; 38(1):29-36.
15. Bowser DM, Rowlands KR, Hariharan D, Gervasio RM, Buckley L, Halasa-Rappel Y, Glaser EL, Nelson CB, Shepard DS. Cost of Respiratory Syncytial Virus Infections in US Infants: Systematic Literature Review and Analysis. J Infect Dis. 2022 Aug 15;226(Suppl 2):S225-S235. doi: 10.1093/infdis/jiac172. PMID: 35968875; PMCID: PMC9377037.
16. Villafana T, et al. Passive and active immunization against respiratory syncytial virus for the young and old. Expert Rev Vaccines. 2017;16:1-39.
17. Synagis - Summary of Product Characteristics (SmPC) - (eMC) [Internet]. Available from: https://www.ema.europa.eu/en/documents/product-information/synagis-epar-product-information_en.pdf Accessed May 2022.
18. Centers for Disease Control and Prevention. Increased respiratory virus activity, especially among children, early in the 2022-2023 Fall and Winter. November 4, 2022 (https://emergency.cdc.gov/han/2022/han00479.asp).
19. Eden J-S, Sikazwe C, Xie R, et al. Off-season RSV epidemics in Australia after easing of COVID-19 restrictions. Nat Commun 2022;13:2884-2884.
20. Zhu Q, McLellan JS, Kallewaard NL, Ulbrandt ND, Palaszynski S, Zhang J, Moldt B, Khan A, Svabek C, McAuliffe JM, Wrapp D, Patel NK, Cook KE, Richter BWM, Ryan PC, Yuan AQ, Suzich JA. A highly potent

extended half-life antibody as a potential RSV vaccine surrogate for all infants. Sci Transl Med. 2017 May 3;9(388):eaaj1928. doi: 10.1126/scitranslmed.aaj1928. PMID: 28469033.
21. Muller WJ, et al. Nirsevimab for Prevention of RSV in Term and Late-Preterm Infants. N Engl J Med. April 5, 2023. doi: 10.1056/NEJMc2214773
22. Hammitt LL, 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.
23. Griffin P, MD et al. Single-Dose Nirsevimab for Prevention of RSV in Preterm Infants. N Engl J Med. 2020;383: 415-425. doi: 10.1056/NEJMoa1913556.
24. 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).
25. US FDA. Beyfortus (nirsevimab-alip) Prescribing Information.
26. Simões EAF, Madhi SA, Muller WJ, et al. Efficacy of nirsevimab against respiratory syncytial virus lower respiratory tract infections in preterm and term infants, and pharmacokinetic extrapolation to infants with congenital heart disease and chronic lung disease: a pooled analysis of randomised controlled trials. Lancet Child Adolesc Health. 2023 Mar;7(3):180-189.
27. Drysdale SB, Cathie K, Flamein F, Knuf M, Collins AM, Hill HC, Kaiser F, Cohen R, Pinquier D, Felter CT, Vassilouthis NC, Jin J, Bangert M, Mari K, Nteene R, Wague S, Roberts M, Tissières P, Royal S, Faust SN; HARMONIE Study Group. Nirsevimab for Prevention of Hospitalizations Due to RSV in Infants. N Engl J Med. 2023 Dec 28;389(26):2425-2435. doi: 10.1056/NEJMoa2309189. PMID: 38157500.
28. Haute Autorité de santé. Recommandation vaccinale contre les infections à VRS chez les femmes enceintes. 27 March 2024. https://www.has-sante.fr/upload/docs/application/pdf/2024-03/recommandation_vaccinale_contre_les_infections_a_vrs_chez_les_femmes_enceintes_-_version_provisoire.pdf [Accessed 2 April 2024
29. Assad Z, et al. N Eng J Med 2024, in press.
30. Ares-Gómez S, Mallah N, Santiago-Pérez MI, Pardo-Seco J, Pérez-Martínez O, Otero-Barrós MT, Suárez-Gaiche N, Kramer R, Jin J, Platero-Alonso L, Alvárez-Gil RM, Ces-Ozores OM, Nartallo-Penas V, Mirás-Carballal S, Piñeiro-Sotelo M, Malvar-Pintos A, González-Pérez JM, Rodríguez-Tenreiro-Sánchez C, Rivero-Calle I, Salas A, Durán-Parrondo C, Martinón-Torres F; NIRSE-GAL study group. Effectiveness and impact of universal prophylaxis with nirsevimab in infants against hospitalisation for respiratory syncytial virus in Galicia, Spain: initial results of a population-based longitudinal study. Lancet Infect Dis. 2024 Apr 30:S1473-3099(24)00215-9. doi: 10.1016/S1473-3099(24)00215-9. Epub ahead of print. PMID: 38701823.

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