A Phase II Trial of Safety, Tolerability, and Immunogenicity of V114, a 15-Valent Pneumococcal Conjugate Vaccine, Compared to 13-Valent Pneumococcal Conjugate Vaccine (PCV13) in Healthy Infants

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Supplemental Digital Content 1, table: Participants Meeting Rescue Criteria at 1 Month PD3

| Participants with PD3 Immunogenicity Data | V114 Lot 1 | V114 Lot 2 | PCV13 | Total |
|------------------------------------------|------------|------------|-------|-------|
| N=311 %                                  | N=309 %    | N=321 %    | N=941 % |       |
| Rescued Participants                     | 9 2.9      | 12 3.9     | 12 3.9 | 33 3.5 |

Rescue Criteria: IgG <0.35 μg/mL for serotype 19A (alone), or for ≥4 serotypes in common between V114 and PCV13 at 1-month PD3.
Supplemental Digital Content 2, figure: Participant Disposition - All Randomized Participants

Enrolled
N = 1051

V114 Lot 1
N = 351

- Vaccination 1
  N = 350

- Vaccination 2
  N = 333

- Vaccination 3
  N = 330

- Vaccination 4
  N = 310

Completed
N = 308 (87.7%)
Reason Discontinued
Adverse Event = 1
Death = 1
Lack of efficacy = 9
Lost to Follow-Up = 7
Physician Decision = 1
Protocol Deviation = 2
Withdrawal by Parent/Guardian = 22

V114 Lot 2
N = 350

- Vaccination 1
  N = 347

- Vaccination 2
  N = 335

- Vaccination 3
  N = 331

- Vaccination 4
  N = 306

Completed
N = 305 (87.1%)
Reason Discontinued
Adverse Event = 1
Death = 0
Lack of efficacy = 12
Lost to Follow-Up = 8
Physician Decision = 6
Protocol Deviation = 1
Withdrawal by Parent/Guardian = 17

PCV13
N = 350

- Vaccination 1
  N = 347

- Vaccination 2
  N = 335

- Vaccination 3
  N = 332

- Vaccination 4
  N = 311

Completed
N = 308 (88.0%)
Reason Discontinued
Adverse Event = 0
Death = 0
Lack of efficacy = 12
Lost to Follow-Up = 4
Physician Decision = 0
Protocol Deviation = 5
Withdrawal by Parent/Guardian = 21
**Supplemental Digital Content 3, table: All Randomized Participant Demographics**

|                                | V114 Lot 1 | V114 Lot 2 | PCV13  | Total  |
|--------------------------------|------------|------------|--------|--------|
| **Participants in population** | 351        | 350        | 350    | 1051   |
| **Gender**                     |            |            |        |        |
| Male, n (%)                    | 187 (53.3) | 164 (46.9) | 177 (50.6) | 528 (50.2) |
| Female, n (%)                  | 164 (46.7) | 186 (53.1) | 173 (49.4) | 523 (49.8) |
| **Age (in weeks)**             |            |            |        |        |
| Mean                           | 8.8        | 8.8        | 8.7    | 8.7    |
| **Race**                       |            |            |        |        |
| White, n (%)                   | 290 (82.6) | 296 (84.6) | 289 (82.6) | 875 (83.3) |
| Black or African American, n (%) | 34 (9.7)  | 24 (6.9)   | 33 (9.4) | 91 (8.7) |
| Multiple/Other,* n (%)         | 27 (7.7)   | 30 (8.6)   | 28 (8.0) | 85 (8.1) |
| **Ethnicity**                  |            |            |        |        |
| Hispanic or Latino, n (%)      | 49 (14.0)  | 36 (10.3)  | 53 (15.1) | 138 (13.1) |

* Multiple/Other includes Multiracial, American Indian, Alaskan Native, Native Hawaiian, Pacific Islander, or missing.
### Supplemental Digital Content 4, table: Adverse Event (AE) Summary – Days 1-to-14 PD1

|                              | V114 Lot 1 | V114 Lot 2 | PCV13 |
|------------------------------|------------|------------|-------|
|                              | n          | %          | n     | %      |
| Participants with Safety Follow-Up | 350 | 347 | 347 |
| Any Injection-site AE        |            |            |       |
| Injection-site pain*         | 164        | 46.9       | 169   | 48.7   | 137   | 39.5 |
| Injection-site erythema*     | 128        | 36.6       | 122   | 35.2   | 99    | 28.5 |
| Injection-site induration*   | 35         | 10.0       | 57    | 16.4   | 33    | 9.5  |
| Injection-site swelling*     | 46         | 13.1       | 47    | 11.5   | 43    | 12.4 |
| Any Systemic AE              |            |            |       |
| Irritability*                | 285        | 81.4       | 303   | 87.3   | 267   | 76.9 |
| Somnolence*                  | 236        | 67.4       | 251   | 72.3   | 213   | 61.4 |
| Pyrexia                      | 146        | 41.7       | 177   | 51.0   | 156   | 45.0 |
| Decreased appetite*          | 30         | 8.6        | 26    | 7.5    | 28    | 8.1  |
| Serious AEs                  |            |            |       |
| Vaccine-related† serious AEs | 4          | 1.1        | 5     | 1.4    | 2     | 0.6  |
| Deaths                       | 0          | 0.0        | 1     | 0.3    | 0     | 0.0  |

* Solicited AEs (days 1 to 14 following any vaccination)
† Determined by the investigator to be related to the vaccine
### Adverse Event (AE) Summary – Days 1-to-14 PD2

|                                | V114 Lot 1 n | %   | V114 Lot 2 n | %   | PCV13 n | %   |
|--------------------------------|--------------|-----|--------------|-----|---------|-----|
| Participants with Safety Follow-Up | 330          |     | 331          |     | 332     |     |
| Any Injection-site AE          |              |     |              |     |         |     |
| Injection-site pain*           | 132          | 40.0| 130          | 39.3| 111     | 33.4|
| Injection-site erythema*       | 88           | 26.7| 84           | 25.4| 67      | 20.2|
| Injection-site induration*     | 62           | 18.8| 57           | 17.2| 52      | 15.7|
| Injection-site swelling*       | 33           | 10.0| 35           | 10.6| 27      | 8.1 |
| Any Systemic AE                |              |     |              |     |         |     |
| Irritability*                  | 246          | 74.5| 270          | 81.6| 263     | 79.2|
| Somnolence*                    | 199          | 60.3| 221          | 66.8| 207     | 62.3|
| Pyrexia                        | 132          | 40.0| 144          | 43.5| 126     | 38.0|
| Decreased appetite*            | 34           | 10.3| 42           | 12.7| 57      | 17.2|
| Serious AEs                    |              |     |              |     |         |     |
| Vaccine-related† serious AEs   | 0            | 0.0 | 0            | 0.0 | 0       | 0.0 |
| Deaths                         | 0            | 0.0 | 0            | 0.0 | 0       | 0.0 |

* Solicited AEs (days 1 to 14 following any vaccination)
† Determined by the investigator to be related to the vaccine
### Supplemental Digital Content 6, table: Adverse Event (AE) Summary – Days 1-to-14 PD3

|                                  | V114 Lot 1 | V114 Lot 2 | PCV13 |
|----------------------------------|------------|------------|-------|
|                                  | n          | %          |       |
| Participants with Safety Follow-Up | 327        | 326        | 331   |
| Any Injection-site AE            |            |            |       |
| Injection-site pain*             | 125        | 38.2       | 133   |
| Injection-site erythema*         | 72         | 22.0       | 82    |
| Injection-site induration*       | 62         | 19.0       | 64    |
| Injection-site swelling*         | 53         | 16.2       | 45    |
|                                  | 38         | 11.6       | 35    |
| Any Systemic AE                  |            |            |       |
| Irritability*                    | 239        | 73.1       | 252   |
| Somnolence*                      | 171        | 52.3       | 194   |
| Pyrexia                          | 85         | 26.0       | 106   |
| Decreased appetite*              | 38         | 11.6       | 61    |
|                                  | 60         | 18.3       | 57    |
| Serious AEs                      |            |            |       |
| Vaccine-related† serious AEs     | 0          | 0.0        | 2     |
| Deaths                           | 0          | 0.0        | 0     |

* Solicited AEs (days 1 to 14 following any vaccination)
† Determined by the investigator to be related to the vaccine
## Supplemental Digital Content 7, table: Adverse Event (AE) Summary – Days 1-to-14 PD4

|                                | V114 Lot 1 |        | V114 Lot 2 |        | PCV13 |        |
|--------------------------------|------------|--------|------------|--------|-------|--------|
|                                | n  | %    | n  | %    | n  | %    |
| Participants with Safety Follow-Up | 296 | 289  | 296 |
| Any Injection-site AE          |     |      |     |      |     |      |
| Injection-site pain*           | 123 | 41.6 | 122 | 42.2 | 122 | 41.2 |
| Injection-site erythema*       | 80  | 27.0 | 85  | 29.4 | 76  | 25.7 |
| Injection-site induration*     | 60  | 20.3 | 56  | 19.4 | 66  | 22.3 |
| Injection-site swelling*       | 51  | 17.2 | 44  | 15.2 | 55  | 18.6 |
| Any Systemic AE                |     |      |     |      |     |      |
| Irritability*                  | 221 | 74.7 | 221 | 76.5 | 217 | 73.3 |
| Somnolence*                    | 165 | 55.7 | 173 | 59.9 | 169 | 57.1 |
| Pyrexia                        | 85  | 28.7 | 97  | 33.6 | 75  | 25.3 |
| Decreased appetite*            | 63  | 21.3 | 56  | 19.4 | 70  | 23.6 |
| Serious AEs                    |     |      |     |      |     |      |
| Vaccine-related† serious AEs   | 3   | 1.0  | 2   | 0.7  | 0   | 0.0  |
| Deaths                         | 0   | 0.0  | 1   | 0.3  | 0   | 0.0  |

* Solicited AEs (days 1 to 14 following any vaccination)
† Determined by the investigator to be related to the vaccine
**Supplemental Digital Content 8, table:** Vaccine-Related Systemic Adverse Events (Incidence ≥ 5% in Any Group) (Days 1 to 14 Following Any Vaccination)

|                              | V114 Lot 1 | V114 Lot 2 | PCV13  | Total  |
|------------------------------|------------|------------|--------|--------|
|                              | n (% )     | n (% )     | n (% ) | n (% ) |
| Subjects in population with follow-up | 350 (88.0) | 347 (92.2) | 347 (91.1) | 1,044 (90.4) |
| with one or more adverse events | 308 (4.0)  | 8 (2.3)    | 20 (5.8) | 42 (4.0) |
| with no adverse events       | 42 (12.0)  | 27 (7.8)   | 31 (8.9) | 100 (9.6) |
| Diarrhoea                    | 14 (4.0)   | 8 (2.3)    | 20 (5.8) | 42 (4.0) |
| Pyrexia                      | 83 (23.7)  | 92 (26.5)  | 110 (31.7) | 285 (27.3) |
| Decreased appetite           | 119 (34.0) | 142 (40.9) | 121 (34.9) | 382 (36.6) |
| Somnolence                   | 205 (58.6) | 223 (64.3) | 222 (64.0) | 650 (62.3) |
| Irritability                 | 277 (79.1) | 293 (84.4) | 281 (81.0) | 851 (81.5) |

Every subject is counted a single time for each applicable row and column.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Irritability, decreased appetite, somnolence, and urticaria were solicited adverse events.
Supplemental Digital Content 9, figure: IgG Antibody Response Rates Pre-Dose 4 V114 vs. PCV13

| Shared Serotypes | V114 % ≥ 0.35 (95% CI) | PCV13 % ≥ 0.35 (95% CI) | Diff (95% CI) |
|------------------|-------------------------|-------------------------|---------------|
| 1                | 280 42.1                | 287 64.5                | -22.3 (-30.2, -14.4) |
| 3                | 280 26.1                | 287 5.2                 | 20.8 (15.2, 26.8)     |
| 4                | 280 30.7                | 287 33.1                | -2.4 (-10.0, 5.3)     |
| 5                | 280 84.9                | 287 93.4                | -8.5 (4.6, 12.4)      |
| 6A               | 280 50.4                | 287 74.9                | -24.6 (-32.1, -16.7)  |
| 6B               | 280 79.3                | 287 68.6                | 10.6 (3.4, 17.8)      |
| 7F               | 280 92.1                | 287 96.9                | -4.7 (-8.8, -0.6)     |
| 9V               | 280 53.9                | 287 67.6                | -13.7 (-21.5, -5.6)   |
| 14               | 280 95.0                | 287 96.2                | -1.2 (-4.8, 2.4)      |
| 18C              | 280 33.2                | 287 46.7                | -13.5 (-21.4, -5.4)   |
| 19A              | 280 49.6                | 287 64.8                | -15.2 (-25.4, -5.6)   |
| 19F              | 280 60.7                | 287 72.1                | -11.4 (-19.1, -3.6)   |
| 23F              | 280 38.2                | 287 44.9                | -6.7 (-14.8, 1.4)     |

**V114 Lot 1 vs. PCV13**

| Percentage Point Difference (V114-PCV13) |
|----------------------------------------|

| Unique V14 serotypes | V114 % ≥ 0.35 (95% CI) | PCV13 % ≥ 0.35 (95% CI) |
|----------------------|-------------------------|-------------------------|
| 23F                  | 280 97.9 (95.39, 99.21) | 287 3.1 (1.44, 4.87)    |
| 33F                  | 280 95.4 (92.10, 97.51) | 286 4.0 (0.36, 7.54)    |

**V114 Lot 2 vs. PCV13**

| Shared Serotypes | V114 % ≥ 0.35 (95% CI) | PCV13 % ≥ 0.35 (95% CI) | Diff (95% CI) |
|------------------|-------------------------|-------------------------|---------------|
| 1                | 283 48.4                | 287 64.5                | -16.1 (-24.0, -7.9) |
| 3                | 283 32.2                | 287 5.2                 | 26.9 (21.0, 33.0)   |
| 4                | 283 28.6                | 287 33.1                | 4.5 (12.0, -3.1)    |
| 5                | 283 89.8                | 287 93.4                | -3.6 (-4.4, 1.0)    |
| 6A               | 283 55.5                | 287 74.9                | -19.4 (-27.0, -11.7)|
| 6B               | 283 73.1                | 287 68.6                | 4.5 (3.0, 11.9)     |
| 7F               | 283 90.8                | 287 96.9                | -6.1 (-10.3, 2.2)   |
| 9V               | 283 58.3                | 287 67.6                | -9.3 (-17.1, 0.4)   |
| 14               | 283 93.6                | 287 96.2                | -2.6 (-4.4, 1.1)    |
| 18C              | 283 55.8                | 287 46.7                | 9.1 (0.9, 17.2)     |
| 19A              | 283 54.4                | 287 64.8                | -10.4 (-18.3, 2.3)  |
| 19F              | 283 86.1                | 287 72.1                | -6.0 (-13.6, 1.6)   |
| 23F              | 283 52.4                | 287 44.9                | 8.4 (0.2, 16.5)     |

**V114 Lot 2 vs. PCV13**

| Percentage Point Difference (V114-PCV13) |
|----------------------------------------|

| Unique V14 serotypes | V114 % ≥ 0.35 (95% CI) | PCV13 % ≥ 0.35 (95% CI) |
|----------------------|-------------------------|-------------------------|
| 23F                  | 283 96.5 (93.60, 99.29) | 287 3.1 (1.44, 5.87)    |
| 33F                  | 283 93.3 (89.71, 95.91) | 286 4.0 (0.38, 7.54)    |
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