

# **Comprehensive Summary of Safety Data on Nirsevimab in Infants and Children from All Pivotal Randomized Clinical Trials**

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## **SUPPLEMENTARY INFORMATION**

## Section S1: Study Designs

In MEDLEY Season 1, treatment-emergent adverse events (AEs) were any AE that started on/after the Season 1 Day 1 dose (start of Season 1) and prior to the end of Season 1, Day 361 (end of Season 1) or the last Day prior to Season 2, Day 1 (start of Season 2). For MEDLEY Season 2, treatment-emergent AEs were any AEs that started on/after the date of the Season 2, Day 1 dose (start of Season 2) and prior to the end of Season 2, Day 361 (end of Season 2). Safety analysis in MEDLEY also included AEs within 30 days post first dose in each season to enable assessment of AEs following the active nirsevimab dose compared with one active palivizumab dose. AEs leading to discontinuation of treatment were evaluated only in MEDLEY, the only study entailing multiple doses of treatment per season whereas AEs leading to discontinuation from the study were captured for all studies.

## Section S2: Subgroups of Interest

Clinically relevant subgroups evaluated in this analysis included neonates (defined as those <28 days age at randomization) and infants weighing <2.5 kg on Day 1 (representing those who had relatively higher nirsevimab exposures of approximately 20–30 mg/kg in their first season) among the healthy preterm and term infants included from the Phase 2b and MELODY trials. Among children at higher risk for severe RSV disease in the MEDLEY trial, subgroups evaluated included infants born <29 weeks gestational age (wGA) (irrespective of congenital heart disease [CHD]/chronic lung disease [CLD] status), infants with CHD, and infants with CLD.

## Section S3: Independent Ethics Committees/Institutional Review Boards consulted

Country	Name/Address of IRB/IEC	Site number
<b>MEDLEY (NCT03959488)</b>		
Austria	Ethikkommission der Medizinischen Universität Graz, Auenbruggerpl. 2, 8036 Graz, Austria	2004190
Belgium	O.L.V. Ziekenhuis, Moorselbaan, 164, Aalst, 9300	2004512, 2005091
Bulgaria	Ethics Committee for Clinical Trials, 8, Damyan Gruev Str., Sofia, 1303	2004194, 2004483, 2004484, 2004511, 2004531, 2004559, 2004580, 2004596, 2004770, 2005099
Canada	UBC C&W Research Ethics Board A2-141A, 950 West 28 <sup>th</sup> Avenue Vancouver, BC V5Z 4H4 Health Research Ethics Board of Alberta, 10104 103 Ave NW #1500, Edmonton, AB T5J 0H8	2004506 2005229
Czech Republic	Multicentricka eticka komise, IKEM a TN, Videnska 800, Praha, 140 59	2004564
Estonia	Research Ethics Committee of the National Institute for Health Development, Hiiu 42, Tallinn, 11619	2004062, 2004591
Finland	Varsinais-Suomen sairaanhoitopiiri Eettinen toimikunta, Kiinamyllynkatu 4-8, PL 52 Turku, 20520	2004592
France	Comité de Protection des Personnes Sud Ouest et Outre Mer III, 146 Rue Léo Saignat, 33000, Bordeaux, France	2004064, 2004196, 2004197, 2004515, 2004561, 2004565, 2004579, 2004586, 2005096
Germany	Ethik-Kommission an der Medizinischen Fakultät der Universität Leipzig, Stephanstraße 9A.1, EG 04103 Leipzig	2004207, 2004211, 2004597
Hungary	Egeszsegügyi Tudományos Tanács Klinikai Farmakológiai Etikai Bizottsága, 25 Alkotmány u., Budapest, H-1054, Hungary	2004066, 2004067, 2004491, 2004566, 2005078
Italy	Comitato Etico per la Sperimentazione Clinica delle Provincie di Verona e Rovigo, P.le Stefani, 1, Verona, 37126	2004069, 2004557
Japan	Fukuoka Children's Hospital IRB, 5 Chome-1-1 Kashiiteriha, Higashi Ward, Fukuoka, 813-0017, Japan	2004472

Country	Name/Address of IRB/IEC	Site number
	Fukui-ken Saiseikai Hospital Institutional Review Board, 7-1 Funabashi, Wadanaka-cho, Fukui-shi, Fukui-Ken "	2004539
	Japanese Red cross Maebashi Hospital IRB, 138-Asakuramachi, Maebashi-Shi Gunma	2004599
	Saitama City Hospital IRB, 2460 Mimuro, Midori Ward, Saitama, 336-8522, Japan	2004698
	JCHO Kyushu Hospital IRB, 1 Chome-8-番 1 号 Kishinoura, Yahatanishi Ward, Kitakyushu, Fukuoka 806-8501, Japan	2004773
	National Center for Child Health and Development IRB, 2-chōme-10-1 Ōkura, Setagaya City, Tokyo 157-0074, Japan	2004774
Latvia	Ethics Committee for Clinical Trials of Medicinal Products, Aizkraukles street 21 - 113, Riga, LV1006	2004246, 2004516, 2004519
Lithuania	Lithuanian Bioethics Committee, Algirdo g. 31, Vilnius, LT-03219	2004247, 2004248
Mexico	Comité de Ética en Investigacion del Hospital Infantil de Mexico Federico Gomez, Calle Doctor Márquez 162 Delegación, Doctores, Cuauhtémoc, 06720 Ciudad de México, CDMX, Mexico	2004529
	Comite de Etica en Investigacion de Investigacion Biomedica para el Desarrollo de Farmaco Insurgentes, Sur #662 PB, Delegación Benito Juárez Del Valle Centro	2004555
Poland	Komisja Bioetyczna przy Okregowej Izbie Lekarskiej w Rzeszowie, ul. Jana Dekerta 2, Rzeszów,35-030	2004133, 2004137, 2004141, 2004467, 2004583
Republic of Korea	Samsung Medical Center Institutional Review Board, (06351) 81 Irwon-Ro Gangnamgu, Seoul, Korea	2004776
	IRB of Ajou University Hospital, San 5, Woncheondong, Yeongtong-gu, Suwon 443-721, Republic of Korea	2004777
	IRB of Korea University Ansan Hospital, 123 Jeokgeum-ro, Danwon-gu, Ansan-si, Gyeonggi-do, South Korea	2004803
Russia	Ethical Council at the MoH of RF, 3 Rakhmanovsky Pereulok, Moscow,127994	2004074, 2004143, 2004144, 2004521, 2004551, 2004568
	LEC at SBHI Novosibirsk City, Clinical Perinatal Center. Ulitsa Adriyena Lezhena, 32, Novosibirsk, Novosibirsk Oblast, Russia, 630089	2005178
South Africa	University of Witwatersrand, Human Research Ethics Committee, 1 Jan Smuts Avenue, Braamfontein 2000, Johannesburg, South Africa	2004076, 2004078, 2004147
	Pharma Ethics, 123 Amcor Road Lyttlelon Manor, South Africa 0157	2004077, 2004079
	1 Military Hospital Human Research Ethics Committee, Department of Neurology, Private bag X 1026 Thaba Tswane 0143	2004080
	Stellenbosch University Human Research Ethics Committee, Stellenbosch University, Private Bag X1, Matieland, 7602, Stellenbosch, South Africa	2004477
Spain	Hospital Universitario Clinico San Carlos, Puerta G - Planta 4ª Norte,C/ Profesor Martin Lagos, s/n Madrid, 28040	2004082, 2004083, 2004084, 2004150, 2004493, 2004500, 2004545, 2004553, 2004587, 2005180, 2005181

Country	Name/Address of IRB/IEC	Site number
Sweden	Etikprövningsmyndigheten, Box 2110,SE-750 02 Uppsala,SE-750 02	2004087
Turkey	Ege University Ethics Committee, Ege Universitesi Tip Fakultesi, Klinik Arastirmalar Etik Kurulu Izmir, 35100	2004152, 2004154, 2004156
Ukraine	Dept of health of Chernivtsi city council, Communal Medical Institution City Clinical Childrens' Hospital, 4 Bukovynska St, Chernivtsi, 58001	2004089
	Vinnytsia regional Children's Clinical Hospital, 108 Khmelnyske shose st, Vinnytsia, 21000. Medical Ethics Commission	2004157
	Ministry of Health of Ukraine, Communal Non- Commercial enterprise Saint Zinaida Children's Clinical Hospital of Sumy City Council, 28 Troiska st, Sumy, 40022	2004159
	Communal Non-Commercial enterprise of Kharkiv Regional Council regional Children's clinical hospital, 5 Ozeryanska st Kharkiv, 61093	2004517
	Odesa Regional State administration, department of health, communal enterprise, Odesa regional Children's clinical hospital, 3 Ac Vorobiov st, Odes- 31, 65031	2004522
	Ethics Commission at Communal Institution Dnipro City Children's Clinical Hospital No 5 of Dnipro City Council, 5 ivana Akinfiieva, st, Dnipro 49027 Ukraine	2004570
	LEC Reg Dniprop Children Clin Hosp, Karavajeva St, 68, Dnipro, Dnipropetrovsk Oblast, Ukraine, 49000	2005230
	LEC Ivano-Frankivsk Regional Children Clinical Hospital, Viacheslava Chornovola St, 44, Ivano- Frankivsk, Ivano-Frankivsk Oblast, Ukraine, 76000	2005231
United Kingdom	NRES Committee South Central - Berkshire,South West REC Centre,Level 3, Block B, Bristol, BS1 2NT	2004482, 2004594, 2005077
United States of America	WCG IRB, 212 Carnegie Center, Suite 301, Princeton, NJ 08540, USA	2004094, 2004161, 2004176, 2004584, 2004164, 2004168, 2004585, 2004169, 2004171, 2004172, 2004461, 2004524, 2004547, 2004549, 2004571, 2004589, 2004606, 2004735, 2005100, 2005182, 2005232
	Institutional Review Board, Ann & Robert H. Lurie Children's Hospital of Chicago, 25 East Chicago Avenue, Chicago, Illinois"	2004177
	Cincinnati Children's Hospital Institutional Review Board, 3333 Burnet Avenue   MLC 7040   Cincinnati, OH 45229	2004179
	Institutional Review Boards, University of Louisville 2301 S 3rd St, Louisville, KY 40292, United States	2004463
	Duke University Health System, Institutional Review Board, 2301 Erwin Rd, Durham, NC 27710, United States	2004603
	Childrens Hospital of Los Angeles-Committee on Clinical Investigations IRB, 4661 Sunset Blvd, Los Angeles, CA 90027, United States	2004705
	East Carolina University, University and Medical Center Institutional Review Board	2005208

Country	Name/Address of IRB/IEC	Site number
<b>Phase 2b (NCT02878330)</b>		
Argentina	Comité de Ética en Investigación Científica. Hospital Pediátrico Dr. Humberto Notti Bandera de Los Andes 2603 Villa Nueva Guaymallén Mendoza	2002905
	Comité Hospitalario de Etica Necochea 675 Bahia Blanca Buenos Aires	2002909
Australia	Monash Health Human Research Ethics Committee (RGO) Level 2, I Block Clayton Victoria	2002910
	Royal Children's Health Services Human Research Ethics Committee (RGO) 50 Flemington Road Parkville Victoria	2002911
	Princess Margaret Hospital for Children Ethics Committee Princess Margaret Hospital Entrance No 6, Hamilton Street Subiaco Western Australia	2002912
Belgium	Comité d'Ethique du CHU Ambroise Paré Boulevard Kennedy 2 Mons	2003274
Brazil	CEP Investiga - Instituto de Pesquisas Avenida Romeu Tortima, 739 - Cidade Universitária Campinas Sao Paulo	2002934
	CEP da Universidade Federal de Minas Gerais Avenida Presidente Antonio Carlos 6627 Unidade Administrativa II Belo Horizonte Minas Gerais	2002935
	CEP da Faculdade de Ciências Médicas e da Saúde de Juiz de Fora SUPREMA/MG Alameda Salvaterra, 200 Bairro Salvaterra Juiz de Fora Minas Gerais	2002939
	CEP da Faculdade de Medicina de Botucatu - UNESP/SP Distrito de Rubião Junior Botucatu Sao Paulo	2003060
	Comitê de Ética em Pesquisa em Seres Humanos do Instituto de Medicina Integral Professor Fernando F Rua dos Coelhoos, 300 -Boa Vista Recife Pernambuco	2002940
	CEP da Universidade Luterana do Brasil -ULBRA Farroupilha, 8001 - Prédio 14 - Sala 224 Bairro São José Canoas Rio Grande do Sul	2002941
	Comitê de Ética em Pesquisa em Seres Humanos do Hospital Pequeno Príncipe Rua Desembargador Motta, 1070 6º andar, sala do NUPE Curitiba Paraná	2002943
	CEP da Universidade de Passo Fundo/RS Universidade de Passo Fundo - BR 285, Bairro São José Passo Fundo Rio Grande do Sul	2002944
Canada	McGill University Health Center-Research Ethics Board 2155 Guy Street 2nd Floor, Room 231 Montreal Quebec	2003277, 2003280
Chile	Comite Etico Cientifico del Servicio de Salud Metropolitano Sur Santa Rosa 3453, Piso 1 San Miguel Santiago	2002998, 2002999
	Comité Etico Científico Servicio de Salud Valdivia Maipú 550, oficina 307 Valdivia	2002953
	Comité Ético Científico Servicio de Salud Metropolitano Central Victoria Subercaseaux 381, piso 4 Santiago	2002956
	Comité Ético-Científico Servicio de Salud Metropolitano Sur Oriente Av Concha y Toro 3459 Puente Alto Santiago	2002954
	Comité Ético-Científico Servicio de Salud Viña del Mar-Quillota Calle Limache #1307 Esquina Peñablanca 2º Piso Viña del Mar	2003257

Country	Name/Address of IRB/IEC	Site number
	Comité de Ética de Investigación en Seres Humanos Av. Independencia 1027, Independencia Santiago	2002955
	Comité de Ética de la Investigación Servicio de Salud Metropolitano Norte San José #1053 Independencia Santiago	2002955
Czech Republic	Etická komise Ústav pro péči o matku a dítě Podolské nabřeží 157/36 Praha 4 - Podolí	2002926
	Etická komise Nemocnice Havlíčkův Brod Husova 2624 Havlíčkův Brod	2002927
	Etická komise IKEM a FTNsP Vídenská 800 Praha 4 - Krc	2002924
Italy	CESC della Provincia di Padova Presso Azienda Ospedaliera di Padova_Via Giustiniani 1 Padova Padova	2003034
	Comitato Etico per la Sperimentazione Clinica delle Province di Verona e Rovigo P.le Stefani, 1 Verona Verona	2003000
	Azienda Ospedaliera Città della Salute e della Scienza di Torino Corso Bramante 88/90. Torino Torino	2003065
	Comitato Etico Regionale della Liguria Largo Rosanna Benzi 10 Farmacia Ospedaliera Genova Genova	2003035
South Africa	Pharma Ethics 123 Amcor Road Lyttelton Manor Centurion Pretoria Gauteng	2002923, 2002919, 2002921, 2002938
	Wits Health Consortium 31 Princess of Wales Terrace Parktown Johannesburg Gauteng	2002918, 2002937
	University of Stellenbosch Ethics Committee Faculty of Health Sciences Francie van Zijl Drive Tygerberg Cape Town Western Cape	2002920
	University of Cape Town HREC Faculty of Health Sciences Research EC E52-24 Old Main Building Groote Schuur Hospital, Observatory Cape Town Western Cape	2002922, 2002946
Spain	CEIC de Galicia C/ San Lázaro, s/n Secretaria Xeral. Conselleria de Sanidade Dirección Santiago de Compostela La Coruña	2002947, 2002948, 2002950, 2002951
United Kingdom	R&D University Hospital Southampton NHS Foundation Trust Tremona Road, Level E, Laboratory & Pathology Block, SCBR - MP 138 Southampton Hampshire	2002967
	R&D - Brighton and Sussex University Hospitals Royal Sussex County Hospital Level 5 Thomas Kemp Tower Eastern Road Brighton East Sussex	2003320
	R&D - Alder Hey Children's NHS Foundation Trust Eaton Road Liverpool Merseyside	2003319
	R&D South West London and St George's Mental Health NHS Trust Department of Mental Health, St George's, University of London, 6th Floor, Hunter Wing, Cranmer Terrace London Greater London	2002968
	R&D - CRN Thames Valley and South Midlands 1st Floor, Manor House The John Radcliffe Hospital, Headley Way Headington Oxford Oxfordshire	2002969
	R&D University Hospitals Bristol NHS Foundation Trust Education & Research Centre Level 3 Upper Maudlin Street Bristol Avon	2002966
United States	MetroHealth Medical Center IRB 2500 MetroHealth Dr. Rammelkamp Bldg. Room 103 Cleveland Ohio	2003359

<b>Country</b>	<b>Name/Address of IRB/IEC</b>	<b>Site number</b>
	Copernicus Group IRB 5000 CentreGreen Way Suite 200 Cary North Carolina	2003395, 2003091, 2002970, 2003007, 2003356, 2003405, 2003355, 2003354, 2003004, 2003353, 2002971, 2003124, 2003350, 2003394, 2003349, 2003092, 2003348, 2003078, 2002974, 2003036, 2003346, 2003340, 2003441, 2003167, 2003338, 2003337, 2003442, 2003068, 2003038, 2003342, 2003335, 2003399, 2003086, 2003444, 2003400, 2003332, 2002976, 2003402, 2003347, 2003403, 2003125, 2003329, 2003336, 2003079, 2003401, 2003407
	Medical University of South Carolina IRB 19 Hagood Avenue 6th floor, Suite 601 Charleston South Carolina	2003358
	UTHSC IRB Office 910 Madison Suite 600 Memphis Tennessee	2003352
	Memorial Health Services Research Council 2801 Atlantic Avenue Attn Research Administration Long Beach California	2003118
	SUNY IRB 750 East Adams Street CWB 218G Syracuse New York	2002972
	WIRB 1019 39th Avenue SE Suite 120 Puyallup Washington	2002973, 2003061, 2003069, 2003093, 2003331, 2003447
	Sharp Healthcare IRB 7930 Frost St Suite 300 San Diego California	2003343
	Winthrop-University Hospital IRB 222 Station Plaza North Suite 521 Mineola New York	2003341
	Marshall University Office of Research Integrity One John Marshall Drive Huntington West Virginia	2003339
	Ann & Robert H. Lurie Children's Hospital of Chicago Institutional Review Board 225 E. Chicago Avenue Box 59 Chicago Illinois	2003011
	Chesapeake IRB 7063 Columbia Gateway Drive Suite 110 Columbia Maryland	2003334
	Cincinnati Children's Hospital Medical Center IRB 3333 Burnet Ave. MLC 5020 Cincinnati Ohio	2003067
	Childrens Hospital of Los Angeles-Committee on Clinical Investigations IRB 4650 Sunset Blvd Mail Stop #23 Dr. Andreas Reiff Los Angeles California	2003333
	University of Texas at San Antonio IRB One UTSA Circle MS 4.01.82 San Antonio Texas	2003005
	Chesapeake IRB 6940 Columbia Gateway Dr #110 Columbia Maryland	2002975
	Arnold Palmer Medical Center Institutional Review Board 1401 Kuhl Avenue MP #21 Research Department Orlando Florida	2003330
	University of Nebraska Medical Center IRB 987830 Nebraska Medical Center Omaha Nebraska	2003328
	Creighton University IRB 2500 California Plaza IRB-Biomedical Omaha Nebraska	2003009
	Oklahoma University Health Sciences Center 1105 North Stonewall Avenue Oklahoma City Oklahoma	2003448
	Connecticut Children's Medical Center IRB 282 Washington Street. Suite 2 K. Hartford Connecticut	2003406

Country	Name/Address of IRB/IEC	Site number
<b>MELODY (NCT03979313)</b>		
Argentina	Independent Ethics Committee for Clinical Pharmacology Trials, Drug and Pharmacology Studies Foundation	2004648, 2004132
Australia	Child and Adolescent Health Service (HREC), Office 5E, Perth Children's Hospital, 15 Hospital Avenue Nedlands, 6009	2004373, 2004327
Austria	Ethikkommission der Medizinischen Universität Graz, Auenbruggerplatz 2, Graz, 8036	2004249, 2004298
Belgium	O.L.V. Ziekenhuis, Moorselbaan 164, Aalst, 9300	2004629, 2004231, 2004270, 2004299, 2004320, 2004398, 2004320
Bulgaria	Ethics Committee for Clinical Trials, 8, Damyan Gruev Str., Sofia, 1303	2004303, 2004234, 2004325, 2004339, 2004343, 2004639, 2004324, 2004401, 2004399
Canada	Conjoint Health Research Ethics Board Research Services Office 2500 University Drive, NW Calgary AB T2N 1N4	2004667
	MUHC Centre for Applied Ethics 5100, boul. de Maisonneuve Ouest, 5th floor, Office 576 Montréal, Québec, H4A 3T2	2004365, 2004351
	UBC C&W Research Ethics Board A2-141A, 950 West 28th Avenue Vancouver, BC V5Z 4H4	2004623
Chile	Servicio De Salud Metropolitano Sur Oriente Comité Etico- Científico, Av. Concha y Toro 3459 – Paradero 30, Vic. Mackenna	2004043
	UNIVERSIDAD DE CHILE [University of Chile] – FACULTAD DE MEDICINA HUMAN RESEARCH ETHICS COMMITTEE, Av. Libertador Bernardo O'Higgins 1058, Santiago de Chile	2004098
	Ministerio de Salud Servicio de Salud Valdivia Scientific Ethics Committee, V. Pérez Rosales 560 - Edificio Prales - Oficina 307 - Piso 3	2004296
	Servicio de Salud Metropolitano Norte Research Ethics Committee, 272, Calle Maruri 8380000 Independencia Metropolitana de Santiago	2004300
Colombia	Universidad Pontificia Bolivariana, Calle 78 B No. 72 A 109	2004233
	CORPORACIÓN CIENTÍFICA PEDIÁTRICA, BIOMEDICAL RESEARCH ETHICS COMMITTEE, Calle 5 B5 No. 37 bis - 28	2004295
	UNIVERSIDAD CES, Calle 10A No. 22 - 04 El Poblado	2004304
	COMITÉ DE ÉTICA EN INVESTIGACIÓN VIT, Calle 24 N° 3-02 este	2004372
	Research Ethics Committee of the Health Sciences Department of the Universidad del Norte, Apartados Aéreos 1569 - 51820, Km. 5 vía Puerto Colombia	2004400
	State Social Enterprise HOSPITAL MENTAL DE ANTIOQUIA [Antioquia Psychiatric Hospital], Calle 38 55- 310 Bello-Colombia	2004669
	Human Research Ethics Committee Fundación Hospital Infantil Universitario de San José, Carrera 52 No. 67 A-71 PBX: 4377540	2004681
Czech Republic	Multicentricka eticka komise IKEM a TN, Videnska 800, Praha, 140 58	2004271
	Multicentricka eticka komise IKEM a TN, Videnska 800, Praha, 140 59	2004272, 2004044



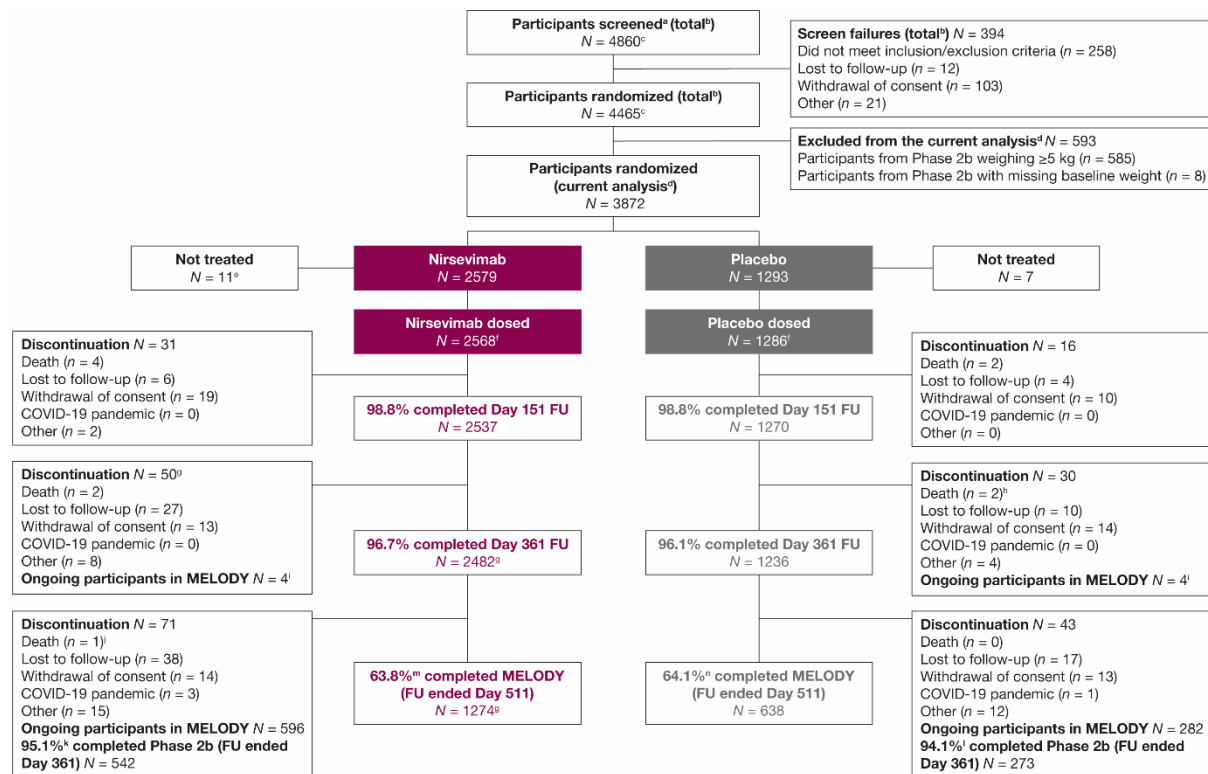
Country	Name/Address of IRB/IEC	Site number
Estonia	Research Ethics Committee of the National Institute for Health Development, Hiiumäe 42, Tallinn, 11619	2004273, 2004045, 2004046, 2004099, 2004047, 2004274
Finland	Varsinais-Suomen sairaanhoitopiiri Eettinen toimikunta, Kiinamyllynkatu 4-8, PL 52 Turku, 20520 Hospital District of Southwest Finland Joint Municipal Authority Ethics Committee, Turku University Hospital, T-Hospital, 6th Floor, Board meeting room A 607	2004742, 2004741, 2004313, 2004743, 2004611, 2004312, 2004644, 2004887, 2004896
France	Comité de Protection des Personnes Ile de France VIII, Hôpital Ambroise Paré, 9 avenue Charles de Gaulle Boulogne Billancourt, 92100	2004654, 2004100, 2004232, 2004374, 2004378, 2004646, 2004653, 2004676, 2005602
Germany	Ethik-Kommission an der Medizinischen Fakultät der Universität Leipzig, Käthe-Kollwitz-Strasse 82, Haus: Karl-Sudhoff-Institut Leipzig, 04109 Landesärztekammer Baden-Württemberg Ethik-Kommission Liebknechtstr. 33 70565 Stuttgart Ethik-Kommission der Bayerischen Landesärztekammer Mühlbauerstr. 16 D-81677 München Ethikkommission der Landesärztekammer Rheinland-Pfalz Deutschhausplatz 3 55116 Mainz	2004185  2004178 2004182  2004359
Israel	Soroka University Medical Center, Itzhak Rager Blv. Beer Sheva 8458900 Laniado Hospital, 16 deuteronomy haim st., kiryat sanz netanya, 42150	2004626 2004672
Italy	Comitato Etico per la Sperimentazione Clinica delle Provincie di Verona e Rovigo, P.le Stefani, 1, Verona, 37126 COMITATO ETICO DELLA FONDAZIONE POLICLINICO UNIVERSITARIO AGOSTINO GEMELLI IRCCS UNIVERSITÀ CATTOLICA DEL SACRO CUORE	2004103 2004396
Japan	Japanese Red cross Maebashi Hospital IRB 138-Asakuramachi, Maebashi-Shi Gunma Yokosuka Kyosai Hospital IRB, 1-16 Yonegahamadori, Yokosuka Kanagawa Jimbo Orthopedic Surgery Institutional Review Board 5-38-41, Honcho Koganei-shi, Tokyo NHO Okayama Medical Center IRB Kita-ku Tamasu 1711-1, Okayama-shi, Okayama-Ken, Japan Kawasaki Municipal Hospital Institutional Review Board 12-1, Shinkawa-dori, Kawasaki-ku, Kawasaki-shi, Kanagawa Fukuyama City Hospital Institutional Review Board 5-23-1 Zao-cho, Fukuyama-shi, Hiroshima KKR Sapporo Medical Center IRB 6-3-40 Hiragishi 1-jo Toyohira-ku, Sapporo-shi, Hokkaido Fukui-ken Saiseikai Hospital Institutional Review Board 7-1 Funabashi, Wadanaka-cho, Fukui-shi, Fukui-Ken Institutional Review Board of Okayama City General Medical Center Okayama City Hospital 3-20-1 Kitanagaseomotomachi, Kita-ku, Okayama-shi, Okayama Local Independent Administrative Corporation Hiroshima City Hospital Organization Hiroshima City Hiroshima Citizens Hospital Institutional Review Board 7-33 Motomachi, Naka-ku, Hiroshima-shi, Hiroshima	2004632 2004660 2004668 2004670 2004671 2004687 2004688 2005029 2005030 2005031

Country	Name/Address of IRB/IEC	Site number
	Review Board of Human Rights and Ethics for Clinical Studies Institutional Review Board 13-2 Ichibancho, Chiyoda-ku, Tokyo	2005032
	Aijinkai Takatsuki General Hospital IRB 1-3-13 Kosobe-cho, Takatsuki, Osaka	2005033
	Review Board of Human Rights and Ethics for Clinical Studies Institutional Review Board 13-2, Ichibancho, Chiyoda-ku, Tokyo, Japan	2005034
	Japanese Red Cross Shizuoka Hospital Institutional Review Board 8-2 Otemachi, Aoi-ku, Shizuoka-shi, Shizuoka	2005035
	JA Shizuoka Kosei Hospital Institutional Review Board 23 Kitabanchō, Aoi-ku, Shizuoka-shi, Shizuoka	2005036
	Hiroshima Red Cross Hospital & Atomicbomb Survivors Hospital Institutional Review Board 1-9-6 Sendamachi, Naka-ku, Hiroshima-shi	2005037
	NHO Shikoku Medical Center for Children and Adults Institutional Review Board 2-1-1, Senyūcho, Zentsūji-shi, Kagawa, Japan	2005038
	Daido Hospital Institutional Review Board 9 Hakusuicho, Minami-ku, Nagoya, Aichi	2005039
	Nagoya Ekisaikai Hospital IRB, 4-66 Shonen-Cho, Nakagawa-ku, Nagoya-Shi, Aich	2005049
	Samsung Medical Center Institutional Review Board Yonsei University Health system, Severance Hospital, Institutional review Board, Yonsei-ro 50-1, Seodaemun-gu, Seoul, 03722	2004768 2004769
	IRB of Korea University Ansan Hospital, 123 Jeokgeum-ro (Gojan-dong) Danwon-gu, Ansan-si, Gyeonggi-do, 15355	2004797
	Inha University Hospital Institutional Review Board, 27 Inhang-ro, Jung-gu, Incheon	2004798
Republic of Korea	Yonsei University Gangnam Severance Hospital, IRB, 2nd Floor, 235 Dogok-ro, Gangnam-gu, Seoul 06230	2004800
Latvia	Ethics Committee for Clinical Trials of Medicinal Products, Aizkraukles street 21 - 113, Riga, LV1006	2004380, 2004199, 2004331, 2004202, 2004198, 2004302
Lithuania	Lithuanian Bioethics Committee, Algirdo g. 31, Vilnius, LT-03219	2004395, 2004204, 2004277, 2004710
Mexico	Federico Gomez Children's hospital of Mexico, National Institute of Health research office	2004404
New Zealand	Northern B Health and Disability Ethics Committee, 20 Aitken Street, Ministry of Health, Ethics Department, Reception - Ground Floor, Thorndon, Wellington, 6011	2004335, 2004405, 2004048, 2004105
Panama	Dr Jose Renan Esquivel Children's hospital, Panama Ave, Balboa, Calle 34 Research Bioethics Committee	2004867, 2004868, 2004869, 2004870, 2004871, 2004872
Poland	Komisja Bioetyczna przy Okręgowej Izbie Lekarskiej w Rzeszowie, ul. Jana Dekerta 2, Rzeszów, 35-030	2004674, 2004371, 2004049, 2004334, 2004206, 2004381, 2004205, 2004208, 2004350, 2004305
Russian Federation	St. Petersburg State Budgetary Institution of Healthcare 'Children's Municipal Polyclinic No. 35' 168 Bldg. 2 Leninskiy Ave., St. Petersburg 196191	2004336, 2004106
	Medical Technologies LLC; 6 Nevzorovoy Str., St. Petersburg 192148;	2004212

Country	Name/Address of IRB/IEC	Site number
	State Budgetary Healthcare Institution of the Perm Territory 'Municipal Children's Clinical Polyclinic No. 5'	2004214
South Africa	Pharma Ethics Independent Research Ethics committee, 123 Amcor Road, Lyttelton Manor Pretoria, 0157	2004034, 2004108, 2004110, 2004712
	Wits Health Consortium, 31 Princess of Wales Terrace, Parktown Johannesburg, 2193	2004217, 2004109, 2004216
	1 Military Hospital Human Research Ethics Committee, Department of Neurology Private bag X 1026 Thaba Tswane 0143	2004111
	Stellenbosch University Human Research Ethics Committee, Stellenbosch University Private Bag X1, Matieland, 7602, Stellenbosch, South Africa	2004039
	University of Cape Town Human Research Ethics Committee, DEPARTMENT OF PAEDIATRICS AND CHILD HEALTH RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL KLIPFONTEIN ROAD RONDEBOSCH 7700	2004036
Spain	Hospital Universitario Clinico San Carlos, Puerta G - Planta 4ª Norte, C/ Profesor Martin Lagos, s/n Madrid, 28040	2004033, 2004112, 2004113, 2004114, 2004115, 2004218, 2004219, 2004311, 2004333, 2004344, 2004363, 2004369, 2004382, 2004385, 2004406, 2004675, 2004407, 2005603
Sweden	Etikprövningsmyndigheten, Box 2110, SE-750 02 Uppsala, SE-750 02	2004402, 2004116
Turkey	Ege University Ethics Committee, Ege Üniversitesi Tıp Fakültesi, Klinik Arastirmalar Etik Kurulu Izmir, 35100	2004222, 2004221, 2004223, 2004224
Ukraine	Dept of health of Chernivtsi city council, Communal Medical Institution City Clinical Children's Hospital, 4 Bukovynska St, Chernivtsi, 58001	2004117
	Ministry of Health of Ukraine, Communal Non-Commercial enterprise Saint Zinaida Children's Clinical Hospital of Sumy City Council, 28 Troiiska st, Sumy, 40022	2004227
	Vinnitsia regional Children's Clinical Hospital, 108 Khmelnytske shose st, Vinnitsia, 21000. Medical Ethics Commission	2004229
	State Institution Academician O.M Lukyanova Institute of Pediatrics, obstetrics and gynecology of national academy of medical sciences of Ukraine, 8 P. Mayborody str Kyiv, 04050	2004294
	Communal Non-Commercial enterprise of Kharkiv Regional Council regional Children's clinical hospital, 5 Ozeryanska st Kharkiv, 61093	2004322
	Odesa Regional State administration, department of health, communal enterprise, Odesa regional Children's clinical hospital, 3 Ac Vorobiov st, Odesa-31, 65031	2004338
	Ethics Commission at Communal Institution Dnipro City Children's Clinical Hospital No 5 of Dnipro City Council, 5 ivana Akinfiieva st, Dnipro 49027 Ukraine	2004633
United Kingdom	NRES Committee South Central - Berkshire, South West REC Centre, Level 3, Block B Bristol, BS1 2NT	2004355, 2004384, 2004682, 2004689, 2004383

Country	Name/Address of IRB/IEC	Site number
United States	WCG IRB 212 Carnegie Center, Suite 301 Princeton, NJ 08540, USA	2004023, 2004025, 2004027, 2004028, 2004030, 2004031, 2004032, 2004118, 2004236, 2004237, 2004239, 2004240, 2004243, 2004253, 2004255, 2004256, 2004258, 2004259, 2004260, 2004261, 2004263, 2004264, 2004267, 2004268, 2004278, 2004279, 2004280, 2004291, 2004292, 2004293, 2004314, 2004315, 2004316, 2004319, 2004323, 2004340, 2004345, 2004376, 2004386, 2004389, 2004394, 2004409, 2004613, 2004614, 2004615, 2004616, 2004618, 2004624, 2004634, 2004650, 2004652, 2004656, 2004657, 2004664, 2004677, 2004679, 2004680, 2004690, 2004697, 2004699, 2004700, 2004702, 2004746, 2004873, 2005604, 2005605, 2005606
	The University of Oklahoma, Institutional Review Board for the Protection of Human Subjects, 1105N. Stone wall Avenue, Oklahoma City, OK73117(FWA 007961)	2004026
	Nemours Office of Human Subjects Protection Nemours/Alfred I. duPont Hospital for Children 1600 Rockland Road Wilmington, DE 19803	2004029
	Institutional Review Board Ann & Robert H. Lurie Children's Hospital of Chicago, 25 East Chicago Avenue, Chicago, Illinois	2004238
	Cincinnati Children's Hospital Institutional Review Board, 3333 Burnet Avenue   MLC 7040   Cincinnati, OH 45229	2004241
	MetroHealth Institutional Review board, 2500 MetroHealth Drive, Cleveland Ohio 44109	2004281
	Creighton University office of the provost Research Compliance, 2500 California Plaza Omaha, NE 68178-0001	2004310
	Medical University of South Carolina, 179 Ashley Ave, Charleston, SC 29425	2004341
	University of Nebraska Medical Center, 42nd and Emile Streets Omaha, NE 68198 402-559-4000	2004391
	Nationwide Children's IRB, Nationwide Children's Hospital 700 Childrens Drive Columbus, OH 43205	2004658
	The University Of Tennessee, Health Science Centre Institutional Review Board 910 Madison Avenue, Suite 600 Memphis, TN 38163	2004662
	Marshfield Clinic Research Institute Institutional Review Board 1000N, Oak Ave Marshfield, WI 54449-5790	2004678
	EMORY UNIVERSITY Institutional Review Board 201 Dowman Dr, Atlanta, GA 30322, United States	2004708
	Navajo Nation Human Research Review Board Navajo Division of Health, P. O. Box 1390, Window Rock, AZ 86515	2004747, 2004748, 2004749

**Figure S1:** Participant disposition (CONSORT diagram): healthy preterm and term infants in the Phase 2b and MELODY trials.



Phase 2b final database lock: February 14, 2019. MELODY data cut-off: November 9, 2022.

<sup>a</sup>Informed consent signed.

<sup>b</sup>Includes all participants from the Phase 2b study and MELODY full enrollment cohort.

<sup>c</sup>One participant from MELODY was randomized twice in the study, was assigned two different subject IDs, and received two doses of nirsevimab 100 mg. One of the two subject IDs was excluded from participants randomized to avoid double counting the same individual in the analysis.

<sup>d</sup>Includes infants from Phase 2b weighing <5 kg and the full MELODY enrollment cohort.

<sup>e</sup>Includes one death of a randomized participant who never received nirsevimab.

<sup>f</sup>Two participants randomized to placebo incorrectly received nirsevimab; both participants were included in the as-treated population under the nirsevimab group. As-treated population: placebo (N = 1284), nirsevimab (N = 2570).

<sup>g</sup>One participant did not complete Day 361 and mistakenly had their end of a study status recorded as completed; this participant is not included among the discontinuations.

<sup>h</sup>Includes one participant from Phase 2b who did not complete the Day 361 visit, was considered an early discontinuation, and died on Day 367 due to bronchopneumonia; this death was considered unrelated to nirsevimab and is not included within the safety analysis.

<sup>i</sup>Four participants in each treatment group completed the Day 361 visit within the allowed 7-Day window but had not completed chronological Day 361 at the time of this safety analysis.

<sup>j</sup>One participant in MELODY died on Day 440 due to an automobile accident; this death is not included within the safety analysis.

<sup>k</sup>Based on 570 participants from Phase 2b weighing <5 kg who were planned to receive nirsevimab and were included in this analysis.

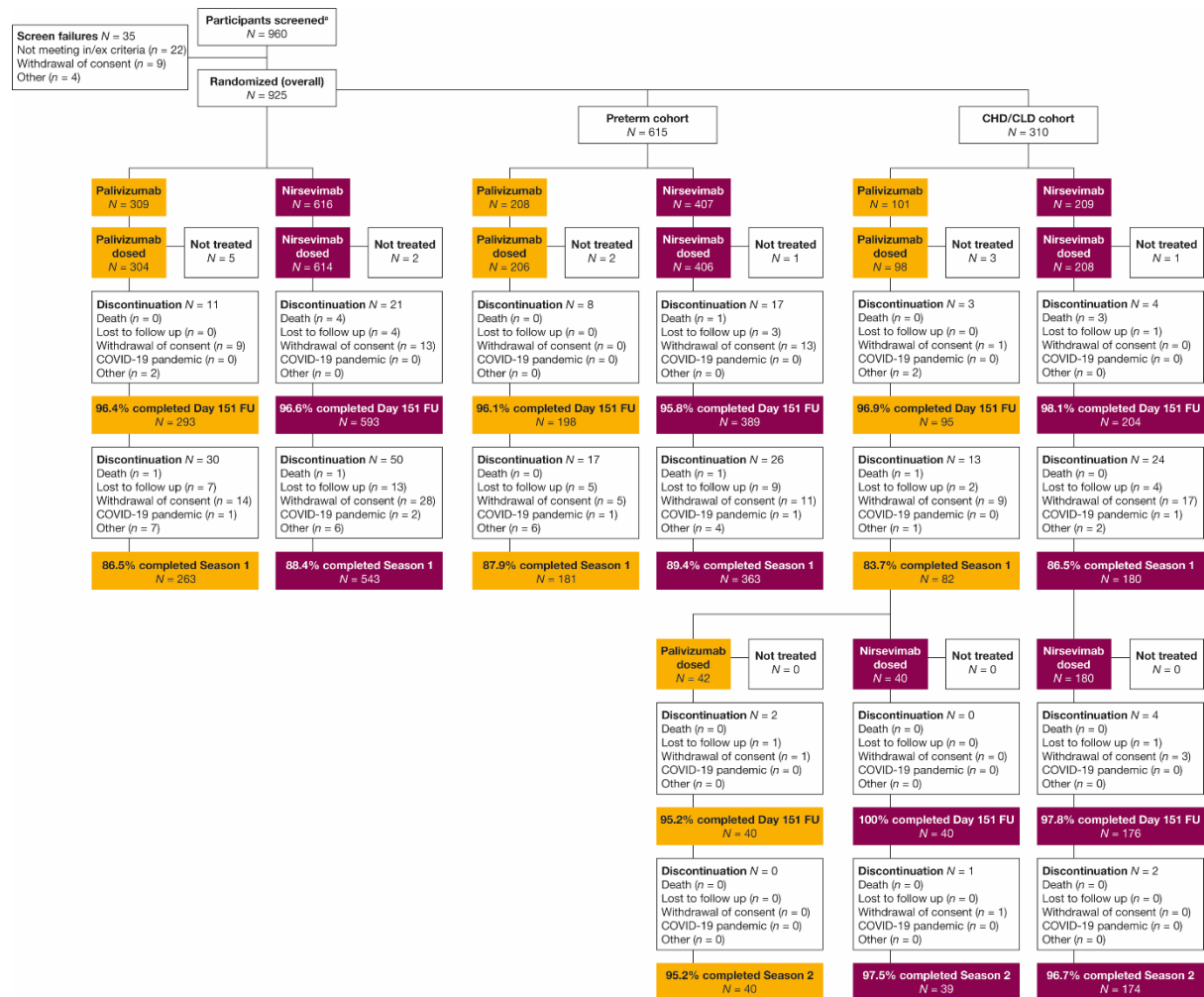
<sup>l</sup>Based on 290 participants from Phase 2b weighing <5 kg who were planned to receive placebo and were included in this analysis.

<sup>m</sup>Based on 1998 participants who received nirsevimab in MELODY.

<sup>n</sup>Based on 996 participants who received placebo in MELODY.

Abbreviations: CONSORT, Consolidated Standards of Reporting Trials; COVID-19, coronavirus disease 2019; FU, follow-up.

**Figure S2:** Participant disposition (CONSORT diagram): infants with CHD/CLD and preterm infants born  $\leq 35$  weeks 0 days GA without CHD/CLD in the MEDLEY trial.

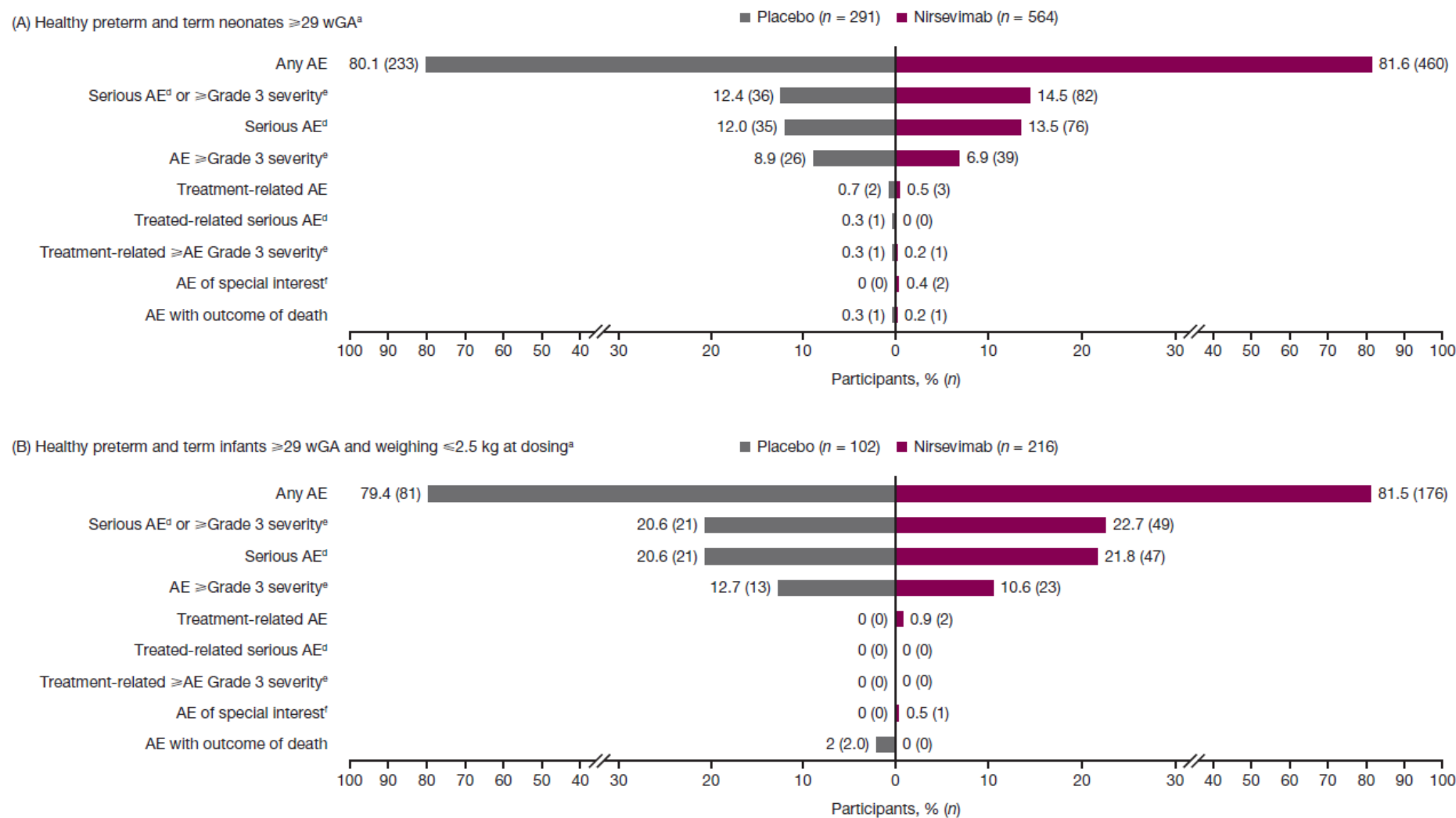


Final database lock: February 22, 2023.

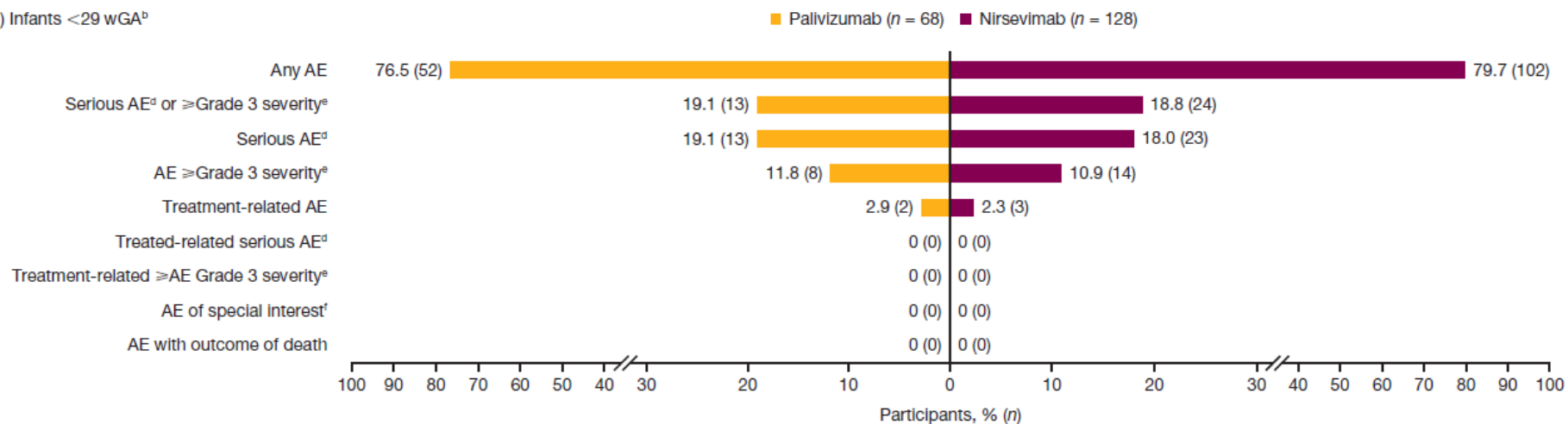
<sup>a</sup>Informed consent signed.

Abbreviations: CONSORT, Consolidated Standards of Reporting Trials; COVID-19, coronavirus disease 2019; FU, follow-up.

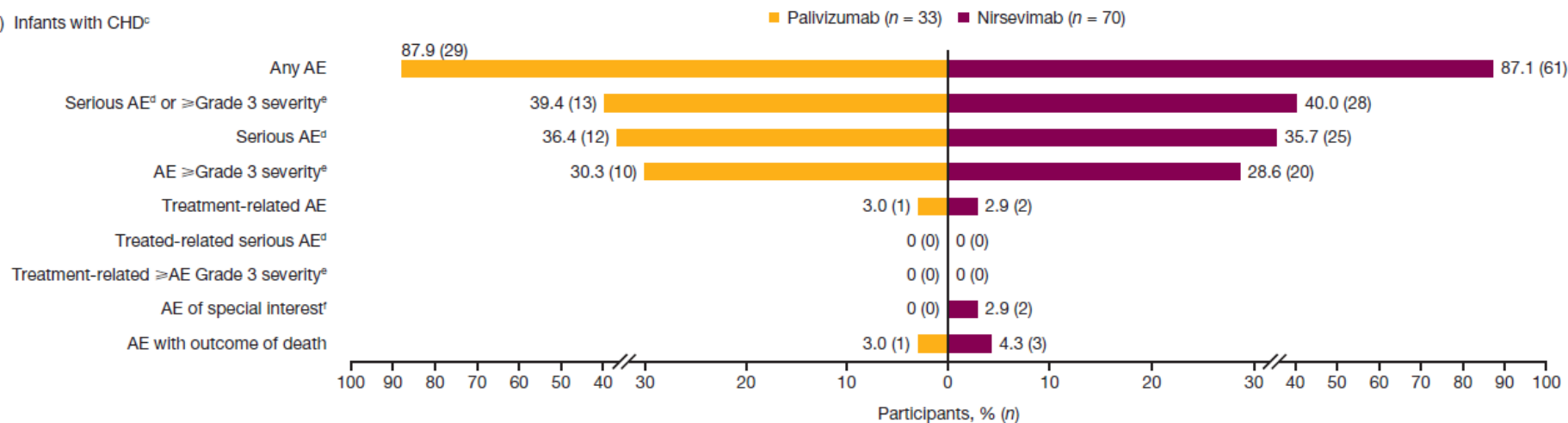
**Figure S3:** Summary of AEs through 360 days post-dose in healthy term and preterm infants born  $\geq 29$  wGA who were (A) neonates or (B) weighed  $< 2.5$  kg at dosing<sup>a</sup> and infants at higher risk of severe disease eligible for palivizumab who were (C) born  $< 29$  wGA,<sup>b</sup> (D) with CHD,<sup>c</sup> or (E) with CLD<sup>c</sup>.



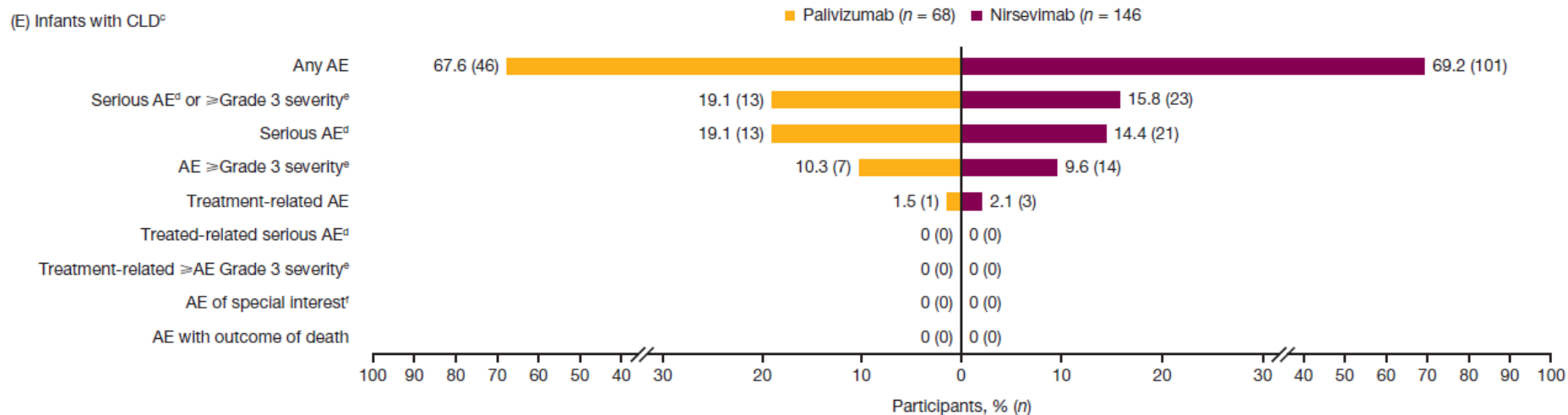
(C) Infants <29 wGA<sup>b</sup>



(D) Infants with CHD<sup>c</sup>







Participants with multiple events in the same category were counted once in that category; participants with events in >1 category were counted once in each category.

<sup>a</sup>Includes infants from Phase 2b weighing <5kg and the full MELODY enrollment cohort.

<sup>b</sup>Includes participants from the MEDLEY Season 1 preterm cohort and CHD/CLD cohort born <29 wGA. <sup>c</sup>Infants with both CHD and CLD were included in both the CHD and the CLD subpopulations.

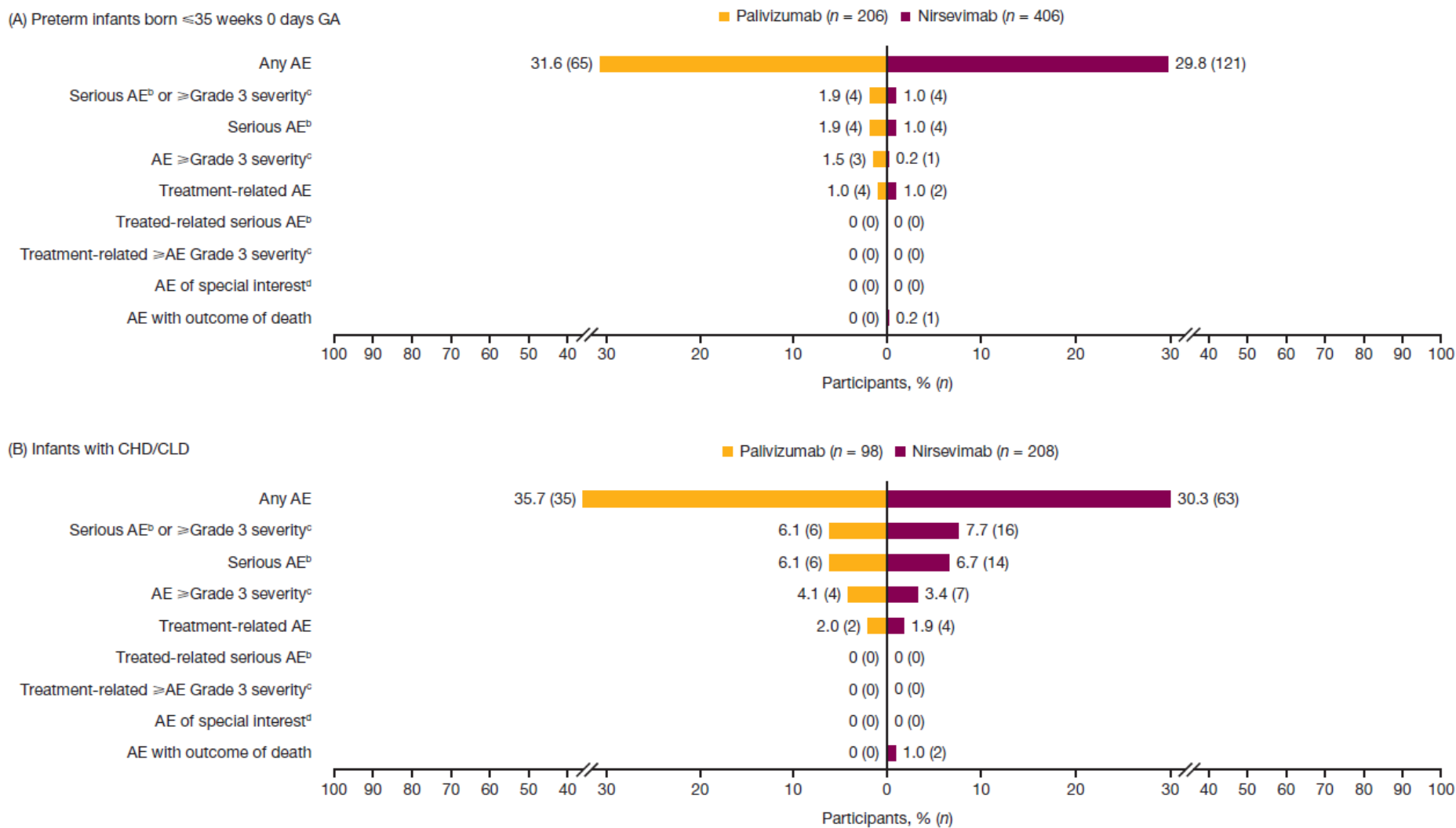
<sup>d</sup>Defined as death, life-threatening, requiring inpatient hospitalization, prolongation of existing hospitalization, persistent or significant disability/incapacity, important medical event, congenital anomaly/birth defect.

<sup>e</sup>Grade 1: mild, Grade 2: moderate; Grade 3: severe; Grade 4: life-threatening; Grade 5: fatal.

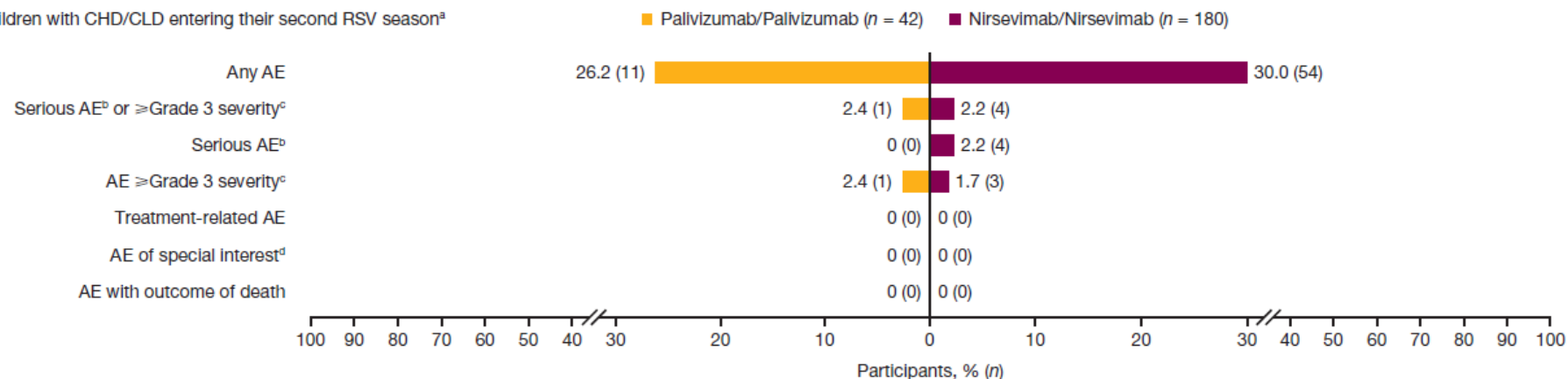
<sup>f</sup>Included immediate type I hypersensitivity reactions (eg, anaphylaxis), immune complex disease, and thrombocytopenia.

Abbreviations: AE, adverse event; CHD, congenital heart disease; CLD, chronic lung disease; wGA, weeks gestational age.

**Figure S4:** Summary of AEs within 30 days of dosing in (A) preterm infants born  $\leq 35$  weeks 0 days GA without CHD/CLD or (B) infants with CHD/CLD entering their first RSV season and (C) children with CHD/CLD entering their second RSV season<sup>a</sup>.



(C) Children with CHD/CLD entering their second RSV season<sup>a</sup>



Participants with multiple events in the same category were counted once in that category; participants with events in >1 category were counted once in each category.

<sup>a</sup>Before the second season, children with CHD/CLD randomized to nirsevimab in the first season received a single IM dose of 200 mg nirsevimab followed by 4x once-monthly IM doses of placebo (nirsevimab/nirsevimab) and those randomized to palivizumab in the first season were re-randomized 1:1 to either a single IM dose of 200 mg nirsevimab followed by 4x once-monthly IM doses of placebo (palivizumab/nirsevimab) or 5x once-monthly IM doses of palivizumab (15 mg/kg per dose; palivizumab/palivizumab).

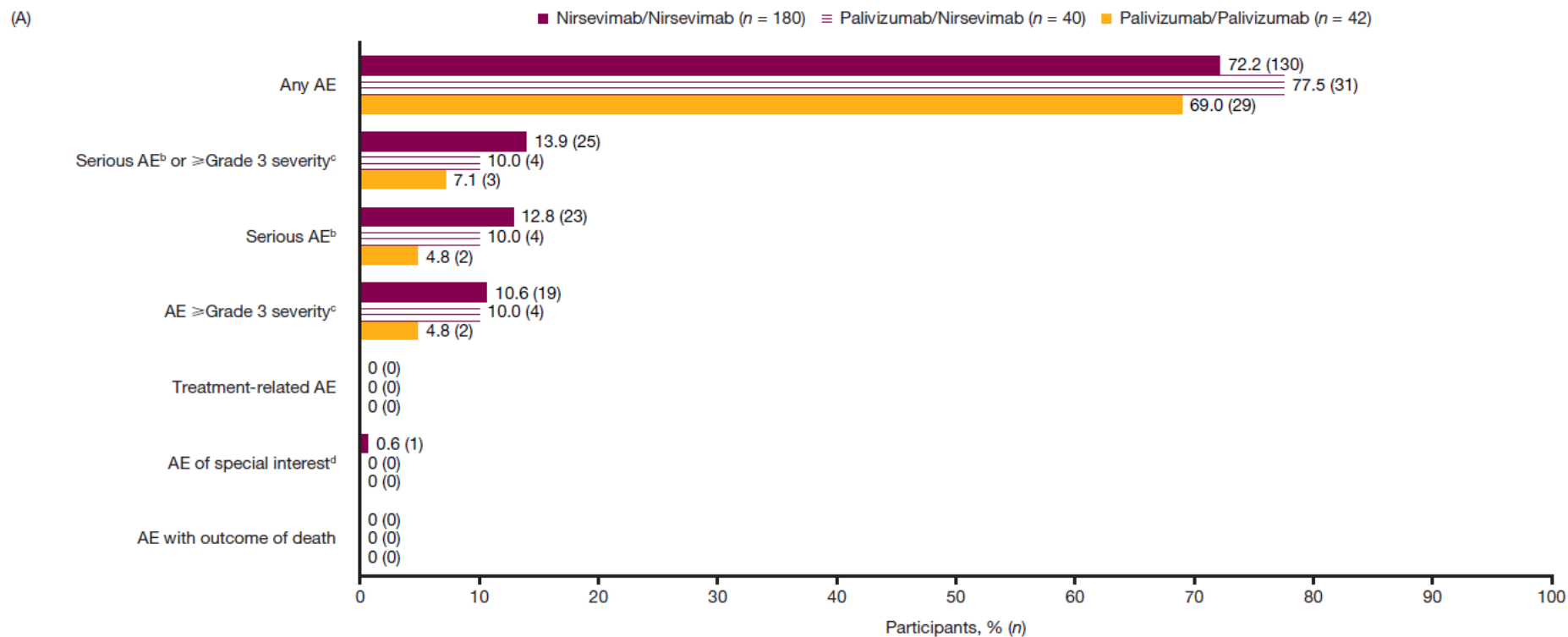
<sup>b</sup>Defined as death, life-threatening, requiring inpatient hospitalization, prolongation of existing hospitalization, persistent or significant disability/incapacity, important medical event, congenital anomaly/birth defect.

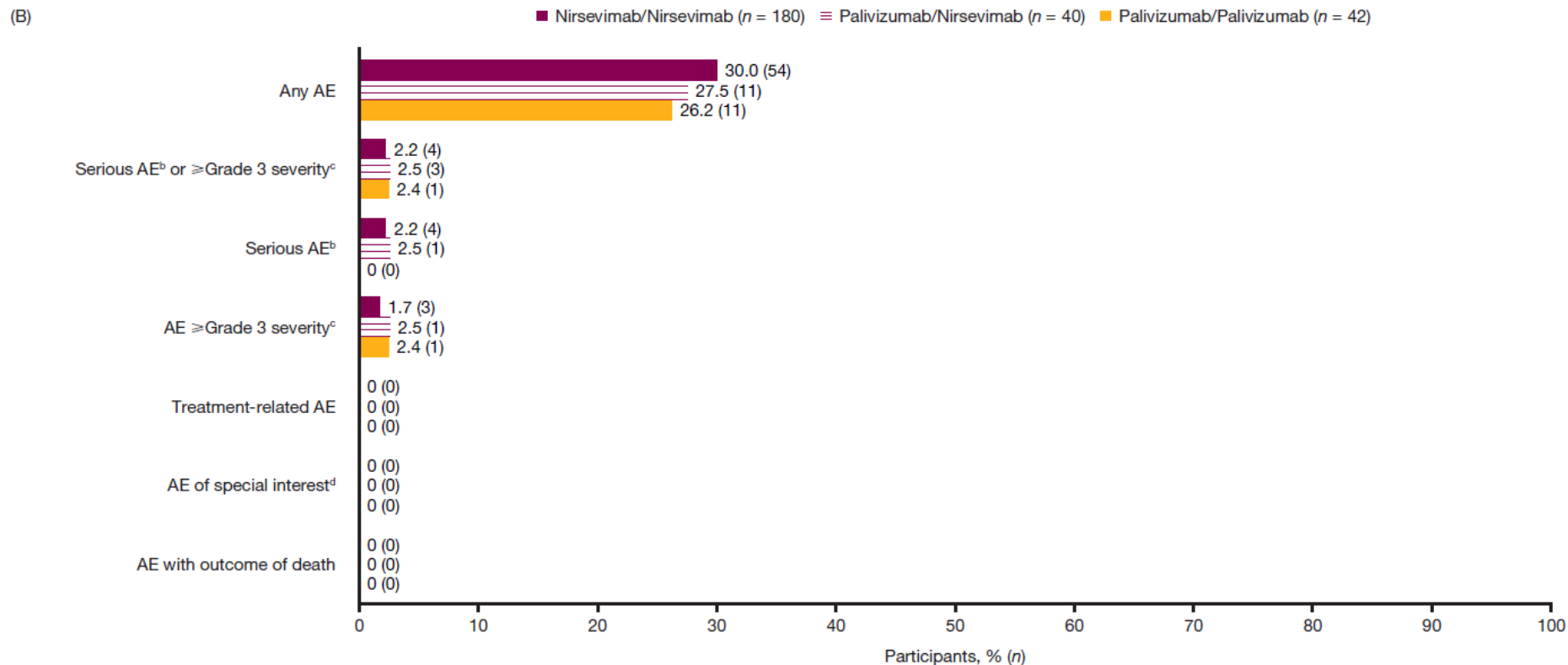
<sup>c</sup>Grade 1: mild; Grade 2: moderate; Grade 3: severe; Grade 4: life-threatening; Grade 5: fatal.

<sup>d</sup>Included immediate type I hypersensitivity reactions (eg, anaphylaxis), immune complex disease, and thrombocytopenia.

Abbreviations: AE, adverse event; CHD, congenital heart disease; CLD, chronic lung disease; GA, gestational age; IM, intramuscular; RSV, respiratory syncytial virus.

**Figure S5:** Summary of AEs in children with CHD/CLD entering their second RSV season through (A) 360 days and (B) 30 days post first dose in the second season<sup>a</sup>.





<sup>a</sup>Before the second season, children with CHD/CLD randomized to nirsevimab in the first season received a single IM dose of 200 mg nirsevimab followed by 4x once-monthly IM doses of placebo (nirsevimab/nirsevimab) and those randomized to palivizumab in the first season were re-randomized 1:1 to either a single IM dose of 200 mg nirsevimab followed by 4x once-monthly IM doses of placebo (palivizumab/nirsevimab) or 5x once-monthly IM doses of palivizumab (15 mg/kg per dose; palivizumab/palivizumab).

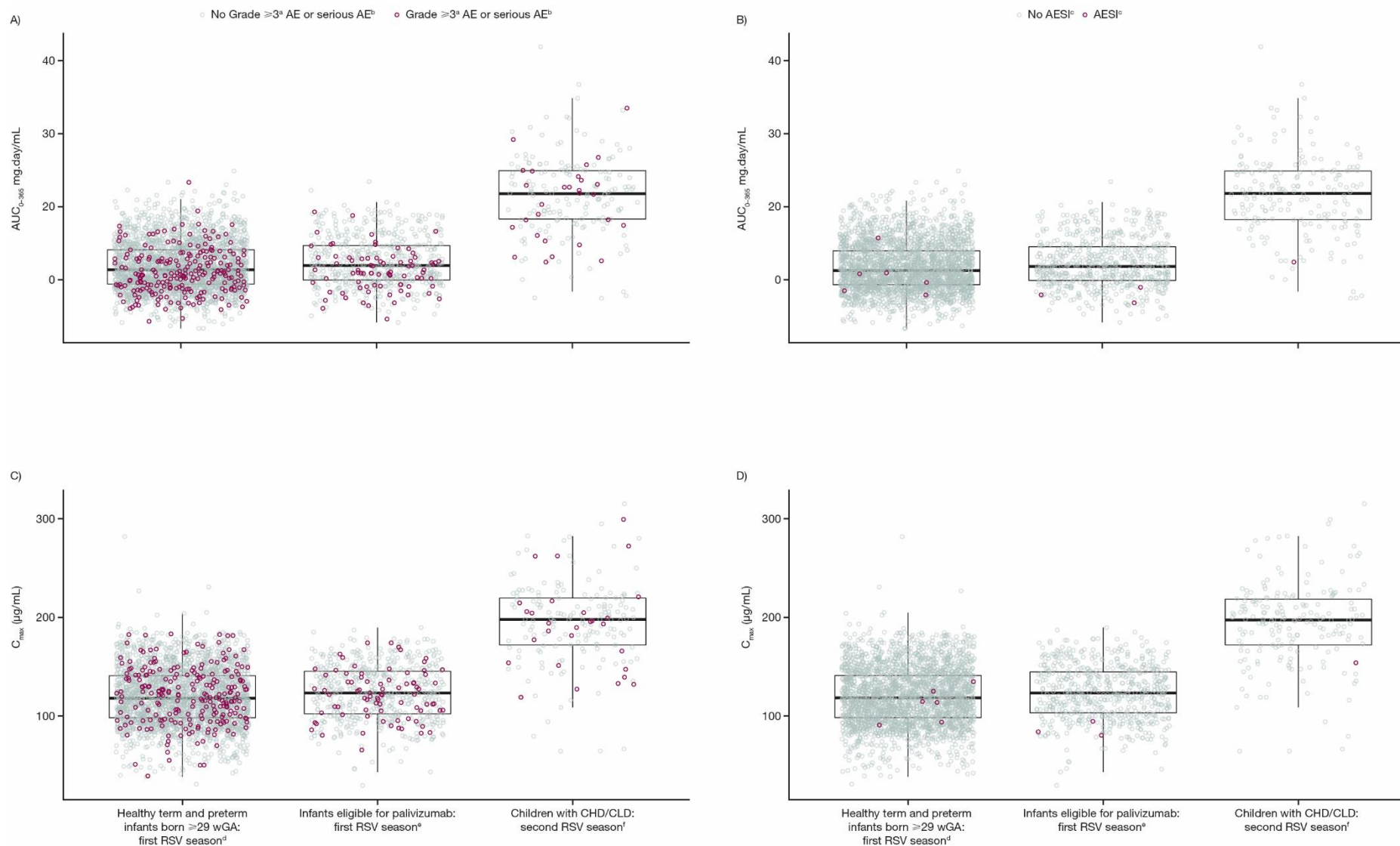
<sup>b</sup>Defined as death, life-threatening, requiring inpatient hospitalization, prolongation of existing hospitalization, persistent or significant disability/incapacity, important medical event, congenital anomaly/birth defect.

<sup>c</sup>Grade 1: mild; Grade 2: moderate; Grade 3: severe; Grade 4: life-threatening; Grade 5: fatal.

<sup>d</sup>Included immediate type I hypersensitivity reactions (eg, anaphylaxis), immune complex disease, and thrombocytopenia.

Abbreviations: AE, adverse event; CHD, congenital heart disease; CLD, congenital lung disease; IM, intramuscular; RSV, respiratory syncytial virus.

**Figure S6:** Nirsevimab serum  $AUC_{0-365}$  (A and B) and  $C_{max}$  (C and D) in participants with  $\geq$ Grade 3 AEs<sup>a</sup> or serious AEs<sup>b</sup> (A and C) and AESI<sup>c</sup> (B and D).



<sup>a</sup>Grade 1: mild; Grade 2: moderate; Grade 3: severe; Grade 4: life-threatening; Grade 5: fatal.

<sup>b</sup>Defined as death, life-threatening, requiring inpatient hospitalization, prolongation of existing hospitalization, persistent or significant disability/incapacity, important medical event, congenital anomaly/birth defect.

<sup>c</sup>Included immediate type I hypersensitivity reactions (eg, anaphylaxis), immune complex disease, and thrombocytopenia.

<sup>d</sup>Includes infants from Phase 2b weighing <5kg and the full MELODY enrollment cohort.

<sup>e</sup>Includes infants with CHD and/or CLD or infants born  $\leq 35$  weeks 0 days GA without CLD or CHD.

<sup>f</sup>Includes participants from the nirsevimab/nirsevimab and palivizumab/nirsevimab groups. Before the second season, children with CHD/CLD randomized to nirsevimab in the first season received a single IM dose of 200 mg nirsevimab followed by 4x once-monthly IM doses of placebo (nirsevimab/nirsevimab) and those randomized to palivizumab in the first season were re-randomized 1:1 to either a single IM dose of 200 mg nirsevimab followed by 4x once-monthly IM doses of placebo (palivizumab/nirsevimab) or 5x once-monthly IM doses of palivizumab (15 mg/kg per dose; palivizumab/palivizumab).

Abbreviations: AE, adverse event; AESI, adverse event of special interest; AUC<sub>0-365</sub>, area under the concentration-time curve from Day 0 to Day 365; CHD, congenital heart disease; CLD, chronic lung disease; C<sub>max</sub>, maximum serum concentration; IM, intramuscular; RSV, respiratory syncytial virus; wGA, weeks gestational age.

**Table S1:** Treatment Exposure and Follow-Up.

Safety Analysis Population	Extent of Exposure	Participants with Safety Follow-Up Through 360 Days Post-Dose, %
Healthy term and preterm infants born $\geq 29$ wGA <sup>a</sup> Phase 2b/MELODY	<ul style="list-style-type: none"> <li>3854 participants received nirsevimab (<math>n = 2570</math>) or placebo (<math>n = 1284</math>) <ul style="list-style-type: none"> <li>Received 50 mg dose: 53.6% of nirsevimab recipients</li> <li>Received 100 mg dose: 46.4% of nirsevimab recipients</li> </ul> </li> </ul>	96.5%
Infants with CHD/CLD or preterm infants born $\leq 35$ weeks 0 days GA without CHD/CLD MEDLEY Season 1	<ul style="list-style-type: none"> <li>Nirsevimab (<math>n = 614</math>): All received at least 1 active dose<sup>b</sup> <ul style="list-style-type: none"> <li>Received 50 mg dose: 56.2% of nirsevimab recipients<sup>c</sup></li> <li>Received 100 mg dose: 43.6% of nirsevimab recipients<sup>c,d</sup></li> </ul> </li> <li>Palivizumab (<math>n = 304</math>): 90.5% received at least 5 active doses<sup>b</sup></li> </ul>	87.8 %
Children with CHD/CLD entering their second RSV season <sup>e</sup> MEDLEY Season 2	<ul style="list-style-type: none"> <li>Nirsevimab/nirsevimab (<math>n = 180</math>): All received at least 1 active dose<sup>b</sup></li> <li>Palivizumab/nirsevimab (<math>n = 40</math>): All received at least 1 active dose<sup>b</sup></li> <li>Palivizumab/palivizumab (<math>n = 42</math>): 90.5% received at least 5 active doses<sup>b</sup></li> </ul>	96.6%

<sup>a</sup>Includes infants from Phase 2b weighing  $< 5$  kg and the full MELODY enrollment cohort.

<sup>b</sup>Participants with CHD could receive an active dose following cardiac surgery with cardiopulmonary bypass.

<sup>c</sup>Refers to the first dose of Season 1.

<sup>d</sup>A single participant weighing 6.1 kg received less than the intended volume due to syringe malfunction and received an estimated dose of 67 mg instead of 100 mg (recorded as a protocol deviation).

<sup>e</sup>Before the second season, children with CHD/CLD randomized to nirsevimab in the first season received a single IM dose of 200 mg nirsevimab followed by 4x once-monthly IM doses of placebo (nirsevimab/nirsevimab) and those randomized to palivizumab in the first season were re-randomized 1:1 to either a single IM dose of 200 mg nirsevimab followed by 4x once-monthly IM doses of placebo (palivizumab/nirsevimab) or 5x once-monthly IM doses of palivizumab (15 mg/kg per dose; palivizumab/palivizumab).

Abbreviations: CHD, congenital heart disease; CLD, chronic lung disease of prematurity; GA, gestational age; IM, intramuscular; RSV, respiratory syncytial virus; wGA, weeks gestational age.



**Table S2:** AESI Among Nirsevimab Recipients Across Pivotal Trials Through 360 Days Post-Dose.

<b>Trial</b>	<b>Relationship to Treatment</b>	<b>Toxicity Grade<sup>a</sup>/ Seriousness<sup>b</sup></b>	<b>Study Day of AE onset</b>	<b>MedDRA Preferred Term</b>	<b>Description</b>	<b>Days to Resolution<sup>c</sup></b>
<b>AESI of hypersensitivity</b>						
Phase 2b	Related	Grade 1/nonserious	Day 3	Rash	Maculopapular rash with generalized and symmetrical distribution on neck and trunk	13 days
Phase 2b	Related	Grade 1/nonserious	Day 120	Petechiae	Based on parental description of skin lesions with a generalized distribution on face, trunk, and arms; no laboratory or healthcare provider assessment	2 days
MELODY	Related	Grade 1/nonserious	Day 1	Rash papular	Erythematous maculopapular rash with generalized distribution on face, trunk, arms, hands and legs	6 days
MELODY	Related	Grade 1/nonserious	Day 1	Rash maculopapular <sup>d</sup>	Erythematous maculopapular rash with symmetrical distribution on legs	1 Day
MELODY	Related	Grade 1/nonserious	Day 1	Rash maculopapular	Erythematous maculopapular rash with a generalized distribution on head, face, neck, trunk, arms, and legs; treated with oral antihistamine	3 days
MELODY	Related	Grade 3/nonserious	Day 7	Rash	Macular rash with a generalized distribution on head, face, neck, trunk, arms, hands, legs, feet, buttocks/groin; exposure to new probiotic	20 days
MEDLEY Season 1 (preterm cohort)	Related	Grade 1/nonserious	Day 93 <sup>e</sup> after a dose of placebo	Rash maculopapular	Maculopapular rash with a generalized distribution on face and trunk following a dose of placebo for nirsevimab; treatment withdrawn	1 Day
<b>AESI of Thrombocytopenia</b>						
MEDLEY Season 1 CHD (hypoplastic	Not related	Grade 2/nonserious	Day 52	Heparin-induced thrombocytopenia	Thrombocytopenia following heparin administration for cardiac catheterization for stent angioplasty of aortic coarctation in an infant with CHD who also received a dose of palivizumab outside the study (Day 22) prior to	5 days

left heart syndrome <sup>f</sup> )					the event. Platelet nadir 23,000/ $\mu$ L 4 days after heparin administration; recovery to 202,000/ $\mu$ L following platelet transfusion	
MEDLEY Season 1 CHD (VSD, <sup>f</sup> ASD, Down syndrome)	Not related	Grade 1/nonserious	Day 40	Thrombocytopenia	Reported as thrombocytopenia due to nosocomial sepsis (on same Day as event of sepsis) during hospitalization for cardiac failure complicated by nosocomial pneumonia (non-RSV), sepsis, and ultimately death (Day 66) from cardiogenic shock following urgent surgery for repair of atrioventricular septal defect. No treatment for thrombocytopenia	12 days
MEDLEY Season 2 CHD (hypoplastic left heart syndrome <sup>f</sup> )	Not related	Grade 2/nonserious	Day 253	Pancytopenia	Thrombocytopenia and leukopenia in the context of aseptic meningitis due to roseola with confirmed Human Herpesvirus 6 infection (CSF sample). Platelet count at presentation (Day 253) was 59,000 / $\mu$ L. Platelet transfusion was required (Day 254) after which platelet count recovered to 105,000 / $\mu$ L at the time of discharge (Day 256). The WBC count was 1800 / $\mu$ L (reference range 4000 – 12,000 / $\mu$ L) at the time of the event and 3600 / $\mu$ L at discharge	78 days

<sup>a</sup>Grade 1: mild, Grade 2: moderate; Grade 3: severe; Grade 4: life-threatening; Grade 5: fatal.

<sup>b</sup>Defined as death, life-threatening, requiring inpatient hospitalization, prolongation of existing hospitalization, persistent or significant disability/incapacity, important medical event, congenital anomaly/birth defect.

<sup>c</sup>Total number of days to resolution includes Day of onset.

<sup>d</sup>Participant who developed antidrug antibodies to nirsevimab which were first detected at the Day 361 visit (actual Study Day 393).

<sup>e</sup>Participant received active dose of nirsevimab Day 1 per protocol and mistakenly received a second active dose of nirsevimab at Day 31, recorded as a protocol deviation.

<sup>f</sup>Primary cardiac lesion as reported by the investigator.

Abbreviations: AE, adverse event; AESI, adverse event of special interest; ASD, atrial septal defect; CHD, congenital heart disease; CSF, cerebrospinal fluid; MedDRA, Medical Dictionary for Medical Activities; RSV, respiratory syncytial virus; VSD, ventricular septal defect; WBC, white blood cell.

**Table S3:** Most Common AEs ( $\geq 1\%$  in Any Group) by Preferred Term within 14 Days Post-Dosing with or without Co-Administered Vaccine<sup>a</sup> in Healthy Term and Preterm Infants Born  $\geq 29$  wGA<sup>b</sup>

AEs, <i>n</i> (%)	Nirsevimab ( <i>n</i> = 2570)		Placebo ( <i>n</i> = 1284)	
	With Vaccine ( <i>n</i> = 695)	Without Vaccine ( <i>n</i> = 1875)	With Vaccine ( <i>n</i> = 374)	Without Vaccine ( <i>n</i> = 910)
Upper respiratory tract infection	26 (3.7)	64 (3.4)	17 (4.5)	19 (2.1)
Nasal congestion	20 (2.9)	24 (1.3)	6 (1.6)	11 (1.2)
Nasopharyngitis	15 (2.2)	38 (2.0)	13 (3.5)	22 (2.4)
Rhinitis	14 (2.0)	37 (2.0)	13 (3.5)	25 (2.7)
Pyrexia	11 (1.6)	15 (0.8)	2 (0.5)	7 (0.8)
Dermatitis diaper	9 (1.3)	23 (1.2)	2 (0.5)	9 (1.0)
Diarrhea	5 (0.7)	19 (1.0)	6 (1.6)	6 (0.7)
Seborrheic dermatitis	3 (0.4)	6 (0.3)	4 (1.1)	0
Constipation	2 (0.3)	6 (0.3)	1 (0.3)	9 (1.0)
Irritability	2 (0.3)	5 (0.3)	4 (1.1)	3 (0.3)

Participants with multiple events in the same preferred term were counted once in each of those preferred terms. Participants with events in more than one preferred term were counted once in each of those preferred terms.

<sup>a</sup>Co-administration within 14 days before or after nirsevimab or placebo with any of 7 pre-specified vaccine groups: polyvalent diphtheria-pertussis-tetanus containing vaccine, measles/mumps/rubella/varicella vaccine, rotavirus vaccine, pneumococcal vaccine, tuberculosis vaccine, hepatitis B vaccine, or influenza vaccine.

<sup>b</sup>Includes infants from Phase 2b weighing  $< 5$  kg and the full MELODY enrollment cohort.

Abbreviations: AE, adverse event; wGA, weeks gestational age.

**Table S4:** Treatment-Related AEs by System Organ Class and Preferred Term in Infants Entering Their First RSV Season Through 360 Days Post-Dose

AEs, <i>n</i> (%)	Healthy Term and Preterm Infants Born $\geq 29$ wGA <sup>a</sup>		Infants Eligible for Palivizumab Entering Their First RSV Season			
	Nirsevimab ( <i>n</i> = 2570)	Placebo ( <i>n</i> = 1284)	Preterm Infants Born $\leq 35$ Weeks 0 days GA		Infants With CHD/CLD	
			Nirsevimab ( <i>n</i> = 406)	Palivizumab ( <i>n</i> = 206)	Nirsevimab ( <i>n</i> = 208)	Palivizumab ( <i>n</i> = 98)
Any treatment-related AE	33 (1.3)	18 (1.4)	6 (1.5)	4 (1.9)	4 (1.9)	2 (2.0)
Blood and lymphatic system disorders	0	2 (0.2)	0	0	0	0
Anemia	0	1 (<0.1)	0	0	0	0
Neutropenia	0	1 (<0.1)	0	0	0	0
Gastrointestinal disorders	2 (<0.1)	2 (0.2)	0	1 (0.5)	0	0
Diarrhea	2 (<0.1)	0	0	1 (0.5)	0	0
Constipation	0	1 (<0.1)	0	0	0	0
Vomiting	0	1 (<0.1)	0	1 (0.5)	0	0
General disorders and administration site conditions	7 (0.3)	4 (0.3)	0	2 (1.0)	1 (0.5)	1 (1.0)
Pyrexia	3 (0.1)	3 (0.2)	0	2 (1.0)	1 (0.5)	0
Injection site pain	2 (<0.1)	0	0	0	0	0
Decreased activity	1 (<0.1)	0	0	0	0	0
Injection site swelling	1 (<0.1)	0	0	0	0	0
Fever neonatal	0	1 (<0.1)	0	0	0	0
Injection site induration	0	0	0	0	0	1 (1.0)
Infections and infestations	1 (<0.1)	2 (0.2)	0	0	0	0
Gastroenteritis	1 (<0.1)	0	0	0	0	0
Pharyngitis	0	1 (<0.1)	0	0	0	0
Upper respiratory tract infection	0	1 (<0.1)	0	0	0	0
Injury, poisoning and procedural complications	0	1 (<0.1)	0	0	0	0
Vaccine complication	0	1 (<0.1)	0	0	0	0
Investigations	1 (<0.1)	2 (0.2)	2 (0.5)	0	0	0
Body temperature increased	0	0	2 (0.5)	0	0	0
Transaminases increased	1 <sup>b</sup> (<0.1)	0	0	0	0	0
Neutrophil count decreased	0	2 (0.2)	0	0	0	0
Metabolism and nutrition disorders	1 (<0.1)	0	0	0	0	0
Decreased appetite	1 (<0.1)	0	0	0	0	0
Musculoskeletal and connective tissue disorders	0	0	1 (0.2)	0	0	0
Myosclerosis <sup>c</sup>	0	0	1 <sup>b</sup> (0.2)	0	0	0

Nervous system disorders	2 (<0.1)	1 (<0.1)	0	0	0	0
Hypersomnia	1 (<0.1)	0	0	0	0	0
Somnolence	1 (<0.1)	1 (<0.1)	0	0	0	0
Psychiatric disorders	4 (0.2)	3 (0.2)	2 (0.5)	0	2 (1.0)	1 (1.0)
Agitation	0	0	1 (0.2)	0	2 (1.0)	0
Irritability	4 (0.2)	3 (0.2)	1 (0.2)	0	0	1 (1.0)
Respiratory, thoracic and mediastinal disorders	1 (<0.1)	1 (<0.1)	0	0	0	0
Nasal congestion	1 (<0.1)	1 (<0.1)	0	0	0	0
Skin and subcutaneous tissue disorders	15 (0.6)	4 (0.3)	1 (0.2)	1 (0.5)	1 (0.5)	0
Rash maculopapular	7 (0.3)	0	1 (0.2)	0	0	0
Rash	3 (0.1)	0	0	0	1 (0.5)	0
Dermatitis	1 (<0.1)	0	0	0	0	0
Drug eruption	1 (<0.1)	0	0	0	0	0
Petechiae	1 (<0.1)	0	0	0	0	0
Rash papular	1 (<0.1)	1 (<0.1)	0	0	0	0
Skin hypopigmentation	1 (<0.1)	0	0	0	0	0
Eczema	0	1 (<0.1)	0	0	0	0
Rash macular	0	0	0	1 (0.5)	0	0

Participants with multiple events in the same preferred term were counted once in each of those preferred terms. Participants with events in more than one preferred term were counted once in each of those preferred terms.

<sup>a</sup>Includes infants from Phase 2b weighing <5kg and the full MELODY enrollment cohort.

<sup>b</sup>Mild (Grade 1) severity elevation of ALT and AST with return to normal reference range on a subsequent laboratory evaluation during the study.

<sup>c</sup>Event was reported by the investigator as "induration of the right thigh (muscular)" at site of injection of treatment and was inadvertently coded to the incorrect MedDRA Preferred Term of myosclerosis rather than injection site induration.

Abbreviations: AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CHD, congenital heart disease; CLD, congenital lung disease; GA, gestational age; RSV, respiratory syncytial virus; wGA, weeks gestational age.

**Table S5:** Nirsevimab Recipients with Post-Baseline Antidrug Antibodies Through 360 Days Post-Dose

<b>ADA Result</b>	<b>Healthy Term and Preterm Infants Born <math>\geq 29</math> wGA<sup>a</sup></b>	<b>Infants Eligible for palivizumab<sup>b</sup></b>	<b>Children with CHD/CLD Entering Their Second RSV Season<sup>c</sup></b>	
	<b>Nirsevimab (<i>n</i> = 2570)</b>	<b>Nirsevimab (<i>n</i> = 614)</b>	<b>Nirsevimab/Nirsevimab (<i>n</i> = 180)</b>	<b>Palivizumab/Nirsevimab (<i>n</i> = 40)<sup>f</sup></b>
Participants with any post-baseline ADA to nirsevimab, % ( <i>n</i> / <i>N</i> )	6.2% (155/2493)	5.8% (34/587) <sup>d</sup>	11.7% (21/180) <sup>e</sup>	2.5% (1/40)

<sup>a</sup>Includes infants from Phase 2b weighing <5kg and the full MELODY enrollment cohort.

<sup>b</sup>Includes infants with CHD/CLD and premature infants born  $\leq 35$  weeks 0 days GA without CHD/CLD.

<sup>c</sup>Before the second season, children with CHD/CLD randomized to nirsevimab in the first season received a single IM dose of 200 mg nirsevimab followed by 4x once-monthly IM doses of placebo (nirsevimab/nirsevimab) and those randomized to palivizumab in the first season were re-randomized 1:1 to either a single IM dose of 200 mg nirsevimab followed by 4x once-monthly IM doses of placebo (palivizumab/nirsevimab) or 5x once-monthly IM doses of palivizumab (15 mg/kg per dose; palivizumab/palivizumab).

<sup>d</sup>24 participants in the preterm cohort and 10 in the CHD/CLD cohort had any post-baseline ADA to nirsevimab.

<sup>e</sup>Reflects the number of participants who had any post-baseline ADA to nirsevimab in Season 1 or Season 2 (baseline defined as prior to Season 1 dose). Of the 180 participants with CHD/CLD who received nirsevimab in 2 consecutive seasons, ADA were detected in 8/180 (4.4%) participants through Day 361 of Season 1. Only one participant had detectable ADA in both Season 1 and Season 2, showing that the second nirsevimab dose (Season 2 Day 1) did not boost the immune response to nirsevimab. At Day 31 and Day 151 of Season 2, ADA were detected in 1/90 (1.1%) and 0/168 (0.0%) participants, respectively, showing that there was no immune priming in participants who received a prior nirsevimab dose.

<sup>f</sup>Participants in the palivizumab/nirsevimab group were evaluated for post-baseline ADA to nirsevimab in Season 2 with baseline defined as prior to the Season 2 nirsevimab dose (either Season 1 Day 361 or Season 2 Day 1).

Abbreviations: ADA, antidrug antibodies; CHD, congenital heart disease; CLD, chronic lung disease of prematurity; IM, intramuscular; RSV, respiratory syncytial virus; wGA, weeks gestational age.

**Table S6:** AEs by Post-Baseline Antidrug Antibody Status Through 360 Days Post-Dose

ADA Status, <i>n</i> (%)	Healthy Term and Preterm Infants Born ≥29 wGA <sup>a</sup>		Infants Eligible for Palivizumab Entering Their First RSV Season <sup>b</sup>	
	Nirsevimab ( <i>n</i> = 2570)	Placebo ( <i>n</i> = 1284)	Nirsevimab ( <i>n</i> = 614)	Palivizumab ( <i>n</i> = 304)
AEs by post-baseline ADA status				
Post-baseline ADA positive with at least 1 AE	143/155 (92.3%)	21/24 (87.5%)	27/34 (79.4%)	15/20 (75.0%)
Post-baseline ADA negative with at least 1 AE	2062/2415 (85.4%)	1067/1260 (84.7%)	417/580 (71.9%)	200/284 (70.4%)
Serious AEs <sup>c</sup> by post-baseline ADA status				
Post-baseline ADA positive with at least 1 serious AE	20/155 (12.9%)	2/24 (8.3%)	8/34 (23.5%)	1/20 (5.0%)
Post-baseline ADA negative with at least 1 serious AE	199/2415 (8.2%)	141/1260 (11.2%)	72/580 (12.4%)	37/284 (13.0%)

<sup>a</sup>Includes infants from Phase 2b weighing <5 kg and the full MELODY enrollment cohort.

<sup>b</sup>Includes infants with CHD/CLD and premature infants born ≤35 wGA without CHD/CLD.

<sup>c</sup>Defined as death, life-threatening, requiring inpatient hospitalization, prolongation of existing hospitalization, persistent or significant disability/incapacity, important medical event, congenital anomaly/birth defect.

Abbreviations: ADA, antidrug antibody; AE, adverse event; AESI, adverse event of special interest; CHD, congenital heart disease; CLD, chronic lung disease of prematurity; RSV, respiratory syncytial virus; wGA, weeks gestational age.

**Table S7:** AEs by Post-Baseline Antidrug Antibody Status in Children with CHD/CLD Entering Their Second RSV Season Through 360 Days Post-Dose

ADA Status, <i>n</i> (%)	Children with CHD/CLD Entering Their Second RSV Season		
	Nirsevimab/nirsevimab ( <i>n</i> = 180)	Palivizumab/nirsevimab ( <i>n</i> = 40)	Palivizumab/palivizumab ( <i>n</i> = 42)
AEs by post-baseline ADA status			
Post-baseline ADA positive with at least 1 AE	15/21 (71.4)	1/1 (100.0)	5/6 (83.3)
Post-baseline ADA negative with at least 1 AE	115/159 (72.3)	30/39 (76.9)	24/36 (66.7)
Serious AEs by post-baseline ADA status			
Post-baseline ADA positive with at least 1 serious AE	1/21 (4.8)	0/1 (0.0)	0/6 (0.0)
Post-baseline ADA negative with at least 1 serious AE	22/159 (13.8)	4/39 (10.3)	2/36 (5.6)

<sup>a</sup>Includes infants from Phase 2b weighing <5 kg and the full MELODY enrollment cohort.

<sup>b</sup>Includes infants with CHD/CLD and premature infants born ≤35 wGA without CHD/CLD.

<sup>c</sup>Defined as death, life-threatening, requiring inpatient hospitalization, prolongation of existing hospitalization, persistent or significant disability/incapacity, important medical event, congenital anomaly/birth defect.

Abbreviations: ADA, antidrug antibody; AE, adverse event; AESI, adverse event of special interest; CHD, congenital heart disease; CLD, chronic lung disease of prematurity; RSV, respiratory syncytial virus; wGA, weeks gestational age.



**Table S8:** Selected AEs Typically Solicited in Vaccine Studies in Infants within 7 Days Post-Dose in Healthy Term and Preterm Infants Born  $\geq 29$  wGA<sup>a</sup>

<b>AE, n (%)</b>	<b>Nirsevimab (n = 2570)</b>	<b>Placebo (n = 1284)</b>
Pyrexia	12 (0.5)	8 (0.6)
Injection site reactions <sup>b</sup>	7 (0.3)	0
Vomiting	6 (0.2)	4 (0.3)
Irritability	5 (0.2)	5 (0.4)
Somnolence	2 (<0.1)	2 (0.2)
Body temperature increased	1 (<0.1)	0
Decreased appetite	1 (<0.1)	0

Participants with multiple events in the same preferred term were counted once in each of those preferred terms. Participants with events in more than one preferred term were counted once in each of those preferred terms.

<sup>a</sup>Includes infants from Phase 2b weighing <5 kg and the full MELODY enrollment cohort.

<sup>b</sup>Grouped term including preferred terms of injection site pain, injection site induration, and injection site swelling.

Abbreviations: AE, adverse event; wGA, weeks gestational age.

**Table S9:** Serious AEs<sup>a</sup> by System Organ Class and Preferred Term in Children with CHD/CLD Entering Their Second RSV Season<sup>b</sup> Through 360 Days Post-Dose

Serious AEs, <i>n</i> (%)	Children with CHD/CLD Entering Their Second RSV Season		
	Nirsevimab/nirsevimab <i>n</i> = 180	Palivizumab/nirsevimab <i>n</i> = 40	Palivizumab/palivizumab <i>n</i> = 42
1 or more events	23 (12.8)	4 (10.0)	2 (4.8)
Cardiac disorders	1 (0.6)	0	0
Arrhythmia	1 (0.6)	0	0
Congenital, familial, and genetic disorders	1 (0.6)	0	0
Fallots tetralogy	1 <sup>c</sup> (0.6)	0	0
Gastrointestinal disorders	2 (1.1)	0	0
Duodenal ulcer	1 (0.6)	0	0
Intestinal obstruction	1 (0.6)	0	0
Infections and infestations	16 (8.9)	4 (10.0)	2 (4.8)
Bronchitis viral	3 (1.7)	0	0
Gastroenteritis	3 (1.7)	1 (2.5)	1 (2.4)
COVID-19	2 (1.1)	0	0
LRTI	2 (1.1)	1 (2.5)	0
Pneumonia	2 (1.1)	2 (5.0)	0
Bronchiolitis	1 (0.6)	0	0
Meningitis aseptic	1 (0.6)	0	0
Pharyngitis	1 (0.6)	0	0
Rotavirus infection	1 (0.6)	0	0
Upper respiratory tract infection	1 (0.6)	0	0
Viral upper respiratory tract infection	1 (0.6)	0	0
Bone abscess	0	1 (2.5)	0
Ear infection	0	1 (2.5)	0
Gastrointestinal infection	0	1 (2.5)	0
LRTI viral	0	0	1 (2.4)
Mastoiditis	0	1 (2.5)	0
Otitis media	0	1 (2.5)	0
Otitis media acute	0	1 (2.5)	0
Investigations	1 (0.6)	0	0
Catheterization cardiac	1 (0.6)	0	0
Metabolism and nutrition disorders	1 (0.6)	0	0
Failure to thrive	1 (0.6)	0	0
Nervous system disorders	1 (0.6)	1 (2.5)	0
Syncope	1 (0.6)	0	0

Nystagmus	0	1 (2.5)	0
Renal and urinary disorders	1 (0.6)	0	0
Calculus urinary	1 (0.6)	0	0
Respiratory, thoracic, and mediastinal disorders	2 (1.1)	0	0
Pleural effusion	2 (1.1)	0	0
Vascular disorders	1 (0.6)	0	0
Cyanosis	1 (0.6)	0	0

Participants with multiple events in the same category were counted once in that category; participants with events in >1 category were counted once in each category.

<sup>a</sup>Defined as death, life-threatening, requiring inpatient hospitalization, prolongation of existing hospitalization, persistent or significant disability/incapacity, important medical event, congenital anomaly/birth defect.

<sup>b</sup>Before the second season, children with CHD/CLD randomized to nirsevimab in the first season received a single IM dose of 200 mg nirsevimab followed by 4x once-monthly IM doses of placebo (nirsevimab/nirsevimab) and those randomized to palivizumab in the first season were re-randomized 1:1 to either a single IM dose of 200 mg nirsevimab followed by 4x once-monthly IM doses of placebo (palivizumab/nirsevimab) or 5x once-monthly IM doses of palivizumab (15 mg/kg per dose; palivizumab/palivizumab).

<sup>c</sup>Cardiac surgery for Tetralogy of Fallot.

Abbreviations: AE, adverse event; CHD, congenital heart disease; CLD, chronic lung disease of prematurity; COVID-19, coronavirus disease 2019; IM, intramuscular; LRTI, lower respiratory tract infection; RSV, respiratory syncytial virus.

**Table S10:** Treatment-Emergent AEs of Grade 3 or Greater Severity<sup>a</sup> by System Organ Class and Preferred Term in Children with CHD/CLD Entering Their Second RSV Season Through 360 Days Post-Dose

AE of Grade 3 or Greater Severity, <i>n</i> (%)	Children with CHD/CLD Entering Their Second RSV Season <sup>b</sup>		
	Nirsevimab/nirsevimab <i>n</i> = 180	Palivizumab/nirsevimab <i>n</i> = 40	Palivizumab/palivizumab <i>n</i> = 42
1 or more events	19 (10.6)	4 (10.0)	2 (4.8)
Cardiac disorders	2 (1.1)	0	0
Arrhythmia	1 (0.6)	0	0
Atrioventricular block	1 (0.6)	0	0
Cardiac failure	1 (0.6)	0	0
Congenital, familial, and genetic disorders	1 (0.6)	0	0
Fallots tetralogy	1 <sup>c</sup> (0.6)	0	0
Gastrointestinal disorders	2 (1.1)	0	0
Duodenal ulcer	1 (0.6)	0	0
Intestinal obstruction	1 (0.6)	0	0
General disorders and administration site conditions	1 (0.6)		
Pyrexia	1 (0.6)		
Infections and infestations	13 (7.2)	4 (10.0)	2 (4.8)
Viral upper respiratory tract infection	3 (1.7)	1 (2.5)	0
Pneumonia	3 (1.7)	0	0
Bronchitis viral	2 (1.1)	0	0
Gastroenteritis	2 (1.1)	0	1 (2.4)
COVID-19	2 (1.1)	0	0
LRTI	2 (1.1)	1 (2.5)	0
Meningitis aseptic	1 (0.6)	0	0
Nasopharyngitis	1 (0.6)	0	0
Pharyngitis	1 (0.6)	0	0
Rotavirus infection	1 (0.6)	0	0
Upper respiratory tract infection	1 (0.6)	0	0
Human herpesvirus 6 infection	1 (0.6)	0	0
Urinary tract infection	1 (0.6)	0	0
Bone abscess	0	1 (2.5)	0
Ear infection	0	1 (2.5)	0
Gastrointestinal infection	0	1 (2.5)	0
LRTI viral	0	0	1 (2.4)
Mastoiditis	0	1 (2.5)	0

Otitis media acute	0	2 (5.0)	0
Investigations	1 (0.6)	0	0
Catheterization cardiac	1 (0.6)	0	0
Nervous system disorders	2 (1.1)	0	0
Ataxia	1 (0.6)	0	0
Syncope	1 (0.6)	0	0
Respiratory, thoracic, and mediastinal disorders	2 (1.1)	0	0
Pleural effusion	2 (1.1)	0	0
Vascular disorders	1 (0.6)	0	0
Cyanosis	1 (0.6)	0	0

Participants with multiple events in the same category were counted once in that category; participants with events in >1 category were counted once in each category.

<sup>a</sup>Grade 1: mild, Grade 2: moderate; Grade 3: severe; Grade 4: life-threatening; Grade 5: fatal.

<sup>b</sup>Before the second season, children with CHD/CLD randomized to nirsevimab in the first season received a single IM dose of 200 mg nirsevimab followed by 4x once-monthly IM doses of placebo (nirsevimab/nirsevimab) and those randomized to palivizumab in the first season were re-randomized 1:1 to either a single IM dose of 200 mg nirsevimab followed by 4x once-monthly IM doses of placebo (palivizumab/nirsevimab) or 5x once-monthly IM doses of palivizumab (15 mg/kg per dose; palivizumab/palivizumab).

<sup>c</sup>Cardiac surgery for Tetralogy of Fallot.

Abbreviations: AE, adverse event; CHD, congenital heart disease; CLD, chronic lung disease of prematurity; COVID-19, coronavirus disease 2019; IM, intramuscular; LRTI, lower respiratory tract infection; RSV, respiratory syncytial virus.

**Supplementary Table S11.** Fatal Events in Healthy Term and Preterm Infants  $\geq 29$  wGA<sup>a</sup> Through 360 Days Post-Dose

Trial	Demographics (Age at Randomization; Sex; Race; wGA at Birth)	Country	Study Day (age) at Death	Underlying Comorbidity	Cause of Death <sup>b</sup>
Placebo group 0.2% (3/1284)					
Phase 2b	3.5 months; male; Black; 32 wGA	South Africa	343 (~15 months)	Moderately preterm	<b>Pericardial effusion;</b> brought to hospital after mother found him not breathing. Died in hospital
Phase 2b	1.1 months; female; Black; 30 wGA	South Africa	26 (~2 months)	Very preterm; respiratory distress syndrome; Klebsiella sepsis (resolved prior to enrollment)	<b>Nosocomial pneumonia;</b> with contributing <i>E coli</i> meningitis
Phase 2b	0.7 months; male; Black; 33 wGA	South Africa	109 (~4 months)	Moderately preterm	<b>Pneumonia;</b> complicated by left-sided empyema; treated with traditional herbal medicine at home and was deceased on arrival to hospital
Nirsevimab group 0.2% (6/2570)					
Phase 2b	3.9 months; female; Black; 31 wGA	South Africa	123 (~8 months)	Very preterm	<b>Unknown;</b> mother reported infant was well when put to bed, found deceased in the morning; twin (nirsevimab group) completed study
Phase 2b	1.9 months; male; White; 32 wGA	Estonia	97 (~5 months)	Moderately preterm; respiratory distress syndrome	<b>Pulmonary vein stenosis;</b> unknown at study entry
MELODY	3.1 months; male; Black; 37 wGA	South Africa	143 (~8 months)	No underlying medical history	<b>Gastroenteritis;</b> No healthcare provider visit for the illness. Pronounced dead on arrival to emergency services. History of two prior episodes of gastroenteritis
MELODY	6.8 months; female; Black; 38 wGA	South Africa	338 (~18 months)	No underlying medical history	<b>Acute gastroenteritis;</b> No healthcare provider visit for the illness. Found lifeless after 2-3 days history of vomiting and diarrhea. Pronounced dead on arrival to emergency services

MELODY	0.03 months; male; White; 40 wGA	Israel	140 (~5 months)	No underlying medical history	<b>Unknown;</b> suspected undiagnosed chronic illness due to failure to thrive, AEs of recurrent vomiting, hypoglycemia, and anemia requiring transfusion <b>Skull base fracture;</b> from automobile accident
MELODY	5.03 months; female; mixed race; 38 wGA	Panama	286 (~14.5 months)	No underlying medical history	

<sup>a</sup>Includes infants from Phase 2b weighing <5 kg and the full MELODY enrollment cohort.

<sup>b</sup>MedDRA Preferred Terms in bold

Abbreviations: AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities; wGA, weeks gestational age.

**Supplementary Table S12.** Fatal Events in Infants At Higher Risk of Severe RSV Disease<sup>a</sup> Through 360 Days Post-Dose

MEDLEY Season	Demographics (Age at Randomization; Sex; Race; wGA)	Country	Study Day (age) at Death	Underlying Comorbidity	Cause of Death <sup>b</sup>
<b>Infants born ≤35 weeks 0 days GA without CHD/CLD – Palivizumab group 0% (0/206)</b>					
<b>Infants born ≤35 weeks 0 days GA without CHD/CLD – Nirsevimab group 0.5% (2/406)</b>					
Season 1	7.5 months; male; White; 29 wGA	Ukraine	162 (~13 months)	Very preterm; Neonatal encephalopathy	Severe <b>COVID-19</b> pneumonia, admitted to ICU and died in the hospital
Season 1	1.2 months; male; White; 32 wGA	Bulgaria	52 (~3 months)	Moderately preterm; Congenital Cytomegalovirus infection	<b>Bronchiolitis</b> , leading to acute cardiovascular and respiratory failure; severe protein calorie malnutrition at presentation
<b>Infants with CLD/CHD – Palivizumab group 1.0% (1/98)</b>					
Season 1	0.8 months; female; White; 38 wGA	Lithuania	155 (~6 months)	CHD (ASD, <sup>c</sup> PDA); agenesis of the corpus callosum; cytogenic abnormality – feminine chromosomal mutation 46XX[11;22][q13.2;11.2])	<b>Respiratory insufficiency</b> due to bronchiolitis
<b>Infants with CLD/CHD – Nirsevimab group 1.4% (3/208)</b>					
Season 1	2.8 months; female; White; 39 wGA	Hungary	19 (~3 months)	CHD (partially corrected VSD, <sup>c</sup> ASD, coarctation of the aorta, PDA); dysgenesis of the corpus callosum; congenital cystic kidney disease	Sudden death due to <b>bronchopneumonia</b>
Season 1	2.3 months; female; other; 38 wGA	Mexico	66 (~4.5 months)	CHD (VSD, <sup>c</sup> ASD); Trisomy 21; Hypothyroidism	<b>Cardiogenic shock</b>
Season 1	6.5 months; female; White; 38 wGA	Russian Federation	19 (~3 months)	CHD (congenital pulmonary valve atresia with VSD, <sup>c</sup> MAPCA with unifocalization and creation of systemic pulmonary anastomosis); cerebral ischemia	<b>Cardiac failure</b> , pulmonary atresia

<sup>a</sup>Additional details on fatal events in the MEDLEY trial have been previously published (Domachowske JB, et al. *N Engl J Med* 2022; 386:892–894).

<sup>b</sup>MedDRA Preferred Terms in bold.

<sup>c</sup>Primary cardiac lesion as reported by the investigator.

Abbreviations: ASD, atrial septal defect; CHD, congenital heart disease; CLD, chronic lung disease of prematurity; COVID-19, coronavirus disease 2019; GA, gestational



age; ICU, intensive care unit; MAPCA, major aortopulmonary collateral arteries; MedDRA, Medical Dictionary for Regulatory Activities; PDA, patent ductus arteriosus; VSD, ventricular septal defect; wGA, weeks gestational age.