# Supplementary information

**Supplementary Note 1. Case narratives of two infants with resistance-associated substitutions**

Two infants in the Phase 2b trial experienced a medically attended (MA) respiratory syncytial virus (RSV) lower respiratory tract infection (LRTI), had their infection subtyped as RSV B, and met the primary case definition had three nirsevimab binding substitutions (I64T, N208S, K68E) associated with clinical resistance. Both had a clinical course in line with RSV disease in premature infants in the first year of life.

The first infant (34 weeks gestational age at birth and 5.9 kg at dosing) had an RSV isolate containing the nirsevimab binding substitutions I64T:K68E. No medical history was reported prior to enrollment; medications included vitamin supplementation. The MA RSV LRTI event was reported as a viral pneumonia due to RSV and occurred 118 days post-dose. The infant became symptomatic 2 days after hospital discharge for a preceding human metapneumovirus (hMPV)-associated LRTI (onset 95 days post-dose), and the investigator suspected the RSV LRTI was a nosocomial infection. The infant was re-hospitalized 2 days after symptom onset. A central nasal swab was positive for RSV B and negative for hMPV; local test was positive for RSV. The infant was hospitalized for 12 days and treated with supplemental oxygen in the intensive care unit (ICU) for 9 days, in addition to bronchodilators, systemic steroids, and an antibiotic. The infant recovered and was discharged from the hospital. Over the course of the study, the infant also had six non-RSV MA LRTIs, five of which required hospitalization with one necessitating ICU admission (the above mentioned hMPV-associated LRTI) with continuous positive airway pressure and high flow nasal cannula in conjunction with supplemental oxygen as maximal respiratory support measures. During a hospitalization for an event of viral pneumonia post-dose, the infant underwent diagnostic evaluations for investigation of tracheal aspiration, cystic fibrosis, and immunologic alterations which were ruled out. The infant was diagnosed with bronchomalacia and subsequently maintained on home oxygen after discharge. All LRTI events resolved with the exception of an event of obstructive bronchitis approximately 1 year post-dose; this event was ongoing at the end of the study.

The second infant (34 weeks gestational age at birth and 5.5 kg at dosing) had an RSV isolate containing the nirsevimab binding site substitution N208K. A medical history of RSV-negative bronchitis prior to enrollment was reported; medications included vitamin supplementation. The MA RSV LRTI event was reported as bronchiolitis and occurred 45 days post-dose. A central nasal swab was positive for RSV B and negative for hMPV; local test was positive for RSV. The infant was hospitalized for total of 14 days, comprising ICU admission, mechanical ventilation, and supplemental oxygen. Treatment included bronchodilators, systemic steroids, inhaled epinephrine, and antibiotics. The infant recovered and was discharged. Over the course of the study, the infant had two non-RSV MA LRTIs reported as events of bronchitis, one of which required hospitalization for 6 days, during which the infant was treated with supplemental oxygen, systemic corticosteroids, and bronchodilator. All LRTI events resolved.

**Supplementary Table S1 |** Summary of case definitions.

| Efficacy endpoint | Investigator assesses to have LRTI based on AE coding URTI/LRTI | Clinical sign of LRT involvement[a] | Indicator of disease severity[b] | Meets per protocol definition of MA RSV LRTI | RSV test result[c] | Setting of care |
|---|---|---|---|---|---|---|
| **Primary** | | | | | | |
| MA RSV LRTI | Yes | Documented as present | Documented as present | Yes | Positive | Inpatient or outpatient |
| **Secondary** | | | | | | |
| MA RSV LRTI with hospitalization | Yes | Documented as present | Documented as present | Yes | Positive | Inpatient |
| **Exploratory, RSV respiratory illness** | | | | | | |
| RSV unscheduled event | Yes or no | May or not be present | May or not be present | No | Positive | Inpatient or Outpatient |
| Non-protocol defined LRTI outpatient event | Yes | May or not be present[d] | May or not be present[d] | No | Positive | Outpatient |
| Hospitalization due to RSV Non-LRTI | Yes or no | May or not be present[d] | May or not be present[d] | No | Positive | Inpatient |

[a]Includes at least one of the following: Rhonchi, rales, crackles, wheeze.

[b]Includes at least one of the following: Hypoxemia, acute hypoxic or ventilatory failure; new onset apnea, nasal flaring, retractions, grunting, dehydration due to respiratory distress.

[c]Confirmed from central test by RT-PCR.

[d]Includes cases where insufficient documentation of the event was available to the investigator.

AE, adverse event; LRT, lower respiratory tract; LRTI, lower respiratory tract infection; MA, medically attended; RSV, respiratory syncytial virus; RT-PCR, reverse transcriptase polymerase chain reaction; URTI, upper respiratory tract infection.

**Supplementary Table S2 |** Prevalence and frequency of all major variant substitutions observed for cases that met the primary case definition in the Phase 2b and MELODY trials.

| Sampling period | Amino acid substitutions in RSV F | Prevalence in surveillance studies (%) | Frequency | | |
|---|---|---|---|---|---|
| | | | Placebo n (%) | Nirsevimab (n (%) | Total n (%) |
| | | **Phase 2b – RSV A** | | | |
| **Through 150 days post-dose** | | | **n = 22** | **n = 11** | **n = 33** |
| | T13A | 4.66 | 0 (0) | 1 (9.1) | 1 (3) |
| | T13I | 0.07 | 1 (4.5) | 0 (0) | 1 (3) |
| | I14V | 0.07 | 1 (4.5) | 0 (0) | 1 (3) |
| | A17V | 0.21 | 1 (4.5) | 1 (9.1) | 2 (6.1) |
| | C21S | NA | 1 (4.5) | 0 (0) | 1 (3) |
| | F22I | 0.07 | 1 (4.5) | 0 (0) | 1 (3) |
| | A23T | 5.32 | 2 (9.1) | 1 (9.1) | 3 (9.1) |
| | S25N | 0.42 | 0 (0) | 1 (9.1) | 1 (3) |
| | G71S | NA | 1 (4.5) | 0 (0) | 1 (3) |
| | V76I | NA | 0 (0) | 1 (9.1) | 1 (3) |
| | S99N | 0.1 | 1 (4.5) | 0 (0) | 1 (3) |
| | A102S | 0.03 | 1 (4.5) | 1 (9.1) | 2 (6.1) |
| | N116Y | NA | 1 (4.5) | 0 (0) | 1 (3) |
| | N120S | 0.35 | 1 (4.5) | 0 (0) | 1 (3) |
| | K123E | 0.03 | 0 (0) | 1 (9.1) | 1 (3) |
| | V127A | 1.15 | 0 (0) | 1 (9.1) | 1 (3) |
| | S213R | 0.1 | 0 (0) | 1 (9.1) | 1 (3) |
| | K419E | 0.1 | 1 (4.5) | 1 (9.1) | 2 (6.1) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| **151–360 days post-dose** | | | **n = 2** | **n = 3** | **n = 5** |
| | I14V | 0.07 | 0 (0) | 1 (33.3) | 1 (20) |
| | A23T | 5.32 | 0 (0) | 2 (66.7) | 2 (40) |

| | | | | | |
|---|---|---|---|---|---|
| | R113K | 0.1 | 1 (50) | 0 (0) | 1 (20) |
| | Y117H | 1.39 | 1 (50) | 0 (0) | 1 (20) |
| | S190N | 0.07 | 0 (0) | 1 (33.3) | 1 (20) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| | | **Phase 2b – RSV B** | | | |
| **Through 150 days post-dose** | | | **n = 22** | **n = 14** | **n = 36** |
| | L4P | 2.25 | 1 (4.5) | 0 (0) | 1 (2.8) |
| | F12L | 7.21 | 1 (4.5) | 2 (14.3) | 3 (8.3) |
| | F15I | NA | 1 (4.5) | 0 (0) | 1 (2.8) |
| | F15L | 99.57 | 21 (95.5) | 14 (100) | 35 (97.2) |
| | A16T | 1.21 | 1 (4.5) | 0 (0) | 1 (2.8) |
| | A16V | 1.57 | 1 (4.5) | 0 (0) | 1 (2.8) |
| | I64T | NA | 0 (0) | 1 (7.1) | 1 (2.8) |
| | K68E | NA | 0 (0) | 1 (7.1) | 1 (2.8) |
| | A103V | 98.5 | 22 (100) | 14 (100) | 36 (100) |
| | T118I | 0.07 | 1 (4.5) | 0 (0) | 1 (2.8) |
| | V127I | 0.07 | 0 (0) | 1 (7.1) | 1 (2.8) |
| | L172Q | 98.61 | 22 (100) | 14 (100) | 36 (100) |
| | S173L | 98.36 | 22 (100) | 14 (100) | 36 (100) |
| | K191R | 68.61 | 8 (36.4) | 4 (28.6) | 12 (33.3) |
| | I206M | 68.89 | 8 (36.4) | 4 (28.6) | 12 (33.3) |
| | N208S | NA | 0 (0) | 1 (7.1) | 1 (2.8) |
| | Q209R | 68.18 | 8 (36.4) | 4 (28.6) | 12 (33.3) |
| | S276N | 7.14 | 2 (9.1) | 2 (14.3) | 4 (11.1) |
| | K327R | 0.11 | 0 (0) | 1 (7.1) | 1 (2.8) |
| | E463D | 7 | 1 (4.5) | 2 (14.3) | 3 (8.3) |

| | | | | | |
|---|---|---|---|---|---|
| | I527M | 0.04 | 1 (4.5) | 0 (0) | 1 (2.8) |
| | A543T | 0.07 | 1 (4.5) | 0 (0) | 1 (2.8) |
| | K574N | 0.07 | 0 (0) | 1 (7.1) | 1 (2.8) |
| | **Nirsevimab binding site** | | | | |
| | I64T | NA | 0 (0) | 1 (7.1) | 1 (2.8) |
| | K68E | NA | 0 (0) | 1 (7.1) | 1 (2.8) |
| | I206M | 68.89 | 8 (36.4) | 4 (28.6) | 12 (33.3) |
| | N208S | NA | 0 (0) | 1 (7.1) | 1 (2.8) |
| | Q209R | 68.18 | 8 (36.4) | 4 (28.6) | 12 (33.3) |
| | **Palivizumab binding site** | | None | | |
| **151–360 days post-dose** | | | **n = 2** | **n = 3** | **n = 5** |
| | F15L | 99.57 | 2 (100) | 3 (100) | 5 (100) |
| | A16V | 1.57 | 0 (0) | 1 (33.3) | 1 (20) |
| | Y33F | 0.07 | 0 (0) | 1 (33.3) | 1 (20) |
| | A103V | 98.5 | 2 (100) | 3 (100) | 5 (100) |
| | V127I | 0.07 | 1 (50) | 0 (0) | 1 (20) |
| | L172Q | 98.61 | 2 (100) | 3 (100) | 5 (100) |
| | S173L | 98.36 | 2 (100) | 3 (100) | 5 (100) |
| | K191R | 68.61 | 1 (50) | 0 (0) | 1 (20) |
| | I206M | 68.89 | 1 (50) | 0 (0) | 1 (20) |
| | Q209R | 68.18 | 1 (50) | 0 (0) | 1 (20) |
| | **Nirsevimab binding site** | | | | |
| | I206M | 68.89 | 1 (50) | 0 (0) | 1 (20) |
| | Q209R | 68.18 | 1 (50) | 0 (0) | 1 (20) |
| | **Palivizumab binding site** | | None | | |

| MELODY full cohort – RSV A | | | | | |
|---|---|---|---|---|---|
| **Through 150 days post-dose** | | | **n = 23** | **n = 13** | **n = 36** |
| | L6H | 0.14 | 1 (4.3) | 0 (0) | 1 (2.8) |
| | T8I | 0.45 | 0 (0) | 1 (7.7) | 1 (2.8) |
| | T12I | 6.75 | 6 (26.1) | 2 (15.4) | 8 (22.2) |
| | T13A | 4.66 | 2 (8.7) | 1 (7.7) | 3 (8.3) |
| | L15F | 2.09 | 0 (0) | 2 (15.4) | 2 (5.6) |
| | L20F | 0.77 | 1 (4.3) | 0 (0) | 1 (2.8) |
| | A23T | 5.32 | 1 (4.3) | 0 (0) | 1 (2.8) |
| | A103T | 1.91 | 1 (4.3) | 1 (7.7) | 2 (5.6) |
| | A107T | 1.04 | 0 (0) | 2 (15.4) | 2 (5.6) |
| | F114S | 0.94 | 2 (8.7) | 0 (0) | 2 (5.6) |
| | M115T | 0.87 | 1 (4.3) | 0 (0) | 1 (2.8) |
| | L119F | 0.07 | 0 (0) | 1 (7.7) | 1 (2.8) |
| | T122A | 11.58 | 3 (13) | 5 (38.5) | 8 (22.2) |
| | K123Q | 3.62 | 0 (0) | 1 (7.7) | 1 (2.8) |
| | V127A | 1.15 | 1 (4.3) | 0 (0) | 1 (2.8) |
| | V127I | 0.21 | 1 (4.3) | 0 (0) | 1 (2.8) |
| | V144I | 0.1 | 1 (4.3) | 0 (0) | 1 (2.8) |
| | T245N | NA | 1 (4.3) | 0 (0) | 1 (2.8) |
| | S255N | 0.03 | 0 (0) | 1 (7.7) | 1 (2.8) |
| | S276N | 2.05 | 2 (8.7) | 0 (0) | 2 (5.6) |
| | Q354R | NA | 0 (0) | 1 (7.7) | 1 (2.8) |
| | I384T | 3.76 | 0 (0) | 1 (7.7) | 1 (2.8) |
| | V406I | 0.66 | 1 (4.3) | 0 (0) | 1 (2.8) |
| | K419E | 0.1 | 0 (0) | 1 (7.7) | 1 (2.8) |

| | | | | | |
|---|---|---|---|---|---|
| | D479N | 0.1 | 0 (0) | 1 (7.7) | 1 (2.8) |
| | D486N | NA | 1 (4.3) | 0 (0) | 1 (2.8) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| **151–360 days post-dose** | | | **n = 6** | **n = 7** | **n = 13** |
| | A23S | 0.1 | 0 (0) | 1 (14.3) | 1 (7.7) |
| | F114S | 0.94 | 0 (0) | 1 (14.3) | 1 (7.7) |
| | T122A | 11.58 | 6 (100) | 6 (85.7) | 12 (92.3) |
| | K123Q | 3.62 | 6 (100) | 5 (71.4) | 11 (84.6) |
| | I384T | 3.76 | 6 (100) | 5 (71.4) | 11 (84.6) |
| | D562N | 0.1 | 1 (16.7) | 0 (0) | 1 (7.7) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| **361–511 days post-dose** | | | **n = 1** | **n = 4** | **n = 5** |
| | T12I | 6.75 | 0 (0) | 1 (25) | 1 (20) |
| | A23S | 0.1 | 1 (100) | 2 (50) | 3 (60) |
| | T122A | 11.58 | 1 (100) | 3 (75) | 4 (80) |
| | K123Q | 3.62 | 0 (0) | 1 (25) | 1 (20) |
| | E378D | 0.03 | 1 (100) | 0 (0) | 1 (20) |
| | I384T | 3.76 | 0 (0) | 1 (25) | 1 (20) |
| | S443T | 0.07 | 0 (0) | 1 (25) | 1 (20) |
| | K551R | 0.03 | 0 (0) | 1 (25) | 1 (20) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |

| MELODY full cohort – RSV B | | | | | |
|---|---|---|---|---|---|
| **Through 150 days post-dose** | | | **n = 29** | **n = 10** | **n = 39** |
| | I11L | NA | 1 (3.4) | 0 (0) | 1 (2.6) |
| | F12I | 0.07 | 7 (24.1) | 5 (50) | 12 (30.8) |
| | F15L | 99.57 | 26 (89.7) | 10 (100) | 36 (92.3) |
| | A16V | 1.57 | 1 (3.4) | 0 (0) | 1 (2.6) |
| | N18S | 0.21 | 1 (3.4) | 0 (0) | 1 (2.6) |
| | L22P | 1.68 | 1 (3.4) | 0 (0) | 1 (2.6) |
| | T91N | NA | 1 (3.4) | 0 (0) | 1 (2.6) |
| | A103V | 98.5 | 29 (100) | 10 (100) | 39 (100) |
| | A111V | 0.07 | 1 (3.4) | 0 (0) | 1 (2.6) |
| | N116S | 0.21 | 1 (3.4) | 0 (0) | 1 (2.6) |
| | L172Q | 98.61 | 29 (100) | 10 (100) | 39 (100) |
| | S173L | 98.36 | 28 (96.6) | 8 (80) | 36 (92.3) |
| | S190N | 2.79 | 22 (75.9) | 9 (90) | 31 (79.5) |
| | K191R | 68.61 | 28 (96.6) | 10 (100) | 38 (97.4) |
| | L204S | NA | 0 (0) | 1 (10) | 1 (2.6) |
| | I206M | 68.89 | 28 (96.6) | 10 (100) | 38 (97.4) |
| | Q209R | 68.18 | 28 (96.6) | 10 (100) | 38 (97.4) |
| | S211N | 1.14 | 22 (75.9) | 9 (90) | 31 (79.5) |
| | V239I | 0.14 | 1 (3.4) | 0 (0) | 1 (2.6) |
| | K272R | 0.04 | 0 (0) | 1 (10) | 1 (2.6) |
| | K327E | 0.04 | 1 (3.4) | 0 (0) | 1 (2.6) |
| | V365I | NA | 1 (3.4) | 0 (0) | 1 (2.6) |
| | P376S | NA | 1 (3.4) | 0 (0) | 1 (2.6) |
| | S389P | 1.07 | 22 (75.9) | 9 (90) | 31 (79.5) |

| | | | | | |
|---|---|---|---|---|---|
| | S436P | NA | 1 (3.4) | 0 (0) | 1 (2.6) |
| | T522A | 0.07 | 1 (3.4) | 0 (0) | 1 (2.6) |
| | A529V | 0.93 | 1 (3.4) | 0 (0) | 1 (2.6) |
| | **Nirsevimab binding site** | | | | |
| | L204S | NA | 0 (0) | 1 (10) | 1 (2.6) |
| | I206M | 68.89 | 28 (96.6) | 10 (100) | 38 (97.4) |
| | Q209R | 68.18 | 28 (96.6) | 10 (100) | 38 (97.4) |
| | S211N | 1.14 | 22 (75.9) | 9 (90) | 31 (79.5) |
| | **Palivizumab binding site** | | | | |
| | K272R | 0.04 | 0 (0) | 1 (10) | 1 (2.6) |
| **151–360 days post-dose** | | | **n = 0** | **n = 6** | **n = 6** |
| | F15L | 99.57 | 0 (0) | 6 (100) | 6 (100) |
| | A103V | 98.5 | 0 (0) | 6 (100) | 6 (100) |
| | L172Q | 98.61 | 0 (0) | 4 (66.7) | 4 (66.7) |
| | S173L | 98.36 | 0 (0) | 4 (66.7) | 4 (66.7) |
| | S190N | 2.79 | 0 (0) | 1 (16.7) | 1 (16.7) |
| | K191R | 68.61 | 0 (0) | 4 (66.7) | 4 (66.7) |
| | I206M | 68.89 | 0 (0) | 4 (66.7) | 4 (66.7) |
| | Q209R | 68.18 | 0 (0) | 4 (66.7) | 4 (66.7) |
| | S211N | 1.14 | 0 (0) | 1 (16.7) | 1 (16.7) |
| | S330T | NA | 0 (0) | 1 (16.7) | 1 (16.7) |
| | S389P | 1.07 | 0 (0) | 2 (33.3) | 2 (33.3) |
| | **Nirsevimab binding site** | | | | |
| | I206M | 68.89 | 0 (0) | 4 (66.7) | 4 (66.7) |
| | Q209R | 68.18 | 0 (0) | 4 (66.7) | 4 (66.7) |
| | S211N | 1.14 | 0 (0) | 1 (16.7) | 1 (16.7) |

| | | | | | |
|---|---|---|---|---|---|
| | **Palivizumab binding site** | | None | | |
| **361–511 days post-dose** | | | **n = 1** | **n = 3** | **n = 4** |
| | F15L | 99.57 | 1 (100) | 3 (100) | 4 (100) |
| | A103V | 98.5 | 1 (100) | 3 (100) | 4 (100) |
| | N120S | 0.11 | 0 (0) | 1 (33.3) | 1 (25) |
| | L172Q | 98.61 | 1 (100) | 3 (100) | 4 (100) |
| | S173L | 98.36 | 1 (100) | 3 (100) | 4 (100) |
| | K191R | 68.61 | 1 (100) | 3 (100) | 4 (100) |
| | I206M | 68.89 | 1 (100) | 3 (100) | 4 (100) |
| | Q209R | 68.18 | 1 (100) | 3 (100) | 4 (100) |
| | S330T | NA | 1 (100) | 0 (0) | 1 (25) |
| | **Nirsevimab binding site** | | | | |
| | I206M | 68.89 | 1 (100) | 3 (100) | 4 (100) |
| | Q209R | 68.18 | 1 (100) | 3 (100) | 4 (100) |
| | **Palivizumab binding site** | | None | | |

Major variants had ≥25% MAF in surveillance studies. Site Ø=AAs 62–96 and 195–227; Site II=AAs 254–277; non-EC regions: signal peptide=AAs 1–23; p27=AAs 110–136; transmembrane and intracellular domains=AAs 525–574; nirsevimab binding site=AAs 62–69 and 196–212; palivizumab binding site=AAs 262–275.

AA, amino acid; EC, extracellular; MAF, molecular allele frequency; NA, not applicable (i.e. not observed); RSV, respiratory syncytial virus.

**Supplementary Table S3 |** Prevalence and frequency of all major variant substitutions observed for cases that met the secondary case definition in the Phase 2b and MELODY trials.

| Sampling period | Amino acid substitutions in RSV F | Prevalence in surveillance studies (%) | Frequency | | |
|---|---|---|---|---|---|
| | | | Placebo n (%) | Nirsevimab n (%) | Total n (%) |
| | | **Phase 2b – RSV A** | | | |
| **Through 150 days post-dose** | | | **n = 12** | **n = 5** | **n = 17** |
| | T13A | 4.66 | 0 (0) | 1 (20) | 1 (5.9) |
| | A17V | 0.21 | 1 (8.3) | 0 (0) | 1 (5.9) |
| | F22I | 0.07 | 1 (8.3) | 0 (0) | 1 (5.9) |
| | A23T | 5.32 | 1 (8.3) | 1 (20) | 2 (11.8) |
| | A102S | 0.03 | 1 (8.3) | 1 (20) | 2 (11.8) |
| | K123E | 0.03 | 0 (0) | 1 (20) | 1 (5.9) |
| | S213R | 0.1 | 0 (0) | 1 (20) | 1 (5.9) |
| | K419E | 0.1 | 1 (8.3) | 1 (20) | 2 (11.8) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| **151–360 days post-dose** | R113K | 0.1 | 1 (100) | 0 (0) | 1 (100) |
| | Y117H | 1.39 | 1 (100) | 0 (0) | 1 (100) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| | | **Phase 2b – RSV B** | | | |
| **Through 150 days post-dose** | | | **n = 8** | **n = 3** | **n = 11** |
| | F12L | 7.21 | 0 (0) | 1 (33.3) | 1 (9.1) |
| | F15I | NA | 1 (12.5) | 0 (0) | 1 (9.1) |
| | F15L | 99.57 | 7 (87.5) | 3 (100) | 10 (90.9) |

| | | | | | |
|---|---|---|---|---|---|
| | A16T | 1.21 | 1 (12.5) | 0 (0) | 1 (9.1) |
| | A16V | 1.57 | 1 (12.5) | 0 (0) | 1 (9.1) |
| | I64T | NA | 0 (0) | 1 (33.3) | 1 (9.1) |
| | K68E | NA | 0 (0) | 1 (33.3) | 1 (9.1) |
| | A103V | 98.5 | 8 (100) | 3 (100) | 11 (100) |
| | L172Q | 98.61 | 8 (100) | 3 (100) | 11 (100) |
| | S173L | 98.36 | 8 (100) | 3 (100) | 11 (100) |
| | K191R | 68.61 | 1 (12.5) | 1 (33.3) | 2 (18.2) |
| | I206M | 68.89 | 1 (12.5) | 1 (33.3) | 2 (18.2) |
| | N208S | NA | 0 (0) | 1 (33.3) | 1 (9.1) |
| | Q209R | 68.18 | 1 (12.5) | 1 (33.3) | 2 (18.2) |
| | S276N | 7.14 | 1 (12.5) | 1 (33.3) | 2 (18.2) |
| | K327R | 0.11 | 0 (0) | 1 (33.3) | 1 (9.1) |
| | E463D | 7 | 0 (0) | 1 (33.3) | 1 (9.1) |
| | K574N | 0.07 | 0 (0) | 1 (33.3) | 1 (9.1) |
| | **Nirsevimab binding site** | | | | |
| | I64T | NA | 0 (0) | 1 (33.3) | 1 (9.1) |
| | K68E | NA | 0 (0) | 1 (33.3) | 1 (9.1) |
| | I206M | 68.89 | 1 (12.5) | 1 (33.3) | 2 (18.2) |
| | N208S | NA | 0 (0) | 1 (33.3) | 1 (9.1) |
| | Q209R | 68.18 | 1 (12.5) | 1 (33.3) | 2 (18.2) |
| | **Palivizumab binding site** | | None | | |
| **151–360 days post-dose** | | | **n = 1** | **n = 1** | **n = 2** |
| | F15L | 99.57 | 1 (100) | 1 (100) | 2 (100) |
| | A103V | 98.5 | 1 (100) | 1 (100) | 2 (100) |
| | V127I | 0.07 | 1 (100) | 0 (0) | 1 (50) |

| | | | | | |
|---|---|---|---|---|---|
| | L172Q | 98.61 | 1 (100) | 1 (100) | 2 (100) |
| | S173L | 98.36 | 1 (100) | 1 (100) | 2 (100) |
| | K191R | 68.61 | 1 (100) | 0 (0) | 1 (50) |
| | I206M | 68.89 | 1 (100) | 0 (0) | 1 (50) |
| | Q209R | 68.18 | 1 (100) | 0 (0) | 1 (50) |
| | **Nirsevimab binding site** | | | | |
| | I206M | 68.89 | 1 (100) | 0 (0) | 1 (50) |
| | Q209R | 68.18 | 1 (100) | 0 (0) | 1 (50) |
| | **Palivizumab binding site** | | None | | |
| | **MELODY full cohort – RSV A** | | | | |
| **Through 150 days post-dose** | | | **n = 8** | **n = 7** | **n = 15** |
| | T8I | 0.45 | 0 (0) | 1 (14.3) | 1 (6.7) |
| | T12I | 6.75 | 2 (25) | 1 (14.3) | 3 (20) |
| | T13A | 4.66 | 1 (12.5) | 1 (14.3) | 2 (13.3) |
| | L15F | 2.09 | 0 (0) | 1 (14.3) | 1 (6.7) |
| | A103T | 1.91 | 1 (12.5) | 0 (0) | 1 (6.7) |
| | A107T | 1.04 | 0 (0) | 2 (28.6) | 2 (13.3) |
| | F114S | 0.94 | 1 (12.5) | 0 (0) | 1 (6.7) |
| | T122A | 11.58 | 1 (12.5) | 2 (28.6) | 3 (20) |
| | V127A | 1.15 | 1 (12.5) | 0 (0) | 1 (6.7) |
| | S276N | 2.05 | 1 (12.5) | 0 (0) | 1 (6.7) |
| | K419E | 0.1 | 0 (0) | 1 (14.3) | 1 (6.7) |
| | D486N | NA | 1 (12.5) | 0 (0) | 1 (6.7) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |

| | | | | | |
|---|---|---|---|---|---|
| **151–360 days post-dose** | | | **n = 2** | **n = 1** | **n = 3** |
| | T122A | 11.58 | 2 (100) | 1 (100) | 3 (100) |
| | K123Q | 3.62 | 2 (100) | 1 (100) | 3 (100) |
| | I384T | 3.76 | 2 (100) | 1 (100) | 3 (100) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| **361–511 days post-dose** | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| | **MELODY full cohort – RSV B** | | | | |
| **Through 150 days post-dose** | | | **n = 12** | **n = 2** | **n = 14** |
| | F12I | 0.07 | 3 (25) | 0 (0) | 3 (21.4) |
| | F15L | 99.57 | 12 (100) | 2 (100) | 14 (100) |
| | A16V | 1.57 | 1 (8.3) | 0 (0) | 1 (7.1) |
| | N18S | 0.21 | 1 (8.3) | 0 (0) | 1 (7.1) |
| | L22P | 1.68 | 1 (8.3) | 0 (0) | 1 (7.1) |
| | A103V | 98.5 | 12 (100) | 2 (100) | 14 (100) |
| | A111V | 0.07 | 1 (8.3) | 0 (0) | 1 (7.1) |
| | L172Q | 98.61 | 12 (100) | 2 (100) | 14 (100) |
| | S173L | 98.36 | 11 (91.7) | 1 (50) | 12 (85.7) |
| | S190N | 2.79 | 10 (83.3) | 1 (50) | 11 (78.6) |
| | K191R | 68.61 | 11 (91.7) | 2 (100) | 13 (92.9) |
| | I206M | 68.89 | 11 (91.7) | 2 (100) | 13 (92.9) |
| | Q209R | 68.18 | 11 (91.7) | 2 (100) | 13 (92.9) |
| | S211N | 1.14 | 10 (83.3) | 1 (50) | 11 (78.6) |
| | V239I | 0.14 | 1 (8.3) | 0 (0) | 1 (7.1) |
| | K327E | 0.04 | 1 (8.3) | 0 (0) | 1 (7.1) |

| | | | | | |
|---|---|---|---|---|---|
| | S389P | 1.07 | 10 (83.3) | 1 (50) | 11 (78.6) |
| | S436P | NA | 1 (8.3) | 0 (0) | 1 (7.1) |
| | T522A | 0.07 | 1 (8.3) | 0 (0) | 1 (7.1) |
| | A529V | 0.93 | 1 (8.3) | 0 (0) | 1 (7.1) |
| | **Nirsevimab binding site** | | | | |
| | I206M | 68.89 | 11 (91.7) | 2 (100) | 13 (92.9) |
| | Q209R | 68.18 | 11 (91.7) | 2 (100) | 13 (92.9) |
| | S211N | 1.14 | 10 (83.3) | 1 (50) | 11 (78.6) |
| | **Palivizumab binding site** | | None | | |
| **151–360 days post-dose** | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| **361–511 days post-dose** | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |

Major variants had ≥25% MAF in surveillance studies. Site Ø=AAs 62–96 and 195–227; Site II=AAs 254–277; non-EC regions: signal peptide=AAs 1–23; p27=AAs 110–136; transmembrane and intracellular domains=AAs 525–574; nirsevimab binding site=AAs 62–69 and 196–212; palivizumab binding site=AAs 262–275.

AA, amino acid; EC, extracellular; MAF, molecular allele frequency; NA, not applicable (i.e. not observed); RSV, respiratory syncytial virus.

**Supplementary Table S4 |** Prevalence and frequency of all major variant substitutions observed for cases that met the exploratory case definition of RSV unscheduled event in the Phase 2b and MELODY trials.

| Sampling period | Amino acid substitutions in RSV F | Prevalence in surveillance studies (%) | Frequency | | |
|---|---|---|---|---|---|
| | | | Placebo n (%) | Nirsevimab n (%) | Total n (%) |
| | | **Phase 2b – RSV A** | | | |
| **Through 150 days post-dose** | | | **n = 0** | **n = 3** | **n = 3** |
| | T13A | 4.66 | 0 (0) | 1 (33.3) | 1 (33.3) |
| | L119I | 0.8 | 0 (0) | 2 (66.7) | 2 (66.7) |
| | K209R | NA | 0 (0) | 2 (66.7) | 2 (66.7) |
| | **Nirsevimab binding site** | | | | |
| | K209R | NA | 0 (0) | 2 (66.7) | 2 (66.7) |
| | **Palivizumab binding site** | | None | | |
| **151–360 days post-dose** | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| | | **Phase 2b – RSV B** | | | |
| **Through 150 days post-dose** | | | **n = 0** | **n = 1** | **n = 1** |
| | F15L | 99.57 | 0 (0) | 1 (100) | 1 (100) |
| | A103V | 98.5 | 0 (0) | 1 (100) | 1 (100) |
| | I129M | 0.43 | 0 (0) | 1 (100) | 1 (100) |
| | L172Q | 98.61 | 0 (0) | 1 (100) | 1 (100) |
| | S173L | 98.36 | 0 (0) | 1 (100) | 1 (100) |
| | K191R | 68.61 | 0 (0) | 1 (100) | 1 (100) |
| | I206M | 68.89 | 0 (0) | 1 (100) | 1 (100) |
| | Q209R | 68.18 | 0 (0) | 1 (100) | 1 (100) |
| | T518I | NA | 0 (0) | 1 (100) | 1 (100) |

| | | | | | |
|---|---|---|---|---|---|
| | **Nirsevimab binding site** | | | | |
| | I206M | 68.89 | 0 (0) | 1 (100) | 1 (100) |
| | Q209R | 68.18 | 0 (0) | 1 (100) | 1 (100) |
| | **Palivizumab binding site** | | None | | |
| **151–360 days post-dose** | | | **n = 1** | **n = 0** | **n = 1** |
| | F12L | 7.21 | 1 (100) | 0 (0) | 1 (100) |
| | F15L | 99.57 | 1 (100) | 0 (0) | 1 (100) |
| | A103V | 98.5 | 1 (100) | 0 (0) | 1 (100) |
| | L172Q | 98.61 | 1 (100) | 0 (0) | 1 (100) |
| | S173L | 98.36 | 1 (100) | 0 (0) | 1 (100) |
| | S190N | 2.79 | 1 (100) | 0 (0) | 1 (100) |
| | K191R | 68.61 | 1 (100) | 0 (0) | 1 (100) |
| | I206M | 68.89 | 1 (100) | 0 (0) | 1 (100) |
| | Q209R | 68.18 | 1 (100) | 0 (0) | 1 (100) |
| | S276N | 7.14 | 1 (100) | 0 (0) | 1 (100) |
| | E463D | 7 | 1 (100) | 0 (0) | 1 (100) |
| | **Nirsevimab binding site** | | | | |
| | I206M | 68.89 | 1 (100) | 0 (0) | 1 (100) |
| | Q209R | 68.18 | 1 (100) | 0 (0) | 1 (100) |
| | **Palivizumab binding site** | | None | | |
| | | **MELODY full cohort – RSV A** | | | |
| **Through 150 days post-dose** | | | **n = 7** | **n = 5** | **n = 12** |
| | T12I | 6.75 | 1 (14.3) | 1 (20) | 2 (16.7) |
| | T13A | 4.66 | 2 (28.6) | 0 (0) | 2 (16.7) |
| | L15F | 2.09 | 1 (14.3) | 0 (0) | 1 (8.3) |
| | A103T | 1.91 | 1 (14.3) | 1 (20) | 2 (16.7) |

| | | | | | |
|---|---|---|---|---|---|
| | T122A | 11.58 | 2 (28.6) | 1 (20) | 3 (25) |
| | S276N | 2.05 | 0 (0) | 1 (20) | 1 (8.3) |
| | N325Y | | 1 (14.3) | 0 (0) | 1 (8.3) |
| | S330T | 0.03 | 1 (14.3) | 0 (0) | 1 (8.3) |
| | S362L | 0.97 | 1 (14.3) | 0 (0) | 1 (8.3) |
| | K419N | 0.03 | 1 (14.3) | 0 (0) | 1 (8.3) |
| | A518V | 0.7 | 0 (0) | 1 (20) | 1 (8.3) |
| | A540V | | 0 (0) | 1 (20) | 1 (8.3) |
| | A552T | 0.14 | 1 (14.3) | 0 (0) | 1 (8.3) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| **151–360 days post-dose** | | | **n = 1** | **n = 1** | **n = 2** |
| | L111I | 0.14 | 0 (0) | 1 (100) | 1 (50) |
| | T122A | 11.58 | 1 (100) | 1 (100) | 2 (100) |
| | K123Q | 3.62 | 1 (100) | 0 (0) | 1 (50) |
| | E378D | 0.03 | 0 (0) | 1 (100) | 1 (50) |
| | I384T | 3.76 | 1 (100) | 0 (0) | 1 (50) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| **361–511 days post-dose** | | | **n = 0** | **n = 1** | **n = 1** |
| | T12I | 6.75 | 0 (0) | 1 (100) | 1 (100) |
| | S105N | 0.45 | 0 (0 | 1 (100) | 1 (100) |
| | E497D | NA | 0 (0) | 1 (100) | 1 (100) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |

| | | MELODY full cohort – RSV B | | | |
|---|---|---|---|---|---|
| **Through 150 days post-dose** | | | **n = 2** | **n = 1** | **n = 3** |
| | F12I | 0.07 | 1 (50) | 0 (0) | 1 (33.3) |
| | F15L | 99.57 | 2 (100) | 1 (100) | 3 (100) |
| | A19T | 2.25 | 0 (0) | 1 (100) | 1 (33.3) |
| | N99T | NA | 1 (50) | 0 (0) | 1 (33.3) |
| | A103V | 98.5 | 2 (100) | 1 (100) | 3 (100) |
| | L172Q | 98.61 | 2 (100) | 1 (100) | 3 (100) |
| | S173L | 98.36 | 1 (50) | 1 (100) | 2 (66.7) |
| | S190N | 2.79 | 2 (100) | 1 (100) | 3 (100) |
| | K191R | 68.61 | 2 (100) | 1 (100) | 3 (100) |
| | I206M | 68.89 | 2 (100) | 1 (100) | 3 (100) |
| | Q209R | 68.18 | 2 (100) | 1 (100) | 3 (100) |
| | S211N | 1.14 | 2 (100) | 1 (100) | 3 (100) |
| | S389P | 1.07 | 2 (100) | 1 (100) | 3 (100) |
| | **Nirsevimab binding site** | | None | | |
| | I206M | 68.89 | 2 (100) | 1 (100) | 3 (100) |
| | Q209R | 68.18 | 2 (100) | 1 (100) | 3 (100) |
| | S211N | 1.14 | 2 (100) | 1 (100) | 3 (100) |
| | **Palivizumab binding site** | | None | | |

Major variants had ≥25% MAF in surveillance studies. Site Ø=AAs 62–96 and 195–227; Site II=AAs 254–277; non-EC regions: signal peptide=AAs 1–23; p27=AAs 110–136; transmembrane and intracellular domains=AAs 525–574; nirsevimab binding site=AAs 62–69 and 196–212; palivizumab binding site=AAs 262–275.

AA, amino acid; EC, extracellular; MAF, molecular allele frequency; NA, not applicable (i.e. not observed); RSV, respiratory syncytial virus.

**Supplementary Table S5 |** Prevalence and frequency of all major variant substitutions observed for cases that met the exploratory case definition of non-protocol defined LRTI outpatient event in the Phase 2b and MELODY trials.

| Sampling period | Amino acid substitutions in RSV F | Prevalence in surveillance studies (%) | Frequency | | |
|---|---|---|---|---|---|
| | | | Placebo n (%) | Nirsevimab n (%) | Total n (%) |
| | | **Phase 2b – RSV A** | | | |
| **Through 150 days post-dose** | | | **n = 1** | **n = 2** | **n = 3** |
| | A103V | 0.28 | 0 (0) | 1 (50) | 1 (33.3) |
| | G329R | 0.07 | 1 (100) | 1 (50) | 2 (66.7) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| | | **Phase 2b – RSV B** | | | |
| **Through 150 days post-dose** | | | **n = 2** | **n = 2** | **n = 4** |
| | F15L | 99.57 | 2 (100) | 2 (100) | 4 (100) |
| | A103V | 98.5 | 2 (100) | 2 (100) | 4 (100) |
| | L172Q | 98.61 | 2 (100) | 2 (100) | 4 (100) |
| | S173L | 98.36 | 2 (100) | 2 (100) | 4 (100) |
| | K191R | 68.61 | 2 (100) | 1 (50) | 3 (75) |
| | I206M | 68.89 | 2 (100) | 1 (50) | 3 (75) |
| | Q209R | 68.18 | 2 (100) | 1 (50) | 3 (75) |
| | V365A | 0.07 | 1 (50) | 1 (50) | 2 (50) |
| | **Nirsevimab binding site** | | None | | |
| | I206M | 68.89 | 2 (100) | 1 (50) | 3 (75) |
| | Q209R | 68.18 | 2 (100) | 1 (50) | 3 (75) |
| | **Palivizumab binding site** | | None | | |

| | | MELODY full cohort RSV A | | | |
|---|---|---|---|---|---|
| **Through 150 days post-dose** | | | **n = 7** | **n = 5** | **n = 12** |
| | T12I | 6.75 | 1 (14.3) | 1 (20) | 2 (16.7) |
| | L15F | 2.09 | 0 (0) | 1 (20) | 1 (8.3) |
| | S24F | 0.45 | 0 (0) | 1 (20) | 1 (8.3) |
| | A103T | 1.91 | 1 (14.3) | 0 (0) | 1 (8.3) |
| | N116S | 0.1 | 1 (14.3) | 0 (0) | 1 (8.3) |
| | T122A | 11.58 | 0 (0) | 2 (40) | 2 (16.7) |
| | T125A | 0.21 | 0 (0) | 1 (20) | 1 (8.3) |
| | S276N | 2.05 | 0 (0) | 1 (20) | 1 (8.3) |
| | A355V | 0.24 | 0 (0) | 1 (20) | 1 (8.3) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| **151–360 days post-dose** | | | **n = 2** | **n = 2** | **n = 4** |
| | T12I | 6.75 | 1 (50) | 0 (0) | 1 (25) |
| | L20F | 0.77 | 1 (50) | 0 (0) | 1 (25) |
| | I57V | NA | 0 (0) | 1 (50) | 1 (25) |
| | L111I | 0.14 | 0 (0) | 1 (50) | 1 (25) |
| | T122A | 11.58 | 1 (50) | 2 (100) | 3 (75) |
| | K123Q | 3.62 | 1 (50) | 1 (50) | 2 (50) |
| | I384T | 3.76 | 1 (50) | 1 (50) | 2 (50) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| **361–511 days post-dose** | | | **n = 1** | **n = 0** | **n = 1** |
| | T122A | 11.58 | 1 (100) | 0 (0) | 1 (100) |
| | K123Q | 3.62 | 1 (100) | 0 (0) | 1 (100) |

| | | | | | |
|---|---|---|---|---|---|
| | I384T | 3.76 | 1 (100) | 0 (0) | 1 (100) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| | **MELODY full cohort RSV B** | | | | |
| **Through 150 days post-dose** | | | **n = 5** | **n = 0** | **n = 5** |
| | F12I | 0.07 | 2 (40) | 0 (0) | 2 (40) |
| | F15L | 99.57 | 5 (100) | 0 (0) | 5 (100) |
| | A103V | 98.5 | 5 (100) | 0 (0) | 5 (100) |
| | L172Q | 98.61 | 5 (100) | 0 (0) | 5 (100) |
| | S173L | 98.36 | 5 (100) | 0 (0) | 5 (100) |
| | S190N | 2.79 | 4 (80) | 0 (0) | 4 (80) |
| | K191R | 68.61 | 5 (100) | 0 (0) | 5 (100) |
| | I206M | 68.89 | 5 (100) | 0 (0) | 5 (100) |
| | Q209R | 68.18 | 5 (100) | 0 (0) | 5 (100) |
| | S211N | 1.14 | 4 (80) | 0 (0) | 4 (80) |
| | S330A | NA | 1 (20) | 0 (0) | 1 (20) |
| | S389P | 1.07 | 4 (80) | 0 (0) | 4 (80) |
| | N437I | NA | 1 (20) | 0 (0) | 1 (20) |
| | **Nirsevimab binding site** | | | | |
| | I206M | 68.89 | 5 (100) | 0 (0) | 5 (100) |
| | Q209R | 68.18 | 5 (100) | 0 (0) | 5 (100) |
| | S211N | 1.14 | 4 (80) | 0 (0) | 4 (80) |
| | **Palivizumab binding site** | | None | | |

Major variants had ≥25% MAF in surveillance studies. Site Ø=AAs 62–96 and 195–227; Site II=AAs 254–277; non-EC regions: signal peptide=AAs 1–23; p27=AAs 110–136; transmembrane and intracellular domains=AAs 525–574; nirsevimab binding site=AAs 62–69 and 196–212; palivizumab binding site=AAs 262–275.

AA, amino acid; EC, extracellular; MAF, molecular allele frequency; NA, not applicable (i.e. not observed); RSV, respiratory syncytial virus.

**Supplementary Table S6 |** Prevalence and frequency of all major variant substitutions observed for cases that met the exploratory case definition of hospitalization due to RSV non-LRTI in the Phase 2b and MELODY trials.

| Sampling period | Amino acid substitutions in RSV F | Prevalence in surveillance studies (%) | Frequency | | |
|---|---|---|---|---|---|
| | | | Placebo n (%) | Nirsevimab n (%) | Total n (%) |
| **Phase 2b – RSV A** | | | | | |
| **Through 150 days post-dose** | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| **151–360 days post-dose** | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| **Phase 2b – RSV B** | | | | | |
| **Through 150 days post-dose** | **Nirsevimab binding site** | | None | | |
| | **Palivizumab Binding Site** | | None | | |
| **151–360 days post-dose** | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| **MELODY full cohort – RSV A** | | | | | |
| **Through 150 days post-dose** | | | **n = 0** | **n = 1** | **n = 1** |
| | T12I | 6.75 | 0 (0) | 1 (100) | 1 (100) |
| | S330T | 0.03 | 0 (0) | 1 (100) | 1 (100) |
| | V360A | NA | 0 (0) | 1 (100) | 1 (100) |
| | A552T | 0.14 | 0 (0) | 1 (100) | 1 (100) |
| | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| **151–360 days post-dose** | **Nirsevimab binding site** | | None | | |
| | **Palivizumab binding site** | | None | | |
| **MELODY full cohort – RSV B** | | | | | |

| | | |
|---|---|---|
| **Through 150 days post-dose** | **Nirsevimab binding site** | None |
| | **Palivizumab binding site** | None |
| **151–360 days post-dose** | **Nirsevimab binding site** | None |
| | **Palivizumab binding site** | None |

Major variants had ≥25% MAF in surveillance studies. Site Ø=AAs 62–96 and 195–227; Site II=AAs 254–277; non-EC regions: signal peptide=AAs 1–23; p27=AAs 110–136; transmembrane and intracellular domains=AAs 525–574; nirsevimab binding site=AAs 62–69 and 196–212; palivizumab binding site=AAs 262–275.

AA, amino acid; EC, extracellular; $IC_{50}$, half maximal inhibitory concentration; MAF, molecular allele frequency; NA, not applicable (i.e. not observed); RSV, respiratory syncytial virus.

**Supplementary Table S7 |** Neutralization potency of nirsevimab and palivizumab on all major variant substitutions in the extracellular domain of the RSV A and RSV B F protein observed for cases that met the primary case definition in the Phase 2b and MELODY trials.

| Sampling period | Amino acid substitutions | Fold change in $IC_{50}$ | |
|---|---|---|---|
| | | Nirsevimab | Palivizumab |
| | **Phase 2b – RSV A** | | |
| **Through 150 days post-dose** | S25N | 2.47 | 1.94 |
| | G71S | QNS | QNS |
| | V76I | 1.23 | 0.88 |
| | S99N | 5.25 | 2.11 |
| | A102S | 1.41 | 0.94 |
| | S213R | 2.24 | 2.57 |
| | K419E | QNS | QNS |
| | **Nirsevimab binding site** | None | |
| | **Palivizumab binding site** | None | |
| **151–360 days post-dose** | S190N | 2.17 | 2.62 |
| | **Nirsevimab binding site** | None | |
| | **Palivizumab binding site** | None | |
| | **Phase 2b – RSV B** | | |
| **Through 150 days post-dose** | I64T | >496.28 | 5.19 |
| | K68E | >283.42 | 2.10 |
| | A103V | 0.89 | 1.76 |
| | L172Q | 1.12 | 2.26 |
| | S173L | 0.88 | 1.88 |
| | K191R | 1.26 | 2.73 |
| | I206M | 5.02 | 1.96 |
| | N208S | >386.60 | 1.81 |

| | | | |
|---|---|---|---|
| | Q209R | 0.47 | 3.12 |
| | S276N | 2.04 | 2.55 |
| | K327R | 0.89 | 1.86 |
| | E463D | 1.39 | 2.12 |
| | **Nirsevimab binding site** | | |
| | I64T | >496.28 | 5.19 |
| | K68E | >283.42 | 2.10 |
| | I206M | 5.02 | 1.96 |
| | N208S | >386.60 | 1.81 |
| | Q209R | 0.47 | 3.12 |
| | **Palivizumab binding site** | None | |
| **151–360 days post-dose** | Y33F | 0.49 | 1.20 |
| | A103V | 0.89 | 1.76 |
| | L172Q | 1.12 | 2.26 |
| | S173L | 0.88 | 1.88 |
| | K191R | 1.26 | 2.73 |
| | I206M | 5.02 | 1.96 |
| | Q209R | 0.47 | 3.12 |
| | **Nirsevimab binding site** | | |
| | I206M | 5.02 | 1.96 |
| | Q209R | 0.47 | 3.12 |
| | **Palivizumab binding site** | None | |
| | **MELODY full cohort – RSV A** | | |
| **Through 150 days post-dose** | A103T | 1.0 | 1.0 |
| | A107T | 2.13 | 2.30 |
| | V144I | 1.14 | 1.13 |

| | | | | |
|---|---|---|---|---|
| | T245N | NA | | NA |
| | S255N | NA | | NA |
| | S276N | 1.0 | | 1.0 |
| | Q354R | 2.12 | | 1.93 |
| | I384T | 2.40 | | 1.35 |
| | V406I | NA | | NA |
| | K419E | QNS | | QNS |
| | D479N | NA | | NA |
| | D486N | NA | | NA |
| | **Nirsevimab binding site** | | None | |
| | **Palivizumab binding site** | | None | |
| **151–360 days post-dose** | I384T | 2.40 | | 1.35 |
| | **Nirsevimab binding site** | | None | |
| | **Palivizumab binding site** | | None | |
| **361–511 days post-dose** | E378D | 2.25 | | 1.36 |
| | I384T | 2.40 | | 1.35 |
| | S443T | NA | | NA |
| | **Nirsevimab binding site** | | None | |
| | **Palivizumab binding site** | | None | |
| | **MELODY full cohort – RSV B** | | | |
| **Through 150 days post-dose** | T91N | NA | | NA |
| | A103V | 0.89 | | 1.76 |
| | L172Q | 1.12 | | 2.26 |
| | S173L | 0.88 | | 1.88 |
| | S190N | QNS | | QNS |
| | K191R | 1.26 | | 2.73 |

| | | | |
|---|---|---|---|
| | L204S | NA | NA |
| | I206M | 5.02 | 1.96 |
| | Q209R | 0.47 | 3.12 |
| | S211N | 1.24 | 1.86 |
| | V239I | NA | NA |
| | K272R | NA | 41.80 |
| | K327E | NA | 1.74 |
| | V365I | NA | NA |
| | P376S | NA | NA |
| | S389P | NA | NA |
| | S436P | NA | NA |
| | T522A | NA | NA |
| | **Nirsevimab binding site** | | |
| | L204S | NA | NA |
| | I206M | 5.02 | 1.96 |
| | Q209R | 0.47 | 3.12 |
| | S211N | 1.24 | 1.86 |
| | **Palivizumab binding site** | | |
| | K272R | NA | 41.80 |
| **151–360 days post-dose** | A103V | 0.89 | 1.76 |
| | L172Q | 1.12 | 2.26 |
| | S173L | 0.88 | 1.88 |
| | S190N | QNS | QNS |
| | K191R | 1.26 | 2.73 |
| | I206M | 5.02 | 1.96 |
| | Q209R | 0.47 | 3.12 |

| | | | | |
|---|---|---|---|---|
| | S211N | 1.24 | | 1.86 |
| | S330T | 0.81 | | 1.89 |
| | S389P | NA | | NA |
| | **Nirsevimab binding site** | | | |
| | I206M | 5.02 | | 1.96 |
| | Q209R | 0.47 | | 3.12 |
| | S211N | 1.24 | | 1.86 |
| | **Palivizumab binding site** | | None | |
| **361–511 days post-dose** | A103V | 0.89 | | 1.76 |
| | L172Q | 1.12 | | 2.26 |
| | S173L | 0.88 | | 1.88 |
| | K191R | 1.26 | | 2.73 |
| | I206M | 5.02 | | 1.96 |
| | Q209R | 0.47 | | 3.12 |
| | S330T | 0.81 | | 1.89 |
| | **Nirsevimab binding site** | | | |
| | I206M | 5.02 | | 1.96 |
| | Q209R | 0.47 | | 3.12 |
| | **Palivizumab binding site** | | None | |

Major variants had ≥25% MAF in surveillance studies. Site Ø=AAs 62–96 and 195–227; Site II=AAs 254–277; non-EC regions: signal peptide=AAs 1–23; p27=AAs 110–136; transmembrane and intracellular domains=AAs 525–574; nirsevimab binding site=AAs 62–69 and 196–212; palivizumab binding site=AAs 262–275.

AA, amino acid; EC, extracellular; $IC_{50}$, half maximal inhibitory concentration; MAF, molecular allele frequency; NA, not applicable (i.e. not observed); QNS, quantity not sufficient; RSV, respiratory syncytial virus.

**Supplementary Table S8 |** Neutralization potency of nirsevimab and palivizumab on all minor variant substitutions in the extracellular domain of the RSV A and RSV B F protein observed for cases that met the primary case definition in the Phase 2b and MELODY trials.

| Sampling period | Amino acid substitutions in RSV F | Fold change in $IC_{50}$ | |
|---|---|---|---|
| | | Nirsevimab | Palivizumab |
| | **Phase 2b – RSV A** | | |
| **Through 150 days post-dose** | R49K | NA | NA |
| | **Nirsevimab binding site** | None | |
| | **Palivizumab binding site** | None | |
| | **Phase 2b – RSV B** | | |
| **Through 150 days post-dose** | L171M | NA | NA |
| | N208K | >350.47 | 2.05 |
| | L381F | NA | NA |
| | Y457H | QNS | QNS |
| | **Nirsevimab binding site** | | |
| | N208K | >350.47 | 2.05 |
| | **Palivizumab binding site** | None | |
| | **MELODY full cohort – RSV A** | | |
| **Through day 150 post-dose** | S105N | 1.0 | 1.0 |
| | N165S | NA | NA |
| | N228S | NA | NA |
| | V247L | NA | NA |
| | S276N | 1.0 | 1.0 |
| | N515H | NA | NA |
| | **Nirsevimab binding site** | None | |
| | **Palivizumab binding site** | None | |

| | | | | |
|---|---|---|---|---|
| **151–360 days post-dose** | K272E | NA | | 41.80 |
| | W341R | NA | | NA |
| | A355V | NA | | NA |
| | I384V | 1.0 | | 1.0 |
| | N515H | NA | | NA |
| | **Nirsevimab binding site** | | None | |
| | **Palivizumab binding site** | | None | |
| | K272E | NA | | 41.80 |
| | K42R | NA | | NA |
| **361–511 days post-dose** | N67T | NA | | NA |
| | A74T | NA | | NA |
| | L78F | NA | | NA |
| | S169N | NA | | NA |
| | D200N | NA | | NA |
| | K201N | NA | | NA |
| | S213R | 2.24 | | 2.57 |
| | N228S | NA | | NA |
| | V247L | NA | | NA |
| | **Nirsevimab binding site** | | | |
| | N67T | NA | | NA |
| | D200N | NA | | NA |
| | K201N | NA | | NA |
| | **Palivizumab binding site** | | None | |
| | **MELODY full cohort – RSV B** | | | |
| **Through 150 days post-dose** | I64T | >496.28 | | 5.19 |
| | K65E | NA | | NA |

| | | | | |
|---|---|---|---|---|
| | K68E | >283.42 | | 2.10 |
| | N200Y | NA | | NA |
| | N208I | NA | | NA |
| | I475M | NA | | NA |
| | Y477H | NA | | NA |
| | **Nirsevimab binding site** | | | |
| | I64T | >496.28 | | 5.19 |
| | K65E | NA | | NA |
| | K68E | >283.42 | | 2.10 |
| | N200Y | NA | | NA |
| | N208I | NA | | NA |
| | **Palivizumab binding site** | | None | |
| **151–360 days post-dose** | K87R | NA | | NA |
| | **Nirsevimab binding site** | | None | |
| | **Palivizumab binding site** | | None | |
| **361–511 days post-dose** | **Nirsevimab binding site** | | None | |
| | **Palivizumab binding site** | | None | |

Minor variants had RSV A ≥4%–<25% MAF; RSV B ≥5%–<25% MAF in surveillance studies. Site Ø=AAs 62–96 and 195–227; Site II=AAs 254–277; non-EC regions: signal peptide=AAs 1–23; p27=AAs 110–136; transmembrane and intracellular domains=AAs 525–574; nirsevimab binding site=AAs 62–69 and 196–212; palivizumab binding site=AAs 262–275.

AA, amino acid; EC, extracellular; $IC_{50}$, half maximal inhibitory concentration; MAF, molecular allele frequency; NA, not applicable (i.e., not observed); QNS, quantity not sufficient; RSV, respiratory syncytial virus.

**Supplementary Table S9 |** Neutralization potency of nirsevimab and palivizumab on all major variant substitutions in the extracellular domain of the RSV A and RSV B F protein observed for cases that met the secondary case definition in the Phase 2b and MELODY trials.

| Sampling period | Amino acid substitutions in RSV F | Fold change in $IC_{50}$ | |
|---|---|---|---|
| | | Nirsevimab | Palivizumab |
| | **Phase 2b – RSV A** | | |
| **Through 150 days post-dose** | A102S | 1.41 | 0.94 |
| | S213R | 2.24 | 2.57 |
| | K419E | QNS | QNS |
| | **Nirsevimab binding site** | None | |
| | **Palivizumab binding site** | None | |
| **151–360 days post-dose** | **Nirsevimab binding site** | None | |
| | **Palivizumab binding site** | None | |
| | **Phase 2b – RSV B** | | |
| **Through 150 days post-dose** | I64T | >496.28 | 5.19 |
| | K68E | >283.42 | 2.10 |
| | A103V | 0.89 | 1.76 |
| | L172Q | 1.12 | 2.26 |
| | S173L | 0.88 | 1.88 |
| | K191R | 1.26 | 2.73 |
| | I206M | 5.02 | 1.96 |
| | N208S | >386.60 | 1.81 |
| | Q209R | 0.47 | 3.12 |
| | S276N | 2.04 | 2.55 |
| | K327R | 0.89 | 1.86 |
| | E463D | 1.39 | 2.12 |
| | **Nirsevimab binding site** | None | |

| | | | | |
|---|---|---|---|---|
| | I64T | >496.28 | | 5.19 |
| | K68E | >283.42 | | 2.10 |
| | I206M | 5.02 | | 1.96 |
| | N208S | >386.60 | | 1.81 |
| | Q209R | 0.47 | | 3.12 |
| | **Palivizumab binding site** | | None | |
| **151–360 days post-dose** | A103V | 0.89 | | 1.76 |
| | L172Q | 1.12 | | 2.26 |
| | S173L | 0.88 | | 1.88 |
| | K191R | 1.26 | | 2.73 |
| | I206M | 5.02 | | 1.96 |
| | Q209R | 0.47 | | 3.12 |
| | **Nirsevimab binding site** | | None | |
| | I206M | 5.02 | | 1.96 |
| | Q209R | 0.47 | | 3.12 |
| | **Palivizumab binding site** | | None | |
| | **MELODY full cohort – RSV A** | | | |
| **Through 150 days post-dose** | A103T | 1.0 | | 1.0 |
| | A107T | 2.13 | | 2.30 |
| | S276N | 1.0 | | 1.0 |
| | K419E | QNS | | QNS |
| | D486N | NA | | NA |
| | **Nirsevimab binding site** | | None | |
| | **Palivizumab binding site** | | None | |
| **151–360 days post-dose** | I384T | 2.40 | | 1.35 |
| | **Nirsevimab binding site** | | None | |

| | | | |
|---|---|---|---|
| | **Palivizumab binding site** | | None |
| **361–511 days post-dose** | **Nirsevimab binding site** | | None |
| | **Palivizumab binding site** | | None |
| | **MELODY full cohort – RSV B** | | |
| **Through 150 days post-dose** | A103V | 0.89 | 1.76 |
| | L172Q | 1.12 | 2.26 |
| | S173L | 0.88 | 1.88 |
| | S190N | NA | NA |
| | K191R | 1.26 | 2.73 |
| | I206M | 5.02 | 1.96 |
| | Q209R | 0.47 | 3.12 |
| | S211N | 1.24 | 1.86 |
| | V239I | NA | NA |
| | K327E | NA | 1.74 |
| | S389P | NA | NA |
| | S436P | NA | NA |
| | T522A | NA | NA |
| | **Nirsevimab binding site** | | |
| | I206M | 5.02 | 1.96 |
| | Q209R | 0.47 | 3.12 |
| | S211N | 1.24 | 1.86 |
| | **Palivizumab binding site** | | None |
| **151–360 days post-dose** | **Nirsevimab binding site** | | None |
| | **Palivizumab binding site** | | None |
| **361–511 days post-dose** | **Nirsevimab binding site** | | None |
| | **Palivizumab binding site** | | None |

Major variants had ≥25% MAF in surveillance studies. Site Ø=AAs 62–96 and 195–227; Site II=AAs 254–277; non-EC regions: signal peptide=AAs 1–23; p27=AAs 110–136; transmembrane and intracellular domains=AAs 525–574; nirsevimab binding site=AAs 62–69 and 196–212; palivizumab binding site=AAs 262–275.

AA, amino acid; EC, extracellular; $IC_{50}$, half maximal inhibitory concentration; NA, not applicable (i.e. not observed); QNS, quantity not sufficient; RSV, respiratory syncytial virus.

**Supplementary Table S10 |** Neutralization potency of nirsevimab and palivizumab on all major variant substitutions in the extracellular domain of the RSV A and RSV B F protein observed for cases that met the exploratory case definition of RSV unscheduled event in the Phase 2b and MELODY trials.

| Sampling period | Amino acid substitutions in RSV F | Fold change in $IC_{50}$ | |
|---|---|---|---|
| | | Nirsevimab | Palivizumab |
| | **Phase 2b – RSV A** | | |
| **Through 150 days post-dose** | K209R | 0.93 | 1.01 |
| | **Nirsevimab binding site** | | |
| | K209R | 0.93 | 1.01 |
| | **Palivizumab binding site** | None | |
| **151–360 days post-dose** | **Nirsevimab binding site** | None | |
| | **Palivizumab binding site** | None | |
| | **Phase 2b – RSV B** | | |
| **Through 150 days post-dose** | A103V | 0.89 | 1.76 |
| | L172Q | 1.12 | 2.26 |
| | S173L | 0.88 | 1.88 |
| | K191R | 1.26 | 2.73 |
| | I206M | 5.02 | 1.96 |
| | Q209R | 0.47 | 3.12 |
| | T518I | 2.97 | 4.39 |
| | **Nirsevimab binding site** | | |
| | I206M | 5.02 | 1.96 |
| | Q209R | 0.47 | 3.12 |
| | **Palivizumab binding site** | None | |
| **151–360 days post-dose** | A103V | 0.89 | 1.76 |
| | L172Q | 1.12 | 2.26 |
| | S173L | 0.88 | 1.88 |

| | | | | |
|---|---|---|---|---|
| | S190N | QNS | | QNS |
| | K191R | 1.26 | | 2.73 |
| | I206M | 5.02 | | 1.96 |
| | Q209R | 0.47 | | 3.12 |
| | S276N | 2.04 | | 2.55 |
| | E463D | 1.39 | | 2.12 |
| | **Nirsevimab binding site** | | | |
| | I206M | 5.02 | | 1.96 |
| | Q209R | 0.47 | | 3.12 |
| | **Palivizumab binding site** | | None | |
| | **MELODY full cohort – RSV A** | | | |
| **Through 150 days post-dose** | A103T | 1.0 | | 1.0 |
| | S276N | 1.0 | | 1.0 |
| | N325Y | 1.83 | | 1.53 |
| | S330T | NA | | 1.07 |
| | S362L | NA | | NA |
| | K419N | NA | | NA |
| | A518V | 0.98 | | 1.24 |
| | **Nirsevimab binding site** | | None | |
| | **Palivizumab binding site** | | None | |
| **151–360 days post-dose** | E378D | 2.25 | | 1.36 |
| | I384T | 2.40 | | 1.35 |
| | **Nirsevimab binding site** | | None | |
| | **Palivizumab binding site** | | None | |
| **361–511 days post-dose** | S105N | 1.0 | | 1.0 |
| | E497D | NA | | NA |

| | | | |
|---|---|---|---|
| | **Nirsevimab binding site** | None | |
| | **Palivizumab binding site** | None | |
| | **MELODY full cohort – RSV B** | | |
| **Through 150 days post-dose** | N99T | NA | NA |
| | A103V | 0.89 | 1.76 |
| | L172Q | 1.12 | 2.26 |
| | S173L | 0.88 | 1.88 |
| | S190N | NA | NA |
| | K191R | 1.26 | 2.73 |
| | I206M | 5.02 | 1.96 |
| | Q209R | 0.47 | 3.12 |
| | S211N | 1.24 | 1.86 |
| | S389P | NA | NA |
| | **Nirsevimab binding site** | None | |
| | I206M | 5.02 | 1.96 |
| | Q209R | 0.47 | 3.12 |
| | S211N | 1.24 | 1.86 |
| | **Palivizumab binding site** | None | |
| **151-360 days post-dose** | **Nirsevimab binding site** | None | |
| | **Palivizumab binding site** | None | |
| **361-511 days post-dose** | **Nirsevimab binding site** | None | |
| | **Palivizumab binding site** | None | |

Major variants had ≥25% MAF in surveillance studies. Site Ø=AAs 62–96 and 195–227; Site II=AAs 254–277; non-EC regions: signal peptide=AAs 1–23; p27=AAs 110–136; transmembrane and intracellular domains=AAs 525–574; nirsevimab binding site=AAs 62–69 and 196–212; palivizumab binding site=AAs 262–275.

AA, amino acid; EC, extracellular; $IC_{50}$, half maximal inhibitory concentration; MAF, molecular allele frequency; NA, not applicable (i.e. not observed); QNS, quality not sufficient; RSV, respiratory syncytial virus.

**Supplementary Table S11** | Neutralization potency of nirsevimab and palivizumab on all major variant substitutions in the extracellular domain of the RSV A and RSV B F protein observed for cases that met the exploratory case definition of non-protocol defined LRTI outpatient event in the Phase 2b and MELODY trials.

| Sampling period | Amino acid substitutions in RSV F | Fold change in $IC_{50}$ | |
|---|---|---|---|
| | | Nirsevimab | Palivizumab |
| | **Phase 2b – RSV A** | | |
| **Through 150 days post-dose** | A103V | 2.18 | 1.53 |
| | G329R | 2.06 | 1.32 |
| | **Nirsevimab binding site** | None | |
| | **Palivizumab binding site** | None | |
| | **Phase 2b – RSV B** | | |
| **Through 150 days post-dose** | A103V | 0.89 | 1.76 |
| | L172Q | 1.12 | 2.26 |
| | S173L | 0.88 | 1.88 |
| | K191R | 1.26 | 2.73 |
| | I206M | 5.02 | 1.96 |
| | Q209R | 0.47 | 3.12 |
| | V365A | 0.79 | 0.95 |
| | **Nirsevimab binding site** | None | |
| | I206M | 5.02 | 1.96 |
| | Q209R | 0.47 | 3.12 |
| | **Palivizumab binding site** | None | |
| | **MELODY full cohort – RSV A** | | |
| **Through 150 days post-dose** | A103T | 1.0 | 1.0 |
| | S276N | 1.0 | 1.0 |
| | A355V | 1.73 | 1.88 |

| | | | | |
|---|---|---|---|---|
| | **Nirsevimab binding site** | | None | |
| | **Palivizumab binding site** | | None | |
| **151–360 days post-dose** | I57V | NA | | NA |
| | I384T | 2.40 | | 1.35 |
| | **Nirsevimab binding site** | | None | |
| | **Palivizumab binding site** | | None | |
| **361–511 days post-dose** | I384T | 2.40 | | 1.35 |
| | **Nirsevimab binding Site** | | None | |
| | **Palivizumab binding site** | | None | |
| | **MELODY full cohort – RSV B** | | | |
| **Through 150 days post-dose** | A103V | 0.89 | | 1.76 |
| | L172Q | 1.12 | | 2.26 |
| | S173L | 0.88 | | 1.88 |
| | S190N | NA | | NA |
| | K191R | 1.26 | | 2.73 |
| | I206M | 5.02 | | 1.96 |
| | Q209R | 0.47 | | 3.12 |
| | S211N | 1.24 | | 1.86 |
| | S330A | NA | | NA |
| | S389P | NA | | NA |
| | N437I | NA | | NA |
| | **Nirsevimab binding site** | | | |
| | I206M | 5.02 | | 1.96 |
| | Q209R | 0.47 | | 3.12 |
| | S211N | 1.24 | | 1.86 |
| | **Palivizumab binding site** | | None | |

Major variants had ≥25% MAF in surveillance studies. Site Ø=AAs 62–96 and 195–227; Site II=AAs 254–277; non-EC regions: signal peptide=AAs 1–23; p27=AAs 110–136; transmembrane and intracellular domains=AAs 525–574; nirsevimab binding site=AAs 62–69 and 196–212; palivizumab binding site=AAs 262–275.

AA, amino acid; EC, extracellular; $IC_{50}$, half maximal inhibitory concentration; MAF, molecular allele frequency; NA, not applicable (i.e. not observed); QNS: quantity not sufficient; RSV, respiratory syncytial virus.

**Supplementary Table S12 |** Neutralization potency of nirsevimab and palivizumab on all major variant substitutions in the extracellular domain of the RSV A and RSV B F protein observed for cases that met the exploratory case definition of hospitalization due to RSV non-LRTI in the Phase 2b and MELODY trials.

| Sampling period | Amino acid substitutions in RSV F | Fold change in $IC_{50}$ | |
|---|---|---|---|
| | | Nirsevimab | Palivizumab |
| | **Phase 2b – RSV A** | | |
| **Through 150 days post-dose** | **Nirsevimab binding site** | None | |
| | **Palivizumab binding site** | None | |
| | **Phase 2b – RSV B** | | |
| **Through 150 days post-dose** | **Nirsevimab binding site** | None | |
| | **Palivizumab binding site** | None | |
| | **MELODY full cohort – RSV A** | | |
| **Through 150 days post-dose** | S330T | NA | 1.07 |
| | V360A | NA | NA |
| | **Nirsevimab binding site** | None | |
| | **Palivizumab binding site** | None | |
| | **MELODY full cohort – RSV B** | | |
| **Through 150 days post-dose** | **Nirsevimab binding site** | None | |
| | **Palivizumab binding site** | None | |

Major variants had ≥25% MAF in surveillance studies. Site Ø=AAs 62–96 and 195–227; Site II=AAs 254–277; non-EC regions: signal peptide=AAs 1–23; p27=AAs 110–136; transmembrane and intracellular domains=AAs 525–574; nirsevimab binding site=AAs 62–69 and 196–212; palivizumab binding site=AAs 262–275.

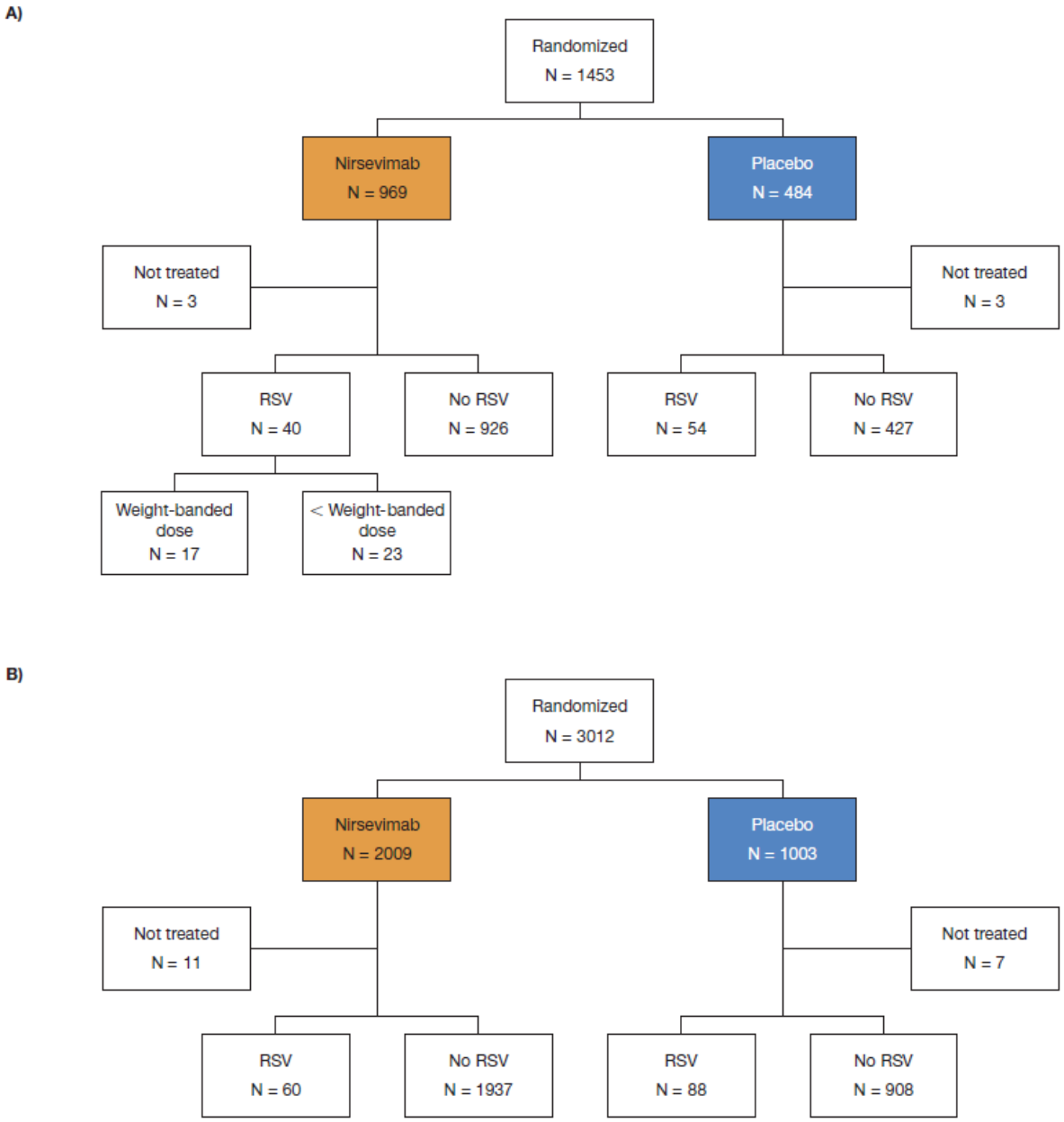
AA, amino acid; EC, extracellular; $IC_{50}$, half maximal inhibitory concentration; MAF, molecular allele frequency; NA, not applicable (i.e. not observed); RSV, respiratory syncytial virus.

**Supplementary Table S13 |** Primer sequences used for qRT-PCR and genotyping.

| Oligonucleotide | Sequence 5’ ---- 3' | Final concentration, nM |
|---|---|---|
| RSV A F1 forward | CRAAATHARMTCTGGGGCAAA | 1600 |
| RSV A F1 reverse | CCARCARGGWGTATCWATWACACCAT | 1600 |
| RSV A F2 forward | TCAATGATATGCCTATAACAAATGATC | 800 |
| RSV A F2 reverse | CAAGCAATGACCTCKAATYTC | 800 |
| RSV B F1 forward | CGAAATTAAATCTGGGGCAAA | 600 |
| RSV B F1 reverse | CCAGCAAGGTGTATCAATTACACCAT | 600 |
| RSV B F2 forward | TCAATGATATGCCTATAACAAATGATC | 600 |
| RSV B F2 reverse | CAAGCAATGACCTCTAATCTC | 600 |

qRT-PCR, quantitative revere-transcriptase polymerase chain reaction; RSV, respiratory syncytial virus.

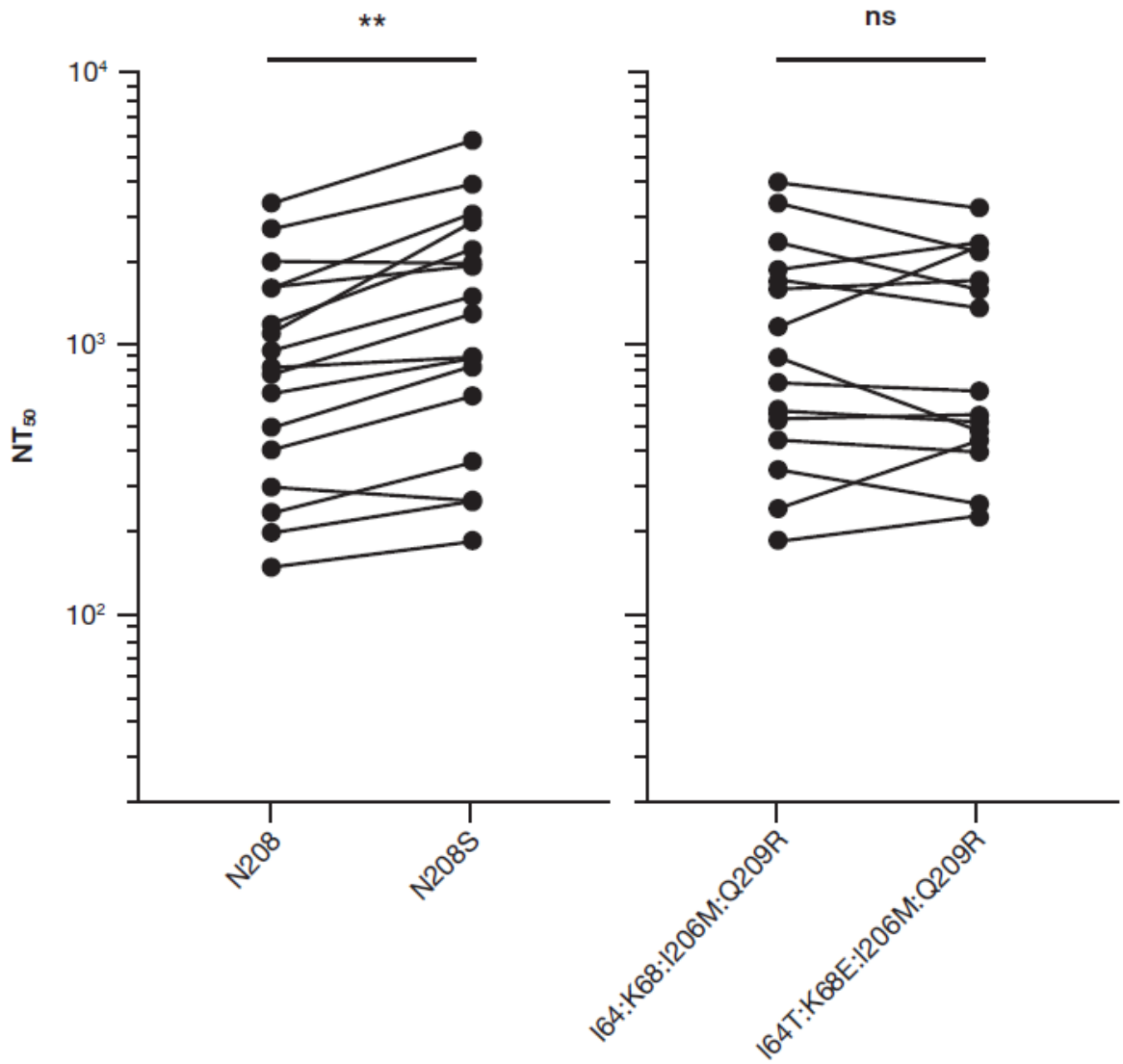
**Supplementary Fig. S1 |** CONSORT diagrams for A) Phase 2b and B) MELODY (full cohort) trials; any RSV infection.




RSV cases shown are those with evaluable NGS data. For the Phase 2b trial, all infants received 50 mg, regardless of weight. For MELODY, nirsevimab was administered according to the weight-banded dosing regimen (participants <5 kg received 50 mg and those ≥5 kg received 100 mg nirsevimab).

NGS, next-generation sequencing; RSV, respiratory syncytial virus.

**Supplementary Fig. S2 |** Susceptibility of resistance-associated nirsevimab binding site substitutions N208S and K68E identified in Phase 2b and MELODY trials to neutralization by antibodies in serum from 17 healthy donors.

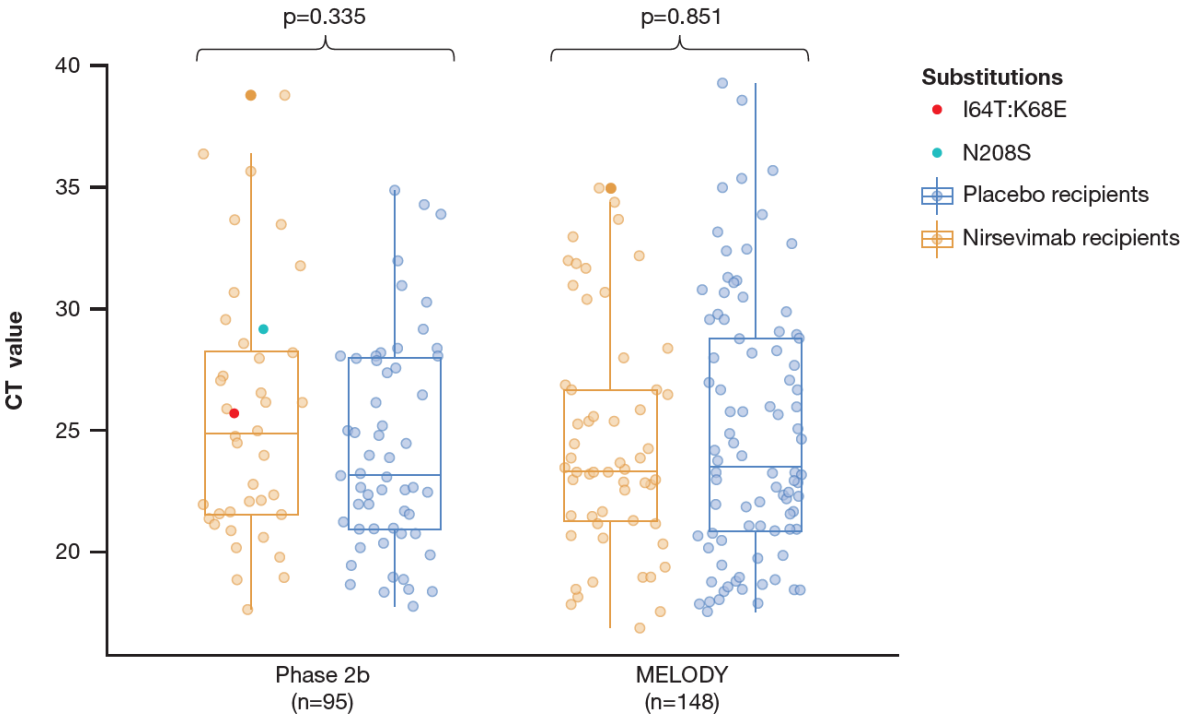



**p<0.05. N208S vs N208, p=0.0028; I64T:K68E:I206M:Q209R vs I64:K68:I206:Q209, p = 0.2639.

$NT_{50}$ values were determined by fitting a four-parameter logistics model using GraphPad Prism 9.4.0. A paired statistical analysis of the corresponding recombinant viruses was performed using a two-tailed t-test. Multiple comparison analysis was not performed.

ns, non-significant; $NT_{50}$, half maximal neutralization titer**.**

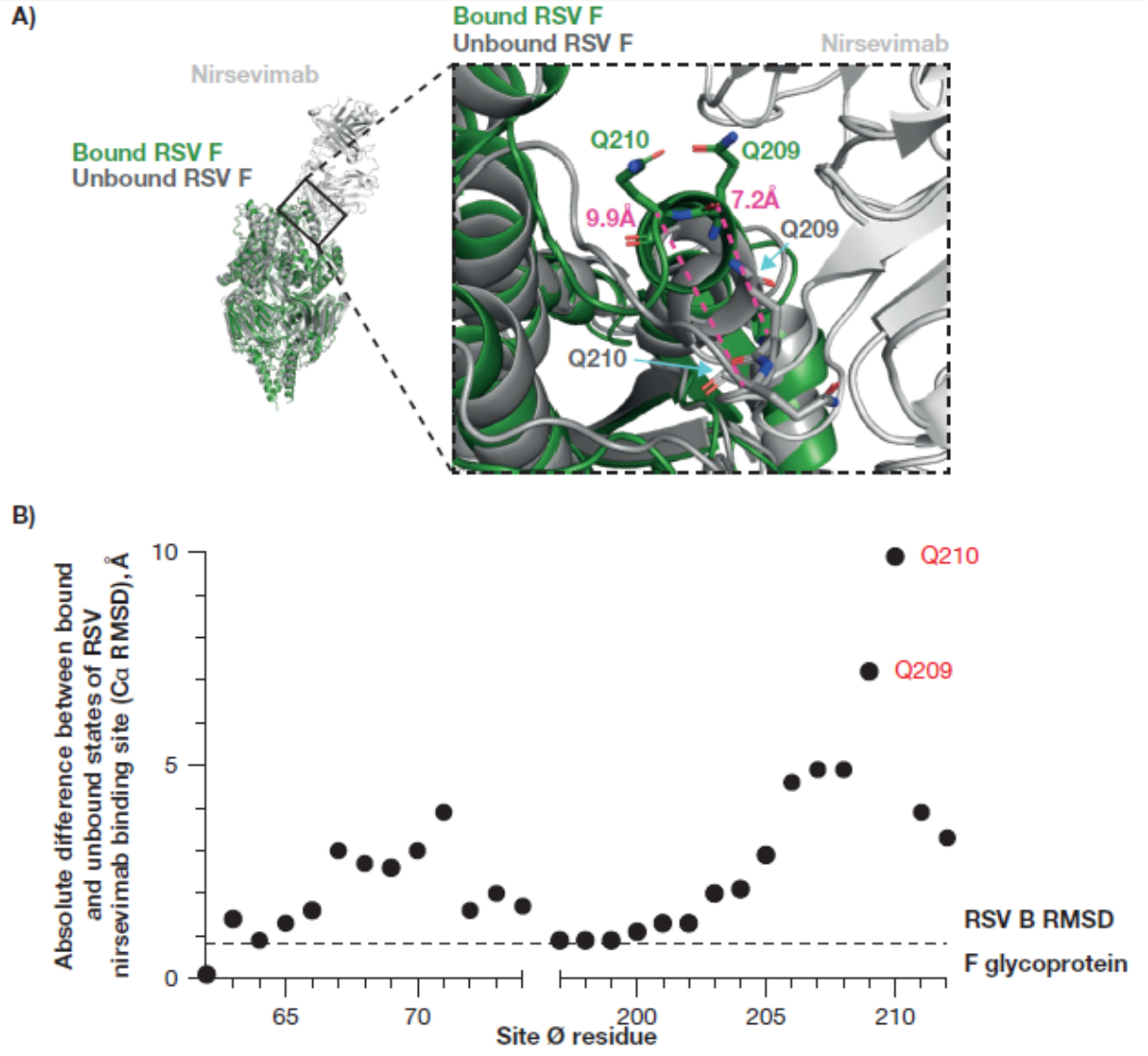
**Supplementary Fig. S3 |** RSV viral titers in participants with resistance-associated substitutions in the Phase 2b and MELODY (primary cohort) studies, as determined by qRT-PCR.

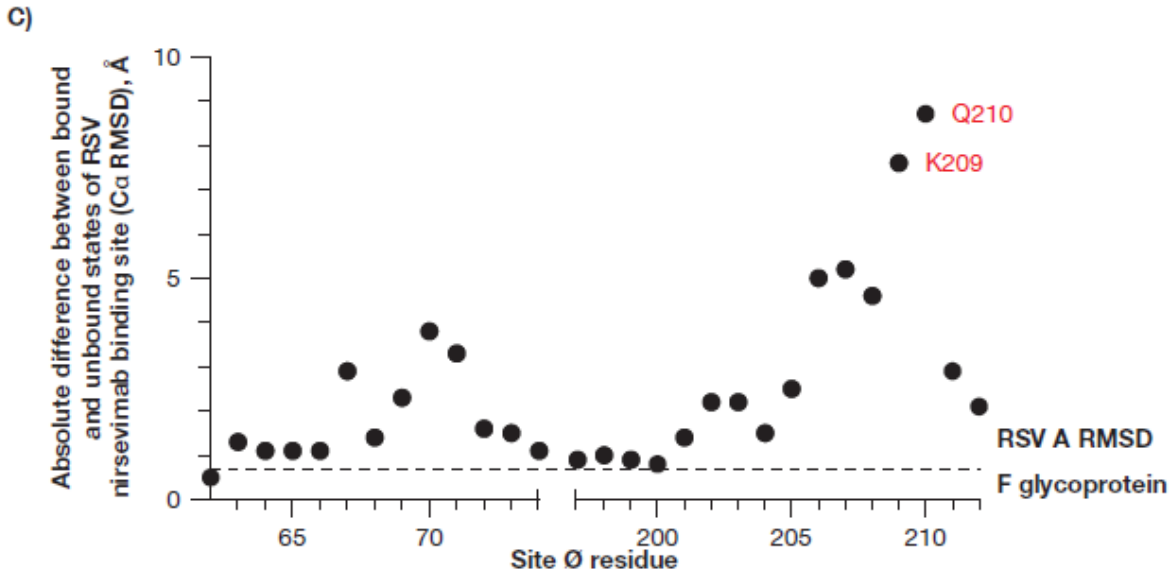



The blue and red dots represent CT values from individuals with N208S and I64T:K68E substitutions, respectively. Boxes indicate the 25th and 75th percentiles, the whiskers are 1.5x inter-quartile range. Filled yellow circles above the whiskers indicates where outliers for nirsevimab recipients fall. P-values were calculated using a two-sided Mann-Whitney test.

CT, cycle threshold; qRT-PCR, quantitative revere-transcriptase polymerase chain reaction; RSV, respiratory syncytial virus.

**Supplementary Fig. S4 |** RSV F protein site Ø conformational changes upon nirsevimab binding. (**A**) Structure and alignment of unbound F glycoprotein site Ø trimer from RSV B (dark green) in complex with nirsevimab (light gray), with largest conformational changes between unbound (dark gray) and bound states shown in angstroms (pink). (**B**) F glycoprotein RSV B monomers bound and unbound and (**C**) F glycoprotein RSV A monomers bound and unbound.

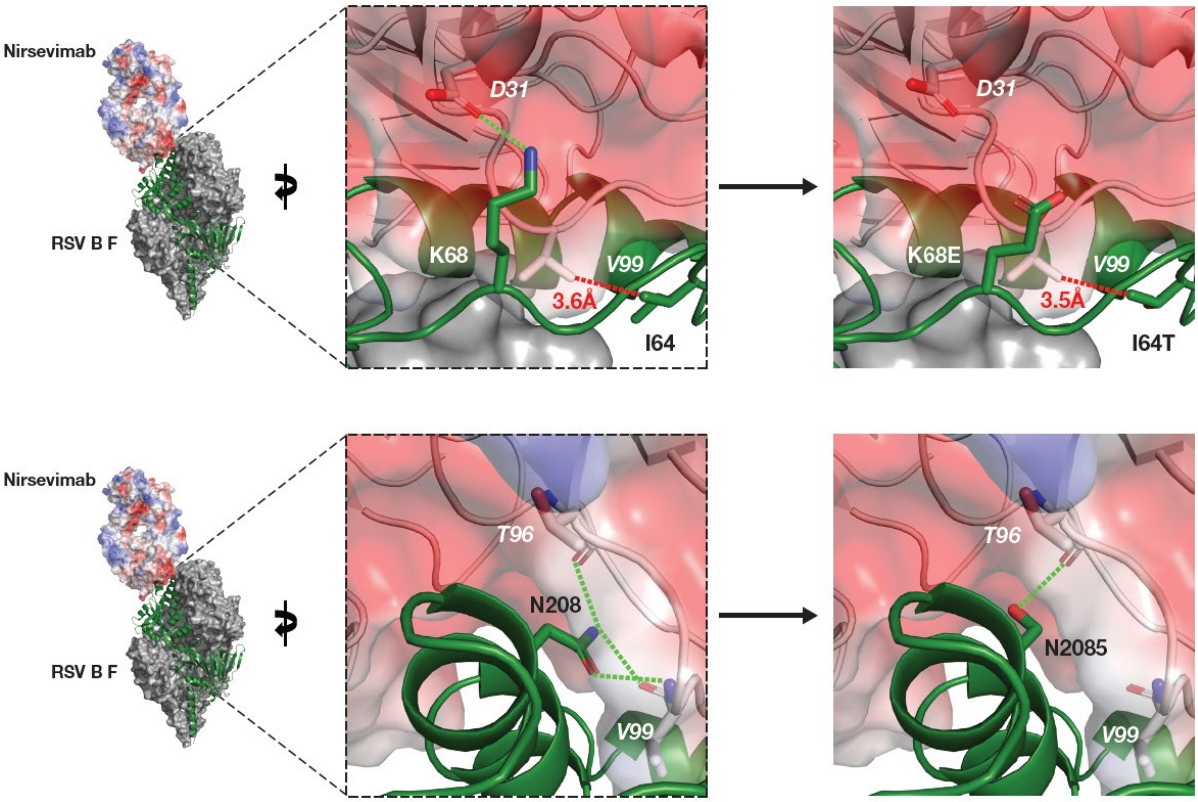





In (**A**) RSV B PDB ID: 5UDE[1]; nirsevimab PDB ID: 5UDD[1]. Site Ø residues Q209 and Q210 in both states are shown as sticks. Light blue arrows indicate the position of Q209 and Q210 in an unbound conformation. The measurements of Q209 and Q210 Cα atoms from unbound to bound states are shown as pink dashed lines, with the distance in angstroms also colored pink. Nirsevimab heavy and light chains are colored light gray. In (**B**) bound F glycoprotein RSV B monomers PDB ID: 5UDD[1]; unbound F glycoprotein RSV B monomers PDB ID: 5UDE[1]. In (**C**) bound F glycoprotein RSV A monomers PDB ID: 5UDC[1]; unbound F glycoprotein RSV B monomers PDB ID: 4MMU[2]. The RMSDs of each site Ø residue between bound and unbound states, as measured by Cα atom distance, were plotted following structural alignment. Residues with the largest conformational changes (Q209, K209, and Q210) are labeled with red text. Black dashed lines along the Y-axis indicate the all-atom RMSD of bound-unbound monomer alignment, with the value in (**A**) equal to 0.8 Å, and the value in (**B**) equal to 0.7 Å. All structural alignment, image capture, and distance measurements were conducted in PyMOL.

PDB, Protein Data Bank; RMSD, root mean squared distance; RSV, respiratory syncytial virus.

**Supplementary Fig. S5 |** Proposed mechanism of decreased RSV B neutralization potency with nirsevimab binding site substitutions K68E and N208S.




Red indicates electrostatics of the negatively charged pocket on nirsevimab. Green dashed lines indicate polar contacts. Red dashed lines are distance measurements.

F, fusion protein; RSV, respiratory syncytial virus

**Independent Ethics Committees/Institutional Review Boards consulted**

| Site Number | Name/Address of IRB/IEC |
|---|---|
| **Phase 2b** | |
| 2002923 | Pharma Ethics 123 Amcor Road Lyttelton Manor Centurion Pretoria, Gauteng |
| 2003359 | MetroHealth Medical Center IRB 2500 MetroHealth Dr. Rammelkamp Bldg. Room 103, Cleveland, Ohio |
| 2002934 | CEP Investiga - Instituto de Pesquisas Avenida Romeu Tortima, 739 - Cidade Universitária Campinas, Sao Paulo |
| 2002970, 2003091, 2003395, 2003007, 2003356, 2003405, 2003355, 2003354, 2003004, 2003353, 2002971, 2003124, 2003350, 2003394, 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 | Copernicus Group IRB 5000 CentreGreen Way Suite 200, Cary, North Carolina |
| 2002935 | CEP da Universidade Federal de Minas Gerais Avenida Presidente Antonio Carlos 6627 Unidade Administrativa II Belo Horizonte Minas Gerais Andrade |
| 2002947 | CEIC de Galicia C/ San Lázaro, s/n Secretaria Xeral. Conselleria de SanidadeDirección Santiago de Compostela La Coruña Ares |
| 2002948 | CEIC de Galicia C/ San Lázaro, s/n Secretaria Xeral. Conselleria de SanidadeDirección Santiago de Compostela La Coruña Arimany Montaña, |
| 2003358 | Medical University of South Carolina IRB 19 Hagood Avenue 6th floor, Suite 601 Charleston South Carolina |
| 2002918 | Wits Health Consortium 31 Princess of Wales Terrace Parktown Johannesburg Gauteng |
| 2002998 | Comite Etico Cientifico del Servicio de Salud Metropolitano Sur Santa Rosa 3453, Piso 1 San Miguel Santiago |
| 2003034 | CESC della Provincia di Padova Presso Azienda Ospedaliera di Padova_Via Giustiniani 1 Padova |
| 2002939 | 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 Bastos |
| 2003060 | CEP da Faculdade de Medicina de Botucatu - UNESP/SP Distrito de Rubião Junior Botucatu Sao Paulo |
| 2003000 | Comitato Etico per la Sperimentazione Clinica delle Provincie di Verona e Rovigo P.le Stefani, 1 Verona |
| 2002919 | Pharma Ethics 123 Amcor Road Lyttelton Manor Centurion Pretoria |

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|---|---|
| 2002910 | Monash Health Human Research Ethics Committee (RGO) Level 2, I Block Clayton Victoria |
| 2002953 | Comité Etico Científico Servicio de Salud Valdivia Maipú 550, oficina 307 Valdivia |
| 2002920 | University of Stellenbosch Ethics Committee Faculty of Health Sciences Francie van Zijl Drive Tygerberg Cape Town Western Cape |
| 2002956 | Comité Ético Científico Servicio de Salud Metropolitano Central Victoria Subercaseaux 381, piso 4 Santiago |
| 2003352 | UTHSC IRB Office 910 Madison Suite 600 Memphis Tennessee |
| 2003118 | Memorial Health Services Research Council 2801 Atlantic Avenue Attn Research Administration Long Beach California |
| 2002972 | SUNY IRB 750 East Adams Street CWB 218G Syracuse New York |
| 2003277 | McGill University Health Center-Research Ethics Board 2155 Guy Street 2nd Floor, Room 231 Montreal Quebec |
| 2002921 | Pharma Ethics 123 Amcor Road Lyttelton Manor Centurion Pretoria Gauteng |
| 2002973, 2003061, 2003069, 2003093, 2003331, 2003447 | WIRB 1019 39th Avenue SE Suite 120 Puyallup Washington |
| 2002905 | Comité de Ética en Investigación Científica. Hospital Pediátrico Dr. Humberto Notti Bandera de Los Andes 2603 Villa Nueva Guaymallén Mendoza |
| 2002967 | R&D University Hospital Southampton NHS Foundation Trust Tremona Road, Level E, Laboratory & Pathology Block, SCBR - MP 138 Southampton, Hampshire |
| 2003320 | R&D - Brighton and Sussex University Hospitals Royal Sussex County Hospital Level 5 Thomas Kemp Tower Eastern Road, Brighton East Sussex |
| 2003065 | Azienda Ospedaliera Città della Salute e della Scienza di Torino Corso Bramante 88/90. Torino |
| 2002940 | Comitê de Ética em Pesquisa em Seres Humanos do Instituto de Medicina Integral Professor Fernando F Rua dos Coelhos, 300 - Boa Vista Recife Pernambuco Gomes |
| 2002922 | University of Cape Town HREC Faculty of Health Sciences Research EC E52-24 Old Main Building Groote Schuur Hospital, Observatory Cape Town Western Cape |
| 2002941 | CEP da Universidade Luterana do Brasil - ULBRA Farroupilha, 8001 - Prédio 14 - Sala 224 Bairro São José Canoas Rio Grande do Sul |
| 2003319 | R&D - Alder Hey Children's NHS Foundation Trust Eaton Road Liverpool Merseyside |
| 2002968 | 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 |
| 2002924 | Eticka komise IKEM a FTNsP Videnska 800 Praha 4 - Krc |
| 2003343 | Sharp Healthcare IRB 7930 Frost St Suite 300 San Diego California |

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|---|---|
| 2003341 | Winthrop-University Hospital IRB 222 Station Plaza North Suite 521 Mineola New York |
| 2002943 | Comitê de Ética em Pesquisa em Seres Humanos do Hospital Pequeno Príncipe Rua Desembargador Motta, 1070 6º andar, sala do NUPE Curitiba Paraná |
| 2003339 | Marshall University Office of Research Integrity One John Marshall Drive Huntington West Virginia |
| 2002937 | Wits Health Consortium 31 Princess of Wales Terrace Parktown Johannesburg Gauteng |
| 2002950 | CEIC de Galicia C/ San Lázaro, s/n Secretaria Xeral. Conselleria de SanidadeDirección Santiago de Compostela La Coruña Martinon |
| 2002944 | CEP da Universidade de Passo Fundo/RS Universidade de Passo Fundo - BR 285, Bairro São José Passo Fundo Rio Grande do Sul |
| 2003011 | Ann & Robert H. Lurie Children's Hospital of Chicago Institutional Review Board 225 E. Chicago Avenue Box 59 Chicago Illinois |
| 2003334, 2002975 | Chesapeake IRB 7063 Columbia Gateway Drive Suite 110 Columbia Maryland |
| 2003067 | Cincinnati Children's Hospital Medical Center IRB 3333 Burnet Ave. MLC 5020 Cincinnati Ohio |
| 2002954 | Comité Ético-Científico Servicio de Salud Metropolitano Sur Oriente Av Concha y Toro 3459 Puente Alto Santiago |
| 2003333 | Childrens Hospital of Los Angeles-Committee on Clinical Investigations IRB 4650 Sunset Blvd Mail Stop #23 Dr. Andreas Reiff Los Angeles California |
| 2003280 | McGill University Health Center-Research Ethics Board 2155 Guy Street 2nd Floor, Room 231 Montreal Quebec |
| 2003005 | University of Texas at San Antonio IRB One UTSA Circle MS 4.01.82 San Antonio Texas |
| 2002951 | CEIC de Galicia C/ San Lázaro, s/n Secretaria Xeral. Conselleria de SanidadeDirección Santiago de Compostela La Coruña |
| 2002911 | Royal Children's Health Services Human Research Ethics Committee (RGO) 50 Flemington Road Parkville Victoria |
| 2002938 | Pharma Ethics 123 Amcor Road Lyttelton Manor Centurion Pretoria Gauteng |
| 2003257 | Comité Ético-Científico Servicio de Salud Viña del Mar-Quillota Calle Limache #1307 Esquina Peñablanca 2º Piso Viña del Mar Quilodran |
| 2003035 | Comitato Etico Regionale della Liguria Largo Rosanna Benzi 10 Farmacia Ospedaliera Genova |
| 2002912 | Princess Margaret Hospital for Children Ethics Committee Princess Margaret Hospital Entrance No 6, Hamilton Street Subiaco Western Australia |
| 2003330 | Arnold Palmer Medical Center Institutional Review Board 1401 Kuhl Avenue MP #21 Research Department Orlando Florida |
| 2003328 | University of Nebraska Medical Center IRB 987830 Nebaska Medical Center, Omaha Nebraska |

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|---|---|
| 2002969 | R&D - CRN Thames Valley and South Midlands 1st Floor, Manor House The John Radcliffe Hospital, Headley Way Headington Oxford Oxfordshire |
| 2002926 | Eticka komise Ustav pro peci o matku a dite Podolske nabrezi 157/36 Praha 4 - Podoli |
| 2002909 | Comité Hospitalario de Etica Necochea 675 Bahia Blanca Buenos Aires |
| 2003274 | Comité d'Ethique du CHU Ambroise Paré Boulevard Kennedy 2 Mons Van |
| 2002955 | Comité de Ética de Investigación en Seres Humanos Av. Independencia 1027, Independencia Santiago Vargas |
| 2003009 | Creighton University IRB 2500 California Plaza IRB-Biomedical Omaha Nebraska |
| 2002966 | R&D University Hospitals Bristol NHS Foundation Trust Education & Research Centre Level 3 Upper Maudlin Street Bristol Avon |
| 2002999 | Comite Etico Cientifico del Servicio de Salud Metropolitano Sur Santa Rosa 3453, Piso 1 San Miguel Santiago Villena |
| 2002927 | Eticka komise Nemocnice Havlickuv Brod Husova 2624 Havlickuv Brod Weberova, |
| 2003448 | Oklahoma University Health Sciences Center 1105 North Stonewall Avenue Oklahoma City Oklahoma |
| 2003406 | Connecticut Children's Medical Center IRB 282 Washington Street. Suite 2 K. Hartford Connecticut |
| 2002946 | University of Cape Town HREC Faculty of Health Sciences Research EC E52-24 Old Main Building Groote Schuur Hospital, Observatory Cape Town Western Cape |
| **MELODY** | |
| 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, 2004618, 2004624, 2004634, 2004650, 2004652, 2004656, 2004657, 2004664, 2004677, 2004679, 2004680, 2004690, 2004697, 2004699, 2004700, 2004702, 2004746, 2004873, 2005604, 2005605, 2005606 | WCG IRB, 212 Carnegie Center, Suite 301, Princeton, NJ 08540, USA |

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|---|---|
| 2004026 | The University of Oklahoma, Institutional Review Board for the Protection of Human Subjects, 1105N. Stone wall Avenue, Oklahoma City, OK73117(FWA 007961) |
| 2004029 | Nemours Office of Human Subjects Protection, Nemours/Alfred I. duPont Hospital for Children, 1600 Rockland Road, Wilmington, DE 19803 |
| 2004036 | 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 |
| 2004039 | Stellenbosch University Human Research Ethics Committee, Stellenbosch University, Private Bag X1, Matieland, 7602, Stellenbosch, South Africa |
| 2004043 | Servicio De Salud Metropolitano Sur Oriente Comite Etico-Cientifico, Av. Concha y Toro 3459 – Paradero 30, Vic. Mackenna |
| 2004098 | UNIVERSIDAD DE CHILE [University of Chile] – FACULTAD DE MEDICINA, HUMAN RESEARCH ETHICS COMMITTEE, Av. Libertador Bernardo O'Higgins 1058, Santiago de Chile |
| 2004103 | Comitato Etico per la Sperimentazione Clinica delle Provincie di Verona e Rovigo,P.le Stefani, 1, Verona,37126 |
| 2004111 | 1 Military Hospital Human Research Ethics Committee, Department of Neurology Private bag X 1026 Thaba Tswane 0143 |
| 2004117 | Dept of health of Chernivtsi city council, Communal Medical Institution City Clinical Childrens' Hospital, 4 Bukovynska St, Chernivtsi, 58001 |
| 2004132 | Independent Ethics Committee for Clinical Pharmacology Trials, Drug and Pharmacology Studies Foundation, LA FUNDACIÓN DE ESTUDIOS FARMACOLOGICOS Y DE MEDICAMENTOS, Pte. J. E. Uriburu 774 1º Piso Ciudad Autónoma de Buenos Aires (C1027AAP), Argentina |
| 2004178 | Landesärztekammer Baden-Württemberg, Ethik-Kommission, Liebknechtstr. 33, 70565 Stuttgart |
| 2004182 | Ethik-Kommission der Bayerischen Landesärztekammer, Mühlbaurstr.16, D-81677 München |
| 2004185 | Ethik-Kommission an der Medizinischen Fakultaet der Universitaet Leipzig,Kaethe-Kollwitz-Strasse 82,Haus: Karl-Sudhoff-Institut Leipzig,04109 |
| 2004222, | Ege University Ethics Committee,Ege Universitesi Tip Fakultesi,Klinik Arastirmalar Etik Kurulu Izmir,35100 |
| 2004227 | Ministy of Health of Ukrain, Communal Non-Commercial enterprise Saint Zinaida Children's Clinical Hospital of Sumy City Council, 28 Troiiska st, Sumy, 40022 |
| 2004229 | Vinnytsia regional Children's Clinical Hospital, 108 Khmelnytske shose st, Vinnytsia, 21000. Medical Ethics Commission |
| 2004233 | Universidad Pontificia Bolivariana, Calle 78 B No. 72 A 109 |
| 2004238 | Institutional Review Board, Ann & Robert H. Lurie Children's Hospital of Chicago, 25 East Chicago Avenue, Chicago, Illinois |
| 2004241 | Cincinnati Children's Hospital Institutional Review Board, 3333 Burnet Avenue \| MLC 7040 \| Cincinnati, OH 45229 |

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|---|---|
| 2004281 | MetroHealth Institutional Review board, 2500 MetroHealth Drive, Cleveland Ohio 44109 |
| 2004294 | 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 |
| 2004295 | CORPORACIÓN CIENTÍFICA PEDIÁTRICA, BIOMEDICAL RESEARCH ETHICS COMMITTEE, Calle 5 B5 No. 37 bis - 28 |
| 2004296 | Ministerio de Salud, Servicio de Salud Valdivia, Scientific Ethics Committee, V. Pérez Rosales 560 - Edificio Prales - Oficina 307 - Piso 3 |
| 2004300 | Servicio de Salud Metropolitano Norte, Research Ethics Committee, 272, Calle Maruri 8380000 Independencia Metropolitana de Santiago |
| 2004304 | UNIVERSIDAD CES, Calle 10A No. 22 - 04 El Poblado |
| 2004310 | Creighton University office of the provost Research Compliance, 2500 California Plaza Omaha, NE 68178-0001 |
| 2004322 | Communal Non-Commercial enterprise of Kharkiv Regional Council Regional Children's clinical hospital, 5 Ozeryanska st Kharkiv, 61093 |
| 2004338 | Odesa Regional State administration, department of health, communal enterprise, Odesa regional Children's clinical hospital, 3 Ac Vorobiov st, Odes-31, 65031 |
| 2004341 | Medical University of South Carolina, 179 Ashley Ave, Charleston, SC 29425 |
| 2004351 | MUHC Centre for Applied Ethics, 5100, boul. de Maisonneuve Ouest, 5th floor, Office 576, Montréal, Québec, H4A 3T2 |
| 2004359 | Ethikkommission der Landesärztekammer Rheinland-Pfalz Deutschhausplatz 3 55116 Mainz |
| 2004365 | MUHC Centre for Applied Ethics, 5100, boul. de Maisonneuve Ouest, 5th floor, Office 576, Montréal, Québec, H4A 3T2 |
| 2004372 | COMITÉ DE ÉTICA EN INVESTIGACIÓN VIT, Calle 24 N° 3-02 este |
| 2004391 | University of Nebraska Medical Center, 42nd and Emile Streets, Omaha, NE 68198, 402-559-4000 |
| 2004396 | COMITATO ETICO DELLA FONDAZIONE POLICLINICO UNIVERSITARIO AGOSTINO GEMELLI IRCCS UNIVERSITÀ CATTOLICA DEL SACRO CUORE |
| 2004400 | Research Ethics Committee of the Health Sciences Department of the Universidad del Norte, Apartados Aéreos 1569 - 51820, Km. 5 vía Puerto Colombia |
| 2004404 | Federico Gomez Children's hospital of Mexico, National Institute of Health research office |
| 2004616 | Stony Brook University, Health Sciences Center Room 031, Stony Brook, NY 11794-8111 |
| 2004623 | UBC C&W Research Ethics Board A2-141A, 950 West 28th Avenue Vancouver, BC V5Z 4H4 |
| 2004626 | Soroka University Medical Center, Itzhak Rager Blv. Beer Sheva 8458900 |
| 2004632 | Japanese Red cross Maebashi Hospital IRB 138-Asakuramachi, Maebashi-Shi Gunma |

| Site Number | Name/Address of IRB/IEC |
|---|---|
| 2004633 | Ethics Commission at Communal Institution Dnipro City Children's Clinical Hospital No 5 of Dnipro City Council, 5 ivana Akinfiieva st, Dnipro 49027 Ukraine |
| 2004648 | Independent Ethics Committee for Clinical Pharmacology Trials, Drug and Pharmacology Studies Foundation, LA FUNDACIÓN DE ESTUDIOS FARMACOLOGICOS Y DE MEDICAMENTOS, Pte. J. E. Uriburu 774 1º Piso Ciudad Autónoma de Buenos Aires (C1027AAP), Argentina |
| 2004658 | Nationwide Children's IRB, Nationwide Children's Hospital, 700 Childrens Drive, Columbus, OH 43205 |
| 2004660 | Yokosuka Kyosai Hospital IRB, 1-16 Yonegahamadori, Yokosuka Kanagawa |
| 2004662 | The University of Tennessee, Health Science Centre Institutional Review Board, 910 Madison Avenue, Suite 600, Memphis, TN 38163 |
| 2004667 | Conjoint Health Research Ethics Board, Research Services Office, 2500 University Drive, NW, Calgary AB T2N 1N4 |
| 2004668 | Jimbo Orthopedic Surgery, Institutional Review Board, 5-38-41, Honcho Koganei-shi, Tokyo |
| 2004669 | State Social Enterprise, HOSPITAL MENTAL DE ANTIOQUIA, [Antioquia Psychiatric Hospital], Calle 38 55-310 Bello-Colombia |
| 2004670 | NHO Okayama Medical Center IRB, Kita-ku Tamasu 1711-1, Okayama-shi, Okayama-Ken, Japan |
| 2004671 | Kawasaki Municipal Hospital Institutional Review Board, 12-1, Shinkawa-dori, Kawasaki-ku, Kawasaki-shi, Kanagawa |
| 2004672 | Laniado Hospital, 16, deuteronomy haim st., kiryat sanz, netanya, 42150 |
| 2004678 | Marshfield Clinic Research Institiute Institutional Review Board, 1000N, Oak Ave, Marshfield, WI 54449-5790 |
| 2004681 | Human Research Ethics Committee, Fundación Hospital Infantil Universitario de San José, Carrera 52 No. 67 A-71 PBX: 4377540 |
| 2004687 | Fukuyama City Hospital Institutional Review Board, 5-23-1 Zao-cho, Fukuyama-shi, Hiroshima |
| 2004688 | KKR Sapporo Medical Center IRB, 6-3-40 Hiragishi 1-jo Toyohira-ku, Sapporo-shi, Hokkaido |
| 2004708 | EMORY UNIVERSITY Institutional Review Board, 201 Dowman Dr, Atlanta, GA 30322, United States |
| 2004747, 2004749 | Navajo Nation Human Research Review Board, Navajo Division of Health, P. O. Box 1390, Window Rock, AZ 86515 |
| 2004748 | Johns Hopkins Bloomberg School Of Public Health, Institutional Review Board Office, 615 N. Wolfe Street / Room E1100 Baltimore, Maryland 21205-2179 |
| 2004768 | Samsung Medical Center Institutional Review Board, (06351) 81 Irwon-Ro Gangnam-gu. Seoul, Korea |
| 2004769 | Yonsei University Health system, Severance Hospital, Institutional review Board, Yonsei-ro 50-1, Seodaemun-gu, Seoul, 03722 |
| 2004797 | human research Protection Program of Korea University medical Center 123 Jeokgeum-ro (Gojan-dong) Danwon-gu, Ansan-si, Gyeonggi-do, 15355 |

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| 2004798 | Inha University Hospital Institutional Review Board, 27 Inhang-ro, Jung-gu, Incheon |
| 2004800 | Yonsei University Gangnam Severance Hospital, IRB, 2nd Floor, 235 Dogok-ro, Gangnam-gu, Seoul 06230 |
| 2005029 | Fukui-ken Saiseikai Hospital Institutional Review Board, 7-1 Funabashi, Wadanaka-cho, Fukui-shi, Fukui-Ken |
| 2005030 | Institutional Review Board of Okayama City General Medical Center Okayama City Hospital, 3-20-1 Kitanagaseomotemachi, Kita-ku, Okayama-shi, Okayama |
| 2005031 | Local Independent Administrative Corporation, Hiroshima City Hospital Organization, Hiroshima City Hiroshima Citizens Hospital Institutional Review Board, 7-33 Motomachi, Naka-ku, Hiroshima-shi, Hiroshima |
| 2005032, 2005034 | Review Board of Human Rights and Ethics for Clinical Studies Institutional Review Board 13-2 Ichibancho, Chiyoda-ku, Tokyo |
| 2005033 | Aijinkai Takatsuki General Hospital IRB, 1-3-13 Kosobe-cho, Takatsuki, Osaka |
| 2005035 | Japanese Red Cross Shizuoka Hospital Institutional Review Board, 8-2 Otemachi, Aoi-ku, Shizuoka-shi, Shizuoka |
| 2005036 | JA Shizuoka Kosei Hospital Institutional Review Board, 23 Kitabancho, Aoi-ku, Shizuoka-shi, Shizuoka |
| 2005037 | Hiroshima Red Cross Hospital & Atomicbomb Survivors Hospital Institutional Review Board, 1-9-6 Sendamachi, Naka-ku, Hiroshima-shI |
| 2005038 | NHO Shikoku Medical Center for Children and Adults Institutional Review Board, 2-1-1, Senyucho, Zentsuji-shi, Kagawa, Japan |
| 2005039 | Daido Hospital Institutional Review Board, 9 Hakusuicho, Minami-ku, Nagoya, Aichi |
| 2005049 | Nagoya Ekisaikai Hospital IRB, 4-66 Shonen-Cho, Nakagawa-ku, Nagoya-Shi, Aichi |
| 2004272, 2004044 | Multicentricka eticka komise IKEM a TN,Videnska 800, Praha,140 59 |
| 2004402, 2004116 | Etikprövningsmyndigheten,Box 2110,SE-750 02 Uppsala,SE-750 02 |
| 2004249, 2004298 | Ethikkommission der Medizinischen Universität Graz,Auenbruggerplatz 2, Graz,8036 |
| 2004373, 2004327 | Child and Adolescent Health Service (HREC), Office 5E, Perth Children's Hospital,15 Hospital Avenue Nedlands,6009 |
| 2004401, 2004399, | Ethics Committee for Multicenter Trials,8 Damyan Gruev Str., Sofia,1303 |
| 2004887, 2004896 | Hospital District of Southwest Finland, Joint Municipal Authority, Ethics Committee, Turku University Hospital, T-Hospital, 6th Floor, Board meeting room A 607 |
| 2004217, 2004109, 2004216 | Wits Health Consortium,31 Princess of Wales Terrace, Parktown Johannesburg, 2193 |
| 2004212, 2004106, 2004214, 2004336 | Ethical Council at the MoH of RF,3 Rakhmanovsky Pereulok, Moscow,127994 |

| Site Number | Name/Address of IRB/IEC |
|---|---|
| 2004335, 2004405, 2004048, 2004105 | Northern B Health and Disability Ethics Committee,20 Aitken Street, Ministry of Health, Ethics Department, Reception - Ground Floor, Thorndon, Wellington,6011 |
| 2004034, 2004108, 2004110, 2004712 | Pharma Ethics Independant Research Ethics committee,123 Amcor Road, Lyttelton Manor Pretoria,0157 |
| 2004395, 2004204, 2004277, 2004710 | Lithuanian Bioethics Committee, Algirdo g. 31, Vilnius,LT-03219 |
| 2004355, 2004384, 2004682, 2004689, 2004383 | NRES Committee South Central - Berkshire, South West REC Centre, Level 3, Block B Bristol,BS1 2NT |
| 2004273, 2004045, 2004046, 2004099, 2004047, 2004274 | Research Ethics Committee of the National Institute for Health Development, Hiiu 42, Tallinn,11619 |
| 2004380, 2004199, 2004331, 2004202, 2004198, 2004302 | Ethics Committee for Clinical Trials of Medicinal Products, Aizkraukles street 21 - 113, Riga,LV1006 |
| 2004867, 2004868, 2004869, 2004870, 2004871, 2004872 | Dr Jose Renan Esquivel Children's hospital, Panama Ave, Balboa, Calle 34 Research Bioethics Committee |
| 2004033, 2004112, 2004113, 2004114, 2004115, 2004218, 2004219, 2004311, 2004333, 2004344, 2004363, 2004369, 2004382, 2004385, 2004406, 2004675, 2004407, 2005603 | Hospital Universitario Clinico San Carlos,Puerta G - Planta 4ª Norte,C/ Profesor Martin Lagos, s/n Madrid, 28040 |
| 2004674, 2004371, 2004049, 2004334, 2004206, 2004381, 2004205, 2004208, 2004350, 2004305 | Komisja Bioetyczna przy Okregowej Izbie Lekarskiej w Rzeszowie,ul. Jana Dekerta 2, Rzeszów, 35-030 |
| 2004629, 2004231, 2004270, 2004299, 2004320, 2004398, 2004320 | O.L.V. Ziekenhuis, Moorselbaan 164, Aalst,9300 |
| 2004303, 2004234, 2004325, 2004339, 2004343, 2004639, 2004324 | Ethics Committee for Clinical Trials,8, Damyan Gruev Str, Sofia, 1303 |
| 2004654, 2004100, 2004232, 2004374, 2004378, 2004646, 2004653, 2004676, 2005602 | Comité de Protection des Personnes Ile de France VIII,Hôpital Ambroise Paré, 9 avenue Charles de Gaulle Boulogne Billancourt, 92100 |
| 2004742, 2004741, 2004313, 2004743, 2004611, 2004312, 2004644 | Varsinais-Suomen sairaanhoitopiiri Eettinen toimikunta, Kiinamyllynkatu 4-8,PL 52 Turku, 20520 |

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