

# Comparative In Vitro Activities of XRP 2868, Pristinamycin, Quinupristin-Dalfopristin, Vancomycin, Daptomycin, Linezolid, Clarithromycin, Telithromycin, Clindamycin, and Ampicillin against Anaerobic Gram-Positive Species, Actinomycetes, and Lactobacilli

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**A comparative study of the in vitro activities of XRP 2868, a new oral streptogramin, against 266 anaerobic gram-positive clinical isolates using the agar dilution method showed that the XRP 2868 MICs for 95% (254 of 266) of isolates were  $\leq 0.5$   $\mu\text{g/ml}$ . XRP 2868 MICs for only two strains, one being *Clostridium clostridioforme* (MIC, 16  $\mu\text{g/ml}$ ) and the other being *Clostridium difficile* (MIC, 32  $\mu\text{g/ml}$ ), were  $> 2$   $\mu\text{g/ml}$ . Depending on its pharmacokinetics and pharmacodynamics, XRP 2868 has potential for use against infections with gram-positive anaerobes and deserves further clinical evaluation.**

Streptogramins are naturally occurring bacteriostatic antibiotics derived from *Streptomyces pristinaspiralis* and act on the 50S ribosome by inhibition of protein synthesis (6). Derivatives include pristinamycin, which has been available in Europe for  $> 30$  years, and quinupristin-dalfopristin, which is available as an injectable combination agent in the United States. While individual streptogramins are bacteriostatic, group A and B streptogramins given in combination act synergistically and may be bactericidal.

XRP 2868 is a new oral streptogramin that is comprised of a mixture of 70% RPR 132552A (group A, PII component) and 30% RPR 202868 (group B, PI component). Pankuch et al. (5) studied the activities of XRP 2868 against 261 pneumococci and 150 *Haemophilus influenzae* strains and found that XRP 2868 “showed potent activity” against all strains “irrespective of their susceptibility to other agents.”

Barriere et al. (J. C. Barriere, E. Bacque, N. Berthaud, G. Dutruc-Rooset, G. Doerflinger, and G. Puchault, Abstr. 41st Intersci. Conf. Antimicrob. Agents Chemother., abstr. F-359, p. 207, 2001) noted that XRP 2868 has an antibacterial spectrum that “includes gram-positive cocci, fastidious gram-negative bacilli, . . . and anaerobes” and suggested that it was of potential value for the therapy of respiratory tract infections. Berthaud et al. (N. Berthaud, N. Diallo, B. Prevost, S. Lannier-Bonnamour, A. De Usatorre, and J. Hodgson, Abstr. 41st Intersci. Conf. Antimicrob. Agents Chemother., abstr. F-360, p. 207, 2001) noted that XRP 2868 has bactericidal activity against *Staphylococcus aureus* in a biofilm model.

In order to extend information about XRP 2868, we studied its comparative in vitro activities against 266 clinical isolates of anaerobic gram-positive organisms.

Strains were isolated from clinical specimens obtained from

adult patients between 1996 and 2002 and identified by standard criteria (2, 3). Strains were consecutive isolates. *S. aureus* ATCC 29213 and *Eubacterium lentum* ATCC 43055 were tested simultaneously. The numbers and species of clinical isolates tested are given in Table 1.

Suppliers of laboratory susceptibility powders were Aventis Pharmaceuticals, Romainville, France, for XRP 2868, pristinamycin, telithromycin, and quinupristin-dalfopristin; Eli Lilly & Co., Indianapolis, Ind., for vancomycin; Cubist Pharmaceuticals, Lexington, Mass., for daptomycin; Pharmacia, Kalamazoo, Mich., for linezolid; and Sigma Chemicals, St. Louis, Mo., for ampicillin and clindamycin.

Susceptibility testing was performed according to methods in National Committee for Clinical Laboratory Standards standards (4), using an agar dilution method with brucella agar supplemented with hemin, vitamin K<sub>1</sub>, and 5% laked sheep blood and an inoculum of  $10^5$  CFU per spot. Daptomycin was supplemented with Ca<sup>2+</sup> (50 mg/liter) as suggested by the manufacturer and in accordance with previously published findings (1). XRP 2868 was dissolved in dimethylformamide, according to the manufacturer’s instructions, in a ratio of 30% RPR 202868 (PI component) and 70% RPR 132552A (PII component).

The results of our study are shown in Table 1. Overall, XRP 2868 had excellent activity against a broad range of gram-positive anaerobic bacteria, including actinomycetes, clostridia, eubacteria, *Propionibacterium* species, and peptostreptococci. Overall, XRP 2868 MICs for 95% (254 of 266) of isolates were  $\leq 0.5$   $\mu\text{g/ml}$ . XRP 2868 MICs for only two strains, one being *Clostridium difficile* and the other being *Clostridium clostridioforme*, were  $> 2$   $\mu\text{g/ml}$ . XRP 2868 was generally similar to or 1 dilution more active in vitro than pristinamycin and often 1 to 4 dilutions more active than quinupristin-dalfopristin. For the *C. clostridioforme* isolate for which the XRP MIC was 16  $\mu\text{g/ml}$ , pristinamycin MICs were 16  $\mu\text{g/ml}$ , quinupristin-dalfopristin MICs were 8

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TABLE 1. Comparative in vitro activities of XRP 2868 against 264 recent clinical isolates of gram-positive anaerobic species, actinomycetes, and lactobacilli

| Organism(s)  | No. of strains  | Antimicrobial             | MIC ( $\mu\text{g/ml}$ ) <sup>a</sup> |             |             |
|--|-----------------|---------------------------|---------------------------------------|-------------|-------------|
|  |                 |                           | Range                                 | 50%         | 90%         |
| <i>Actinomyces israelii</i>                            | 13              | XRP 2868                  | $\leq 0.03-0.06$                      | 0.06        | 0.06        |
|  |                 | Pristinamycin             | $\leq 0.03-0.12$                      | 0.12        | 0.12        |
|  |                 | Quinupristin-dalfopristin | 0.12-0.5                              | 0.25        | 0.25        |
|  |                 | Vancomycin                | 0.5-1                                 | 0.5         | 1           |
|  |                 | Daptomycin                | 0.12->32                              | 2           | 4           |
|  |                 | Linezolid                 | 0.25-16                               | 0.5         | 16          |
|  |                 | Clarithromycin            | $\leq 0.03-0.06$                      | $\leq 0.03$ | 0.06        |
|  |                 | Telithromycin             | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|  |                 | Clindamycin               | $\leq 0.03-0.5$                       | 0.12        | 0.25        |
|  |                 | Ampicillin                | $\leq 0.03-0.5$                       | $\leq 0.03$ | 0.5         |
| <i>Actinomyces meyeri-Actinomyces turicensis</i> group | 12 <sup>b</sup> | XRP 2868                  | $\leq 0.03-0.06$                      | $\leq 0.03$ | $\leq 0.03$ |
|  |                 | Pristinamycin             | $\leq 0.03-0.12$                      | $\leq 0.03$ | $\leq 0.03$ |
|  |                 | Quinupristin-dalfopristin | 0.06-0.5                              | 0.12        | 0.12        |
|  |                 | Vancomycin                | 0.25-1                                | 0.5         | 0.5         |
|  |                 | Daptomycin                | 0.5-16                                | 2           | 8           |
|  |                 | Linezolid                 | 0.12-1                                | 0.5         | 0.5         |
|  |                 | Clarithromycin            | $\leq 0.03-1$                         | $\leq 0.03$ | $\leq 0.03$ |
|  |                 | Telithromycin             | $\leq 0.03-0.06$                      | $\leq 0.03$ | $\leq 0.03$ |
|  |                 | Clindamycin               | $\leq 0.03-0.12$                      | 0.06        | 0.12        |
|  |                 | Ampicillin                | $\leq 0.03-0.25$                      | 0.06        | 0.12        |
| <i>Actinomyces odontolyticus</i>                       | 10              | XRP 2868                  | $\leq 0.03-0.12$                      | 0.06        | 0.12        |
|  |                 | Pristinamycin             | $\leq 0.03-0.12$                      | $\leq 0.03$ | 0.12        |
|  |                 | Quinupristin-dalfopristin | 0.12-0.5                              | 0.25        | 0.25        |
|  |                 | Vancomycin                | 0.5-1                                 | 1           | 1           |
|  |                 | Daptomycin                | 16->32                                | 16          | 32          |
|  |                 | Linezolid                 | 0.5-1                                 | 0.5         | 0.5         |
|  |                 | Clarithromycin            | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|  |                 | Telithromycin             | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|  |                 | Clindamycin               | 0.06->32                              | 0.25        | 0.5         |
|  |                 | Ampicillin                | 0.06-0.5                              | 0.12        | 0.5         |
| <i>Actinomyces viscosus</i>                            | 10              | XRP 2868                  | $\leq 0.03-0.12$                      | 0.06        | 0.06        |
|  |                 | Pristinamycin             | $\leq 0.03-0.12$                      | 0.06        | 0.06        |
|  |                 | Quinupristin-dalfopristin | 0.06-0.5                              | 0.25        | 0.25        |
|  |                 | Vancomycin                | 0.5                                   | 0.5         | 0.5         |
|  |                 | Daptomycin                | 0.5-8                                 | 4           | 8           |
|  |                 | Linezolid                 | 0.5                                   | 0.5         | 0.5         |
|  |                 | Clarithromycin            | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|  |                 | Telithromycin             | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|  |                 | Clindamycin               | $\leq 0.03-1$                         | 0.25        | 0.25        |
|  |                 | Ampicillin                | $\leq 0.03-0.06$                      | 0.06        | 0.06        |
| <i>Clostridium clostridioforme</i>                     | 15              | XRP 2868                  | 0.12-16                               | 0.25        | 4           |
|  |                 | Pristinamycin             | 0.25-16                               | 0.5         | 16          |
|  |                 | Quinupristin-dalfopristin | 0.12-8                                | 0.5         | 4           |
|  |                 | Vancomycin                | 0.25->32                              | 0.5         | 1           |
|  |                 | Daptomycin                | 0.25-8                                | 1           | 4           |
|  |                 | Linezolid                 | 2-4                                   | 2           | 4           |
|  |                 | Clarithromycin            | 0.06->64                              | >64         | >64         |
|  |                 | Telithromycin             | $\leq 0.03->32$                       | >32         | >32         |
|  |                 | Clindamycin               | $\leq 0.03-32$                        | 0.5         | 4           |
|  |                 | Ampicillin                | 0.5->32                               | 1           | 1           |
| <i>Clostridium difficile</i>                           | 14              | XRP 2868                  | 0.12-32                               | 0.12        | 2           |
|  |                 | Pristinamycin             | 0.12-16                               | 0.12        | 4           |
|  |                 | Quinupristin-dalfopristin | 0.25-2                                | 0.25        | 1           |
|  |                 | Vancomycin                | 0.25-2                                | 0.5         | 1           |
|  |                 | Daptomycin                | 0.5-2                                 | 0.5         | 2           |
|  |                 | Linezolid                 | 2-8                                   | 2           | 8           |
|  |                 | Clarithromycin            | 0.25->64                              | 0.5         | >64         |
|  |                 | Telithromycin             | 0.12->32                              | 4           | >32         |
|  |                 | Clindamycin               | 1->32                                 | 4           | >32         |
|  |                 | Ampicillin                | 0.5-2                                 | 1           | 2           |

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TABLE 1—Continued

| Organism(s)                    | No. of strains    | Antimicrobial             | MIC ( $\mu\text{g/ml}$ ) <sup>a</sup> |             |      |
|--------------------------------|-------------------|---------------------------|---------------------------------------|-------------|------|
|                                |                   |                           | Range                                 | 50%         | 90%  |
| <i>Clostridium innocuum</i>    | 15                | XRP 2868                  | 0.06–0.5                              | 0.12        | 0.25 |
|                                |                   | Pristinamycin             | 0.12–2                                | 0.12        | 0.25 |
|                                |                   | Quinupristin-dalfopristin | 0.12–1                                | 0.25        | 0.25 |
|                                |                   | Vancomycin                | 8–16                                  | 16          | 16   |
|                                |                   | Daptomycin                | 2–8                                   | 4           | 8    |
|                                |                   | Linezolid                 | 2–4                                   | 2           | 2    |
|                                |                   | Clarithromycin            | 0.12–>64                              | >64         | >64  |
|                                |                   | Telithromycin             | $\leq 0.03$ –>32                      | 2           | >32  |
|                                |                   | Clindamycin               | 0.25–>32                              | 0.5         | >32  |
| Ampicillin                     | 0.12–0.25         | 0.12                      | 0.25                                  |             |      |
| <i>Clostridium perfringens</i> | 12                | XRP 2868                  | 0.06–0.12                             | 0.06        | 0.06 |
|                                |                   | Pristinamycin             | 0.12                                  | 0.12        | 0.12 |
|                                |                   | Quinupristin-dalfopristin | 0.12–0.5                              | 0.25        | 0.25 |
|                                |                   | Vancomycin                | 0.5                                   | 0.5         | 0.5  |
|                                |                   | Daptomycin                | 0.25–1                                | 1           | 1    |
|                                |                   | Linezolid                 | 2                                     | 2           | 2    |
|                                |                   | Clarithromycin            | 0.5–1                                 | 0.5         | 1    |
|                                |                   | Telithromycin             | 0.12–0.25                             | 0.12        | 0.12 |
|                                |                   | Clindamycin               | 0.06–1                                | 1           | 1    |
| Ampicillin                     | $\leq 0.03$ –0.06 | $\leq 0.03$               | 0.06                                  |             |      |
| <i>Clostridium ramosum</i>     | 16                | XRP 2868                  | 0.06–1                                | 0.5         | 1    |
|                                |                   | Pristinamycin             | 0.25–2                                | 0.25        | 2    |
|                                |                   | Quinupristin-dalfopristin | 0.12–2                                | 0.25        | 2    |
|                                |                   | Vancomycin                | 1–8                                   | 4           | 4    |
|                                |                   | Daptomycin                | 8–>32                                 | 32          | 32   |
|                                |                   | Linezolid                 | 4–8                                   | 8           | 8    |
|                                |                   | Clarithromycin            | 0.25–>64                              | >64         | >64  |
|                                |                   | Telithromycin             | $\leq 0.03$ –>32                      | >32         | >32  |
|                                |                   | Clindamycin               | 0.25–>32                              | 4           | 4    |
| Ampicillin                     | $\leq 0.03$ –1    | 0.06                      | 0.25                                  |             |      |
| <i>Eubacterium lentum</i>      | 9                 | XRP 2868                  | 0.06–0.25                             | 0.12        |      |
|                                |                   | Pristinamycin             | 0.06–0.12                             | 0.06        |      |
|                                |                   | Quinupristin-dalfopristin | 0.12–0.5                              | 0.25        |      |
|                                |                   | Vancomycin                | 0.5–1                                 | 1           |      |
|                                |                   | Daptomycin                | 8–32                                  | 16          |      |
|                                |                   | Linezolid                 | 1–2                                   | 2           |      |
|                                |                   | Clarithromycin            | $\leq 0.03$ –>64                      | $\leq 0.03$ |      |
|                                |                   | Telithromycin             | $\leq 0.03$ –2                        | $\leq 0.03$ |      |
|                                |                   | Clindamycin               | 0.12–0.5                              | 0.12        |      |
| Ampicillin                     | 0.12–0.5          | 0.25                      |                                       |             |      |
| <i>Eubacterium limosum</i>     | 10                | XRP 2868                  | $\leq 0.03$ –1                        | 0.25        | 1    |
|                                |                   | Pristinamycin             | $\leq 0.03$ –2                        | 0.12        | 1    |
|                                |                   | Quinupristin-dalfopristin | 0.12–2                                | 0.25        | 1    |
|                                |                   | Vancomycin                | 0.25–2                                | 2           | 2    |
|                                |                   | Daptomycin                | 0.06–0.5                              | 0.25        | 0.25 |
|                                |                   | Linezolid                 | 1–4                                   | 2           | 4    |
|                                |                   | Clarithromycin            | $\leq 0.03$ –>64                      | 0.06        | >64  |
|                                |                   | Telithromycin             | $\leq 0.03$ –>32                      | $\leq 0.03$ | >32  |
|                                |                   | Clindamycin               | $\leq 0.03$ –>32                      | 1           | 2    |
| Ampicillin                     | $\leq 0.03$ –0.12 | $\leq 0.03$               | 0.06                                  |             |      |
| <i>Eubacterium</i> group       | 13 <sup>c</sup>   | XRP 2868                  | $\leq 0.03$ –1                        | 0.12        | 0.5  |
|                                |                   | Pristinamycin             | $\leq 0.03$ –1                        | 0.12        | 1    |
|                                |                   | Quinupristin-dalfopristin | $\leq 0.03$ –1                        | 0.5         | 1    |
|                                |                   | Vancomycin                | 0.25–4                                | 1           | 2    |
|                                |                   | Daptomycin                | 0.06–8                                | 0.5         | 0.5  |
|                                |                   | Linezolid                 | 0.5–2                                 | 2           | 2    |
|                                |                   | Clarithromycin            | $\leq 0.03$ –>64                      | 0.5         | >64  |
|                                |                   | Telithromycin             | $\leq 0.03$ –>32                      | 0.12        | >32  |
|                                |                   | Clindamycin               | $\leq 0.03$ –32                       | 0.06        | 1    |
| Ampicillin                     | $\leq 0.03$ –0.25 | $\leq 0.03$               | 0.06                                  |             |      |

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TABLE 1—Continued

| Organism(s)                         | No. of strains  | Antimicrobial             | MIC ( $\mu\text{g/ml}$ ) <sup>a</sup> |             |             |
|-------------------------------------|-----------------|---------------------------|---------------------------------------|-------------|-------------|
|                                     |                 |                           | Range                                 | 50%         | 90%         |
| <i>Lactobacillus plantarum</i>      | 10              | XRP 2868                  | 0.12–0.5                              | 0.12        | 0.5         |
|                                     |                 | Pristinamycin             | 0.12–1                                | 0.25        | 1           |
|                                     |                 | Quinupristin-dalfopristin | 0.5–2                                 | 0.5         | 2           |
|                                     |                 | Vancomycin                | 0.5–4                                 | 4           | 4           |
|                                     |                 | Daptomycin                | 8–>32                                 | 32          | >32         |
|                                     |                 | Linezolid                 | 4–8                                   | 8           | 8           |
|                                     |                 | Clarithromycin            | $\leq 0.03$ –>64                      | 0.25        | >64         |
|                                     |                 | Telithromycin             | $\leq 0.03$ –>32                      | $\leq 0.03$ | >32         |
|                                     |                 | Clindamycin               | 2–8                                   | 2           | 4           |
|                                     |                 | Ampicillin                | $\leq 0.03$ –0.5                      | $\leq 0.03$ | 0.25        |
| <i>Lactobacillus casei</i>          | 6               | XRP 2868                  | 0.12–0.5                              | 0.25        |             |
|                                     |                 | Pristinamycin             | 0.12–0.25                             | 0.25        |             |
|                                     |                 | Quinupristin-dalfopristin | 0.5–1                                 | 1           |             |
|                                     |                 | Vancomycin                | >32                                   | >32         |             |
|                                     |                 | Daptomycin                | 1–4                                   | 2           |             |
|                                     |                 | Linezolid                 | 4                                     | 4           |             |
|                                     |                 | Clarithromycin            | 0.12                                  | 0.12        |             |
|                                     |                 | Telithromycin             | $\leq 0.03$                           | 0.02        |             |
|                                     |                 | Clindamycin               | 0.12                                  | 0.12        |             |
|                                     |                 | Ampicillin                | 0.5–4                                 | 1           |             |
| <i>Lactobacillus</i> spp.           | 16 <sup>d</sup> | XRP 2868                  | $\leq 0.03$ –1                        | 0.12        | 0.25        |
|                                     |                 | Pristinamycin             | $\leq 0.03$ –2                        | 0.12        | 0.25        |
|                                     |                 | Quinupristin-dalfopristin | 0.12–4                                | 0.25        | 1           |
|                                     |                 | Vancomycin                | 0.25–8                                | 1           | 4           |
|                                     |                 | Daptomycin                | 0.25–>32                              | 4           | >32         |
|                                     |                 | Linezolid                 | 1–8                                   | 4           | 8           |
|                                     |                 | Clarithromycin            | $\leq 0.03$ –>64                      | 0.25        | >64         |
|                                     |                 | Telithromycin             | $\leq 0.03$ –>32                      | 0.06        | >32         |
|                                     |                 | Clindamycin               | $\leq 0.03$ –>32                      | 0.5         | 4           |
|                                     |                 | Ampicillin                | $\leq 0.03$ –1                        | 0.12        | 0.5         |
| <i>Propionibacterium acnes</i>      | 10              | XRP 2868                  | $\leq 0.03$ –0.12                     | $\leq 0.03$ | $\leq 0.03$ |
|                                     |                 | Pristinamycin             | $\leq 0.03$ –0.12                     | $\leq 0.03$ | $\leq 0.03$ |
|                                     |                 | Quinupristin-dalfopristin | $\leq 0.03$ –0.5                      | 0.12        | 0.12        |
|                                     |                 | Vancomycin                | 0.25–0.5                              | 0.5         | 0.5         |
|                                     |                 | Daptomycin                | 0.12–1                                | 0.5         | 1           |
|                                     |                 | Linezolid                 | 0.25–0.5                              | 0.5         | 0.5         |
|                                     |                 | Clarithromycin            | $\leq 0.03$ –0.12                     | $\leq 0.03$ | $\leq 0.03$ |
|                                     |                 | Telithromycin             | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|                                     |                 | Clindamycin               | $\leq 0.03$ –0.12                     | $\leq 0.03$ | 0.06        |
|                                     |                 | Ampicillin                | $\leq 0.03$ –0.12                     | 0.06        | 0.06        |
| <i>Propionibacterium avidum</i>     | 12              | XRP 2868                  | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|                                     |                 | Pristinamycin             | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|                                     |                 | Quinupristin-dalfopristin | 0.12                                  | 0.12        | 0.12        |
|                                     |                 | Vancomycin                | 0.5                                   | 0.5         | 0.5         |
|                                     |                 | Daptomycin                | 1–2                                   | 2           | 2           |
|                                     |                 | Linezolid                 | $\leq 0.5$                            | $\leq 0.5$  | $\leq 0.5$  |
|                                     |                 | Clarithromycin            | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|                                     |                 | Telithromycin             | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|                                     |                 | Clindamycin               | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|                                     |                 | Ampicillin                | $\leq 0.03$ –0.12                     | 0.12        | 0.12        |
| <i>Propionibacterium granulosum</i> | 10              | XRP 2868                  | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|                                     |                 | Pristinamycin             | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|                                     |                 | Quinupristin-dalfopristin | 0.06–0.12                             | 0.12        | 0.12        |
|                                     |                 | Vancomycin                | 0.5–1                                 | 0.5         | 1           |
|                                     |                 | Daptomycin                | 0.12–1                                | 0.5         | 1           |
|                                     |                 | Linezolid                 | 0.25–0.5                              | 0.25        | 0.25        |
|                                     |                 | Clarithromycin            | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|                                     |                 | Telithromycin             | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|                                     |                 | Clindamycin               | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|                                     |                 | Ampicillin                | $\leq 0.03$ –0.5                      | 0.06        | 0.06        |

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TABLE 1—Continued

| Organism(s)                           | No. of strains    | Antimicrobial             | MIC ( $\mu\text{g/ml}$ ) <sup>a</sup> |             |             |
|---------------------------------------|-------------------|---------------------------|---------------------------------------|-------------|-------------|
|                                       |                   |                           | Range                                 | 50%         | 90%         |
| <i>Peptostreptococcus anaerobius</i>  | 10                | XRP 2868                  | $\leq 0.03$ –0.12                     | 0.06        | 0.06        |
|                                       |                   | Pristinamycin             | $\leq 0.03$ –0.12                     | $\leq 0.03$ | 0.12        |
|                                       |                   | Quinupristin-dalfopristin | 0.06–0.5                              | 0.12        | 0.25        |
|                                       |                   | dalfopristin              |                                       |             |             |
|                                       |                   | Vancomycin                | 0.25–0.5                              | 0.25        | 0.5         |
|                                       |                   | Daptomycin                | 0.25–4                                | 0.25        | 0.5         |
|                                       |                   | Linezolid                 | 0.5–8                                 | 0.5         | 8           |
|                                       |                   | Clarithromycin            | $\leq 0.03$ –>64                      | $\leq 0.03$ | 0.12        |
|                                       |                   | Telithromycin             | $\leq 0.03$ –0.5                      | $\leq 0.03$ | $\leq 0.03$ |
|                                       |                   | Clindamycin               | $\leq 0.03$ –8                        | $\leq 0.03$ | 0.25        |
| Ampicillin                            | $\leq 0.03$ –0.12 | 0.06                      | 0.12                                  |             |             |
| <i>Peptoniphilus asaccharolyticus</i> | 10                | XRP 2868                  | $\leq 0.03$ –0.25                     | 0.12        | 0.12        |
|                                       |                   | Pristinamycin             | $\leq 0.03$ –0.12                     | 0.12        | 0.12        |
|                                       |                   | Quinupristin-dalfopristin | 0.25–0.5                              | 0.5         | 0.5         |
|                                       |                   | Vancomycin                | 0.06–0.5                              | 0.12        | 0.12        |
|                                       |                   | Daptomycin                | $\leq 0.03$ –0.25                     | $\leq 0.03$ | $\leq 0.03$ |
|                                       |                   | Linezolid                 | 0.5–1                                 | 0.5         | 1           |
|                                       |                   | Clarithromycin            | 0.25–>64                              | 1           | >64         |
|                                       |                   | Telithromycin             | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|                                       |                   | Clindamycin               | $\leq 0.03$ –1                        | 0.12        | 1           |
|                                       |                   | Ampicillin                | $\leq 0.03$ –0.12                     | $\leq 0.03$ | 0.06        |
| <i>Finegoldia magna</i>               | 11 <sup>e</sup>   | XRP 2868                  | $\leq 0.03$ –0.25                     | 0.12        | 0.12        |
|                                       |                   | Pristinamycin             | 0.06–0.12                             | 0.12        | 0.12        |
|                                       |                   | Quinupristin-dalfopristin | 0.25–0.5                              | 0.25        | 0.5         |
|                                       |                   | Vancomycin                | 0.25–1                                | 0.25        | 0.5         |
|                                       |                   | Daptomycin                | 0.25–4                                | 0.5         | 1           |
|                                       |                   | Linezolid                 | 0.5–2                                 | 1           | 2           |
|                                       |                   | Clarithromycin            | $\leq 0.03$ –>64                      | >64         | >64         |
|                                       |                   | Telithromycin             | $\leq 0.03$ –1                        | $\leq 0.03$ | 0.06        |
|                                       |                   | Clindamycin               | $\leq 0.03$ –>32                      | 0.25        | 4           |
|                                       |                   | Ampicillin                | $\leq 0.03$ –0.25                     | 0.12        | 0.25        |
| <i>Micromonas micros</i>              | 11 <sup>e</sup>   | XRP 2868                  | $\leq 0.03$ –0.12                     | 0.12        | 0.12        |
|                                       |                   | Pristinamycin             | 0.06–0.25                             | 0.06        | 0.12        |
|                                       |                   | Quinupristin-dalfopristin | 0.5–1                                 | 0.5         | 1           |
|                                       |                   | Vancomycin                | 0.25–0.5                              | 0.5         | 0.5         |
|                                       |                   | Daptomycin                | 0.25–1                                | 0.5         | 0.5         |
|                                       |                   | Linezolid                 | 0.05–1                                | 0.5         | 0.5         |
|                                       |                   | Clarithromycin            | 0.12–0.25                             | 0.12        | 0.25        |
|                                       |                   | Telithromycin             | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
|                                       |                   | Clindamycin               | 0.06–0.25                             | 0.12        | 0.12        |
|                                       |                   | Ampicillin                | $\leq 0.03$                           | $\leq 0.03$ | $\leq 0.03$ |
| <i>Anaerococcus prevotii</i>          | 11 <sup>e</sup>   | XRP 2868                  | $\leq 0.03$ –0.12                     | $\leq 0.03$ | 0.12        |
|                                       |                   | Pristinamycin             | $\leq 0.03$ –0.12                     | 0.06        | 0.12        |
|                                       |                   | Quinupristin-dalfopristin | $\leq 0.03$ –1                        | 0.25        | 0.5         |
|                                       |                   | Vancomycin                | 0.12–1                                | 0.5         | 0.5         |
|                                       |                   | Daptomycin                | $\leq 0.03$ –16                       | 0.06        | 0.12        |
|                                       |                   | Linezolid                 | $\leq 0.03$ –2                        | 0.5         | 1           |
|                                       |                   | Clarithromycin            | $\leq 0.03$ –32                       | $\leq 0.03$ | 0.06        |
|                                       |                   | Telithromycin             | $\leq 0.03$ –32                       | $\leq 0.03$ | 0.06        |
|                                       |                   | Clindamycin               | $\leq 0.03$ –8                        | 0.06        | 1           |
|                                       |                   | Ampicillin                | $\leq 0.03$ –0.12                     | $\leq 0.03$ | 0.06        |

<sup>a</sup> 50% and 90%, MICs at which 50 and 90% of isolates tested, respectively, were inhibited.

<sup>b</sup> *Actinomyces meyeri* ( $n = 5$ ) and *Actinomyces turicensis* ( $n = 7$ ).

<sup>c</sup> *Eubacterium contortum* ( $n = 2$ ), *Eubacterium moniliforme* ( $n = 1$ ), *Eubacterium tenue* ( $n = 2$ ), *Pseudoramibacter alactolyticus* ( $n = 7$ ), and *Eubacterium* sp., no good fit ( $n = 1$ ).

<sup>d</sup> Includes *Lactobacillus acidophilus* ( $n = 2$ ), *Lactobacillus catenaforme* ( $n = 8$ ), *Lactobacillus gasseri* ( $n = 1$ ), *Lactobacillus jensenii* ( $n = 2$ ), *Lactobacillus leichmannii* ( $n = 1$ ), *Lactobacillus rhamnosus* ( $n = 1$ ) and *Lactobacillus uli* ( $n = 1$ ).

<sup>e</sup> Formerly *Peptostreptococcus* sp.

$\mu\text{g/ml}$ , daptomycin MICs were 8  $\mu\text{g/ml}$ , and ampicillin, clarithromycin, and telithromycin MICs were >32  $\mu\text{g/ml}$ . The vancomycin MICs were 1  $\mu\text{g/ml}$ , and the linezolid and clindamycin MICs were 2  $\mu\text{g/ml}$ . In comparison, for the *C.*

*difficile* isolate for which the XRP MIC was 32  $\mu\text{g/ml}$ , pristinamycin MICs were 16  $\mu\text{g/ml}$ ; clarithromycin, telithromycin, and clindamycin MICs were >32  $\mu\text{g/ml}$ ; linezolid MICs were 8  $\mu\text{g/ml}$ ; ampicillin and quinupristin-dalfopristin MICs

were 2 µg/ml; daptomycin MICs were 1 µg/ml; and vancomycin MICs were 0.5 µg/ml.

Daptomycin had decreased activity (MIC > 4 µg/ml) against 14 strains of *Actinomyces* spp. and all *Clostridium ramosum*, *E. lentum*, and *Lactobacillus plantarum* strains. Linezolid showed decreased activity (MIC, 4 µg/ml) against all strains of *C. ramosum*, 2 strains of *C. difficile*, and 15 strains of *Lactobacillus* spp. Ampicillin MICs were >1 µg/ml for eight strains of *Clostridium* spp. and three strains of *Lactobacillus casei*.

Depending on its pharmacokinetics and pharmacodynamics, XRP 2868 has potential for use against infections with gram-positive anaerobes and deserves further clinical evaluation.

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