METHOD FOR TREATING, PREVENTING, OR REDUCING THE RISK OF SKIN INFECTION

RELATED APPLICATIONS

[0001] This application claims the benefit of priority under 35 U.S.C. § 119(e) of United States Provisional Application No. 62/080,212, filed November 14, 2014, the contents of which are hereby incorporated in their entirety.

FIELD OF THE INVENTION

[0002] The present invention relates to methods for treating, preventing, or reducing the risk of acne and other skin infections caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient by administering a safe and effective amount of an antibiotic compound.

BACKGROUND

[0003] Acne is a common inflammatory pilosebaceous disease characterized by comedones, papules, pustules, inflamed nodules, superficial pus-filled cysts, and in extreme cases, sinus formation and deep inflammation, sometimes associated with purulent sacs.

[0004] The pathogenesis of acne is complex. An interaction between hormones, keratinization, sebum, and bacteria somehow determines the course and severity of the disease. Acne usually begins at puberty when the increase of androgens causes an increase in the size and activity of the pilosebaceous glands. The earliest microscopic change is intrafollicular hyperkeratosis, which leads to restriction of the pilosebaceous follicle with consequent formation of the comedone composed of sebum, keratin, and microorganisms, particularly *Propionibacterium acnes*. Lipases from *Propionibacterium acnes* break down triglycerides in the sebum to form free fatty acids (FFA), which irritate the follicular wall. Retention of sebaceous secretions and dilation of the follicle may lead to cyst formation. Rupture of the follicle with release of the contents into the tissues induces an inflammatory reaction which heals with scarring in severe cases.

[0005] Acne tends to appear during puberty and to fade away again, usually spontaneously when growth has stopped. Occasionally it is still to be found in older adults. The face, back, and shoulders are the predominant areas affected. Particularly with the face, severe cases can cause

alterations resulting in considerable disfigurement with significant psychological burdens for the afflicted person.

[0006] Over the years, many compositions have been developed for the treatment or prevention of acne. For example, acne can be treated by topical application of various lotions, salves, and the like or by, for example, localized treatment with sulfur, resorcinol, salicylic acid, benzoyl peroxide, vitamin A acids, retinoic acid, antibiotics such as erythromycin, and the like. Acne has also been treated orally with antibiotics and tretinoin. However, the effectiveness, reliability, and convenience of current treatments have not always met with patient expectations.

[0007] Salicylic acid is a long-known anti-acne active ingredient which is believed to cause a reduction in intercellular cohesion of the corneocytes (*see* C. Huber et al., *Arch. Derm. Res.* 257, pp. 293-297, 1977). It has also been postulated that salicylic acid works by dissolving the existing keratin plugs, as well as by preventing the formation of new ones. In order to best exert its skin benefits, the ideal anti-acne composition should deliver and retain optimal concentrations of salicylic acid in the stratum corneum with less penetration through the skin and into the general circulation. Also, compliance by the user to a regimen of treatment involving repeated applications is important. However, salicylic acid tends to be somewhat drying and irritating and can often cause peeling, thereby causing individuals to refrain from using salicylic acid products as frequently and copiously as is necessary to obtain an optimum benefit. Thus, user compliance with current salicylic acid compositions is less than ideal.

[0008] Benzoyl peroxide has been used as a keratolytic agent and an antibacterial agent in the topical treatment of skin lesions such as acne. *See e.g.*, Levine et al., Ohio State Med. J., 65, 492 (1969); U.S. Pat. No. 3,535,422, to Cox et al., issued Oct. 20, 1970; British Patent Application Nos. 1,185,685, to Fisher, published Mar. 25, 1970; 1,163,004, to Stiefel Laboratories, Inc., published Sep. 4, 1969; and 1,407,937, to Stiefel Laboratories, Inc. published Oct. 1, 1975. The topical application of benzoyl peroxide for skin lesion therapy is thoroughly detailed in the medical literature. *See* Brogdne et al., *Drugs*, 4, 417 (1974); Poole et al., *Arch Derm.*, 102, 400 (1972); Eaglstein, *Arch Derm.*, 97, 527 (1968); Pace, *Can. Med. Assoc. J.*, 93,252 (1965); Vasarinsh, *Arch. Derm.*, 98, 183 (1968); Mysliborski et al., *AFP*, 15, 86 (1977); Nare, *Br. J. Clin. Prac,*, 29, 63 (1975); Fulton et al., *Arch. Derm.*, 1, 10, 83 (1974); and Wilkinson et al., *Can. Med. Assoc. J.*, 95, 28 (1966).

[0009] While benzoyl peroxide can be a useful topical treatment of skin lesions from acne, seborrhea, and other conditions, it has the undesirable side effect of being a contact irritant. The irritation associated with benzoyl peroxide therapy has also been detailed in the medical literature

cited in the previous paragraph. Additionally, the redness induced by benzoyl peroxide may impair a patient's ability to perceive the improvement in acne condition initially. Accordingly, some patients are denied the benefits of benzoyl peroxide therapy because of the irritation problem. When used in the treatment of acne, benzoyl peroxide produces dryness, exfoliation, increased redness and a decrease in bacterial flora.

[0010] Other agents, such as retinoic acid, are used for the treatment of acne. However, retinoic acid can be extremely drying and irritating when applied topically and can adversely affect the structure of the skin. Also, retinoic acid can be administered orally. However, retinoic acid can be teratogenic and have other undesired side effects.

[0011] Antibiotic agents, such as erythromycin, clindamycin, tetracycline, and beta lactams have also been used both orally and topically in the treatment of acne. However, as is a problem with the use of most antibiotic agents in general, bacteria can become resistant making the underlying condition more difficult to treat. Resistant strains of *Propionibacterium acnes*, *Staphylococcus aureus*, *Propionibacterium granulosum*, *Gardnerella vaginalis* and other bacteria involved in acne have begun to emerge. *See*, *e.g.*, Eady E.A., et al. The effects of acne treatment with a combination of benzoyl peroxide and erythromycin on skin carriage of erythromycin-resistant propionibacteria. *Br. J. Dermatol.* 1996; *134*:107-113; McLean, N. W.; McGroarty, J. A. *Appl. Environ. Microbiol.* **1996,** *62*(3), 1089-1092; Nagaraja, P. *Indian J. Med. Microbiol.* **2008,** *26*(2), 155-157; Tomusiak, A. *et al. Ginekol. Pol.* **2011,** *82*(12), 900-904; Eschenbach, D. A. *Clin. Infectious Dis.* **2007,** *44*(2), 220-221. Furthermore, bacteria, including resistant strains of bacteria, can also cause further complications such as skin infections, eye infections, bone and joint infections, central nervous system infections, and endocarditis. Therefore, with antibiotic treatments for acne, it would be highly desirable to have effective treatments which are also useful against resistant bacteria. See Tan, A.W. and Tan, H.H., "Acne vulgaris,: a review of antibiotic therapy", *Expert Opin. Pharmacother.*, 2005 Mar 6(3), 409-418; Oprica, C. et al., "European surveillance study on the antibiotic susceptibility of *Propionibacterium acnes",* Clinical Microbiology and Infection, Volume 11, Number 3, March 2005, pp. 204-312; and Goldstein, E., et al., "Comparative In Vitro Activities of retapamulin (SB-275833) against 141 Clinical isolates of *propionibacterium* spp., Including 117 *P. acnes* Isolates", Antimicrobial Agents and Chemotherapy, Jan. 2006, p. 379-381, vol. 50, no. 1.

[0012] From the foregoing, and especially in view of the development of resistant strains of bacteria, it is seen that there is a continuing need for safe, effective, and convenient means for

treating, preventing, or reducing the risk of acne and other skin infections caused or mediated by *Propionibacterium acnes, Staphylococcus aureus*, or *Gardneralla vaginalis*.

[0013] Bacterial vaginosis (BV) is one of the most common vaginal diseases in women of reproductive age. Since BV is caused by an imbalance of normal vaginal microorganisms, there are multiple risk factors, including the use of intrauterine devices, the use of douches, and new sexual partners. *Gardnerella vaginalis* is a causative agent of BV. BV may present with a burning sensation when urinating and white or gray discharge with a fish-like odor. Additionally, BV can increase the risk of contracting sexually transmitted diseases, including HIV/AIDS. Treatment of BV with current antibiotics has high rates of failure and recurrence. Thus, it is important for there to be safe, effective, and convenient alternatives for treating, preventing, or reducing the risk of BV.

[0014] The present invention provides methods for treating, preventing, and reducing the risk of acne and other skin infections caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus*, in a patient by administering a safe and effective amount of an antibiotic compound, *e.g.*, a topically applied oxazolidinone compound.

SUMMARY OF THE INVENTION

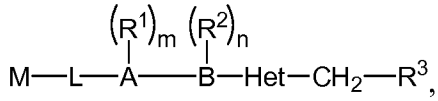
[0015] The present invention relates to methods for treating, preventing, or reducing the risk of acne and other skin infections caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* by administering to a patient in need thereof a safe and effective amount of an antibiotic compound, *e.g.*, an oxazolidinone compound.

[0016] The present invention relates to compounds for use in methods for treating, preventing, or reducing the risk of acne and other skin infections caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient in need thereof. For example, the compounds for use are administered in a safe and effective amount. The compound can be, *e.g.*, an oxazolidinone compound.

[0017] In addition, the present invention provides formulations useful in the present invention and provides the use of an antibiotic compound in the manufacture of a medicament useful for topically treating, preventing, or reducing the risk of acne and other skin infections caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus*.

[0018] In one aspect, disclosed herein is a method of treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes, Gardnerella vaginalis,* or

Staphylococcus aureus in a patient, the method comprising administering a pharmaceutically effective amount of a compound having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, wherein:

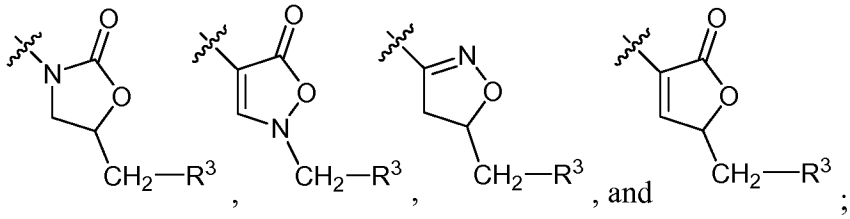
A is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

B is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

Het-CH_2-R^3 is selected from the group consisting of:



M is selected from the group consisting of:

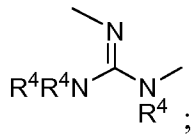
a) saturated, unsaturated, or aromatic C_{3-14} carbocycle, and b) saturated, unsaturated, or aromatic 3-14 membered heterocycle containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, wherein a) or b) optionally is substituted with one or more R^5 groups;

M-L is selected from the group consisting of:

a) M-X, b) M-L^1, c) M-L^1-X, d) M-X-L^2, e) M-L^1-X-L^2, f) M-X-L^1-X-L^2, g) M-L^1-X-L^2-X, h) M-X-X-, i) M-L^1-X-X-, j) M-X-X-L^2, and k) M-L^1-X-X-L^2, wherein

X, at each occurrence, independently is selected from the group consisting of:

a) -O-, b) -NR^4-, c) –N(O)-, d) –N(OR^4)-, e) -$S(O)_p$-, f) -SO_2NR^4-, g) -NR^4SO_2-, h) -NR^4-N=, i) =N-NR^4-, j) -O-N=, k) =N-O-, l) -N=, m) =N-, n) -NR^4-NR^4-, o) -$NR^4C(O)O$-, p) -$OC(O)NR^4$-, q) -$NR^4C(O)NR^4$- r) -$NR^4C(NR^4)NR^4$-, and s)



L^1 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups; and

L^2 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups;

R^1, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) $-CF_3$, f) $-OR^4$, g) -CN, h) $-NO_2$, i) $-NR^4R^4$, j) $-C(O)R^4$, k) $-C(O)OR^4$, l) $-OC(O)R^4$, m) $-C(O)NR^4R^4$, n) $-NR^4C(O)R^4$, o) $-OC(O)NR^4R^4$, p) $-NR^4C(O)OR^4$, q) $-NR^4C(O)NR^4R^4$, r) $-C(S)R^4$, s) $-C(S)OR^4$, t) $-OC(S)R^4$, u) $-C(S)NR^4R^4$, v) $-NR^4C(S)R^4$, w) $-OC(S)NR^4R^4$, x) $-NR^4C(S)OR^4$, y) $-NR^4C(S)NR^4R^4$, z) $-NR^4C(NR^4)NR^4R^4$, aa) $-S(O)_pR^4$, bb) $-SO_2NR^4R^4$, and cc) R^4;

R^2, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) $-CF_3$, f) $-OR^4$, g) -CN, h) $-NO_2$, i) $-NR^4R^4$, j) $-C(O)R^4$, k) $-C(O)OR^4$, l) $-OC(O)R^4$, m) $-C(O)NR^4R^4$, n) $-NR^4C(O)R^4$, o) $-OC(O)NR^4R^4$, p) $-NR^4C(O)OR^4$, q) $-NR^4C(O)NR^4R^4$, r) $-C(S)R^4$, s) $-C(S)OR^4$, t) $-OC(S)R^4$, u) $-C(S)NR^4R^4$, v) $-NR^4C(S)R^4$, w) $-OC(S)NR^4R^4$, x) $-NR^4C(S)OR^4$, y) $-NR^4C(S)NR^4R^4$, z) $-NR^4C(NR^4)NR^4R^4$, aa) $-S(O)_pR^4$, bb) $-SO_2NR^4R^4$, and cc) R^4;

R^3 is selected from the group consisting of:

a) $-OR^4$, b) $-NR^4R^4$, c) $-C(O)R^4$, d) $-C(O)OR^4$, e) $-OC(O)R^4$, f) $-C(O)NR^4R^4$, g) $-NR^4C(O)R^4$, h) $-OC(O)NR^4R^4$, i) $-NR^4C(O)OR^4$, j) $-NR^4C(O)NR^4R^4$, k) $-C(S)R^4$, l) $-C(S)OR^4$, m) $-OC(S)R^4$, n) $-C(S)NR^4R^4$, o) $-NR^4C(S)R^4$, p) $-OC(S)NR^4R^4$, q) $-NR^4C(S)OR^4$, r) $-NR^4C(S)NR^4R^4$, s) $-NR^4C(NR^4)NR^4R^4$, t) $-S(O)_pR^4$, u) $-SO_2NR^4R^4$, and v) R^4;

R^4, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) $-C(O)-C_{1-6}$ alkyl, h) $-C(O)-C_{2-6}$ alkenyl, i) $-C(O)-C_{2-6}$ alkynyl, j) $-C(O)-C_{3-14}$ saturated,

unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated,

unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^5 groups;

R^5, at each occurrence, is independently selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) =NR^6, h) =NOR^6, i) =N-NR^6R^6, j) -CF_3, k) -OR^6, l) -CN, m) -NO_2, n) –NR^6R^6, o) -C(O)R^6, p) -C(O)OR^6, q) -OC(O)R^6, r) -C(O)NR^6R^6, s) –NR^6C(O)R^6, t) -OC(O)NR^6R^6, u) -NR^6C(O)OR^6, v) -NR^6C(O)NR^6R^6, w) -C(S)R^6, x) -C(S)OR^6, y) -OC(S)R^6, z) -C(S)NR^6R^6, aa) -NR^6C(S)R^6, bb) -OC(S)NR^6R^6, cc) -NR^6C(S)OR^6, dd) –NR^6C(S)NR^6R^6, ee) –NR^6C(NR^6)NR^6R^6, ff) -$S(O)_pR^6$, gg) -$SO_2NR^6R^6$, and hh) R^6;

R^6, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) -C(O)-C_{1-6} alkyl, h) -C(O)-C_{2-6} alkenyl, i) –C(O)-C_{2-6} alkynyl, j) -C(O)-C_{3-14} saturated,

unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^7 groups;

R^7, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) =NR^8, h) =NOR^8, i) =N-NR^8R^8, j) -CF_3, k) -OR^8, l) -CN, m) -NO_2, n) –NR^8R^8, o) -C(O)R^8, p) -C(O)OR^8, q) -OC(O)R^8, r) -C(O)NR^8R^8, s) –NR^8C(O)R^8, t) -OC(O)NR^8R^8, u) -NR^8C(O)OR^8, v) -NR^8C(O)NR^8R^8, w) -C(S)R^8, x) -C(S)OR^8, y) -OC(S)R^8, z) -C(S)NR^8R^8,

aa) -$NR^8C(S)R^8$, bb) -$OC(S)NR^8R^8$, cc) -$NR^8C(S)OR^8$, dd) –$NR^8C(S)NR^8R^8$, ee) -$NR^8C(NR^8)NR^8R^8$, ff) -$S(O)_pR^8$, gg) -$SO_2NR^8R^8$, hh) C_{1-6} alkyl, ii) C_{2-6} alkenyl, jj) C_{2-6} alkynyl, kk) C_{3-14} saturated, unsaturated, or aromatic carbocycle, and ll) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of hh) – ll) optionally is substituted with one or more moieties selected from the group consisting of R^8, F, Cl, Br, I, -CF_3, –OR^8, –SR^8, -CN, -NO_2, –NR^8R^8, -$C(O)R^8$, -$C(O)OR^8$, -$OC(O)R^8$, -$C(O)NR^8R^8$, -$NR^8C(O)R^8$, -$OC(O)NR^8R^8$, –$NR^8C(O)OR^8$, -$NR^8C(O)NR^8R^8$, -$C(S)R^8$, -$C(S)OR^8$, -$OC(S)R^8$, -$C(S)NR^8R^8$, -$NR^8C(S)R^8$, -$OC(S)NR^8R^8$, -$NR^8C(S)OR^8$, -$NR^8C(S)NR^8R^8$, -$NR^8C(NR^8)NR^8R^8$, -$SO_2NR^8R^8$, and-$S(O)_pR^8$;

R^8, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) -$C(O)$-C_{1-6} alkyl, h) -$C(O)$-C_{2-6} alkenyl, i) –$C(O)$-C_{2-6} alkynyl, j) -$C(O)$-C_{3-14} saturated, unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -$C(O)O$-C_{1-6} alkyl, m) -$C(O)O$-C_{2-6} alkenyl, n) –$C(O)O$-C_{2-6} alkynyl, o) -$C(O)O$-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

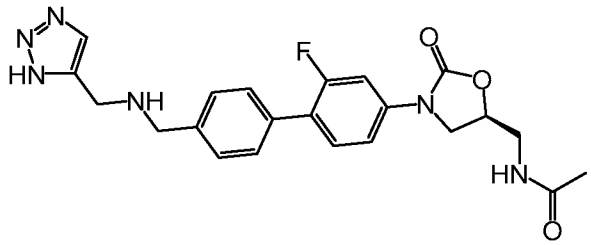
wherein any of b) – p) optionally is substituted with one or more moieties selected from the group consisting of F, Cl, Br, I, -CF_3, -OH, -OCH_3, -SH, -SCH_3, -CN, -NO_2, –NH_2, -$NHCH_3$, -$N(CH_3)_2$, -$C(O)CH_3$, -$C(O)OCH_3$, -$C(O)NH_2$, –$NHC(O)CH_3$, -SO_2NH_2, -SO_2NHCH_3, -$SO_2N(CH_3)_2$, and-$S(O)_pCH_3$;

m, at each occurrence, independently is 0, 1, 2, 3, or 4;

n, at each occurrence, independently is 0, 1, 2, 3, or 4; and

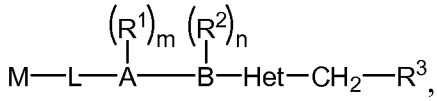
p, at each occurrence, independently is 0, 1, or 2.

[0019] In another aspect, disclosed herein is a method of treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient, the method comprising administering a pharmaceutically effective amount of a compound having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof.

[0020] In another aspect, disclosed herein is a topical formulation for use in treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes, Gardnerella vaginalis,* or *Staphylococcus aureus* in a patient, the formulation comprising one or more dermatologically acceptable carriers and one or more compounds having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, wherein:

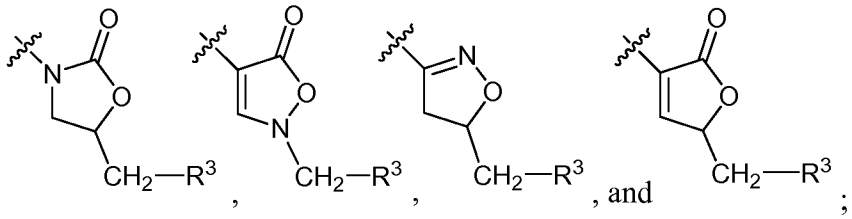
A is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

B is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

Het-CH_2-R^3 is selected from the group consisting of:



M is selected from the group consisting of:

a) saturated, unsaturated, or aromatic C_{3-14} carbocycle, and b) saturated, unsaturated, or aromatic 3-14 membered heterocycle containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

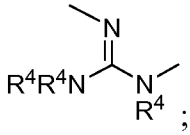
wherein a) or b) optionally is substituted with one or more R^5 groups;

M-L is selected from the group consisting of:

a) M-X, b) M-L^1, c) M-L^1-X, d) M-X-L^2, e) M-L^1-X-L^2, f) M-X-L^1-X-L^2, g) M-L^1-X-L^2-X, h) M-X-X-, i) M-L^1-X-X-, j) M-X-X-L^2, and k) M-L^1-X-X-L^2, wherein

X, at each occurrence, independently is selected from the group consisting of:

a) -O-, b) -NR^4-, c) –N(O)-, d) –N(OR^4)-, e) -$S(O)_p$-, f) -SO_2NR^4-, g) -NR^4SO_2-, h) -NR^4-N=, i) =N-NR^4-, j) -O-N=, k) =N-O-, l) -N=, m) =N-, n) -NR^4-NR^4-, o) -$NR^4C(O)O$-, p) -$OC(O)NR^4$-, q) -$NR^4C(O)NR^4$- r) -$NR^4C(NR^4)NR^4$-, and s)



;

L^1 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups; and

L^2 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups;

R^1, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) -CF_3, f) –OR^4, g) -CN, h) -NO_2, i) -NR^4R^4, j) -$C(O)R^4$, k) -$C(O)OR^4$, l) -$OC(O)R^4$, m) -$C(O)NR^4R^4$, n) -$NR^4C(O)R^4$, o) -$OC(O)NR^4R^4$, p -$NR^4C(O)OR^4$, q) –$NR^4C(O)NR^4R^4$, r) -$C(S)R^4$, s) -$C(S)OR^4$, t) -$OC(S)R^4$, u) -$C(S)NR^4R^4$, v) –$NR^4C(S)R^4$, w) -$OC(S)NR^4R^4$, x) –$NR^4C(S)OR^4$, y) -$NR^4C(S)NR^4R^4$, z) -$NR^4C(NR^4)NR^4R^4$, aa) -$S(O)_pR^4$, bb) -$SO_2NR^4R^4$, and cc) R^4;

R^2, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) -CF_3, f) –OR^4, g) -CN, h) -NO_2, i) -NR^4R^4, j) -$C(O)R^4$, k) -$C(O)OR^4$, l) -$OC(O)R^4$, m) -$C(O)NR^4R^4$, n) -$NR^4C(O)R^4$, o) -$OC(O)NR^4R^4$, p) -$NR^4C(O)OR^4$, q) –$NR^4C(O)NR^4R^4$, r) -$C(S)R^4$, s) -$C(S)OR^4$, t) -$OC(S)R^4$, u) -$C(S)NR^4R^4$, v) –$NR^4C(S)R^4$, w) -$OC(S)NR^4R^4$, x) –$NR^4C(S)OR^4$, y) -$NR^4C(S)NR^4R^4$, z) -$NR^4C(NR^4)NR^4R^4$, aa) -$S(O)_pR^4$, bb) -$SO_2NR^4R^4$, and cc) R^4;

R^3 is selected from the group consisting of:

a) $-OR^4$, b) $-NR^4R^4$, c) $-C(O)R^4$, d) $-C(O)OR^4$, e) $-OC(O)R^4$, f) $-C(O)NR^4R^4$, g) $-NR^4C(O)R^4$, h) $-OC(O)NR^4R^4$, i) $-NR^4C(O)OR^4$, j) $-NR^4C(O)NR^4R^4$, k) $-C(S)R^4$, l) $-C(S)OR^4$, m) $-OC(S)R^4$, n) $-C(S)NR^4R^4$, o) $-NR^4C(S)R^4$, p) $-OC(S)NR^4R^4$, q $-NR^4C(S)OR^4$, r) $-NR^4C(S)NR^4R^4$, s) $-NR^4C(NR^4)NR^4R^4$, t) $-S(O)_pR^4$, u) $-SO_2NR^4R^4$, and v) R^4;

R^4, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) $-C(O)-C_{1-6}$ alkyl, h) $-C(O)-C_{2-6}$ alkenyl, i) $-C(O)-C_{2-6}$ alkynyl, j) $-C(O)-C_{3-14}$ saturated,
unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) $-C(O)O-C_{1-6}$ alkyl, m) $-C(O)O-C_{2-6}$ alkenyl, n) $-C(O)O-C_{2-6}$ alkynyl, o) $-C(O)O-C_{3-14}$ saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^5 groups;

R^5, at each occurrence, is independently selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) $=NR^6$, h) $=NOR^6$, i) $=N-NR^6R^6$, j) $-CF_3$, k) $-OR^6$, l) -CN, m) $-NO_2$, n) $-NR^6R^6$, o) $-C(O)R^6$, p) $-C(O)OR^6$, q) $-OC(O)R^6$, r) $-C(O)NR^6R^6$, s) $-NR^6C(O)R^6$, t) $-OC(O)NR^6R^6$, u) $-NR^6C(O)OR^6$, v) $-NR^6C(O)NR^6R^6$, w) $-C(S)R^6$, x) $-C(S)OR^6$, y) $-OC(S)R^6$, z) $-C(S)NR^6R^6$, aa) $-NR^6C(S)R^6$, bb) $-OC(S)NR^6R^6$, cc) $-NR^6C(S)OR^6$, dd) $-NR^6C(S)NR^6R^6$, ee) $-NR^6C(NR^6)NR^6R^6$, ff) $-S(O)_pR^6$, gg) $-SO_2NR^6R^6$, and hh) R^6;

R^6, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) $-C(O)-C_{1-6}$ alkyl, h) $-C(O)-C_{2-6}$ alkenyl, i) $-C(O)-C_{2-6}$ alkynyl, j) $-C(O)-C_{3-14}$ saturated,

unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^7 groups;

R^7, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) =NR^8, h) =NOR^8, i) =N-NR^8R^8, j) -CF_3, k) -OR^8, l) -CN, m) -NO_2, n) –NR^8R^8, o) -C(O)R^8, p) -C(O)OR^8, q) -OC(O)R^8, r) -C(O)NR^8R^8, s) –NR^8C(O)R^8, t) -OC(O)NR^8R^8, u) -NR^8C(O)OR^8, v) -NR^8C(O)NR^8R^8, w) -C(S)R^8, x) -C(S)OR^8, y) -OC(S)R^8, z) -C(S)NR^8R^8, aa) -NR^8C(S)R^8, bb) -OC(S)NR^8R^8, cc) -NR^8C(S)OR^8, dd) –NR^8C(S)NR^8R^8, ee) -NR^8C(NR^8)NR^8R^8, ff) -$S(O)_pR^8$, gg) -$SO_2NR^8R^8$, hh) C_{1-6} alkyl, ii) C_{2-6} alkenyl, jj) C_{2-6} alkynyl, kk) C_{3-14} saturated, unsaturated, or aromatic carbocycle, and ll) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of hh) – ll) optionally is substituted with one or more moieties selected from the group consisting of R^8, F, Cl, Br, I, -CF_3, –OR^8, –SR^8, -CN, -NO_2, –NR^8R^8, -C(O)R^8, -C(O)OR^8, -OC(O)R^8, -C(O)NR^8R^8, –NR^8C(O)R^8, -OC(O)NR^8R^8, –NR^8C(O)OR^8, -NR^8C(O)NR^8R^8, -C(S)R^8, -C(S)OR^8, -OC(S)R^8, -C(S)NR^8R^8, -NR^8C(S)R^8, -OC(S)NR^8R^8, -NR^8C(S)OR^8, -NR^8C(S)NR^8R^8, -NR^8C(NR^8)NR^8R^8, -$SO_2NR^8R^8$, and-$S(O)_pR^8$;

R^8, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) -C(O)-C_{1-6} alkyl, h) -C(O)-C_{2-6} alkenyl, i) –C(O)-C_{2-6} alkynyl, j) -C(O)-C_{3-14} saturated,
unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated,

unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

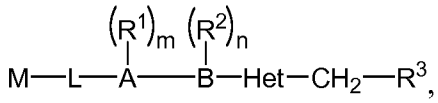
wherein any of b) – p) optionally is substituted with one or more moieties selected from the group consisting of F, Cl, Br, I, -CF_3, -OH, -OCH_3, -SH, -SCH_3, -CN, -NO_2, –NH_2, -$NHCH_3$, -$N(CH_3)_2$, -$C(O)CH_3$, -$C(O)OCH_3$, -$C(O)NH_2$, –$NHC(O)CH_3$, -SO_2NH_2, -SO_2NHCH_3, -$SO_2N(CH_3)_2$, and-$S(O)_pCH_3$;

m, at each occurrence, independently is 0, 1, 2, 3, or 4;

n, at each occurrence, independently is 0, 1, 2, 3, or 4; and

p, at each occurrence, independently is 0, 1, or 2.

[0021] In another aspect, disclosed herein is a topical formulation for use in treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes, Gardnerella vaginalis,* or *Staphylococcus aureus* in a patient, the formulation comprising one or more dermatologically acceptable carriers and one or more compounds having the formula:

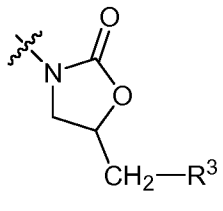


or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, wherein:

A is a phenyl;

B is a phenyl;

Het-CH_2-R^3 is:



M is a 5-membered unsaturated heterocycle containing one or more nitrogen heteroatoms optionally substituted with one or more R^5 groups, wherein the heterocycle contains only nitrogen atoms;

M-L is M-L^1-X-L^2, wherein

X, at each occurrence, independently is selected from the group consisting of:

a) $-NR^4-$, b) $-SO_2NR^4-$

L^1 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups; and

L^2 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups;

R^1, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) ;

R^2, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d);

R^3 is $-NR^4C(O)R^4$;

R^4, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl;

R^5, at each occurrence, is independently selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) $-CF_3$, h) -CN, i) $-NO_2$, j) $-NR^6R^6$, k) $-C(O)R^6$, l) $-C(O)NR^6R^6$, m) $-S(O)_pR^6$, and n) R^6;

R^6, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl,

wherein any of b) – d) optionally is substituted with one or more R^7 groups;

R^7, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) $=NR^8$, f) $-CF_3$, g) $-OR^8$, h) -CN, i) $-NO_2$, j) $-NR^8R^8$, k) $-C(O)R^8$, and l) $-C(O)OR^8$;

R^8, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl,

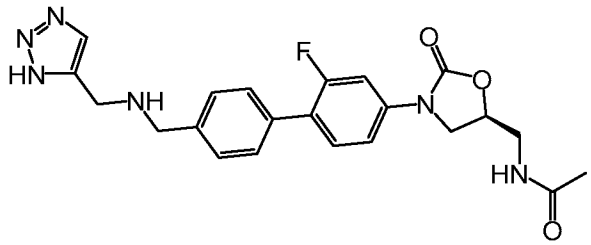
wherein any of b) – d) optionally is substituted with one or more moieties selected from the group consisting of F, Cl, Br, I, $-CF_3$, and -OH;

m is 0, 1, 2, 3, or 4;

n is 0, 1, 2, 3, or 4; and

p, at each occurrence, independently is 0, 1, or 2.

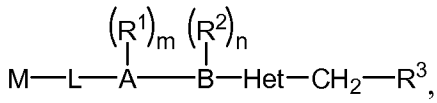
[0022] In another aspect, disclosed herein is a topical formulation for use in treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes, Gardnerella vaginalis,* or *Staphylococcus aureus* in a patient, the formulation comprising one or more dermatologically acceptable carriers and a compound having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof.

[0023] In another aspect, disclosed herein is a method of treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient, the method comprising administering a pharmaceutically effective amount of the topical formulation according to any one of claims 32 through 39.

[0024] In another aspect, disclosed herein is a use of a compound having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, wherein:

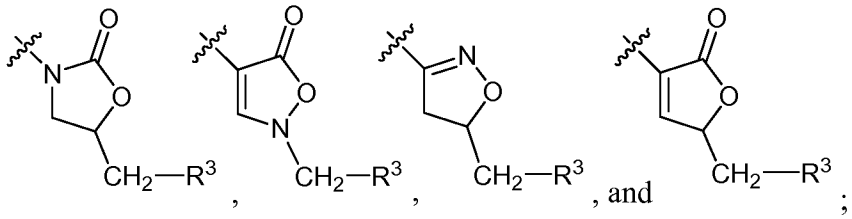
A is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

B is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

Het-CH_2-R^3 is selected from the group consisting of:



;

M is selected from the group consisting of:

a) saturated, unsaturated, or aromatic C_{3-14} carbocycle, and b) saturated, unsaturated, or aromatic 3-14 membered heterocycle containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

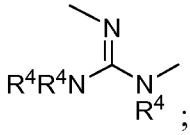
wherein a) or b) optionally is substituted with one or more R^5 groups;

M-L is selected from the group consisting of:

a) M-X, b) M-L^1, c) M-L^1-X, d) M-X-L^2, e) M-L^1-X-L^2, f) M-X-L^1-X-L^2, g) M-L^1-X-L^2-X, h) M-X-X-, i) M-L^1-X-X-, j) M-X-X-L^2, and k) M-L^1-X-X-L^2, wherein

X, at each occurrence, independently is selected from the group consisting of:

a) -O-, b) -NR^4-, c) –N(O)-, d) –N(OR^4)-, e) -$S(O)_p$-, f) -SO_2NR^4-, g) -NR^4SO_2-, h) -NR^4-N=, i) =N-NR^4-, j) -O-N=, k) =N-O-, l) -N=, m) =N-, n) -NR^4-NR^4-, o) -$NR^4C(O)O$-, p) -$OC(O)NR^4$-, q) -$NR^4C(O)NR^4$- r) -$NR^4C(NR^4)NR^4$-, and s)



;

L^1 is selected from the group consisting of:

a) $C_{1\text{-}6}$ alkyl, b) $C_{2\text{-}6}$ alkenyl, and c) $C_{2\text{-}6}$ alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups; and

L^2 is selected from the group consisting of:

a) $C_{1\text{-}6}$ alkyl, b) $C_{2\text{-}6}$ alkenyl, and c) $C_{2\text{-}6}$ alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups;

R^1, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) -CF_3, f) –OR^4, g) -CN, h) -NO_2, i) -NR^4R^4, j) -$C(O)R^4$, k) -$C(O)OR^4$, l) -$OC(O)R^4$, m) -$C(O)NR^4R^4$, n) -$NR^4C(O)R^4$, o) -$OC(O)NR^4R^4$, p) -$NR^4C(O)OR^4$, q) –$NR^4C(O)NR^4R^4$, r) -$C(S)R^4$, s) -$C(S)OR^4$, t) -$OC(S)R^4$, u) -$C(S)NR^4R^4$, v) –$NR^4C(S)R^4$, w) -$OC(S)NR^4R^4$, x) –$NR^4C(S)OR^4$, y) -$NR^4C(S)NR^4R^4$, z) -$NR^4C(NR^4)NR^4R^4$, aa) -$S(O)_pR^4$, bb) -$SO_2NR^4R^4$, and cc) R^4;

R^2, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) -CF_3, f) –OR^4, g) -CN, h) -NO_2, i) -NR^4R^4, j) -$C(O)R^4$, k) -$C(O)OR^4$, l) -$OC(O)R^4$, m) -$C(O)NR^4R^4$, n) -$NR^4C(O)R^4$, o) -$OC(O)NR^4R^4$, p) -$NR^4C(O)OR^4$, q) –$NR^4C(O)NR^4R^4$, r) -$C(S)R^4$, s) -$C(S)OR^4$, t) -$OC(S)R^4$, u) -$C(S)NR^4R^4$, v) –$NR^4C(S)R^4$, w) -$OC(S)NR^4R^4$, x) –$NR^4C(S)OR^4$, y) -$NR^4C(S)NR^4R^4$, z) -$NR^4C(NR^4)NR^4R^4$, aa) -$S(O)_pR^4$, bb) -$SO_2NR^4R^4$, and cc) R^4;

R^3 is selected from the group consisting of:

a) $-OR^4$, b) $-NR^4R^4$, c) $-C(O)R^4$, d) $-C(O)OR^4$, e) $-OC(O)R^4$, f) $-C(O)NR^4R^4$, g) $-NR^4C(O)R^4$, h) $-OC(O)NR^4R^4$, i) $-NR^4C(O)OR^4$, j) $-NR^4C(O)NR^4R^4$, k) $-C(S)R^4$, l) $-C(S)OR^4$, m) $-OC(S)R^4$, n) $-C(S)NR^4R^4$, o) $-NR^4C(S)R^4$, p) $-OC(S)NR^4R^4$, q) $-NR^4C(S)OR^4$, r) $-NR^4C(S)NR^4R^4$, s) $-NR^4C(NR^4)NR^4R^4$, t) $-S(O)_pR^4$, u) $-SO_2NR^4R^4$, and v) R^4;

R^4, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) $-C(O)-C_{1-6}$ alkyl, h) $-C(O)-C_{2-6}$ alkenyl, i) $-C(O)-C_{2-6}$ alkynyl, j) $-C(O)-C_{3-14}$ saturated,
unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) $-C(O)O-C_{1-6}$ alkyl, m) $-C(O)O-C_{2-6}$ alkenyl, n) $-C(O)O-C_{2-6}$ alkynyl, o) $-C(O)O-C_{3-14}$ saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^5 groups;

R^5, at each occurrence, is independently selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) $=NR^6$, h) $=NOR^6$, i) $=N-NR^6R^6$, j) $-CF_3$, k) $-OR^6$, l) -CN, m) $-NO_2$, n) $-NR^6R^6$, o) $-C(O)R^6$, p) $-C(O)OR^6$, q) $-OC(O)R^6$, r) $-C(O)NR^6R^6$, s) $-NR^6C(O)R^6$, t) $-OC(O)NR^6R^6$, u) $-NR^6C(O)OR^6$, v) $-NR^6C(O)NR^6R^6$, w) $-C(S)R^6$, x) $-C(S)OR^6$, y) $-OC(S)R^6$, z) $-C(S)NR^6R^6$, aa) $-NR^6C(S)R^6$, bb) $-OC(S)NR^6R^6$, cc) $-NR^6C(S)OR^6$, dd) $-NR^6C(S)NR^6R^6$, ee) $-NR^6C(NR^6)NR^6R^6$, ff) $-S(O)_pR^6$, gg) $-SO_2NR^6R^6$, and hh) R^6;

R^6, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) $-C(O)-C_{1-6}$ alkyl, h) $-C(O)-C_{2-6}$ alkenyl, i) $-C(O)-C_{2-6}$ alkynyl, j) $-C(O)-C_{3-14}$ saturated,

unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^7 groups;

R^7, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) =NR^8, h) =NOR^8, i) =N-NR^8R^8, j) -CF_3, k) -OR^8, l) -CN, m) -NO_2, n) –NR^8R^8, o) -C(O)R^8, p) -C(O)OR^8, q) -OC(O)R^8, r) -C(O)NR^8R^8, s) –NR^8C(O)R^8, t) -OC(O)NR^8R^8, u) -NR^8C(O)OR^8, v) -NR^8C(O)NR^8R^8, w) -C(S)R^8, x) -C(S)OR^8, y) -OC(S)R^8, z) -C(S)NR^8R^8, aa) -NR^8C(S)R^8, bb) -OC(S)NR^8R^8, cc) -NR^8C(S)OR^8, dd) –NR^8C(S)NR^8R^8, ee) -NR^8C(NR^8)NR^8R^8, ff) -$S(O)_pR^8$, gg) -$SO_2NR^8R^8$, hh) C_{1-6} alkyl, ii) C_{2-6} alkenyl, jj) C_{2-6} alkynyl, kk) C_{3-14} saturated, unsaturated, or aromatic carbocycle, and ll) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of hh) – ll) optionally is substituted with one or more moieties selected from the group consisting of R^8, F, Cl, Br, I, -CF_3, –OR^8, –SR^8, -CN, -NO_2, –NR^8R^8, -C(O)R^8, -C(O)OR^8, -OC(O)R^8, -C(O)NR^8R^8, -NR^8C(O)R^8, -OC(O)NR^8R^8, –NR^8C(O)OR^8, -NR^8C(O)NR^8R^8, -C(S)R^8, -C(S)OR^8, -OC(S)R^8, -C(S)NR^8R^8, -NR^8C(S)R^8, -OC(S)NR^8R^8, -NR^8C(S)OR^8, -NR^8C(S)NR^8R^8, -NR^8C(NR^8)NR^8R^8, -$SO_2NR^8R^8$, and-$S(O)_pR^8$;

R^8, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) -C(O)-C_{1-6} alkyl, h) -C(O)-C_{2-6} alkenyl, i) –C(O)-C_{2-6} alkynyl, j) -C(O)-C_{3-14} saturated,
unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated,

unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more moieties selected from the group consisting of F, Cl, Br, I, -CF_3, -OH, -OCH_3, -SH, -SCH_3, -CN, -NO_2, –NH_2, -$NHCH_3$, -$N(CH_3)_2$, -C(O)CH_3, -C(O)OCH_3, -C(O)NH_2, –$NHC(O)CH_3$, -SO_2NH_2, -SO_2NHCH_3, -$SO_2N(CH_3)_2$, and-$S(O)_pCH_3$;

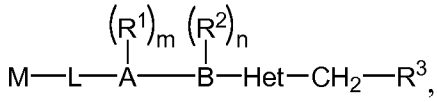
m, at each occurrence, independently is 0, 1, 2, 3, or 4;

n, at each occurrence, independently is 0, 1, 2, 3, or 4; and

p, at each occurrence, independently is 0, 1, or 2,

in the manufacture of a medicament for treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient.

[0025] In another aspect, disclosed herein is a use of a compound having the formula:

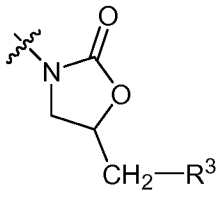


or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, wherein:

A is a phenyl;

B is a phenyl;

Het-CH_2-R^3 is:



;

M is a 5-membered unsaturated heterocycle containing one or more nitrogen heteroatoms optionally substituted with one or more R^5 groups, wherein the heterocycle contains only nitrogen atoms;

M-L is M-L^1-X-L^2, wherein

X, at each occurrence, independently is selected from the group consisting of:

a) $-NR^4-$, b) $-SO_2NR^4-$

L^1 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups; and

L^2 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups;

R^1, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) ;

R^2, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d);

R^3 is $-NR^4C(O)R^4$;

R^4, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl;

R^5, at each occurrence, is independently selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) $-CF_3$, h) -CN, i) $-NO_2$, j) $-NR^6R^6$, k) $-C(O)R^6$, l) $-C(O)NR^6R^6$, m) $-S(O)_pR^6$, and n) R^6;

R^6, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl,

wherein any of b) – d) optionally is substituted with one or more R^7 groups;

R^7, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) $=NR^8$, f) $-CF_3$, g) $-OR^8$, h) -CN, i) $-NO_2$, j) $-NR^8R^8$, k) $-C(O)R^8$, and l) $-C(O)OR^8$;

R^8, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl,

wherein any of b) – d) optionally is substituted with one or more moieties selected from the group consisting of F, Cl, Br, I, $-CF_3$, and -OH;

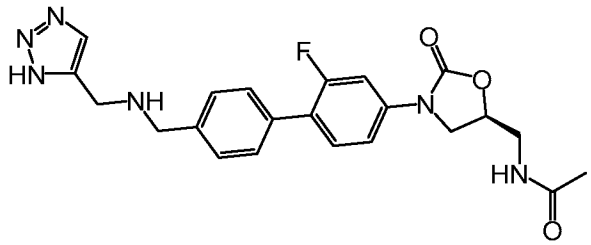
m is 0, 1, 2, 3, or 4;

n is 0, 1, 2, 3, or 4; and

p, at each occurrence, independently is 0, 1, or 2,

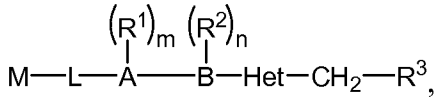
in the manufacture of a medicament for treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient comprising.

[0026] In another aspect, disclosed herein is a use of a compound having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, in the manufacture of a medicament for treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient.

[0027] In another aspect, disclosed herein is a use of a compound having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, wherein:

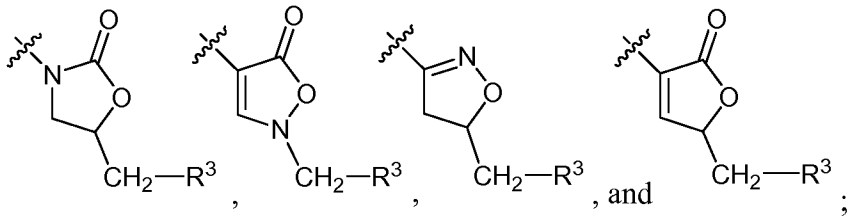
A is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

B is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

Het-CH_2-R^3 is selected from the group consisting of:



;

M is selected from the group consisting of:

a) saturated, unsaturated, or aromatic C_{3-14} carbocycle, and b) saturated, unsaturated, or aromatic 3-14 membered heterocycle containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

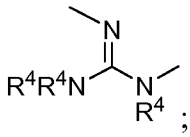
wherein a) or b) optionally is substituted with one or more R^5 groups;

M-L is selected from the group consisting of:

a) M-X, b) M-L^1, c) M-L^1-X, d) M-X-L^2, e) M-L^1-X-L^2, f) M-X-L^1-X-L^2, g) M-L^1-X-L^2-X, h) M-X-X-, i) M-L^1-X-X-, j) M-X-X-L^2, and k) M-L^1-X-X-L^2, wherein

X, at each occurrence, independently is selected from the group consisting of:

a) -O-, b) -NR^4-, c) –N(O)-, d) –N(OR^4)-, e) -$S(O)_p$-, f) -SO_2NR^4-, g) -NR^4SO_2-, h) -NR^4-N=, i) =N-NR^4-, j) -O-N=, k) =N-O-, l) -N=, m) =N-, n) -NR^4-NR^4-, o) -$NR^4C(O)O$-, p) -$OC(O)NR^4$-, q) -$NR^4C(O)NR^4$- r) -$NR^4C(NR^4)NR^4$-, and s)



;

L^1 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups; and

L^2 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups;

R^1, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) -CF_3, f) –OR^4, g) -CN, h) -NO_2, i) -NR^4R^4, j) -$C(O)R^4$, k) -$C(O)OR^4$, l) -$OC(O)R^4$, m) -$C(O)NR^4R^4$, n) -$NR^4C(O)R^4$, o) -$OC(O)NR^4R^4$, p) -$NR^4C(O)OR^4$, q) –$NR^4C(O)NR^4R^4$, r) -$C(S)R^4$, s) -$C(S)OR^4$, t) -$OC(S)R^4$, u) -$C(S)NR^4R^4$, v) –$NR^4C(S)R^4$, w) -$OC(S)NR^4R^4$, x) –$NR^4C(S)OR^4$, y) -$NR^4C(S)NR^4R^4$, z) -$NR^4C(NR^4)NR^4R^4$, aa) -$S(O)_pR^4$, bb) -$SO_2NR^4R^4$, and cc) R^4;

R^2, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) -CF_3, f) –OR^4, g) -CN, h) -NO_2, i) -NR^4R^4, j) -$C(O)R^4$, k) -$C(O)OR^4$, l) -$OC(O)R^4$, m) -$C(O)NR^4R^4$, n) -$NR^4C(O)R^4$, o) -$OC(O)NR^4R^4$, p) -$NR^4C(O)OR^4$, q) –$NR^4C(O)NR^4R^4$, r) -$C(S)R^4$, s) -$C(S)OR^4$, t) -$OC(S)R^4$, u) -$C(S)NR^4R^4$, v) –$NR^4C(S)R^4$, w) -$OC(S)NR^4R^4$, x) –$NR^4C(S)OR^4$, y) -$NR^4C(S)NR^4R^4$, z) -$NR^4C(NR^4)NR^4R^4$, aa) -$S(O)_pR^4$, bb) -$SO_2NR^4R^4$, and cc) R^4;

R^3 is selected from the group consisting of:

a) $-OR^4$, b) $-NR^4R^4$, c) $-C(O)R^4$, d) $-C(O)OR^4$, e) $-OC(O)R^4$, f) $-C(O)NR^4R^4$, g) $-NR^4C(O)R^4$, h) $-OC(O)NR^4R^4$, i) $-NR^4C(O)OR^4$, j) $-NR^4C(O)NR^4R^4$, k) $-C(S)R^4$, l) $-C(S)OR^4$, m) $-OC(S)R^4$, n) $-C(S)NR^4R^4$, o) $-NR^4C(S)R^4$, p) $-OC(S)NR^4R^4$, q) $-NR^4C(S)OR^4$, r) $-NR^4C(S)NR^4R^4$, s) $-NR^4C(NR^4)NR^4R^4$, t) $-S(O)_pR^4$, u) $-SO_2NR^4R^4$, and v) R^4;

R^4, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) $-C(O)-C_{1-6}$ alkyl, h) $-C(O)-C_{2-6}$ alkenyl, i) $-C(O)-C_{2-6}$ alkynyl, j) $-C(O)-C_{3-14}$ saturated,

unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) $-C(O)O-C_{1-6}$ alkyl, m) $-C(O)O-C_{2-6}$ alkenyl, n) $-C(O)O-C_{2-6}$ alkynyl, o) $-C(O)O-C_{3-14}$ saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^5 groups;

R^5, at each occurrence, is independently selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) $=NR^6$, h) $=NOR^6$, i) $=N-NR^6R^6$, j) $-CF_3$, k) $-OR^6$, l) -CN, m) $-NO_2$, n) $-NR^6R^6$, o) $-C(O)R^6$, p) $-C(O)OR^6$, q) $-OC(O)R^6$, r) $-C(O)NR^6R^6$, s) $-NR^6C(O)R^6$, t) $-OC(O)NR^6R^6$, u) $-NR^6C(O)OR^6$, v) $-NR^6C(O)NR^6R^6$, w) $-C(S)R^6$, x) $-C(S)OR^6$, y) $-OC(S)R^6$, z) $-C(S)NR^6R^6$, aa) $-NR^6C(S)R^6$, bb) $-OC(S)NR^6R^6$, cc) $-NR^6C(S)OR^6$, dd) $-NR^6C(S)NR^6R^6$, ee) $-NR^6C(NR^6)NR^6R^6$, ff) $-S(O)_pR^6$, gg) $-SO_2NR^6R^6$, and hh) R^6;

R^6, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) $-C(O)-C_{1-6}$ alkyl, h) $-C(O)-C_{2-6}$ alkenyl, i) $-C(O)-C_{2-6}$ alkynyl, j) $-C(O)-C_{3-14}$ saturated,

unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated,

unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^7 groups;

R^7, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) =NR^8, h) =NOR^8, i) =N-NR^8R^8, j) -CF_3, k) -OR^8, l) -CN, m) -NO_2, n) –NR^8R^8, o) -C(O)R^8, p) -C(O)OR^8, q) -OC(O)R^8, r) -C(O)NR^8R^8, s) –NR^8C(O)R^8, t) -OC(O)NR^8R^8, u) -NR^8C(O)OR^8, v) -NR^8C(O)NR^8R^8, w) -C(S)R^8, x) -C(S)OR^8, y) -OC(S)R^8, z) -C(S)NR^8R^8, aa) -NR^8C(S)R^8, bb) -OC(S)NR^8R^8, cc) -NR^8C(S)OR^8, dd) –NR^8C(S)NR^8R^8, ee) -NR^8C(NR^8)NR^8R^8, ff) -$S(O)_pR^8$, gg) -$SO_2NR^8R^8$, hh) C_{1-6} alkyl, ii) C_{2-6} alkenyl, jj) C_{2-6} alkynyl, kk) C_{3-14} saturated, unsaturated, or aromatic carbocycle, and ll) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of hh) – ll) optionally is substituted with one or more moieties selected from the group consisting of R^8, F, Cl, Br, I, -CF_3, –OR^8, –SR^8, -CN, -NO_2, –NR^8R^8, -C(O)R^8, -C(O)OR^8, -OC(O)R^8, -C(O)NR^8R^8, -NR^8C(O)R^8, -OC(O)NR^8R^8, -NR^8C(O)OR^8, -NR^8C(O)NR^8R^8, -C(S)R^8, -C(S)OR^8, -OC(S)R^8, -C(S)NR^8R^8, -NR^8C(S)R^8, -OC(S)NR^8R^8, -NR^8C(S)OR^8, -NR^8C(S)NR^8R^8, -NR^8C(NR^8)NR^8R^8, -$SO_2NR^8R^8$, and-$S(O)_pR^8$;

R^8, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) -C(O)-C_{1-6} alkyl, h) -C(O)-C_{2-6} alkenyl, i) –C(O)-C_{2-6} alkynyl, j) -C(O)-C_{3-14} saturated, unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected

from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more moieties selected from the group consisting of F, Cl, Br, I, -CF_3, -OH, -OCH_3, -SH, -SCH_3, -CN, -NO_2, –NH_2, -$NHCH_3$, -$N(CH_3)_2$, -C(O)CH_3, -C(O)OCH_3, -C(O)NH_2, –$NHC(O)CH_3$, -SO_2NH_2, -SO_2NHCH_3, -$SO_2N(CH_3)_2$, and-$S(O)_pCH_3$;

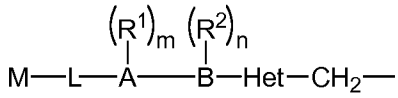
m, at each occurrence, independently is 0, 1, 2, 3, or 4;

n, at each occurrence, independently is 0, 1, 2, 3, or 4; and

p, at each occurrence, independently is 0, 1, or 2,

for treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient.

[0028] In another aspect, disclosed herein is a use of a compound having the formula:

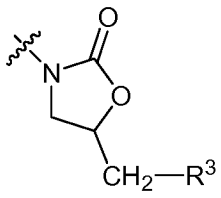


or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, wherein:

A is a phenyl;

B is a phenyl;

Het-CH_2-R^3 is:


;

M is a 5-membered unsaturated heterocycle containing one or more nitrogen heteroatoms optionally substituted with one or more R^5 groups, wherein the heterocycle contains only nitrogen atoms;

M-L is M-L^1-X-L^2, wherein

X, at each occurrence, independently is selected from the group consisting of:

a) -NR^4-, b) -SO_2NR^4-

L^1 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups; and

L^2 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups;

R^1, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) ;

R^2, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d);

R^3 is $-NR^4C(O)R^4$;

R^4, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl;

R^5, at each occurrence, is independently selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) $-CF_3$, h) -CN, i) $-NO_2$, j) $-NR^6R^6$, k) $-C(O)R^6$, l) $-C(O)NR^6R^6$, m) $-S(O)_pR^6$, and n) R^6;

R^6, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl,

wherein any of b) – d) optionally is substituted with one or more R^7 groups;

R^7, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) $=NR^8$, f) $-CF_3$, g) $-OR^8$, h) -CN, i) $-NO_2$, j) $-NR^8R^8$, k) $-C(O)R^8$, and l) $-C(O)OR^8$;

R^8, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl,

wherein any of b) – d) optionally is substituted with one or more moieties selected from the group consisting of F, Cl, Br, I, $-CF_3$, and -OH;

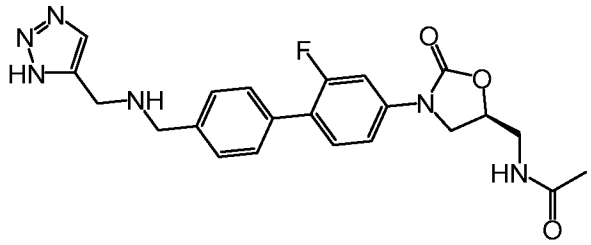
m is 0, 1, 2, 3, or 4;

n is 0, 1, 2, 3, or 4; and

p, at each occurrence, independently is 0, 1, or 2,

for treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient.

[0029] In another aspect, disclosed herein is a use of a compound having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, for treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient.

[0030] The foregoing and other aspects and embodiments of the present invention can be more fully understood by reference to the following detailed description and claims.

BRIEF DESCRIPTION OF THE FIGURES

[**0031**] **FIG 1.** shows radezolid safety in a long-term rat study, as indicated by average body weight over time.

[**0032**] **FIG 2.** shows linezolid safety in a long-term rat study, as indicated by average body weight over time.

[**0033**] **FIG 3.** shows bacterial burden in pouch over time when treated with radezolid.

[**0034**] **FIG 4.** shows radezolid levels in pouch and plasma over time when treated with radezolid.

[0035] **FIG 5.** shows the results of the 2-step dissolution test performed following Method 1. Dissolution of the radezolid formulation was tested in a buffer at pH 4.0 for 0-30 minutes and then after transferring to a buffer at pH 5.4 for 30-90 minutes.

[0036] **FIG 6.** shows the results of the 2-step dissolution test performed following Method 2. Dissolution of the radezolid formulation was tested in a buffer at pH 4.0 for 0-30 minutes and then after transferring to a buffer at pH 6.5 for 30-90 minutes.

[0037] **FIG 7.** shows the results of the 2-step dissolution test performed following Method 3. Dissolution of the radezolid formulation was tested in a buffer at pH 4.0 for 0-30 minutes and then after transferring to a buffer at pH 6.5 for 30-90 minutes. Both buffers had 0.9% NaC1. The two-step dissolution with 0.9% NaC1 was used to simulate the common ion effect.

[0038] **FIG 8.** shows the results of the 2-step dissolution test performed following Method 4. Dissolution of the radezolid formulation was tested in a buffer at pH 4 containing NaC1 for 0-30 minutes, and then transferred to a buffer at pH 6.5 containing bile salt, surfactant and KC1 for 30-90 minutes.

[0039] **FIG 9.** shows the pharmacokinetic profiles of the radezolid formulations in beagle dogs (n=3).

DETAILED DESCRIPTION OF THE INVENTION

[0040] The present invention relates to methods for treating, preventing, or reducing the risk of acne and other skin infections caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient a safe and effective amount of an antibiotic, *i.e.*, an antimicrobial compound such as, *e.g.*, an oxazolidinone compound as described herein.

1. Definitions

[0041] The term "patient," as used herein, means the human or animal (in the case of an animal, more typically a mammal) subject that would be considered to be in need of the methods of treating, preventing, or reducing the risk of acne or a pilosebaceous disorder.

[0042] As used herein, the phrase "pharmaceutically acceptable" refers to those compounds, materials, compositions, carriers, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

[0043] The term "treating," as used herein, means to cure an already present acne outbreak or other undesirable other skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient or subject.

[0044] The term "preventing," as used herein means, to completely or almost completely stop an acne outbreak or other undesirable pilosebaceous disorder from occurring in a patient or subject, especially when the patient or subject is predisposed to such. Preventing can also include inhibiting, *i.e.*, arresting the development of, an acne outbreak or other undesirable pilosebaceous disorder, and relieving or ameliorating, *i.e.*, causing regression of the acne outbreak or pilosebaceous disorder.

[0045] The term "reducing the risk of," as used herein, means to lower the likelihood or probability of an acne outbreak or other undesirable pilosebaceous disorder from occurring, especially when the patient or subject is predisposed to such occurrence.

[0046] As used herein, the term "pharmaceutically effective amount" refers to an amount of a compound, or a combination of compounds, of the present invention effective when administered alone or in combination with other active ingredients useful to treat, prevent, or reduce the risk of

acne or a pilosebaceous disorder. For example, a pharmaceutically effective amount refers to an amount of the compound present in a formulation or on a medical device given to a recipient patient or subject sufficient to elicit biological activity, for example, activity against acne or other undesirable pilosebaceous disorder. The combination of compounds optionally is a synergistic combination. Synergy, as described, for example, by Chou and Talalay, *Adv. Enzyme Regul.* vol. 22, pp. 27-55 (1984), occurs when the effect of the compounds when administered in combination is greater than the additive effect of the compounds when administered alone as a single agent. In general, a synergistic effect is most clearly demonstrated at sub-optimal concentrations of the compounds. Synergy can be in terms of lower cytotoxicity, increased anti-proliferative and/or anti-infective effect, or some other beneficial effect of the combination compared with the individual components.

[0047] The term "prophylactically effective amount" means an effective amount of a compound or compounds, of the present invention that is administered to prevent or reduce the risk of an acne outbreak or other undesirable pilosebaceous disorder. In other words, an amount that can be administered to provide a preventative or prophylactic effect.

[0048] As used herein, "topically applying" and "topical administration" means that compounds of the present invention are applied to the skin of the patient directly laying or spreading said compound or compounds on the outer skin, scalp, hair, fur, feathers, scales, shells, eyes, or ears of the patient, *e.g.*, by use of the hands or an applicator such as a wipe, roller, or spray.

[0049] As used herein, "dermatologically acceptable" means that the ingredients the term describes are suitable for use in contact with tissues (*e.g.*, the skin or hair) without undue toxicity, incompatibility, instability, irritation, allergic response, or the like.

[0050] With respect to the antibiotic compounds useful in the present invention, the following terms can be applicable, however, it should be kept in mind that more specific definitions are also given in the references referred to and incorporated by reference herein:

[0051] The chemical compounds described herein can have asymmetric centers. Compounds of the present invention containing an asymmetrically substituted atom can be isolated in optically active or racemic forms. It is well known in the art how to prepare optically active forms, such as by resolution of racemic forms or by synthesis from optically active starting materials. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds described herein, and all such stable isomers are contemplated in the present invention. Cis and trans geometric isomers of the compounds of the present invention are

described and can be isolated as a mixture of isomers or as separated isomeric forms. All chiral, diastereomeric, racemic, and geometric isomeric forms of a structure are intended, unless the specific stereochemistry or isomeric form is specifically indicated. All processes used to prepare compounds of the present invention and intermediates made therein are, where appropriate, considered to be part of the present invention. All tautomers of shown or described compounds are also, where appropriate, considered to be part of the present invention.

[0052] When a bond to a substituent is shown to cross a bond connecting two atoms in a ring, then such substituent can be bonded to any atom in the ring. When a substituent is listed without indicating the atom via which such substituent is bonded to the rest of the compound of a given formula, then such substituent can be bonded via any atom in such substituent. Combinations of substituents and/or variables are permissible, but only if such combinations result in stable compounds.

[0053] As used herein, "pharmaceutically acceptable salts" refer to derivatives of the disclosed compounds wherein the parent compound is modified by making acid or base salts thereof. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines, alkali or organic salts of acidic residues such as carboxylic acids, and the like. The pharmaceutically acceptable salts include the conventional non-toxic salts or the quaternary ammonium salts of the parent compound formed, for example, from non-toxic inorganic or organic acids. For example, such conventional non-toxic salts include, but are not limited to, those derived from inorganic and organic acids selected from 2-acetoxybenzoic, 2-hydroxyethane sulfonic, acetic, ascorbic, benzene sulfonic, benzoic, bicarbonic, carbonic, citric, edetic, ethane disulfonic, ethane sulfonic, fumaric, glucoheptonic, gluconic, glutamic, glycolic, glycollyarsanilic, hexylresorcinic, hydrabamic, hydrobromic, hydrochloric, hydroiodic, hydroxymaleic, hydroxynaphthoic, isethionic, lactic, lactobionic, lauryl sulfonic, maleic, malic, mandelic, methane sulfonic, napsylic, nitric, oxalic, pamoic, pantothenic, phenylacetic, phosphoric, polygalacturonic, propionic, salicylic, stearic, subacetic, succinic, sulfamic, sulfanilic, sulfuric, tannic, tartaric, toluene sulfonic, and the commonly occurring amine acids, *e.g.*, glycine, alanine, phenylalanine, arginine, etc.

[0054] The pharmaceutically acceptable salts of the present invention can be synthesized from a parent compound that contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent, or in a mixture of the two; generally, non-aqueous media like ether, ethyl acetate,

ethanol, isopropanol, or acetonitrile are preferred. Lists of suitable salts are found in *Remington's Pharmaceutical Sciences*, 18th ed. (Mack Publishing Company, 1990). For example, salts can include, but are not limited to, the hydrochloride and acetate salts of the aliphatic amine-containing, hydroxyl amine-containing, and imine-containing compounds of the present invention.

[0055] Additionally, the compounds of the present invention, for example, the salts of the compounds, can exist in either hydrated or unhydrated (the anhydrous) form or as solvates with other solvent molecules. Nonlimiting examples of hydrates include monohydrates, dihydrates, etc. Nonlimiting examples of solvates include ethanol solvates, acetone solvates, etc.

[0056] The compounds of the present invention can also be prepared as esters, for example pharmaceutically acceptable esters. For example a carboxylic acid functional group in a compound can be converted to its corresponding ester, *e.g.*, a methyl, ethyl, or other ester. Also, an alcohol group in a compound can be converted to its corresponding ester, *e.g.*, an acetate, propionate, or other ester.

[0057] The compounds of the present invention can also be prepared as prodrugs, for example pharmaceutically acceptable prodrugs. Since prodrugs are known to enhance numerous desirable qualities of pharmaceuticals (*e.g.*, solubility, bioavailability, manufacturing, etc.) the compounds of the present invention can be delivered in prodrug form. Thus, the present invention is intended to cover prodrugs of the presently claimed compounds, methods of delivering the same and compositions containing the same. "Prodrugs" are intended to include any covalently bonded carriers that release an active parent drug of the present invention *in vivo* when such prodrug is administered to a mammalian subject. Prodrugs the present invention are prepared by modifying functional groups present in the compound in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*, to the parent compound. Prodrugs include compounds of the present invention wherein a hydroxy, amino, or sulfhydryl group is bonded to any group that, when the prodrug of the present invention is administered to a mammalian subject, cleaves to form a free hydroxyl, free amino, or free sulfhydryl group, respectively. Examples of prodrugs include, but are not limited to, acetate, formate, and benzoate derivatives of alcohol and amine functional groups in the compounds of the present invention.

[0058] "Stable compound" and "stable structure" are meant to indicate a compound that is sufficiently robust to survive isolation, and as appropriate, purification from a reaction mixture, and formulation into an efficacious therapeutic agent.

[0059] As used herein, "skin infection" includes but is not limited to acne vulgaris, rosacea, impetigo, otitis externa, bacterial conjunctivitis, and bacterial vaginosis.

[0060] As used herein, "treating acne" refers to a mitigating, reducing, preventing, improving, or eliminating the presence or signs of disorders resulting from the actions of hormones and other substances on the sebaceous glands and hair follicles, typically leading to clogged pores and the formation of inflammatory or non-inflammatory lesions on the skin. Specifically, it relates to the treatment or prevention of blemishes, lesions, or pimples, pre-emergent pimples, blackheads, and/or whiteheads.

[0061] As used herein, "treating bacterial vaginosis" refers to mitigating, reducing, preventing, improving, or eliminating the presence or signs of disorders resulting from the actions of *Gardnerella vaginalis* in the vagina.

[0062] In the specification, the singular forms also include the plural, unless the context clearly dictates otherwise. Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. In the case of conflict, the present specification will control.

[0063] All percentages and ratios used herein, unless otherwise indicated, are by weight.

[0064] Throughout the description, where compositions are described as having, including, or comprising specific components, it is contemplated that compositions also consist essentially of, or consist of, the recited components. Similarly, where methods or processes are described as having, including, or comprising specific process steps, the processes also consist essentially of, or consist of, the recited processing steps. Further, it should be understood that the order of steps or order for performing certain actions is immaterial so long as the invention remains operable. Moreover, two or more steps or actions can be conducted simultaneously.

2. Methods of the Invention

[0065] The present invention relates to methods for treating acne and other skin infections caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient in need thereof a safe and effective amount of an antibiotic.

[0066] The present invention relates to methods for preventing acne and other skin infections caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient in need thereof a safe and effective amount of an antibiotic compound.

[0067] The present invention relates to methods for reducing the risk of acne and other skin infections caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or

Staphylococcus aureus in a patient with a safe and prophylactically effective amount of an antibiotic compound.

[0068] As discussed above, acne and other skin infections can be caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus*. It has been found that the antibiotic compounds of the present invention are useful for treating, preventing, or reducing the risk of these microbial infections and the associated acne or other skin infections caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus*. The methods of the present invention can be usefully applied to patients, whether human or animal.

[0069] As discussed above, bacterial vaginosis can be caused or mediated by *Gardnerella vaginalis*. It has been found that the antibiotic compounds of the present invention are useful for treating, preventing, or reducing the risk of bacterial vaginosis caused or mediated by *Gardnerella vaginalis*. The methods of the present invention can be usefully applied to patients, whether human or animal.

[0070] In practicing the methods of the present invention, it is desired that the tissue level, or sometimes the blood level in the patient or subject, of the compound used to provide the effect be of an appropriate level for a sufficient time interval. Also, because it often takes a finite amount of time to achieve such blood or tissue levels, it is important that the compound is administered at some appropriate time. The appropriate time for administration of the compound will depend upon the pharmacokinetic profile of the compound and its formulation, route of administration, time required for completing administration, patient characteristics, desired clinical outcome, etc.

[0071] The compounds used in the methods of the present invention are generally provided to the patient or subject by topical administration, including, but not limited to administration to the skin, hair, fur, feathers, ears, or eyes.

3. Antibiotic Compounds Useful in the Present Invention

[0072] The antibiotic, *i.e.* antimicrobial, compounds or antibiotic agents useful herein are those that are particularly effective against bacteria that cause or mediate or are involved in acne and other undesirable skin infections caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus*, and that are especially effective against resistant strains of such bacteria.

[0073] A wide range of antibiotic compounds can be used in the methods, compositions, and uses of the present invention. These antibiotic compounds can provide their therapeutic effect by

a variety of biochemical or biophysical mechanisms. Antibiotic compounds useful in the present invention can include those which bind to or modulate ribosomal RNA, for example bacterial ribosomal RNA. Antibiotic compounds also useful in the present invention can include those which bind to or modulate the large ribosomal subunit, for example the large ribosomal subunit of a bacterial organism. Nonlimiting classes of antibiotic compounds useful herein include oxazolidinone antibiotics and antibiotics. Oxazolidinone antibiotics are characterized in having an oxazolidinone ring. Antibiotics are characterized in having a macrocyclic ring, typically a 13-16-membered macrocyclic ring, more typically a 14-15-memebered macrocyclic ring.

[0074] The antibiotic compounds useful in the present invention can include their pharmaceutically acceptable salts, esters, or prodrugs thereof. The invention further provides methods for synthesizing any one of the antibiotic compounds of the present invention. The invention also provides pharmaceutical compositions comprising an effective amount of one or more of the antibiotic compounds of the present invention and a pharmaceutically acceptable carrier. The present invention further provides methods for making these pharmaceutical compositions.

[0075] Nonlimiting examples of antibiotic compounds useful herein and their pharmaceutically acceptable salts, esters, tautomers, and prodrugs thereof are disclosed and incorporated by reference here in the following Table 1.

Table 1
References Disclosing Antibiotic Compounds of the Present Invention

PCT Publication No., U.S. Patent or Publication No., or U.S. Application Serial No.	Applicant or Assignee	Title	Publication or Issue Date	International or U.S. Filing Date
WO 2004/029066	Rib-X Pharmaceuticals, Inc.	Bifunctional Heterocyclic Compounds and Methods of Making and Using Same	April 8, 2004	September 25, 2003
WO 2004/078770	Rib-X Pharmaceuticals, Inc.	Bifunctional Heterocyclic Compounds and Methods of Making and Using the Same	September 16, 2004	March 5, 2004
WO 2007/025284	Rib-X Pharmaceuticals, Inc.	Triazole Compounds and Methods of Making and Using the Same	March 1, 2007	August 24, 2006
WO 2007/025098	Rib-X Pharmaceuticals, Inc.	Triazole Compounds and Methods of Making and Using the Same	March 1, 2007	August 24, 2006
WO 2007/025089	Rib-X Pharmaceuticals, Inc.	Triazole Compounds and Methods of Making and Using the Same	March 1, 2007	August 24, 2006
WO 2006/133397	Rib-X Pharmaceuticals, Inc.	Process for the Synthesis of Triazoles	December 14, 2006	June 8, 2006
7,148,219 B2	Rib-X Pharmaceuticals, Inc.	Biaryl Heterocyclic Compounds and Methods of Making and Using The Same	December 12, 2006	April 29, 2005
7,129,259, B2 and its	Rib-X Pharmaceuticals,	Halogenated Biaryl Heterocyclic Compounds and	October 31, 2006	December 1, 2004

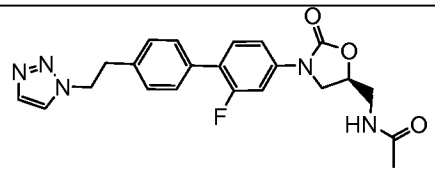
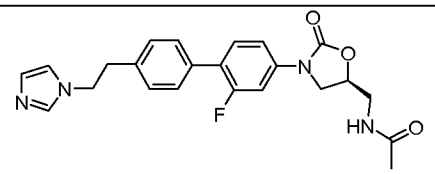
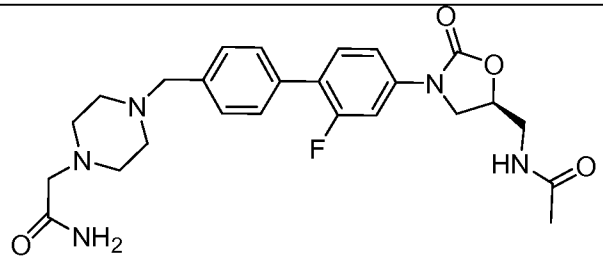
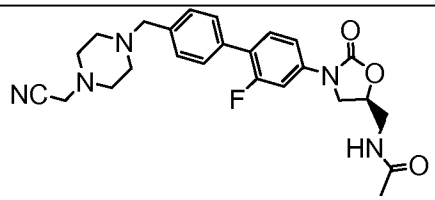
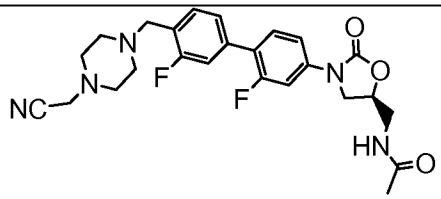
Certificate of Correction of March 6, 2007	Inc.	Methods of Making and Using the Same		
7,091,196 B2	Rib-X Pharmaceuticals, Inc.	Bifunctional Heterocyclic Compounds and Methods of Making and Using Same	August 15, 2006	September 25, 2003
6,969,726 B2 and its Certificate of Correction of February 27, 2007	Melinta Therapeutics, Inc.	Biaryl Heterocyclic Compounds and Methods of Making and Using The Same	November 29, 2005	June 2, 2004
US 2005/0043317 A1	Rib-X Pharmaceuticals, Inc.	Biaryl Heterocyclic Compounds and Methods of Making and Using The Same	February 24, 2005	June 2, 2004
US 2005/0203147 A1	Rib-X Pharmaceuticals, Inc.	Biaryl Heterocyclic Compounds and Methods of Making and Using The Same	September 15, 2005	June 2, 2004
US 2005/0153971 A1	Rib-X Pharmaceuticals, Inc.	Halogenated Biaryl Heterocyclic Compounds and Methods of Making and Using The Same	July 14, 2005	December 1, 2004
WO 2005/019211	Rib-X Pharmaceuticals, Inc.	Biaryl Heterocyclic Compounds and Methods of Making and Using The Same	March 3, 2005	June 2, 2004
WO 2006/022794	Rib-X Pharmaceuticals, Inc.	Biaryl Heterocyclic Compounds and Methods of Making and Using The Same	March 2, 2006	December 1, 2004
WO 2005/061468	Rib-X Pharmaceuticals, Inc.	Halogenated Biaryl Heterocyclic Compounds and Methods of Making and	July 7, 2005	December 1, 2004

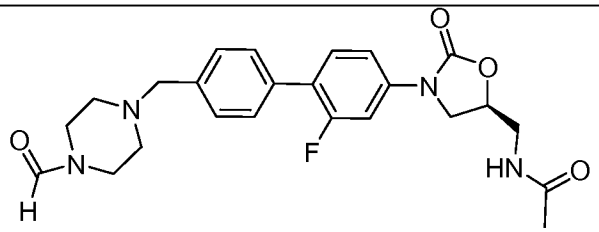
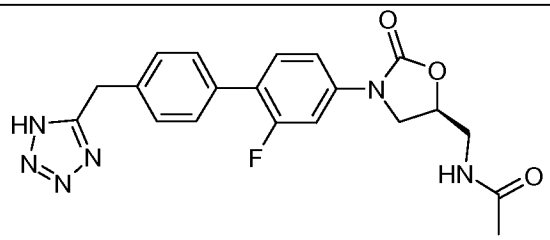
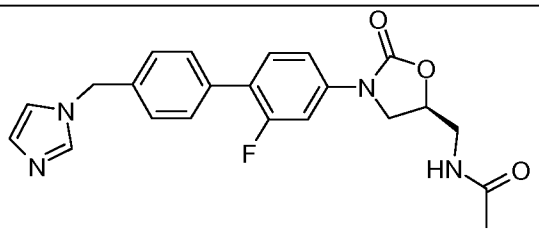
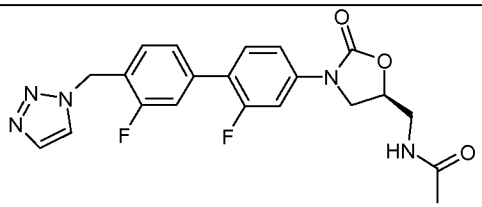
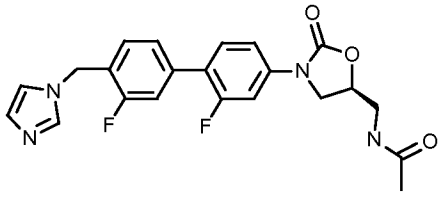
		Using The Same		
WO 2005/070904	Rib-X Pharmaceuticals, Inc.	Sulfonamide Compounds and Methods of Making and Using The Same	August 4, 2005	June 2, 2004
WO 2005/012270	Rib-X Pharmaceuticals, Inc.	Biaryl Heterocyclic Amides, Amides, and Sulfur-Containing Compounds and Methods of Making and Using the Same	February 10, 2005	July 28, 2004
WO 2005/012271	Rib-X Pharmaceuticals, Inc.	Process for the Synthesis of Biaryl Oxazolidinones	February 10, 2005	July 28, 2004
US 6,559,303 B1	Pharmacia & Upjohn Company	Linezolid -Crystal Form II	May 6, 2003	May 23, 2002
US 5,688,792	Pharmacia & Upjohn Company	Substituted Oxazine and Thiazine Oxazolidinone Antimicrobials	November 18, 1997	§ 371 Date March 5, 1996
US 5,654,435	Pharmacia & Upjohn Company	Substituted Arylphenyloxazolidinones	August 5, 1997	June 6, 1995
WO 2001/094342	Dong A Pharm. Co., Ltd.	Novel Oxazolidinone Derivatives and a Process for the Preparation Thereof	December 13, 2001	May 18, 2001
WO 01/081350	AstraZeneca AB and AstraZeneca UK Limited	Oxazolidinone Derivatives with Antibiotic Activity	November 1, 2001	April 23, 2001
US 6,133,284	Wakunaga Pharmaceutical Co., Ltd.	Pyridone Carboxylic Acid Derivatives or their Salts, and Antibacterial Agents Containing the Same as Their Effective Components	October 17, 2000	June 10, 1999
US 5,998,436 and its certificate of	Wakunaga Pharmaceutical Co., Ltd.	Pyridone Carboxylic Acid Derivatives or their Salts and Antibacterial Agent	December 7, 1999	PCT Filed September 20, 1996

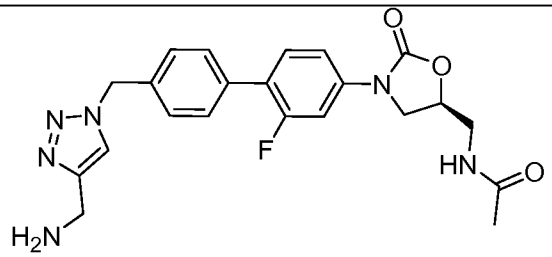
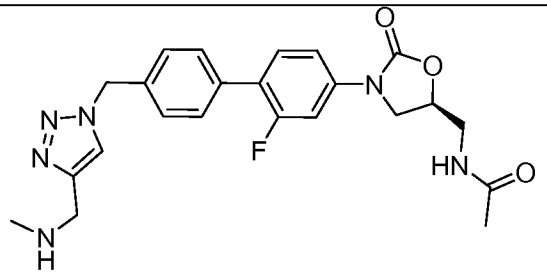
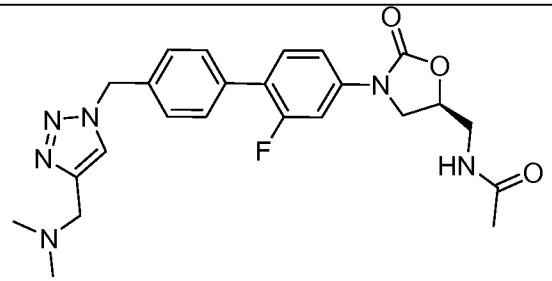
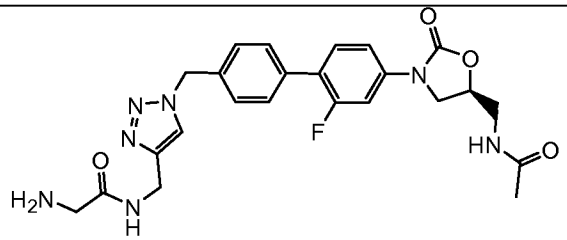
correction of December 17, 2002		Comprising the Same as the Active Ingredient		
US 6,156,903	Wakunaga Pharmaceutical Co., Ltd.	Pyridone Carboxylic Acid Derivatives or their Salts, and Antibacterial Agents Containing the Same as Their Effective Components	December 5, 2000	June 10, 1999
WO 1997/11068	Wakunaga Pharmaceutical Co., Ltd.	Novel Pyridone Carboxylic Acid Derivatives or their Salts and Antibacterial Agent Comprising the Same as the Active Ingredient	March 27, 1997	September 20, 1996
WO 2006/015194	Abbott Laboratories	Preparation of Pyridone Carboxylic Acid Antibacterials	February 9, 2006	July 29, 2005
WO 2006/042034	Abbott Laboratories	Salt and Crystalline Forms Thereof of a Drug	April 20, 2006	October 9, 2005
WO 2006/110815	Abbott Laboratories	Pharmaceutical Compositions Having Improved Dissolution Profiles for Poorly Soluble Drugs	October 19, 2006	April 11, 2006

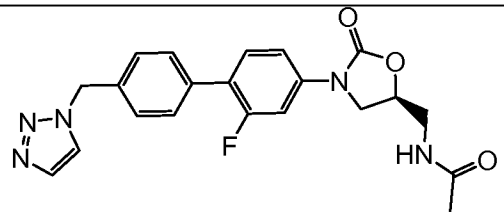
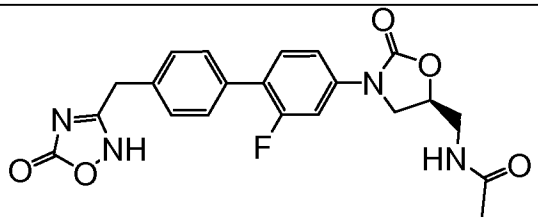
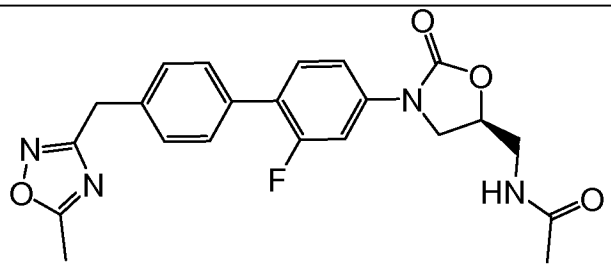
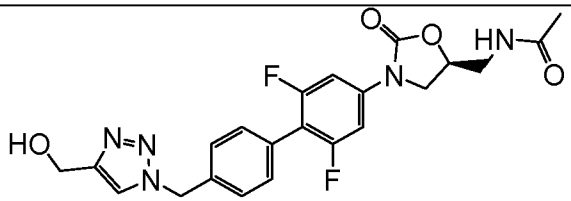
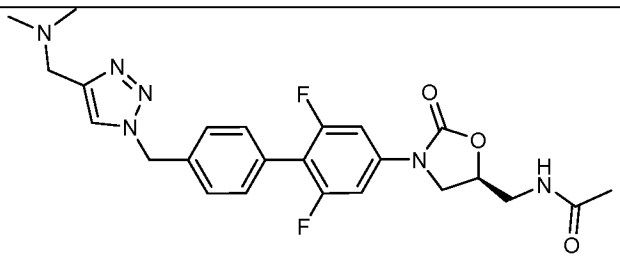
[0076] Exemplary compounds in accordance with the invention are listed in Table 2 with their minimum inhibitory concentrations (MICs) (μg/mL) for *S. aureus*:

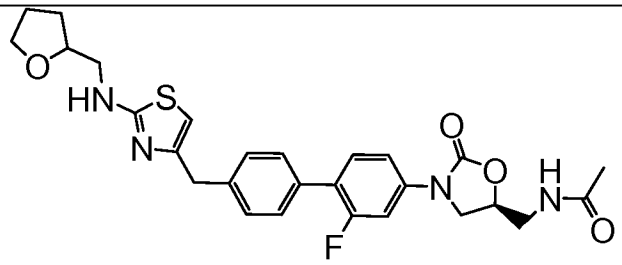
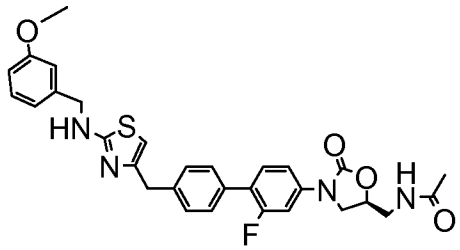
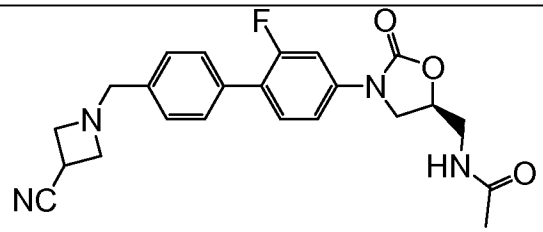
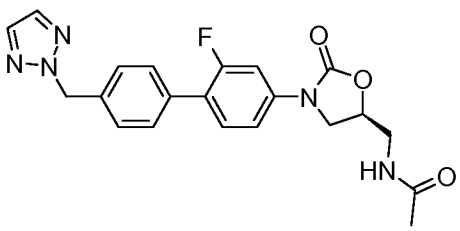
Table 2

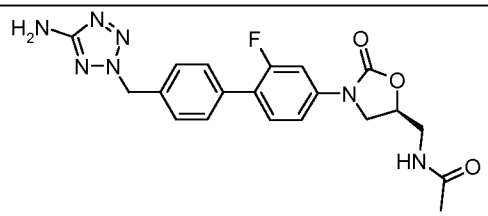
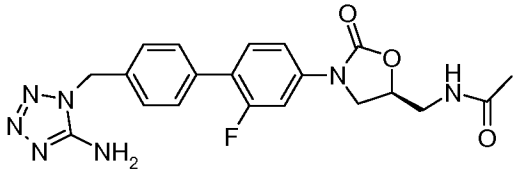
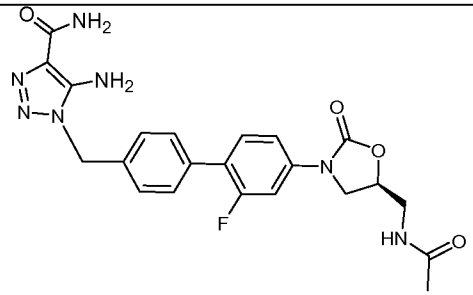
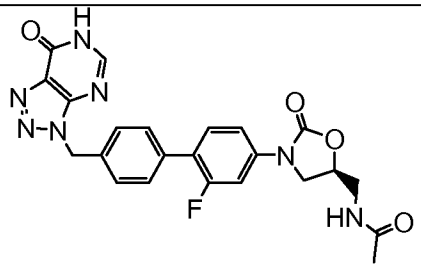
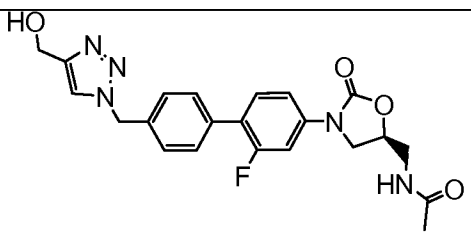
Compound Number	Structure	MICs
1001		2
	N-{3-[2-Fluoro-4'-(2-[1,2,3]triazol-1-yl-ethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1002		2
	N-{3-[2-Fluoro-4'-(2-imidazol-1-yl-ethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1003		2
	2-(4-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-piperazin-1-yl)-acetamide	
1004		2
	N-{3-[4'-(4-Cyanomethyl-piperazin-1-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1005		2
	N-{3-[4'-(4-Cyanomethyl-piperazin-1-ylmethyl)-2,3'-difluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

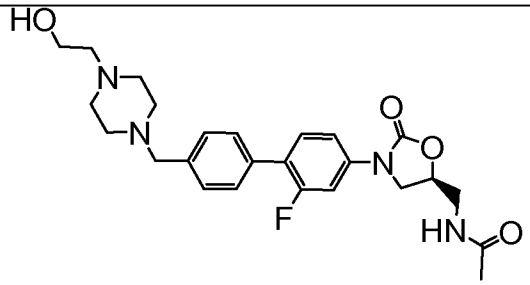
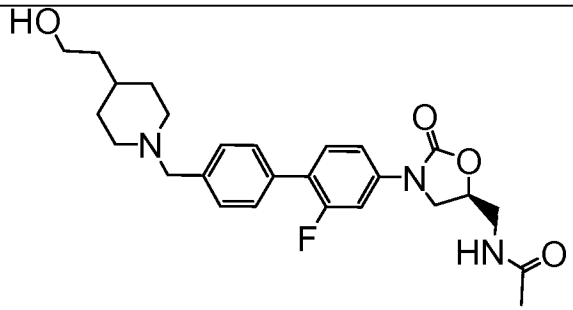
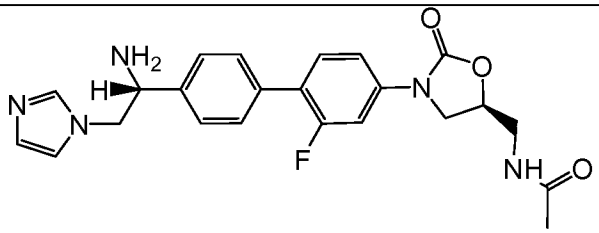
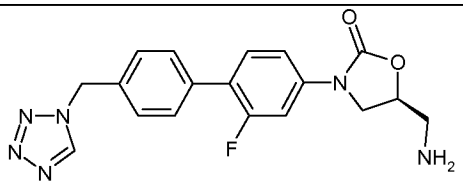
1006		0.5
	N-{3-[2-Fluoro-4'-(4-formyl-piperazin-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1007		8
	N-{3-[2-Fluoro-4'-(1H-tetrazol-5-(S)-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1008		0.5
	N-[3-(2-Fluoro-4'-imidazol-1-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
1009		0.25
	N-[3-(2,3'-Difluoro-4'-[1,2,3]triazol-1-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
1010		1
	N-[3-(2,3'-Difluoro-4'-imidazol-1-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

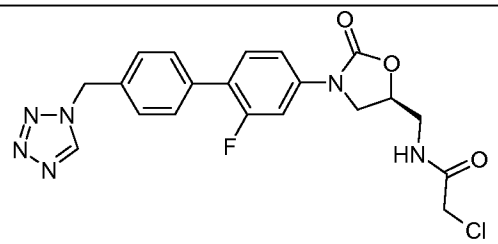
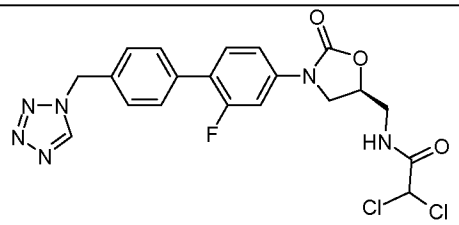
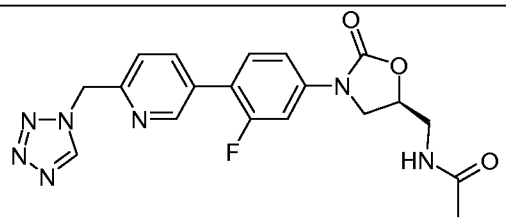
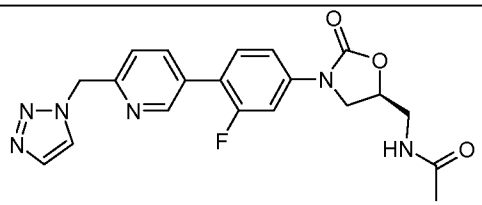
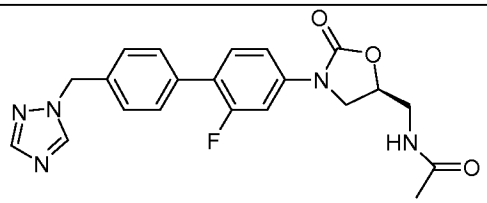
1011		1
	N-{3-[4'-(4-Aminomethyl-[1,2,3]triazol-1-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1012		2
	N-{3-[2-Fluoro-4'-(4-methylaminomethyl-[1,2,3]triazol-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1013		4
	N-{3-[4'-(4-Dimethylaminomethyl-[1,2,3]triazol-1-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1014		8
	N-(1-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-1H-[1,2,3]triazol-4-ylmethyl)-2-amino-acetamide	

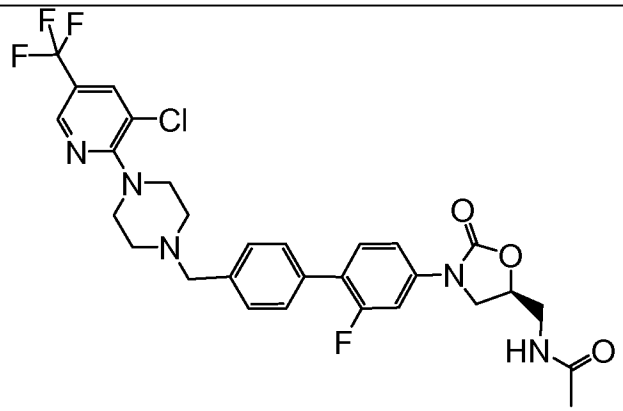
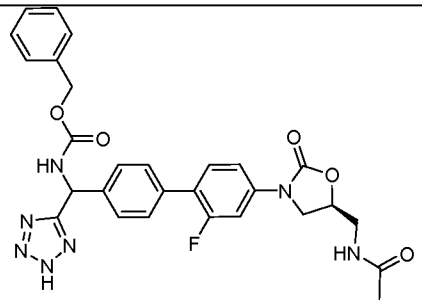
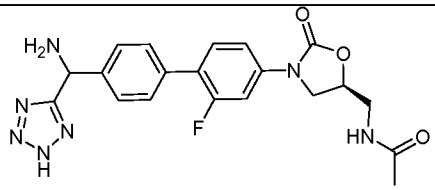
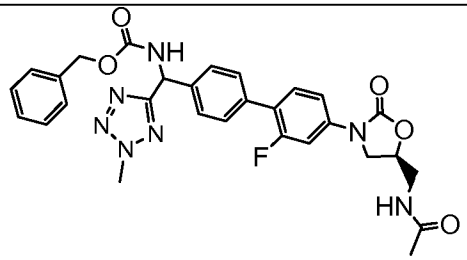
1015		0.25
	N-[3-(2-Fluoro-4'-[1,2,3]triazol-1-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
1016		4
	N-{3-[2-Fluoro-4'-(5-(S)-oxo-2,5-(S)-dihydro-[1,2,4]oxadiazol-3-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1017		1
	N-{3-[2-Fluoro-4'-(5-(S)-methyl-[1,2,4]oxadiazol-3-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1018		1
	N-{3-[2,6-Difluoro-4'-(4-hydroxymethyl-[1,2,3]triazol-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1019		2
	N-{3-[4'-(4-Dimethylaminomethyl-[1,2,3]triazol-1-ylmethyl)-	

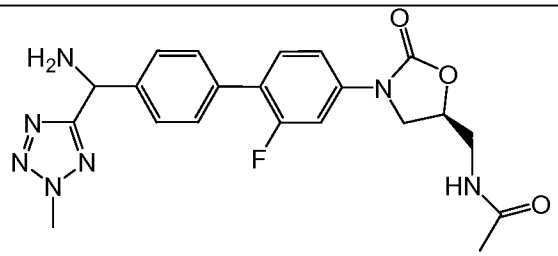
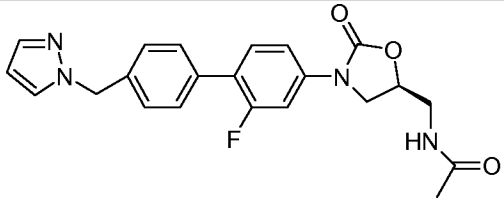
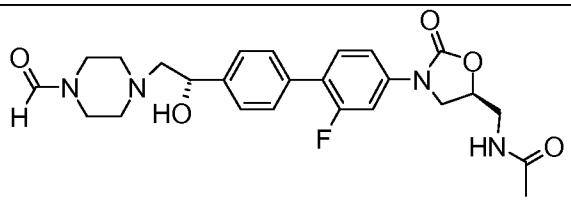
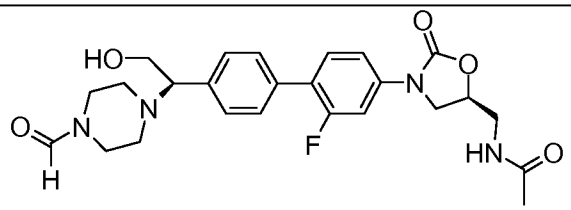
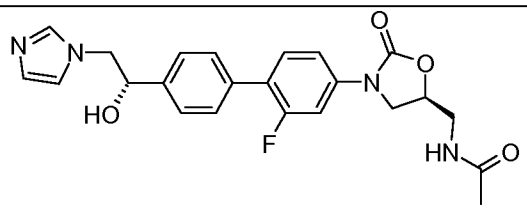
	2,6-difluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1020		1
	N-[3-(2-Fluoro-4'-{2-[(tetrahydro-furan-2-ylmethyl)-amino]-thiazol-4-ylmethyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
1021		1
	N-(3-{2-Fluoro-4'-[2-(3-methoxy-benzylamino)-thiazol-4-ylmethyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
1022		0.25
	N-{3-[4'-(3-Cyano-azetidin-1-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1023		0.25
	N-[3-(2-Fluoro-4'-[1,2,3]triazol-2-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

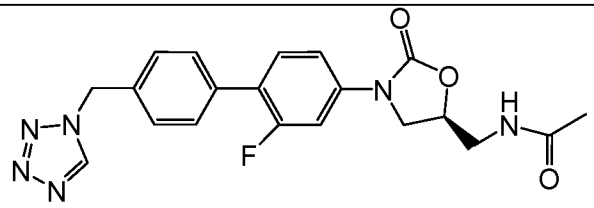
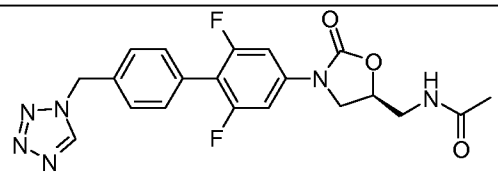
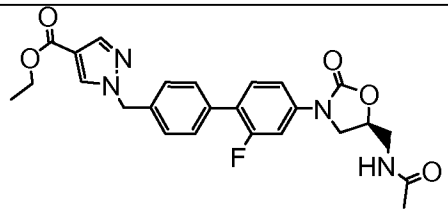
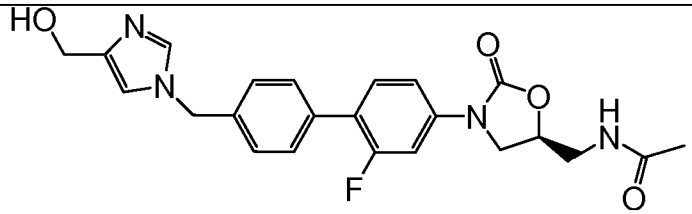
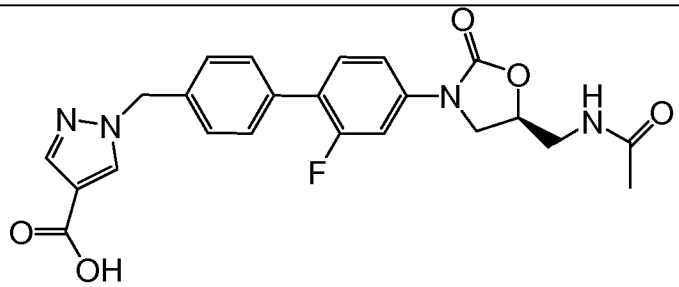
1024		0.25
	N-{3-[4'-(5-Amino-tetrazol-2-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1025		0.5
	N-{3-[4'-(5-Amino-tetrazol-1-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1026		2
	1-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-5-amino-1H-[1,2,3]triazole-4-carboxylic acid amide	
1027		1
	N-{3-[2-Fluoro-4'-(7-oxo-6,7-dihydro-[1,2,3]triazolo[4,5-d]pyrimidin-3-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1028		1

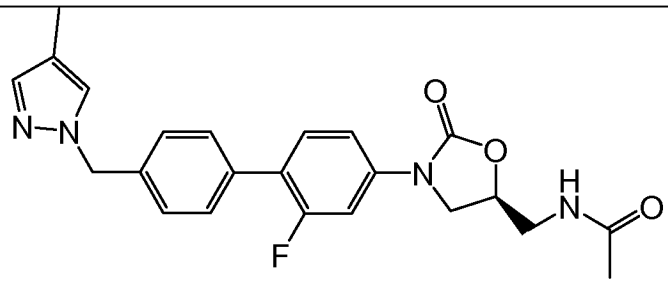
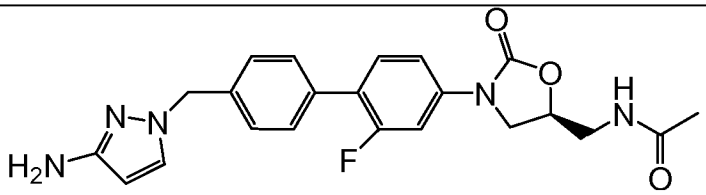
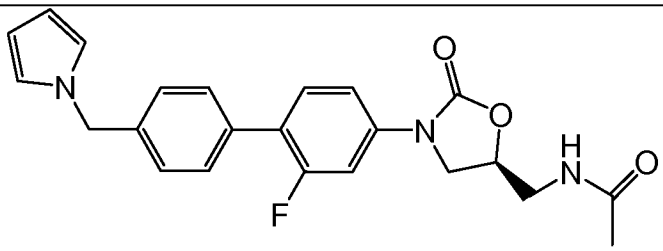
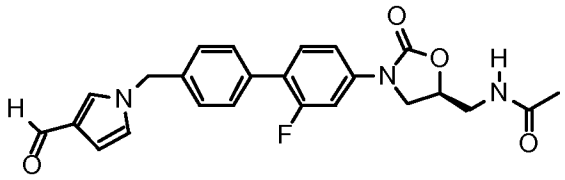
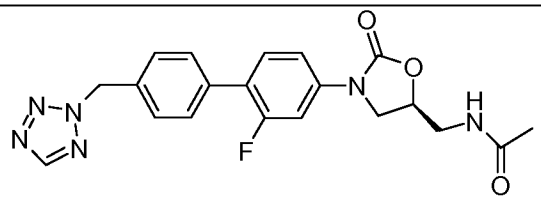
	N-{3-[2-Fluoro-4'-(4-hydroxymethyl-[1,2,3]triazol-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1029		2
	N-(3-{2-Fluoro-4'-[4-(2-hydroxy-ethyl)-piperazin-1-ylmethyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
1030		2
	N-(3-{2-Fluoro-4'-[4-(2-hydroxy-ethyl)-piperidin-1-ylmethyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
1031		8
	N-{3-[4'-(R)-(1-Amino-2-imidazol-1-yl-ethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1032		32
	5-(S)-Aminomethyl-3-(2-fluoro-4'-tetrazol-1-ylmethyl-biphenyl-4-yl)-oxazolidin-2-one	

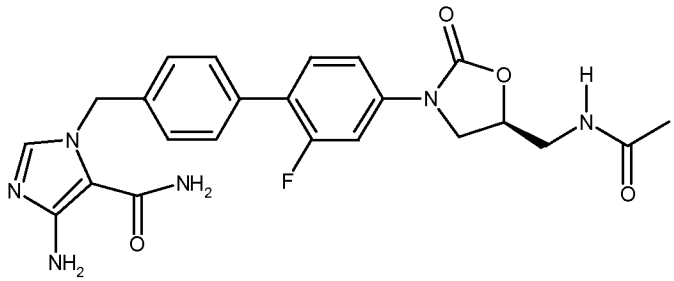
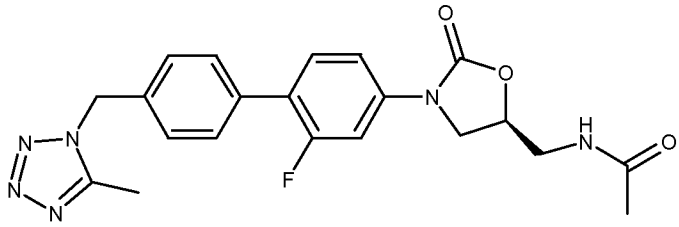
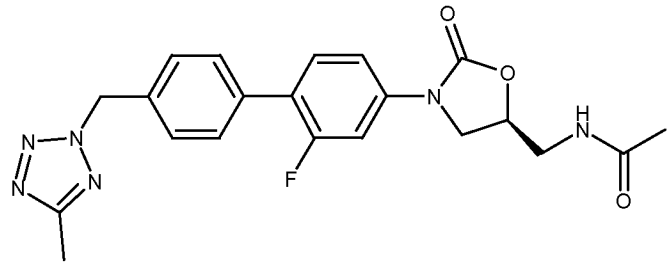
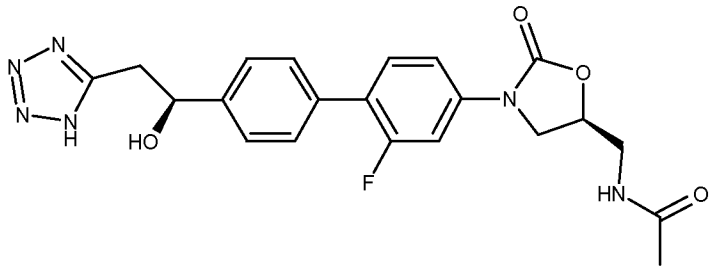
1033		0.25
	2-Chloro-N-[3-(2-fluoro-4'-tetrazol-1-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
1034		0.5
	2,2-Dichloro-N-[3-(2-fluoro-4'-tetrazol-1-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
1035		0.5
	N-{3-[3-Fluoro-4-(6-tetrazol-1-ylmethyl-pyridin-3-yl)-phenyl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1036		1
	N-{3-[3-Fluoro-4-(6-[1,2,3]triazol-1-ylmethyl-pyridin-3-yl)-phenyl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1037		0.5
	N-[3-(2-Fluoro-4'-[1,2,4]triazol-1-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

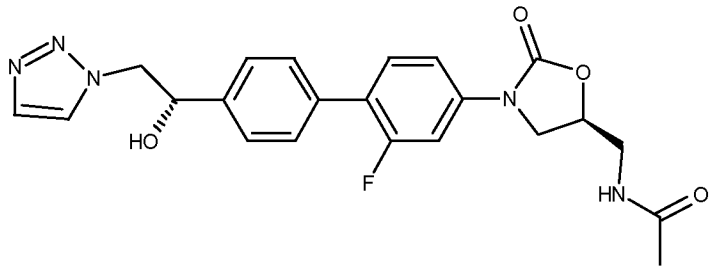
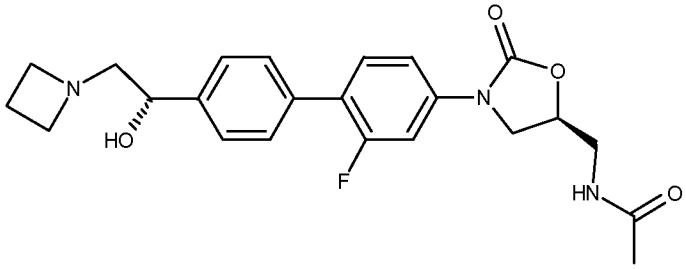
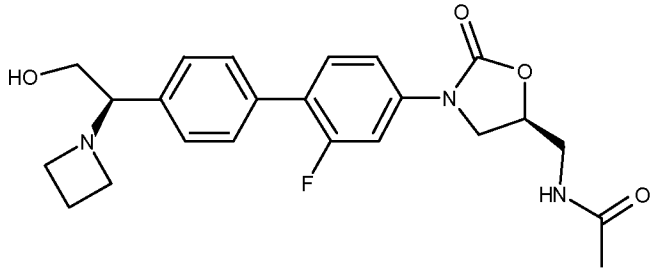
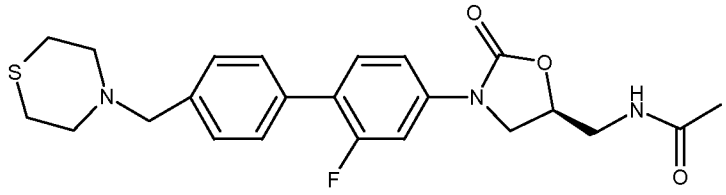
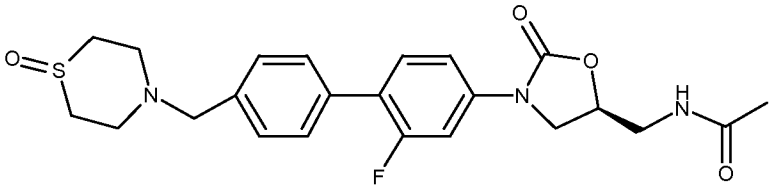
1038		128
	N-(3-{4'-[4-(3-Chloro-5-trifluoromethyl-pyridin-2-yl)-piperazin-1-ylmethyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
1039		128
	[{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-yl}-(2H-tetrazol-5-(R/S)-yl)-methyl]-carbamic acid benzyl ester	
1040		128
	N-(3-{4'-[Amino-(2H-tetrazol-5-(R/S)-yl)-methyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
1041		1
	[{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-yl}-(2-methyl-2H-tetrazol-5-(R/S)-yl)-methyl]-carbamic acid benzyl ester	

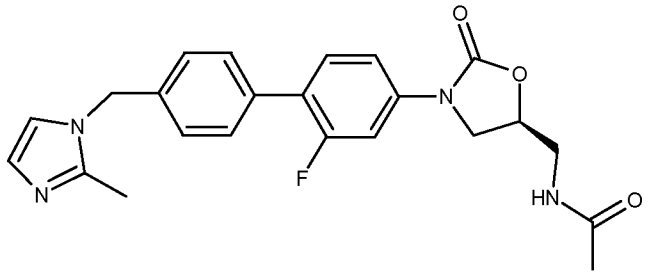
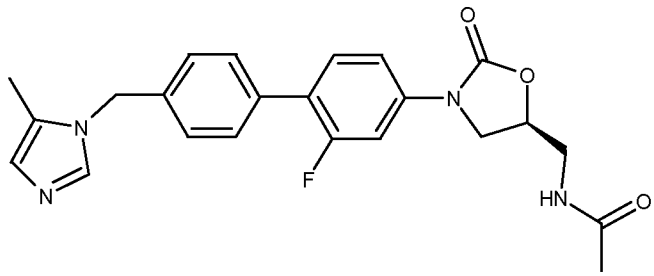
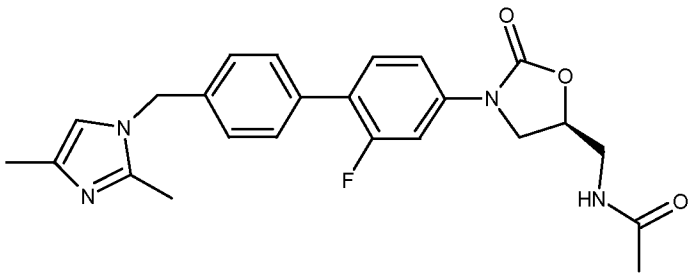
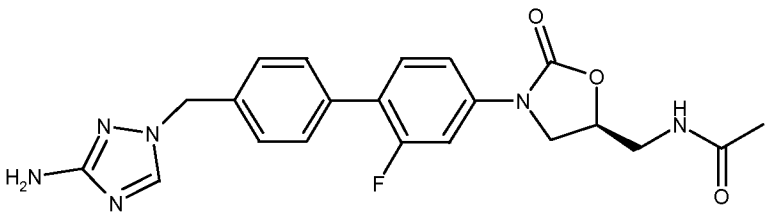
1042		64
	N-(3-{4'-[Amino-(2-methyl-2H-tetrazol-5-(R/S)-yl)-methyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
1043		0.25
	N-[3-(2-Fluoro-4'-pyrazol-1-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
1044		0.5
	N-(3-{2-Fluoro-4'-[2-(4-formyl-piperazin-1-yl)-1-(S)-hydroxy-ethyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
1045		0.5
	N-(3-{2-Fluoro-4'-[1-(R)-(4-formyl-piperazin-1-yl)-2-hydroxy-ethyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
1046		1
	N-{3-[2-Fluoro-4'-(1-(S)-hydroxy-2-imidazol-1-yl-ethyl)-	

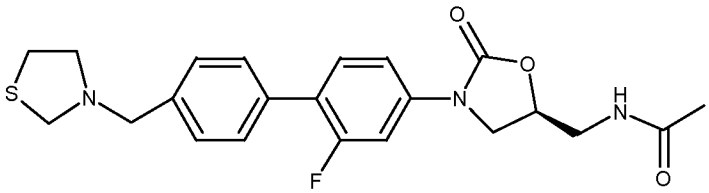
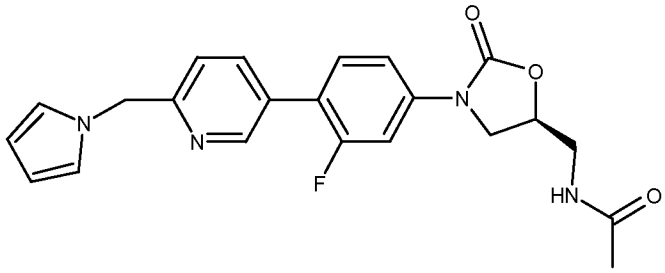
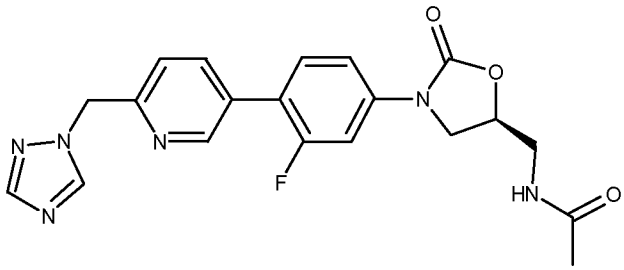
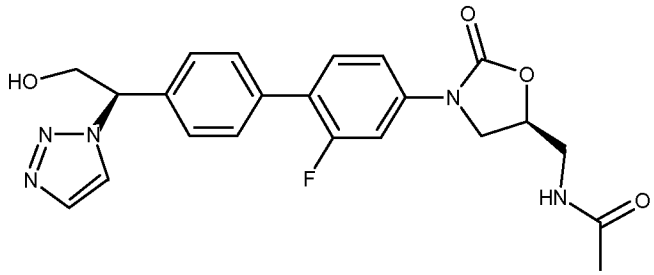
	biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1047		0.25
	N-[3-(2-Fluoro-4'-tetrazol-1-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
1048		1
	N-[3-(2,6-Difluoro-4'-tetrazol-1-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
1049		0.5
	1-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-1H-pyrazole-4-carboxylic acid ethyl ester	
1050		2
	N-{3-[2-Fluoro-4'-(4-hydroxymethyl-imidazol-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1051		1
	1-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-1H-pyrazole-4-carboxylic acid	

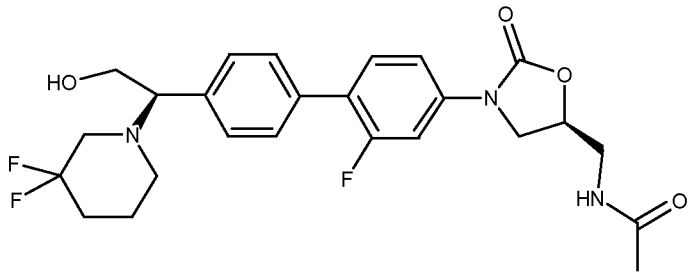
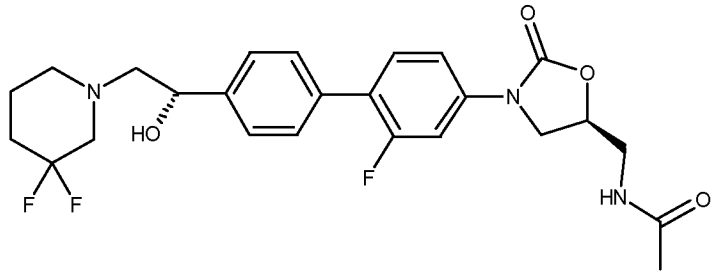
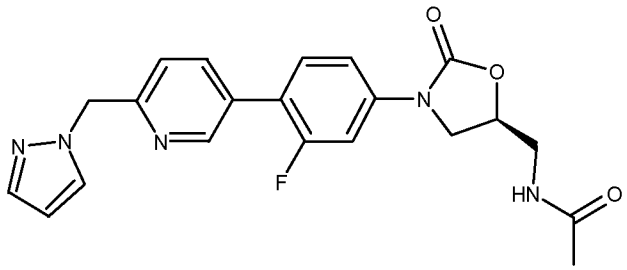
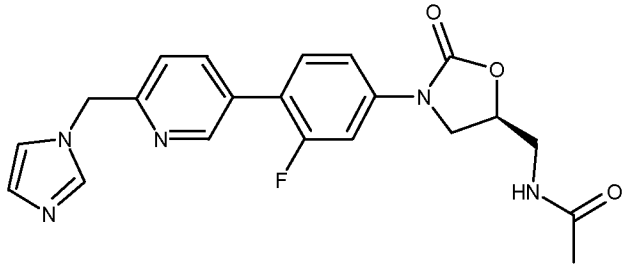
1052		1
	N-{3-[2-Fluoro-4'-(4-methyl-pyrazol-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1053		1
	N-{3-[4'-(3-Amino-pyrazol-1-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1054		0.5
	N-[3-(2-Fluoro-4'-pyrrol-1-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
1055		0.25
	N-{3-[2-Fluoro-4'-(3-formyl-pyrrol-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1056		0.25
	N-[3-(2-Fluoro-4'-tetrazol-2-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

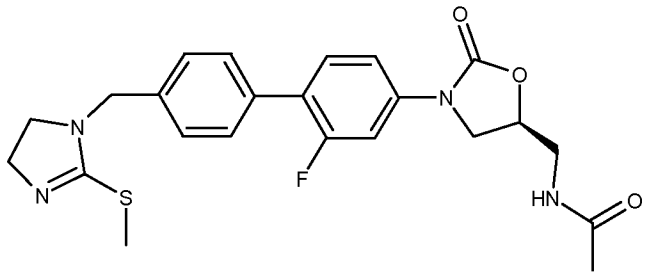
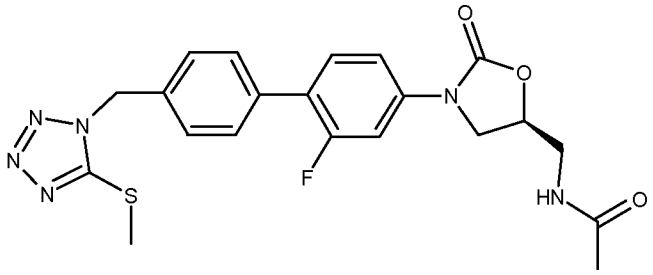
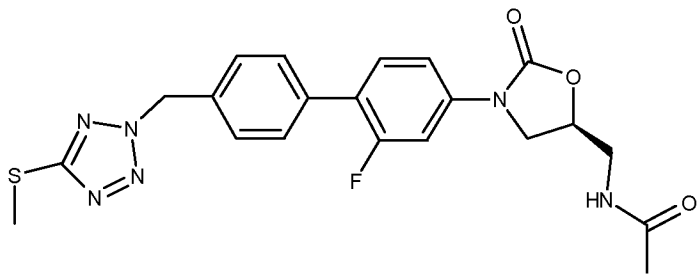
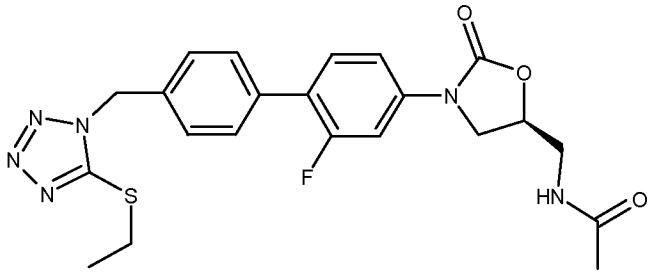
1057		1
	3-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-5-amino-3H-imidazole-4-carboxylic acid amide	
1058		0.5
	N-{3-[2-Fluoro-4'-(5-methyl-tetrazol-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1059		0.5
	N-{3-[2-Fluoro-4'-(5-methyl-tetrazol-2-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1060		64
	N-(3-{2-Fluoro-4'-[1-(R)-hydroxy-2-(1H-tetrazol-5-yl)-ethyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	

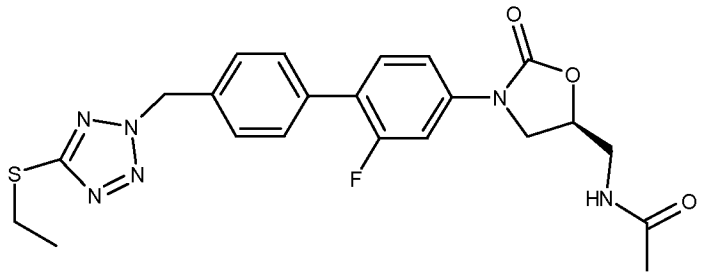
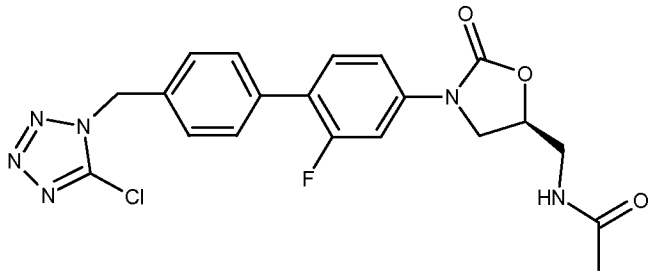
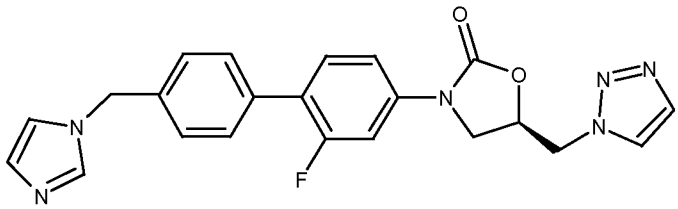
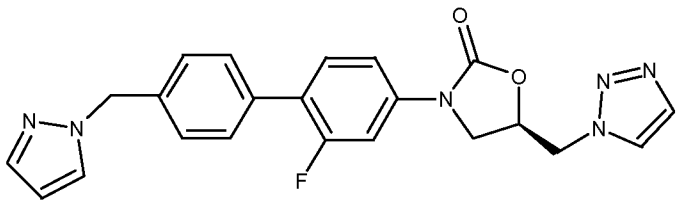
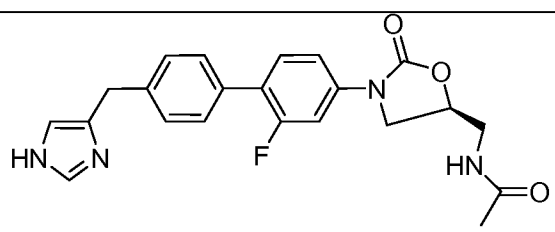
1061		1
	N-{3-[2-Fluoro-4'-(1-(S)-hydroxy-2-[1,2,3]triazol-1-yl-ethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1062		8
	N-{3-[4'-(2-Azetidin-1-yl-1-(S)-hydroxy-ethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1063		8
	N-{3-[4'-(1-(R)-Azetidin-1-yl-2-hydroxy-ethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1064		2
	N-[3-(2-Fluoro-4'-thiomorpholin-4-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
1065		2

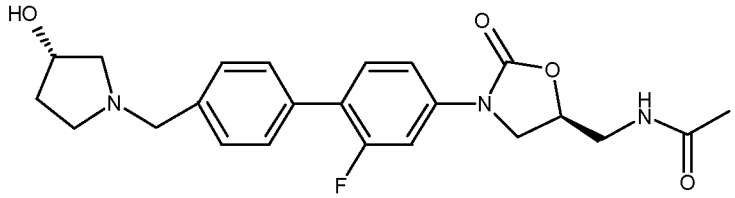
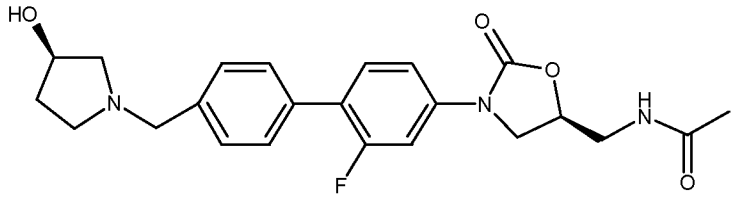
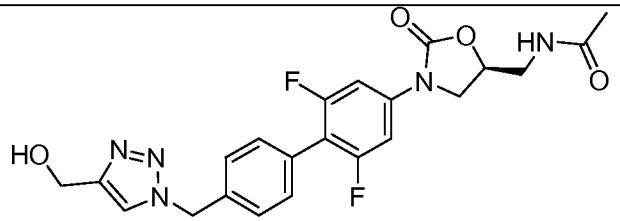
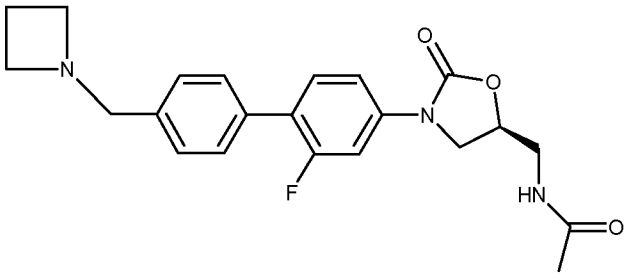
	N-{3-[2-Fluoro-4'-(1-oxo-1lambda*4*-thiomorpholin-4-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1066		1
	N-{3-[2-Fluoro-4'-(2-methyl-imidazol-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1067		1
	N-{3-[2-Fluoro-4'-(5-methyl-imidazol-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1068		1
	N-{3-[4'-(2,4-Dimethyl-imidazol-1-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1069		1
	N-{3-[4'-(3-Amino-[1,2,4]triazol-1-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

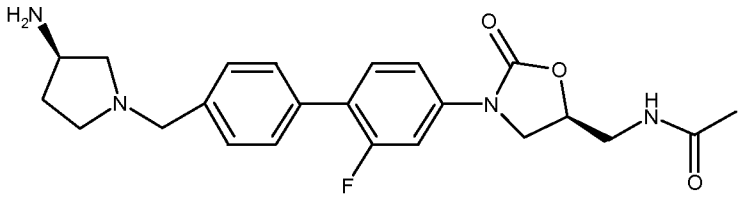
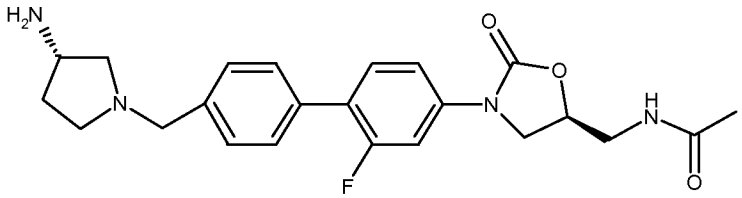
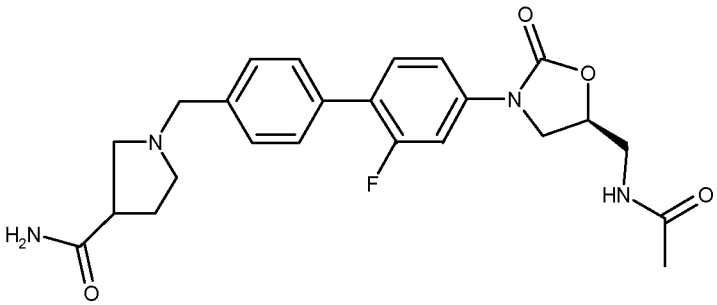
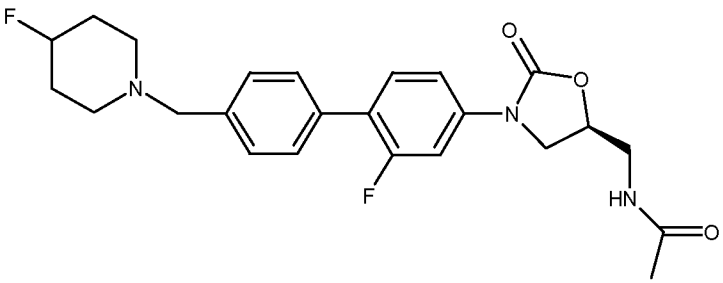
1070		
	N-[3-(2-Fluoro-4'-thiazolidin-3-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
1071		0.25
	N-{3-[3-Fluoro-4-(6-pyrrol-1-ylmethyl-pyridin-3-yl)-phenyl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1072		1
	N-{3-[3-Fluoro-4-(6-[1,2,4]triazol-1-ylmethyl-pyridin-3-yl)-phenyl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1073		1
	N-{3-[2-Fluoro-4'-(2-hydroxy-1-(R)-[1,2,3]triazol-1-yl-ethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

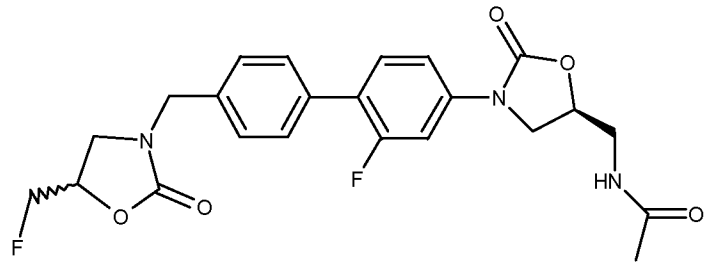
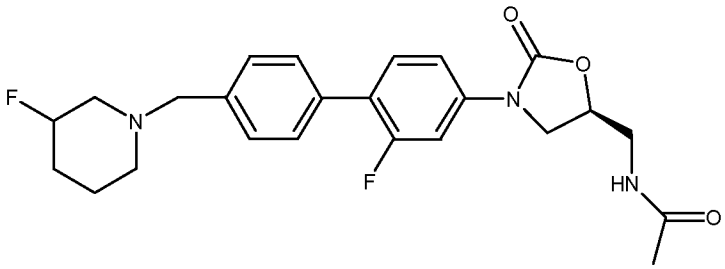
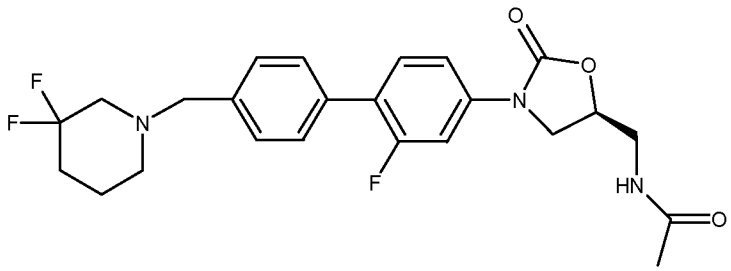
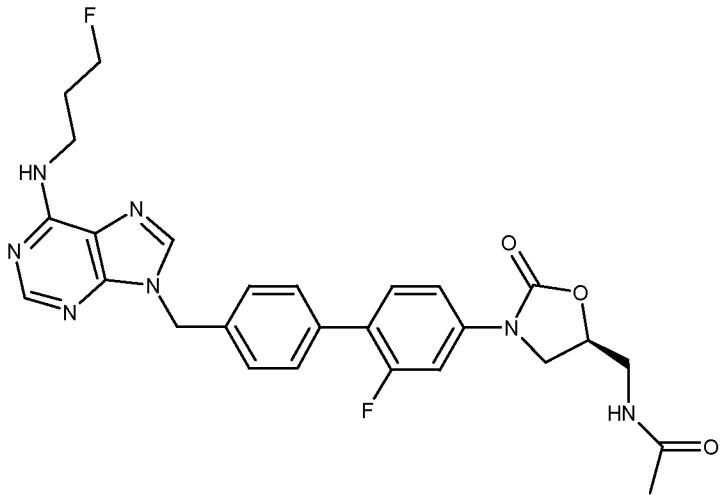
1074		4
	N-(3-{4'-[1-(R)-(3,3-Difluoro-piperidin-1-yl)-2-hydroxy-ethyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
1075		2
	N-(3-{4'-[2-(3,3-Difluoro-piperidin-1-yl)-1-(S)-hydroxy-ethyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
1076		1
	N-{3-[3-Fluoro-4-(6-pyrazol-1-ylmethyl-pyridin-3-yl)-phenyl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1077		4
	N-{3-[3-Fluoro-4-(6-imidazol-1-ylmethyl-pyridin-3-yl)-phenyl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

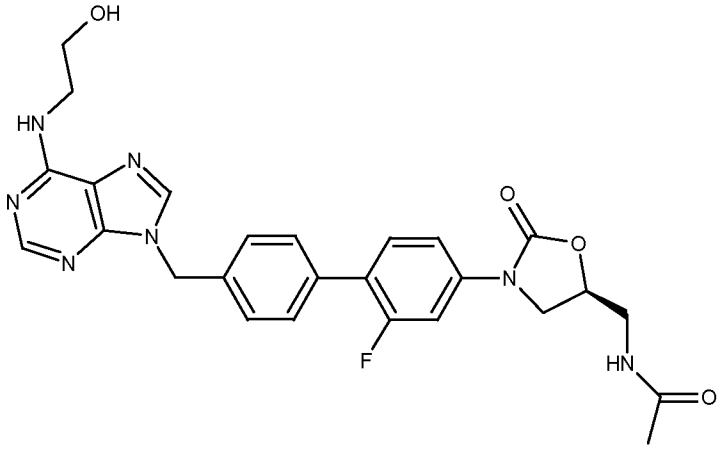
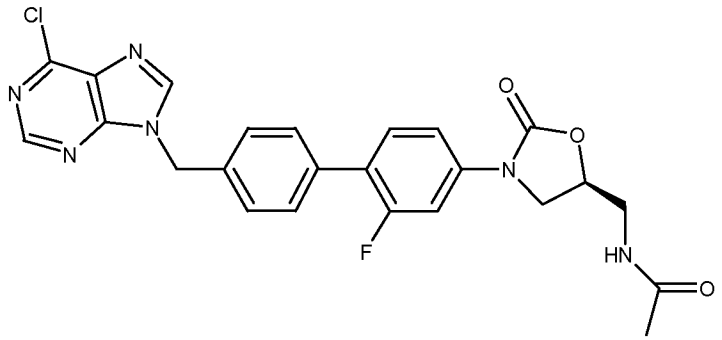
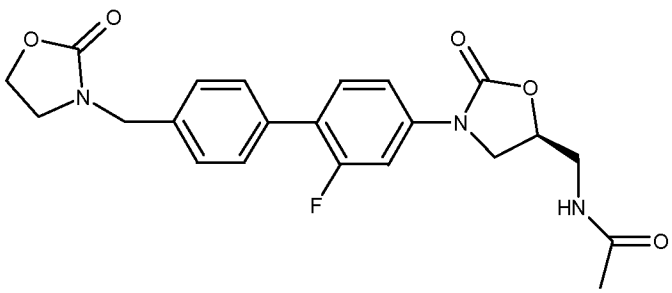
1078		2
	N-{3-[2-Fluoro-4'-(2-methylsulfanyl-4,5-dihydro-imidazol-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1079		2
	N-{3-[2-Fluoro-4'-(5-methylsulfanyl-tetrazol-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1080		0.25
	N-{3-[2-Fluoro-4'-(5-methylsulfanyl-tetrazol-2-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1081		2
	N-{3-[4'-(5-Ethylsulfanyl-tetrazol-1-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

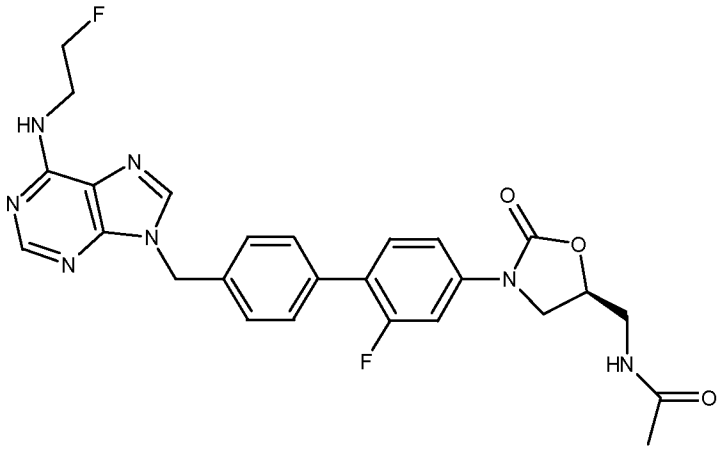
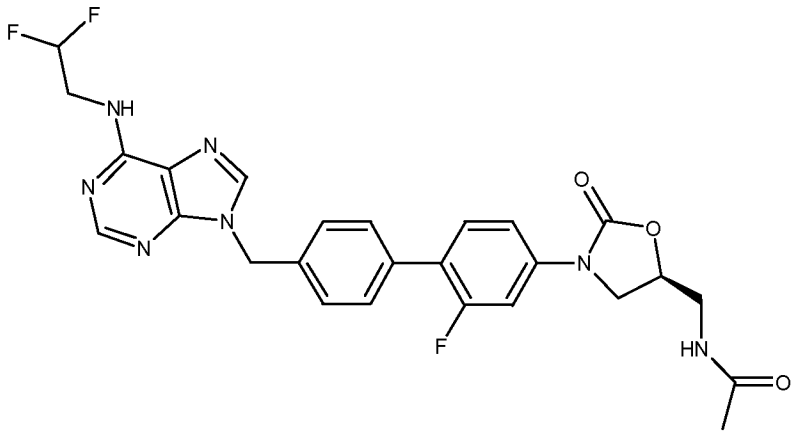
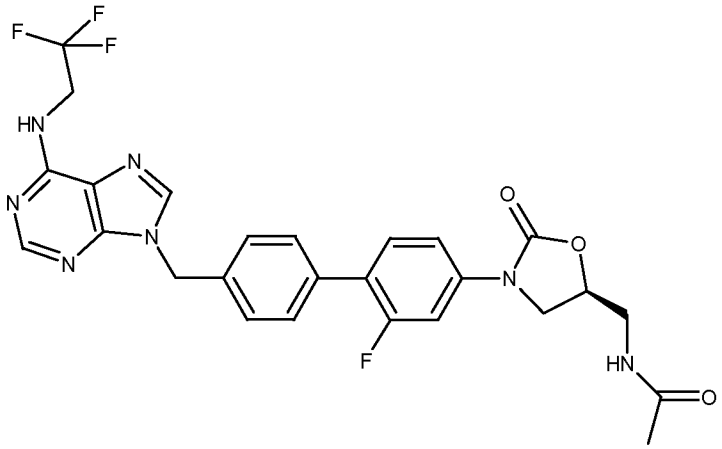
1082		0.5
	N-{3-[4'-(5-Ethylsulfanyl-tetrazol-2-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1083		0.5
	N-{3-[4'-(5-Chloro-tetrazol-1-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1084		0.25
	3-(2-Fluoro-4'-imidazol-1-ylmethyl-biphenyl-4-yl)-5-(R)-[1,2,3]triazol-1-ylmethyl-oxazolidin-2-one	
1085		0.5
	3-(2-Fluoro-4'-pyrazol-1-ylmethyl-biphenyl-4-yl)-5-(R)-[1,2,3]triazol-1-ylmethyl-oxazolidin-2-one	
1086		0.5

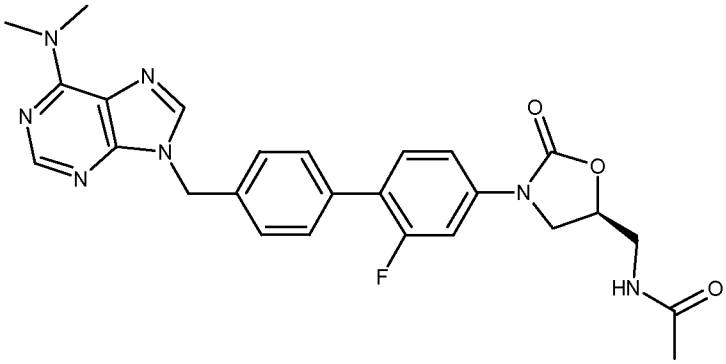
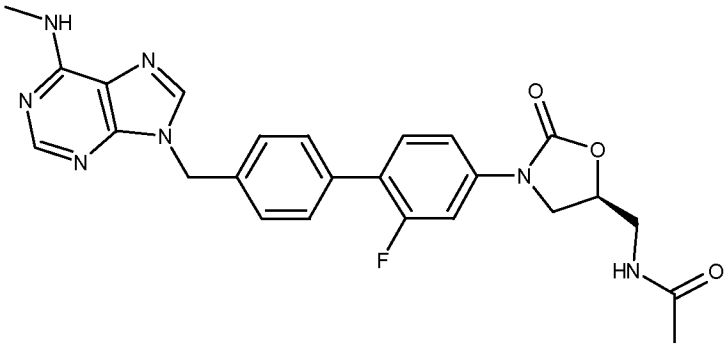
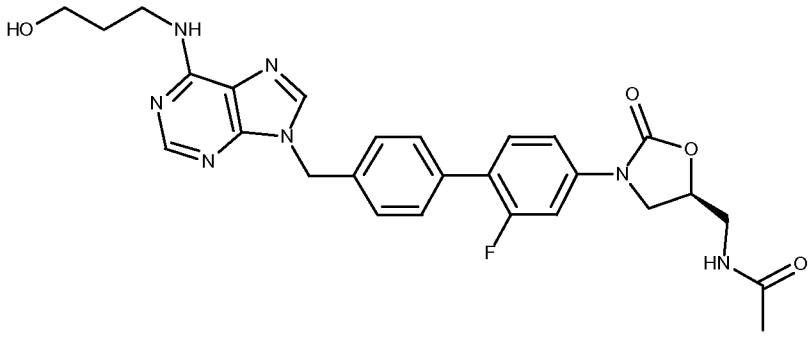
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1087		4
	N-{3-[2-Fluoro-4'-(3-(S)-hydroxy-pyrrolidin-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1088		4
	N-{3-[2-Fluoro-4'-(3-(R)-hydroxy-pyrrolidin-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1089		1
	N-{3-[2,6-Difluoro-4'-(4-hydroxymethyl-[1,2,3]triazol-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1090		2
	N-[3-(4'-Azetidin-1-ylmethyl-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

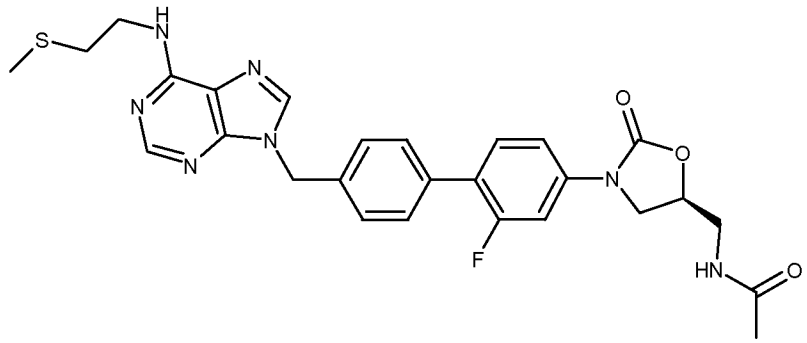
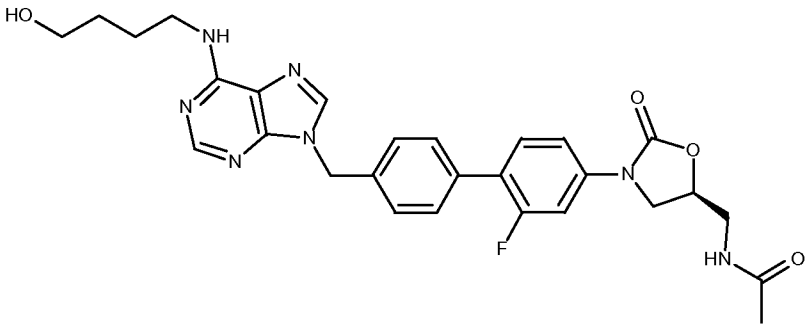
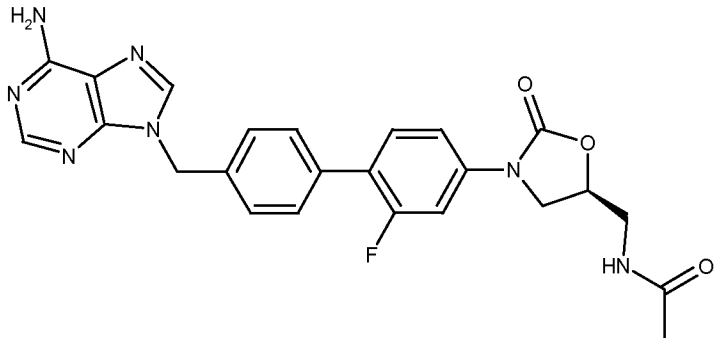
1091		2
	N-{3-[4'-(3-(R)-Amino-pyrrolidin-1-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1092		4
	N-{3-[4'-(3-(S)-Amino-pyrrolidin-1-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1093		2
	1-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-pyrrolidine-3-(R/S)-carboxylic acid amide	
1094		1
	N-{3-[2-Fluoro-4'-(4-fluoro-piperidin-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

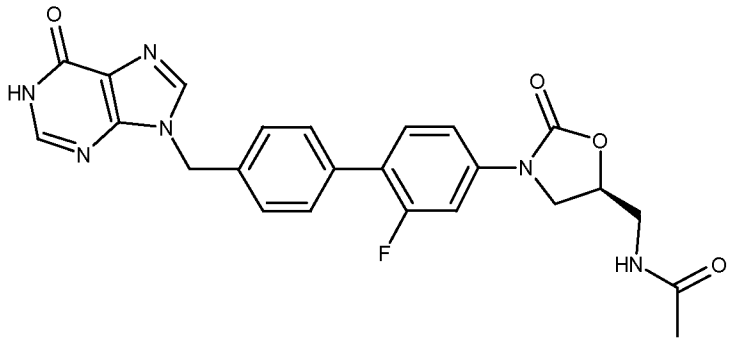
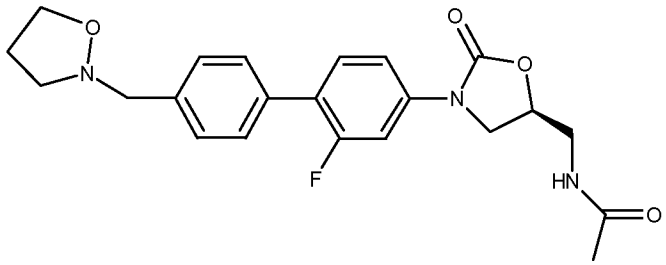
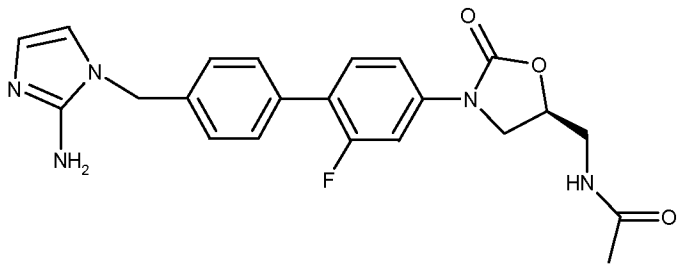
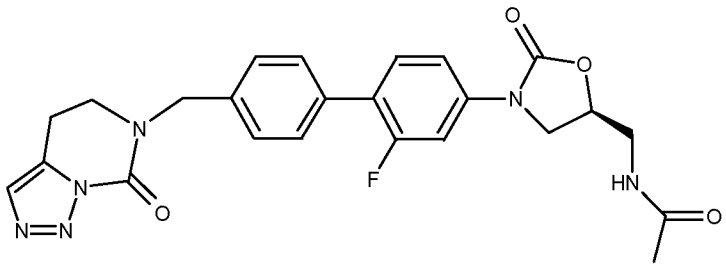
1095		0.5
	N-{3-[2-Fluoro-4'-(5-fluoromethyl-2-oxo-oxazolidin-3-(R/S)ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1096		1
	N-{3-[2-Fluoro-4'-(3-(R/S)-fluoro-piperidin-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1097		2
	N-{3-[4'-(3,3-Difluoro-piperidin-1-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1098		2

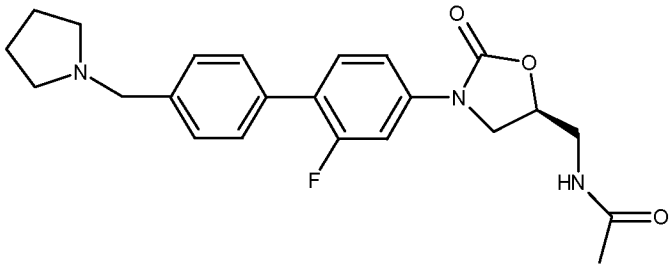
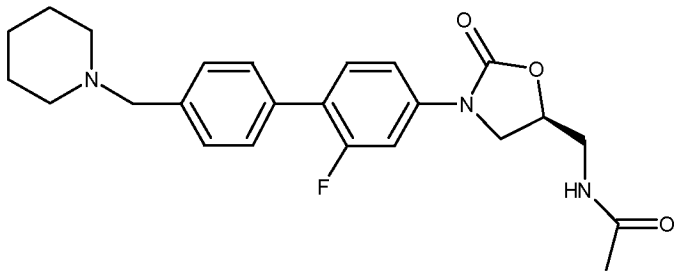
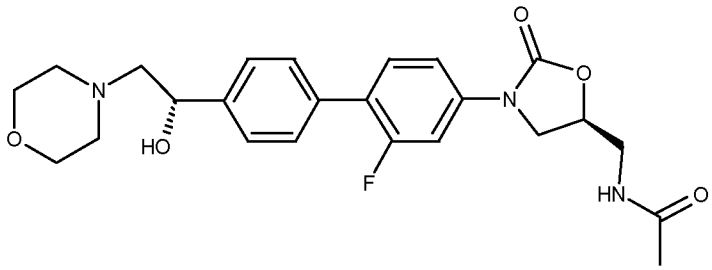
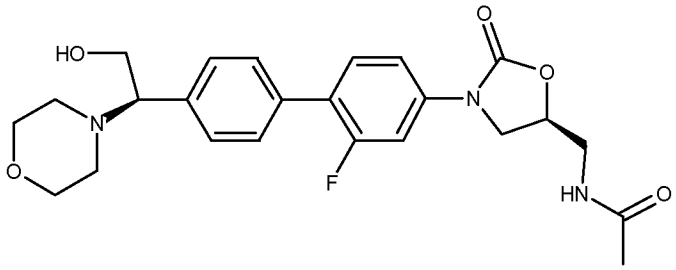
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1099		2
	N-(3-{2-Fluoro-4'-[6-(2-hydroxy-ethylamino)-purin-9-ylmethyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
1100		1
	N-{3-[4'-(6-Chloro-purin-9-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1101		0.25
	N-{3-[2-Fluoro-4'-(2-oxo-oxazolidin-3-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

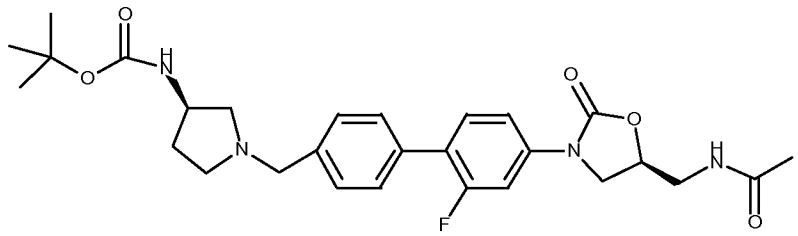
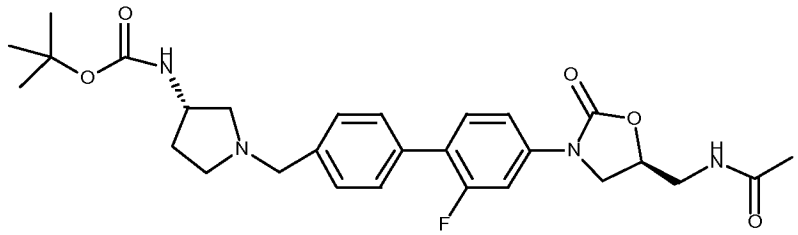
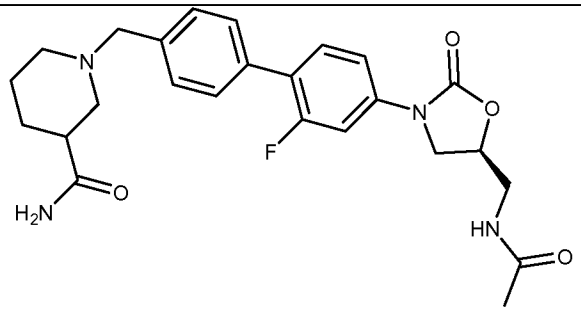
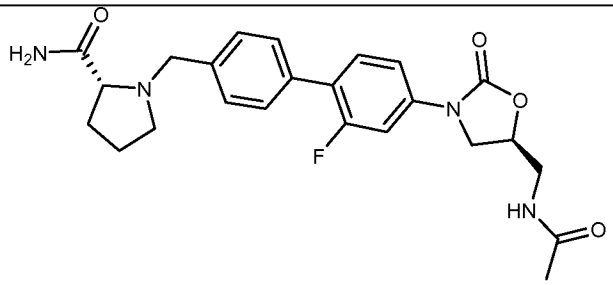
1102		1
	N-(3-{2-Fluoro-4'-[6-(2-fluoro-ethylamino)-purin-9-ylmethyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
1103		1
	N-(3-{4'-[6-(2,2-Difluoro-ethylamino)-purin-9-ylmethyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
1104		1

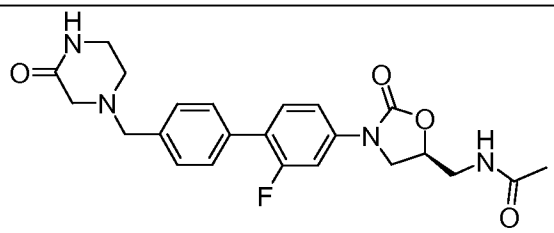
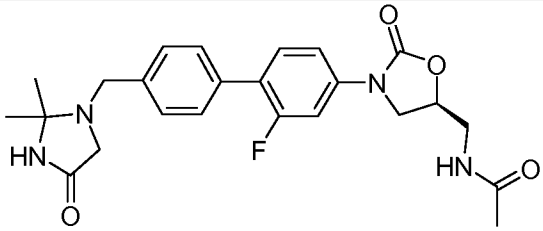
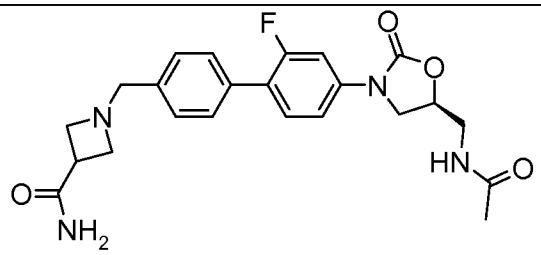
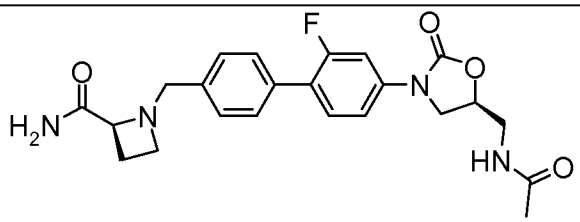
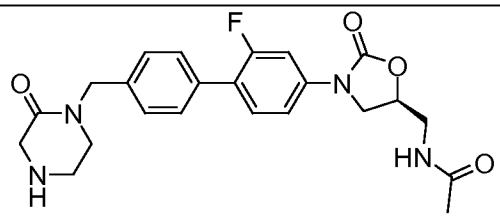
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1105		1
	N-{3-[4'-(6-Dimethylamino-purin-9-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1106		1
	N-{3-[2-Fluoro-4'-(6-methylamino-purin-9-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1107		2
	N-(3-{2-Fluoro-4'-[6-(3-hydroxy-propylamino)-purin-9-ylmethyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	

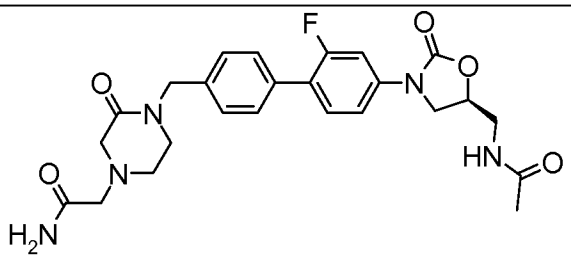
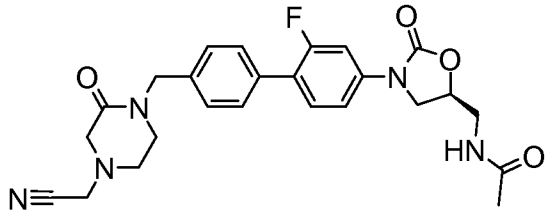
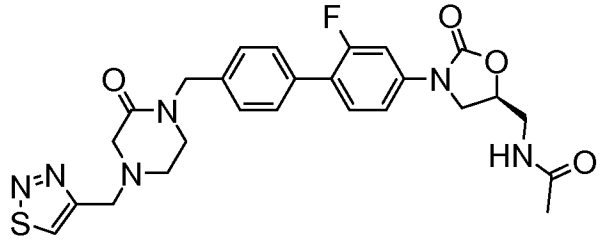
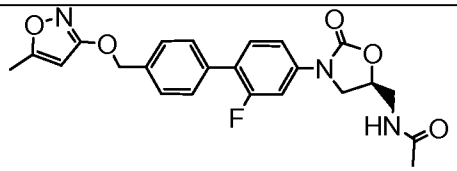
1108		2
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1109		2
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1110		1
	N-{3-[4'-(6-Amino-purin-9-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

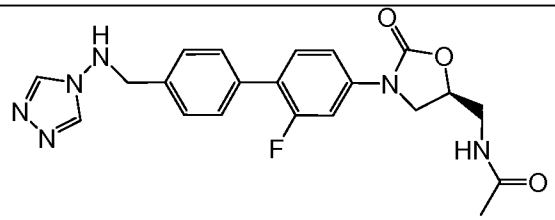
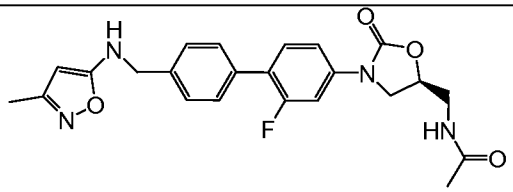
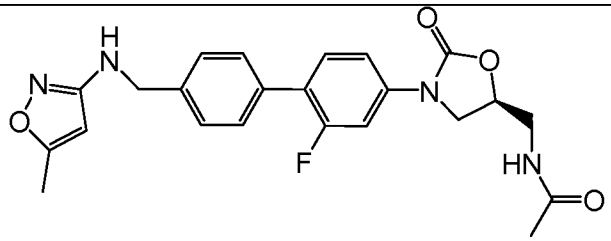
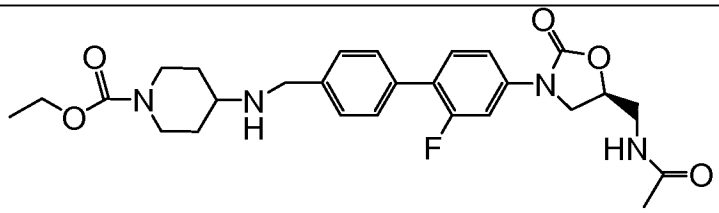
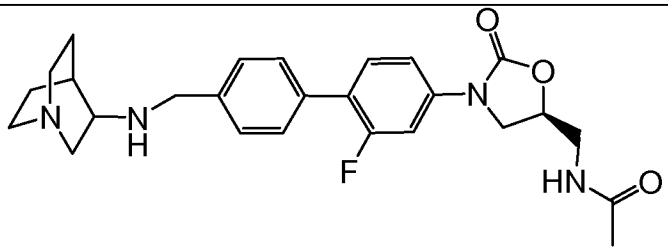
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	N-{3-[2-Fluoro-4'-(6-oxo-1,6-dihydro-purin-9-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1112		1
	N-[3-(2-Fluoro-4'-isoxazolidin-2-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
1113		2
	N-{3-[4'-(2-Amino-imidazol-1-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1114		
	N-{3-[2-Fluoro-4'-(7-oxo-4,5-dihydro-[1,2,3]triazolo[1,5-c]pyrimidin-6-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

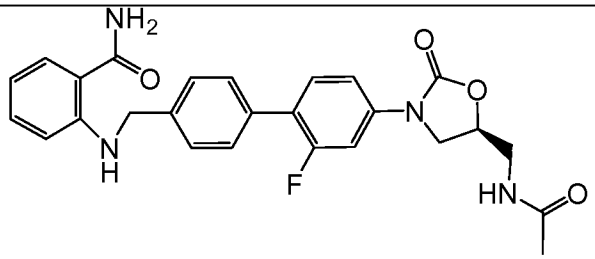
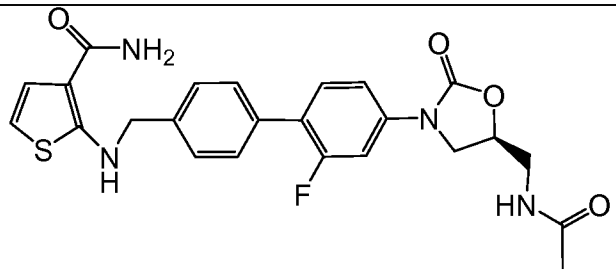
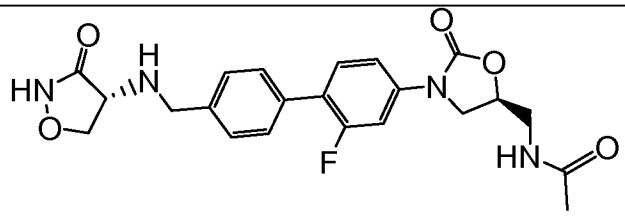
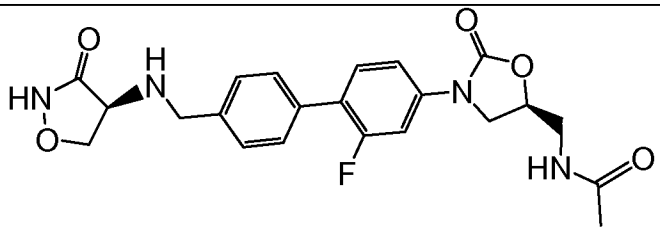
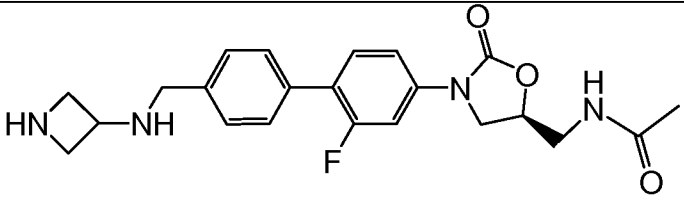
1115		
	N-[3-(2-Fluoro-4'-pyrrolidin-1-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
1116		
	N-[3-(2-Fluoro-4'-piperidin-1-ylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
1117		
	N-{3-[2-Fluoro-4'-(1-(S)-hydroxy-2-morpholin-4-yl-ethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1118		
	N-{3-[2-Fluoro-4'-(2-hydroxy-1-(R)-morpholin-4-yl-ethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

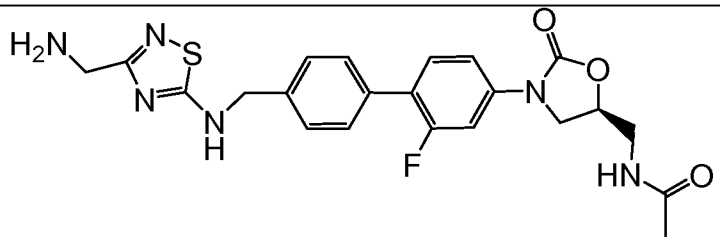
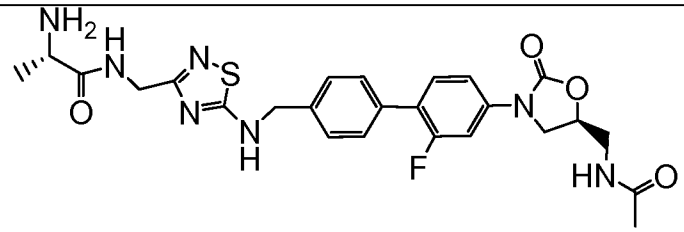
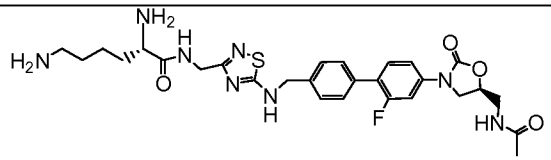
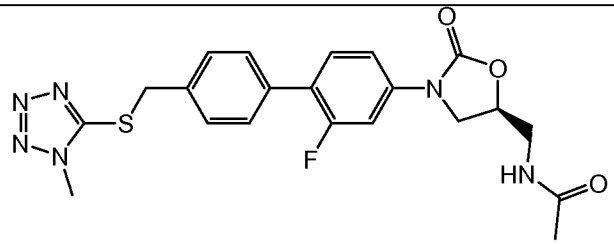
1119		
	(1-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-pyrrolidin-3-(R)-yl)-carbamic acid tert-butyl ester	
1120		
	(1-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-pyrrolidin-3-(S)-yl)-carbamic acid tert-butyl ester	
1121		
	1-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-piperidine-3-(R/S)-carboxylic acid amide	
1122		
	1-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-pyrrolidine-2-(S)-carboxylic acid amide	

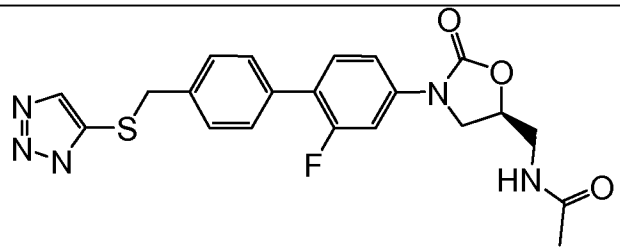
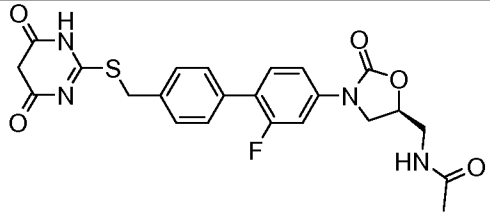
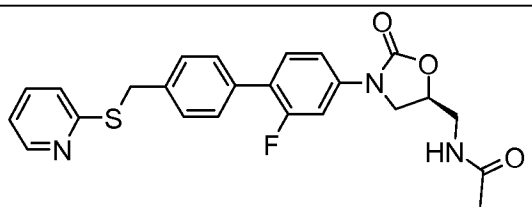
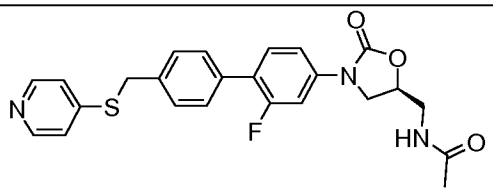
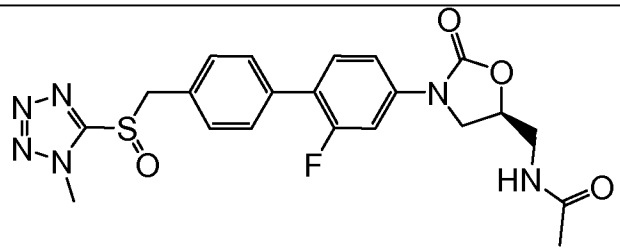
1123		
	N-{3-[2-Fluoro-4'-(3-oxo-piperazin-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1124		
	N-{3-[4'-(2,2-Dimethyl-4-oxo-imidazolidin-1-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1125		
	1-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-azetidine-3-(R/S)-carboxylic acid amide	
1126		
	1-{4'-[5-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-azetidine-2-carboxylic acid amide	
1127		

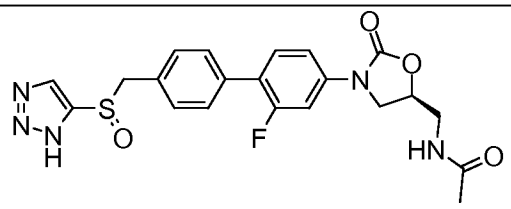
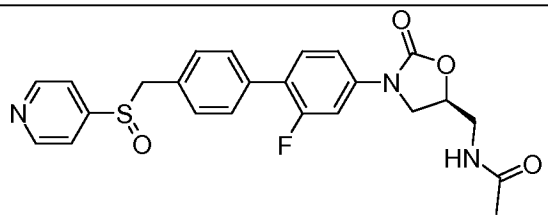
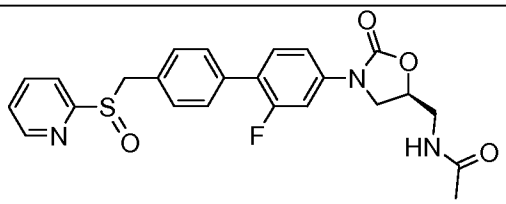
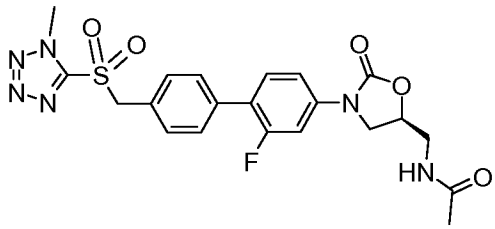
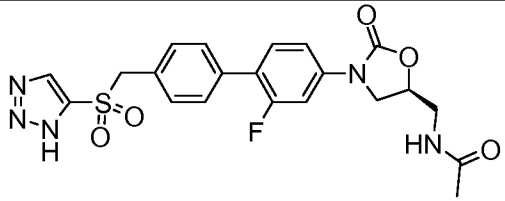
	N-{3-[2-Fluoro-4'-(2-oxo-piperazin-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1128		
	2-(4-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-3-oxo-piperazin-1-yl)-acetamide	
1129		
	N-{3-[4'-(4-Cyanomethyl-2-oxo-piperazin-1-ylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
1130		
	N-{3-[2-Fluoro-4'-(2-oxo-4-[1,2,3]thiadiazol-4-ylmethyl-piperazin-1-ylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2001		
	N-{3-[2-Fluoro-4'-(5-methyl-isoxazol-3-yloxymethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

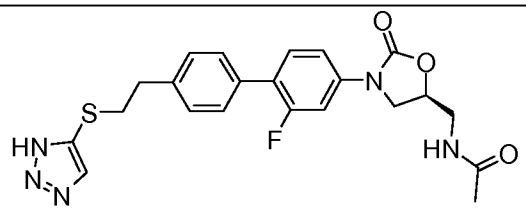
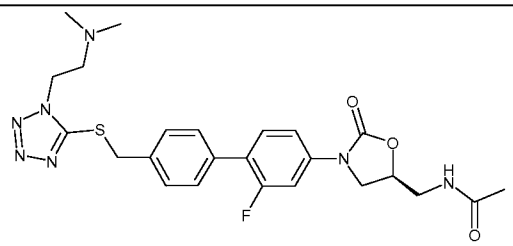
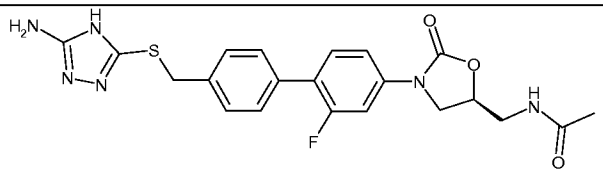
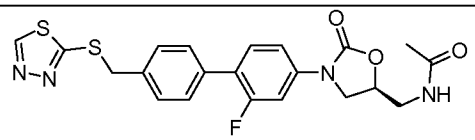
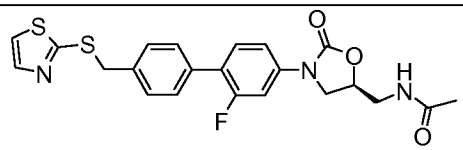
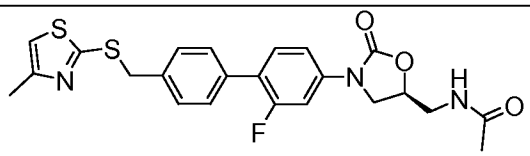
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	N-{3-[2-Fluoro-4'-([1,2,4]triazol-4-ylaminomethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2003		
	N-(3-{2-Fluoro-4'-[(3-methyl-isoxazol-5-ylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
2004		
	N-(3-{2-Fluoro-4'-[(5-methyl-isoxazol-3-ylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
2005		
	4-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-piperidine-1-carboxylic acid ethyl ester	
2006		
	N-(3-{4'-[(1-Aza-bicyclo[2.2.2]oct-3-ylamino)-methyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	

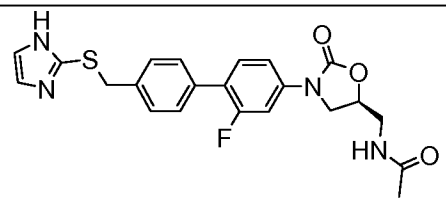
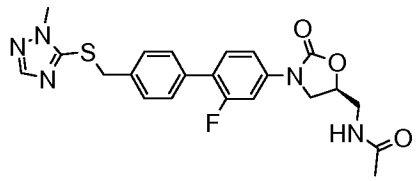
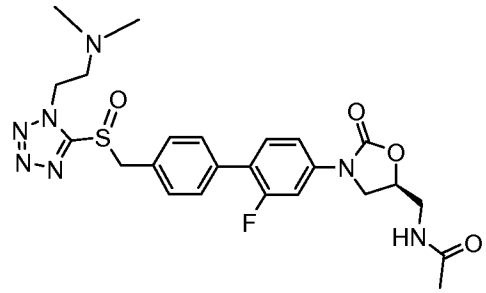
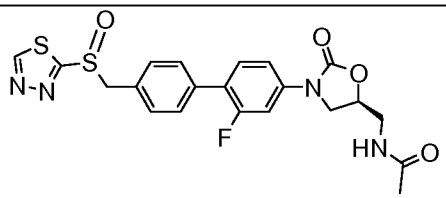
2007		
	2-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-benzamide	
2008		
	2-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-thiophene-3-carboxylic acid amide	
2009		
	N-(3-{2-Fluoro-4'-[(3-oxo-isoxazolidin-4-(R)-ylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
2010		
	N-(3-{2-Fluoro-4'-[(3-oxo-isoxazolidin-4-(S)-ylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
2011		8

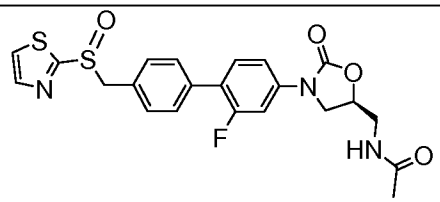
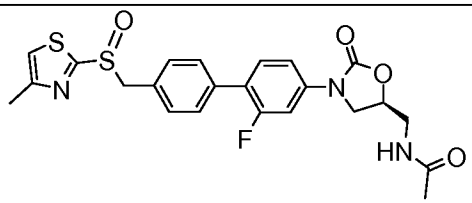
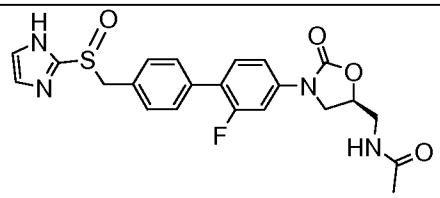
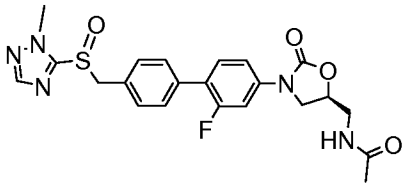
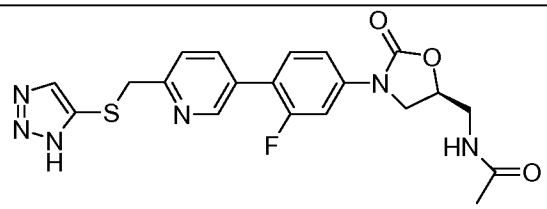
	N-{3-[4'-(Azetidin-3-(R/S)-ylaminomethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2012		1
	N-(3-{4'-[(3-Aminomethyl-[1,2,4]thiadiazol-5-ylamino)-methyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
2013		1
	N-[5-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-[1,2,4]thiadiazol-3-ylmethyl]-2-(S)-amino-propionamide	
2014		2
	2,6-Diamino-hexanoic acid [5-({4'-[5-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-[1,2,4]thiadiazol-3-ylmethyl]-amide	
2015		0.25
	N-{3-[2-Fluoro-4'-(1-methyl-1H-tetrazol-5-ylsulfanylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

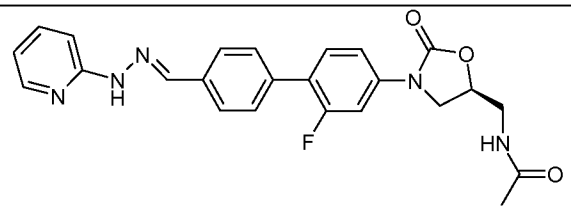
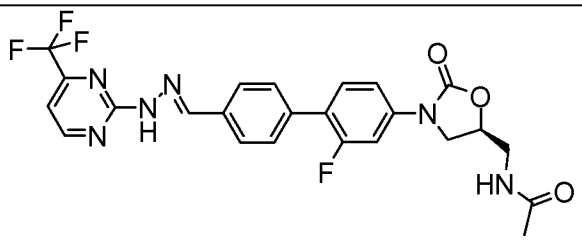
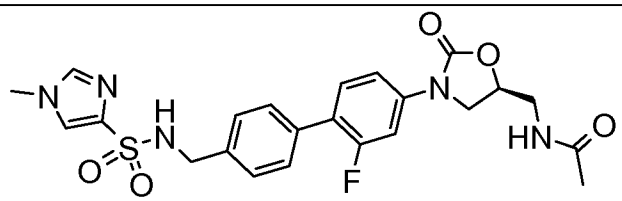
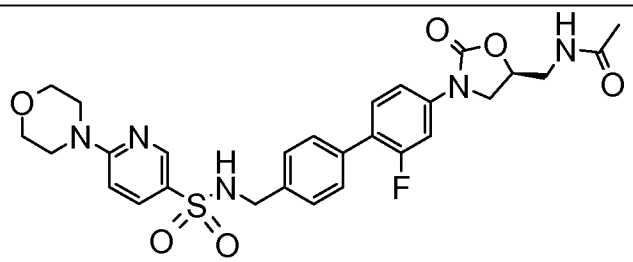
2016		0.25
	N-{3-[2-Fluoro-4'-(3H-[1,2,3]triazol-4-ylsulfanylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2017		16
	N-{3-[4'-(4,6-Dioxo-1,4,5,6-tetrahydro-pyrimidin-2-ylsulfanylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2018		0.25
	N-{3-[2-Fluoro-4'-(pyridin-2-ylsulfanylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2019		1
	N-{3-[2-Fluoro-4'-(pyridin-4-ylsulfanylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2020		0.25
	N-{3-[2-Fluoro-4'-(1-methyl-1H-tetrazole-5-sulfinylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

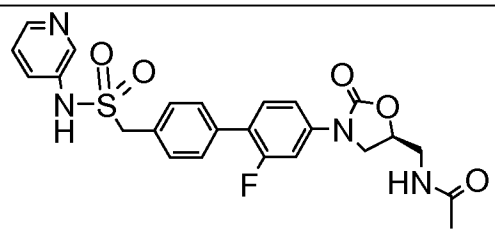
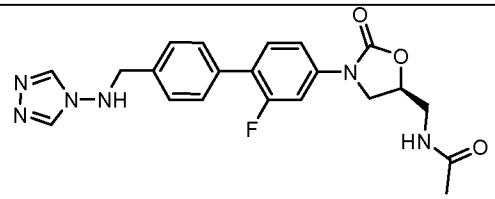
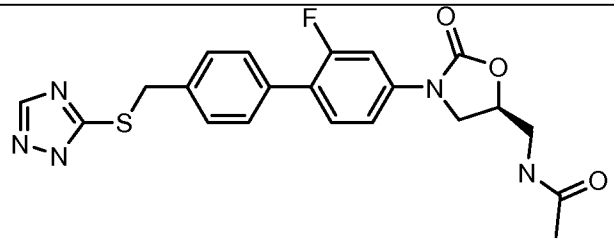
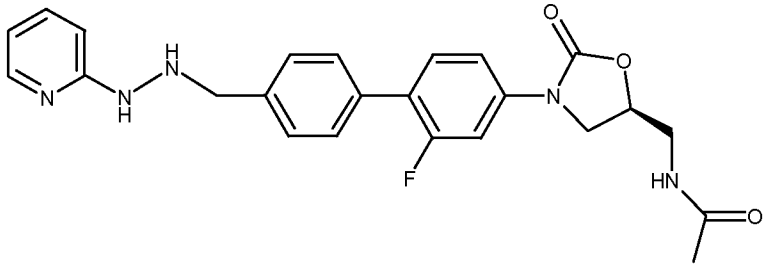
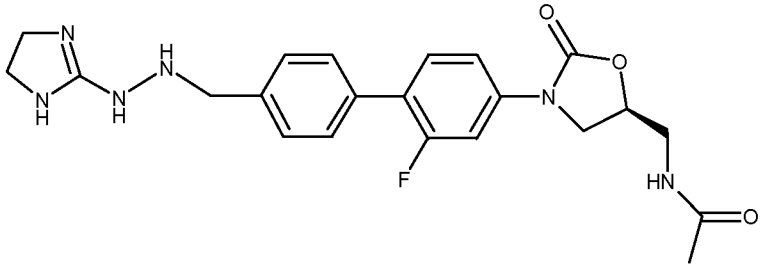
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	N-{3-[2-Fluoro-4'-(3H-[1,2,3]triazole-4-sulfinylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2022		2
	N-{3-[2-Fluoro-4'-(pyridine-4-sulfinylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2023		1
	N-{3-[2-Fluoro-4'-(pyridine-2-sulfinylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2024		0.25
	N-{3-[2-Fluoro-4'-(1-methyl-1H-tetrazole-5-sulfonylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2025		8
	N-{3-[2-Fluoro-4'-(3H-[1,2,3]triazole-4-sulfonylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

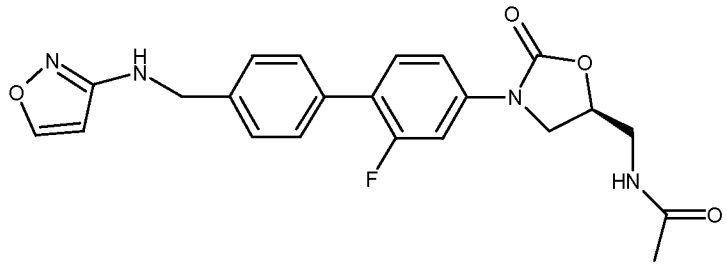
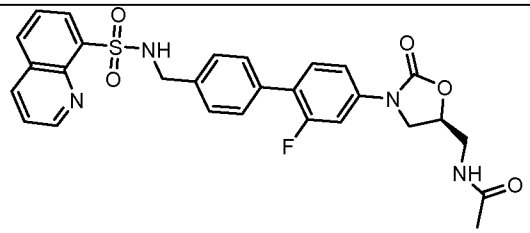
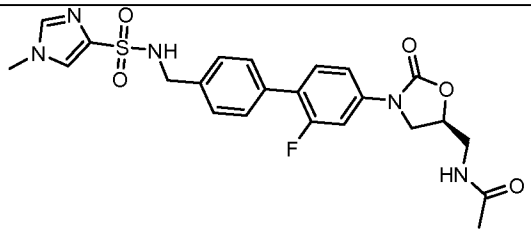
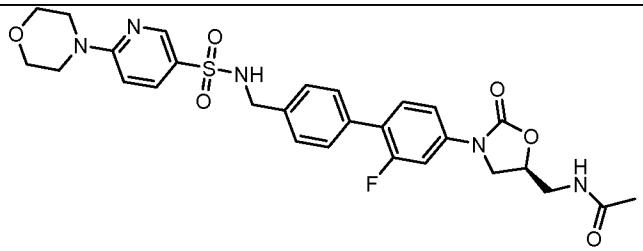
2026		0.25
	N-(3-{2-Fluoro-4'-[2-(3H-[1,2,3]triazol-4-ylsulfanyl)-ethyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
2027		1
	N-(3-{4'-[1-(2-Dimethylamino-ethyl)-1H-tetrazol-5-ylsulfanylmethyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
2028		0.25
	N-{3-[4'-(5-Amino-4H-[1,2,4]triazol-3-ylsulfanylmethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2029		0.25
	N-{3-[2-Fluoro-4'-([1,3,4]thiadiazol-2-ylsulfanylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2030		1
	N-{3-[2-Fluoro-4'-(thiazol-2-ylsulfanylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2031		1

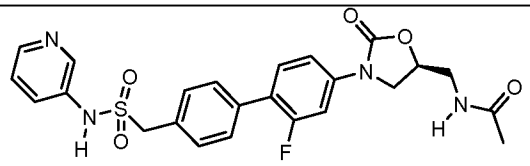
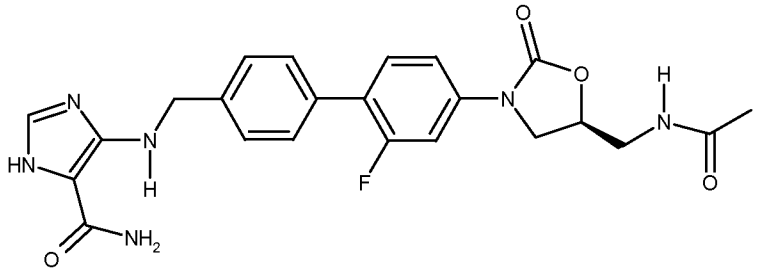
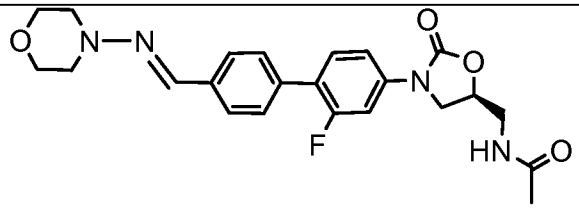
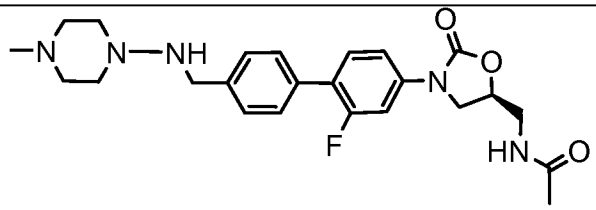
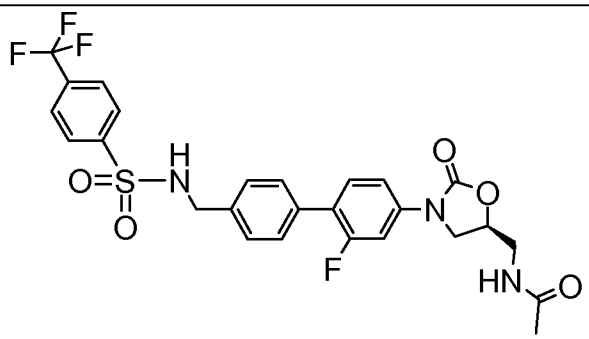
	N-{3-[2-Fluoro-4'-(4-methyl-thiazol-2-ylsulfanylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2032		1
	N-{3-[2-Fluoro-4'-(1H-imidazol-2-ylsulfanylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2033		1
	N-{3-[2-Fluoro-4'-(2-methyl-2H-[1,2,4]triazol-3-ylsulfanylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2034		2
	N-{3-[2-Fluoro-4'-(2-methyl-2H-[1,2,4]triazol-3-ylsulfanylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2035		1
	N-{3-[2-Fluoro-4'-([1,3,4]thiadiazole-2-sulfinylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

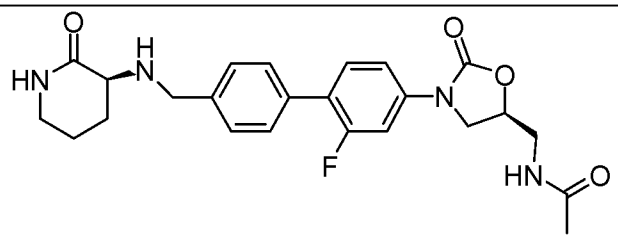
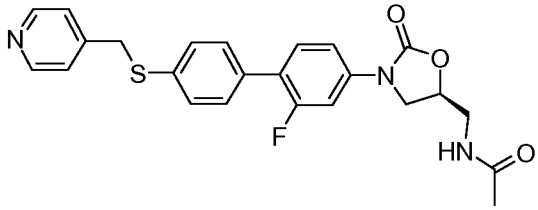
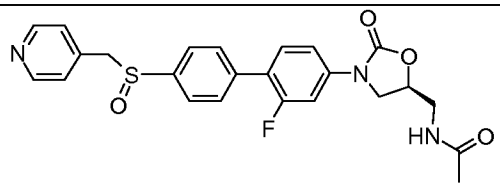
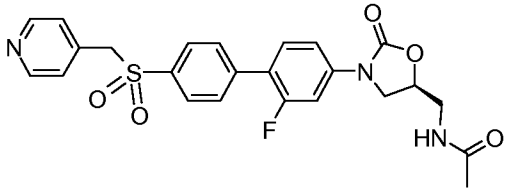
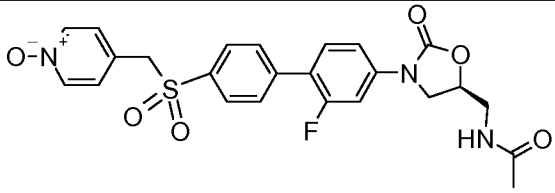
2036		1
	N-{3-[2-Fluoro-4'-(thiazole-2-sulfinylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2037		1
	N-{3-[2-Fluoro-4'-(4-methyl-thiazole-2-sulfinylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2038		2
	N-{3-[2-Fluoro-4'-(1H-imidazole-2-sulfinylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2039		2
	N-{3-[2-Fluoro-4'-(2-methyl-2H-[1,2,4]triazole-3-sulfinylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2040		0.25
	N-(3-{3-Fluoro-4-[6-(3H-[1,2,3]triazol-4-ylsulfanylmethyl)-pyridin-3-yl]-phenyl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	

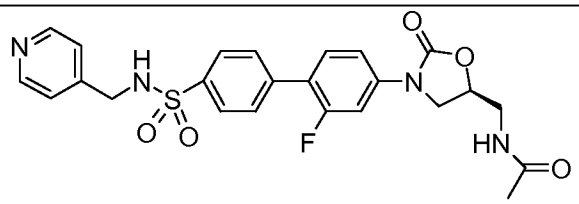
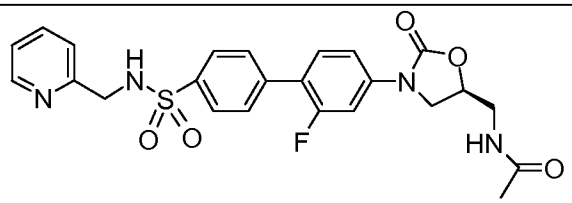
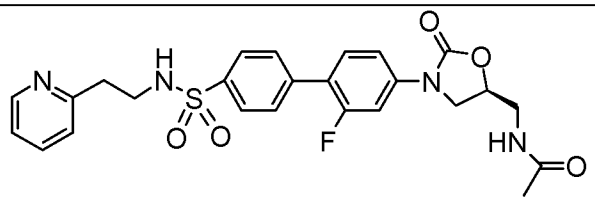
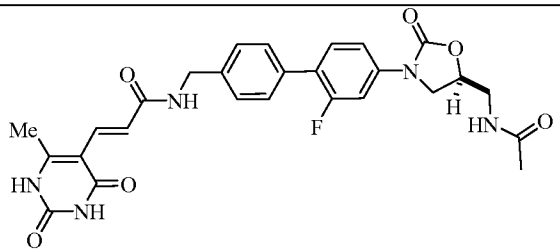
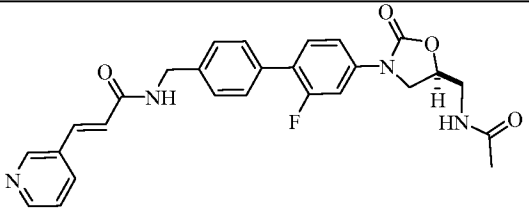
2041		1
	N-{3-[2-Fluoro-4'-(pyridin-2-yl-hydrazonomethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2042		128
	N-(3-{2-Fluoro-4'-[(4-trifluoromethyl-pyrimidin-2-yl)-hydrazonomethyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
2043		2
	N-(3-{2-Fluoro-4'-[(1-methyl-1H-imidazole-4-sulfonylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
2044		128
	N-(3-{2-Fluoro-4'-[(6-morpholin-4-yl-pyridine-3-sulfonylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	

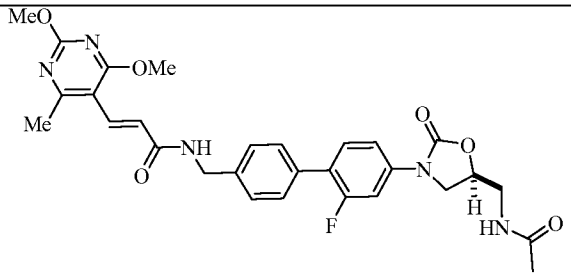
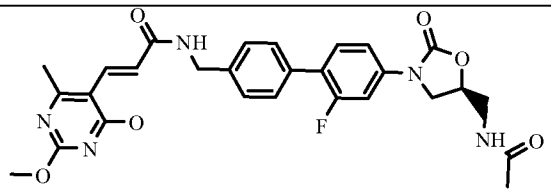
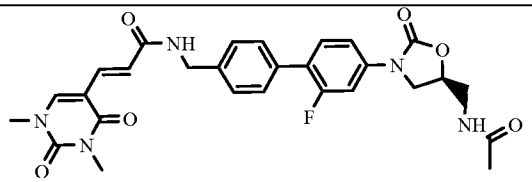
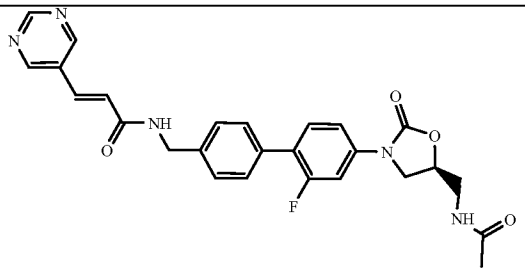
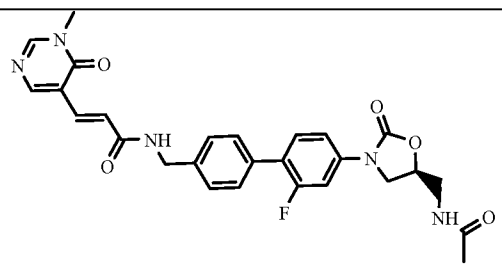
2045		2
	N-{3-[2-Fluoro-4'-(pyridin-3-ylsulfamoylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2046		1
	N-{3-[2-Fluoro-4'-([1,2,4]triazol-4-ylaminomethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2047		0.25
	N-{3-[2-Fluoro-4'-(2H-[1,2,4]triazol-3-ylsulfanylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2048		0.5
	N-{3-[2-Fluoro-4'-(N'-pyridin-2-yl-hydrazinomethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2049		2
	N-(3-{4'-[N'-(4,5-Dihydro-1H-imidazol-2-yl)-	

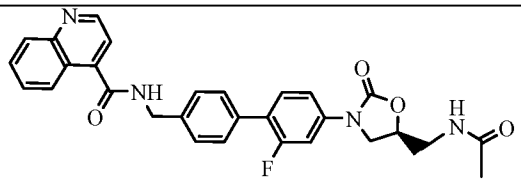
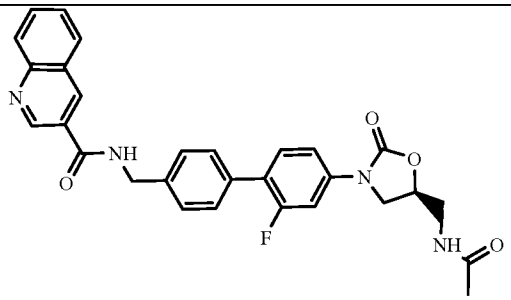
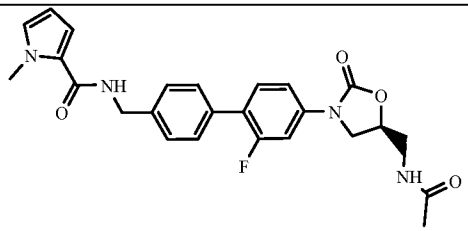
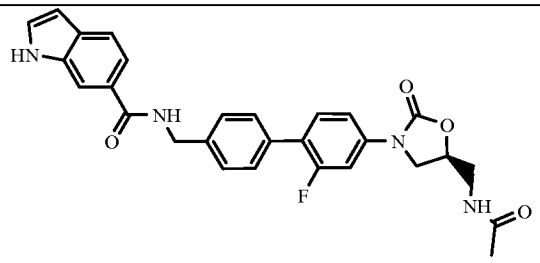
	hydrazinomethyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
2050		0.25
	N-{3-[2-Fluoro-4'-(isoxazol-3-ylaminomethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2051		4
	N-(3-{2-Fluoro-4'-[(quinoline-8-sulfonylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
2052		2
	N-(3-{2-Fluoro-4'-[(1-methyl-1H-imidazole-4-sulfonylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
2053		128
	N-(3-{2-Fluoro-4'-[(6-morpholin-4-yl-pyridine-3-sulfonylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	

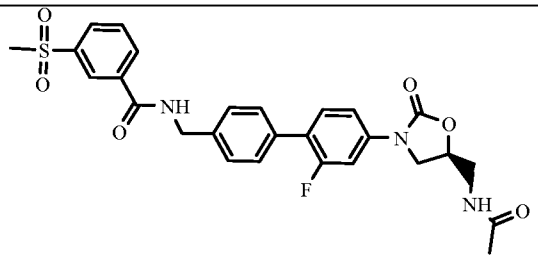
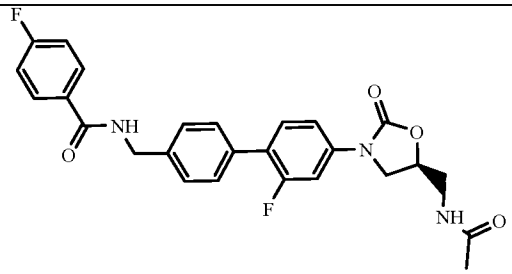
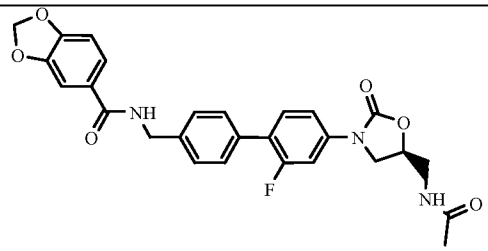
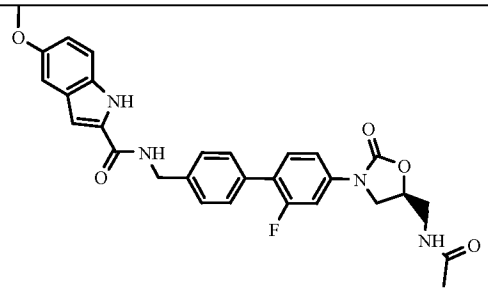
2054		2
	N-{3-[2-Fluoro-4‘-pyridin-3-ylsulfamoylmethyl)-biphenyl-4-yl]2-oxo-oxazolidin-5-(S)-ylmethyl}acetamide	
2055		4
	5-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-3H-imidazole-4-carboxylic acid amide	
2056		0.25
	N-{3-[2-Fluoro-4'-(morpholin-4-yliminomethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
2057		1
	N-(3-{2-Fluoro-4'-[(4-methyl-piperazin-1-ylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
2058		32
	N-(3-{2-Fluoro-4'-[(4-trifluoromethyl-benzenesulfonylamino)-	

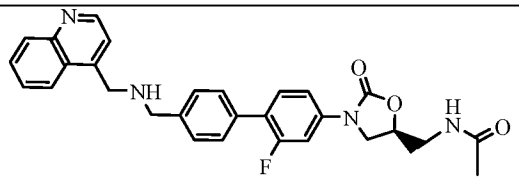
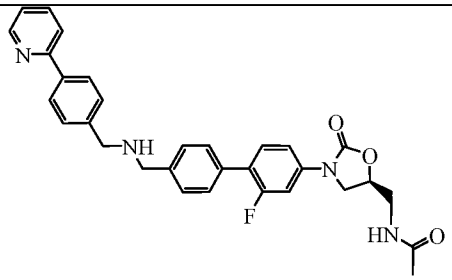
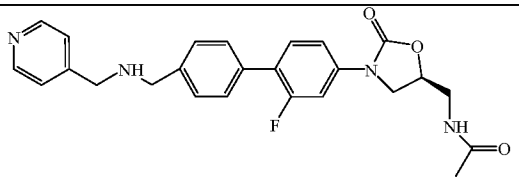
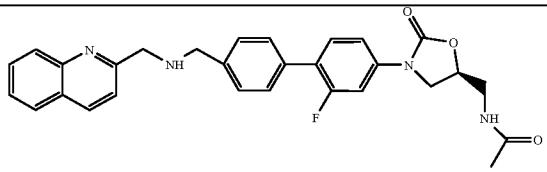
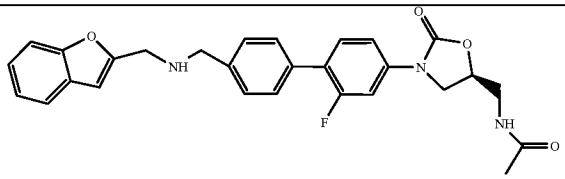
	methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
2059		2
	N-(3-{2-Fluoro-4'-[(2-oxo-piperidin-3-(S)-ylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
3001		1
	N-{3-[2-Fluoro-4'-(pyridin-4-ylmethylsulfanyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
3002		1
	N-{3-[2-Fluoro-4'-(pyridin-4-ylmethanesulfinyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
3003		2
	N-{3-[2-Fluoro-4'-(pyridin-4-ylmethanesulfonyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
3004		4
	N-{3-[2-Fluoro-4'-(1-oxy-pyridin-4-ylmethanesulfonyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

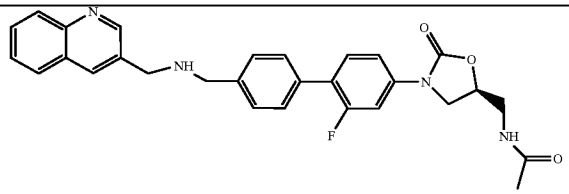
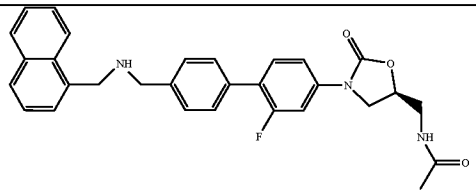
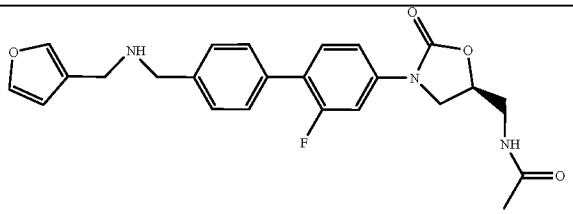
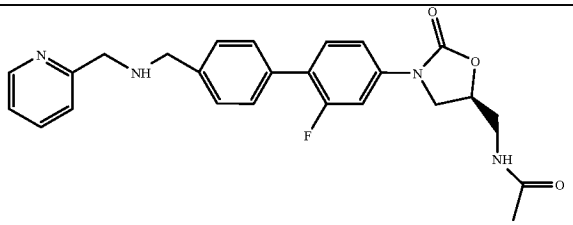
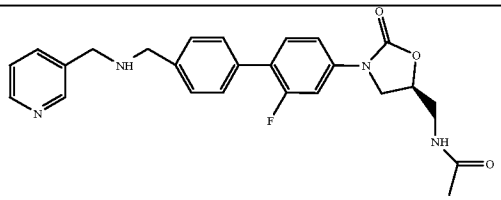
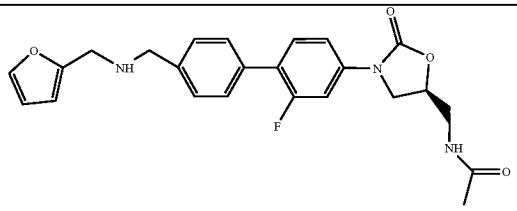
3005		2
	N-(3-{2-Fluoro-4'-[(pyridin-4-ylmethyl)-sulfamoyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
3006		16
	N-(3-{2-Fluoro-4'-[(pyridin-2-ylmethyl)-sulfamoyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
3007		1
	N-{3-[2-Fluoro-4'-(2-pyridin-2-yl-ethylsulfamoyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4001		0.25
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-3-(6-methyl-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidin-5-yl)-acrylamide	
4002		4
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-3-pyridin-3-yl-acrylamide	

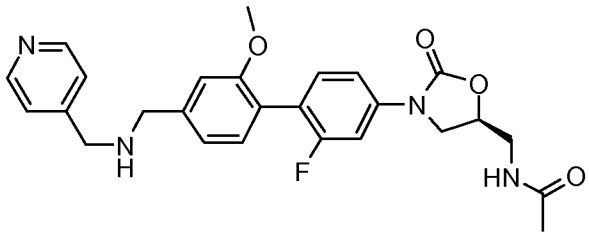
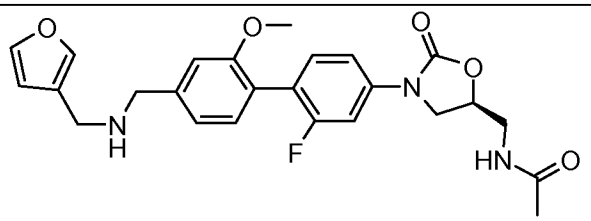
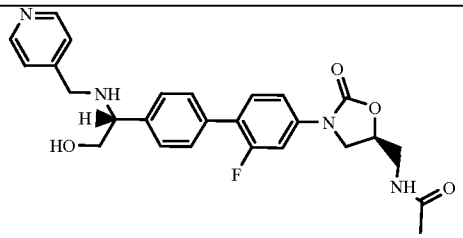
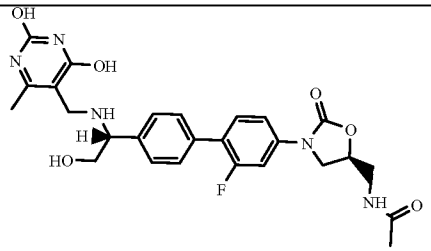
4003		128
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-3-(2,4-dimethoxy-6-methyl-pyrimidin-5-yl)-acrylamide	
4004		2
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-3-(4-hydroxy-2-methoxy-6-methyl-pyrimidin-5-yl)-acrylamide	
4005		2
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-3-(1,3-dimethyl-2,4-dioxo-1,1,2,3,4-tetrahydro-pyrimidin-5-yl)-acrylamide	
4006		8
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-3-pyrimidin-5-yl-acrylamide	
4007		1

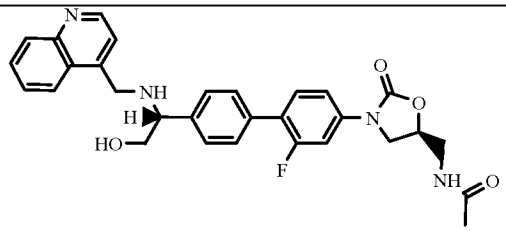
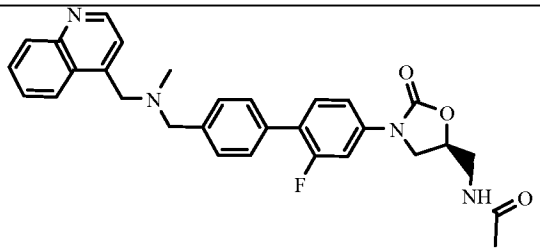
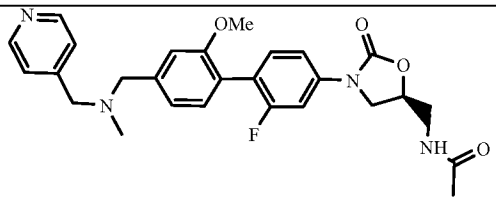
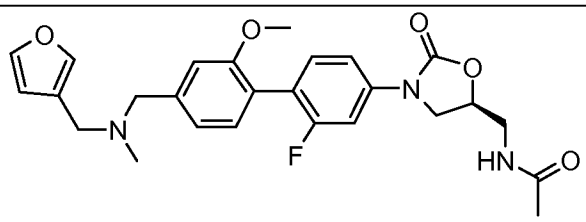
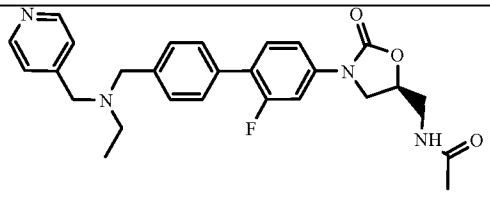
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-3-(1-methyl-6-oxo-1,6-dihydro-pyrimidin-5-yl)-acrylamide	
4008		1
	Quinoline-4-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	
4009		32
	Quinoline-3-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	
4010		1
	1-Methyl-1H-pyrrole-2-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	
4011		1
	1H-Indole-6-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	

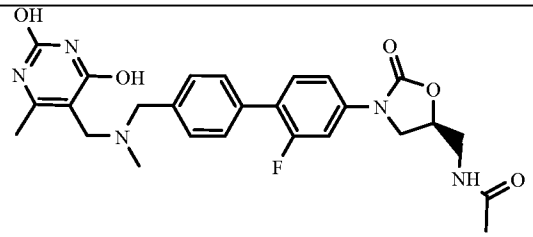
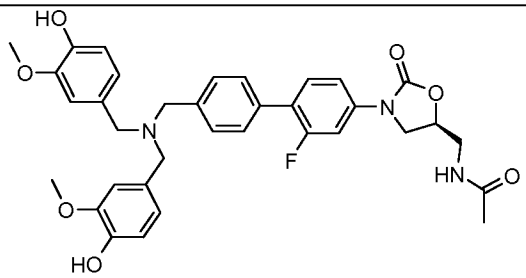
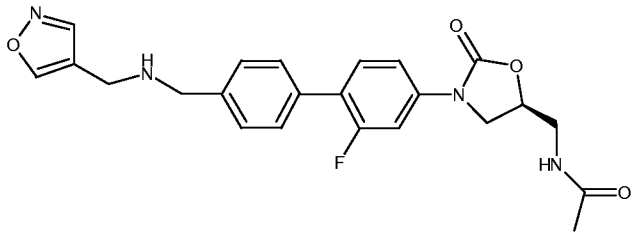
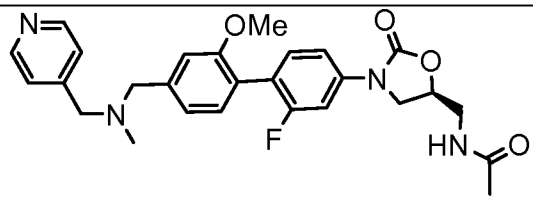
4012		4
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-3-methanesulfonyl-benzamide	
4013		8
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-4-fluoro-benzamide	
4014		4
	Benzo[1,3]dioxole-5-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	
4015		4
	5-Methoxy-1H-indole-2-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	

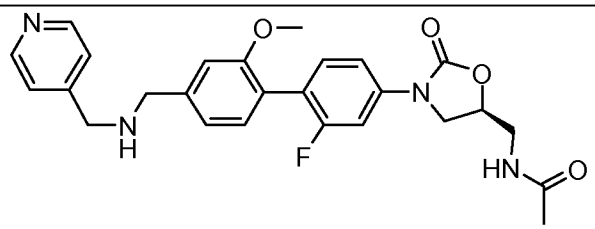
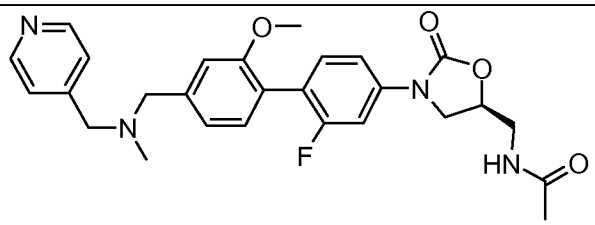
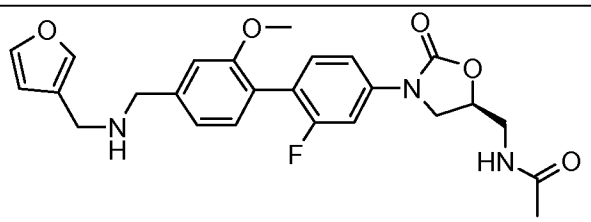
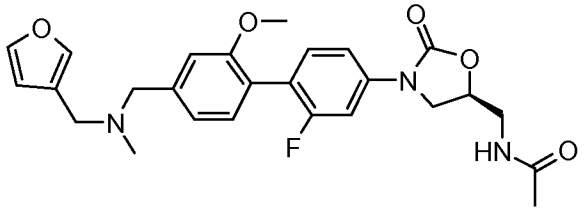
4016		1
	N-[3-(2-Fluoro-4'-{[(quinolin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4017		2
	N-(3-{2-Fluoro-4'-[(4-pyridin-2-yl-benzylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4018		1
	N-[3-(2-Fluoro-4'-{[(pyridin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4019		0.5
	N-[3-(2-Fluoro-4'-{[(quinolin-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4020		2
	N-[3-(4'-{[(Benzofuran-2-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

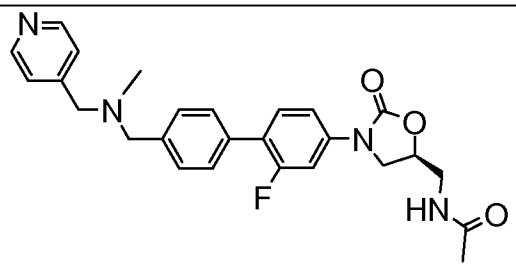
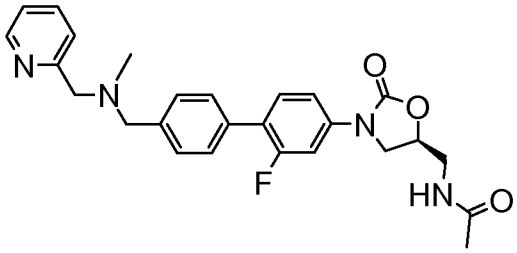
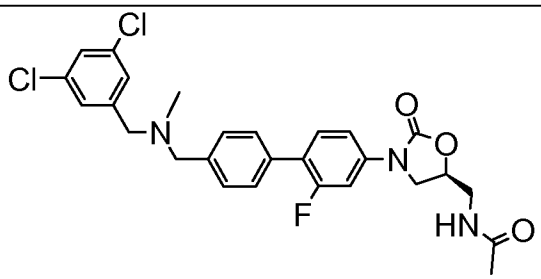
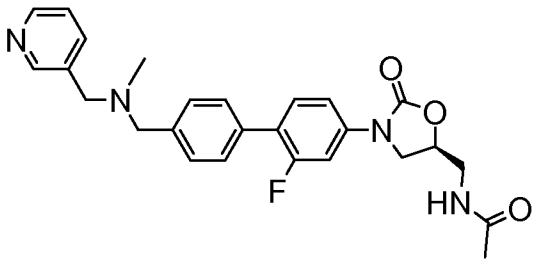
4021		0.25
	N-[3-(2-Fluoro-4'-{[(quinolin-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4022		4
	N-[3-(2-Fluoro-4'-{[(naphthalen-1-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4023		1
	N-[3-(2-Fluoro-4'-{[(furan-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4024		1
	N-[3-(2-Fluoro-4'-{[(pyridin-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4025		1
	N-[3-(2-Fluoro-4'-{[(pyridin-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4026		1

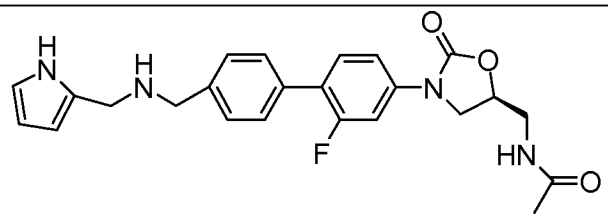
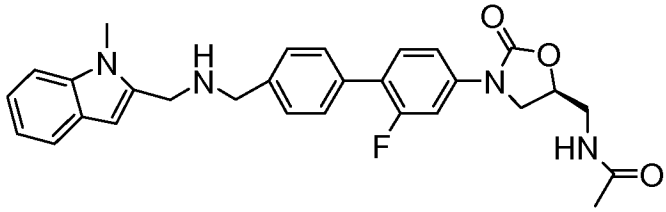
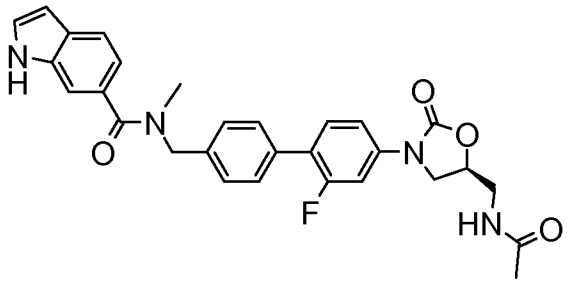
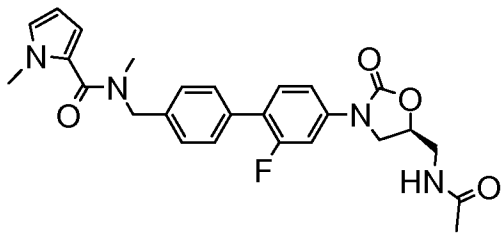
	N-[3-(2-Fluoro-4'-{[(furan-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4027		8
	N-[3-(2-Fluoro-2'-methoxy-4'-{[(pyridin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4028		8
	N-[3-(2-Fluoro-4'-{[(furan-3-ylmethyl)-amino]-methyl}-2'-methoxy-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4029		4
	N-[3-(2-Fluoro-4'-{2-hydroxy-1-(R)-[(pyridin-4-ylmethyl)-amino]-ethyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4030		64
	N-[3-(4'-{1-(R)-[(2,4-Dihydroxy-6-methyl-pyrimidin-5-ylmethyl)-amino]-2-hydroxy-ethyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

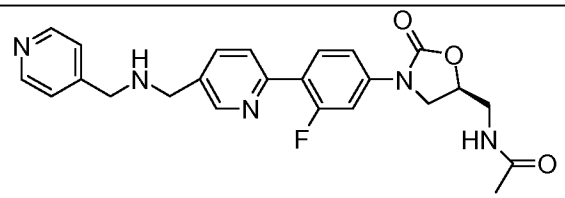
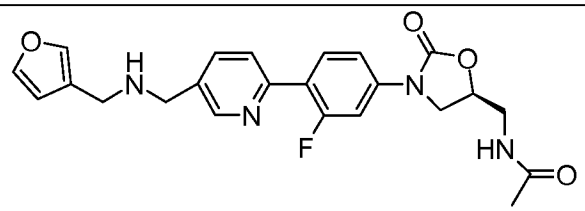
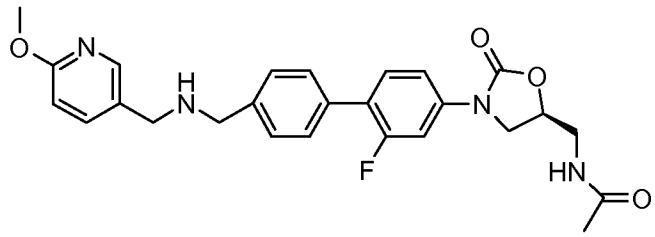
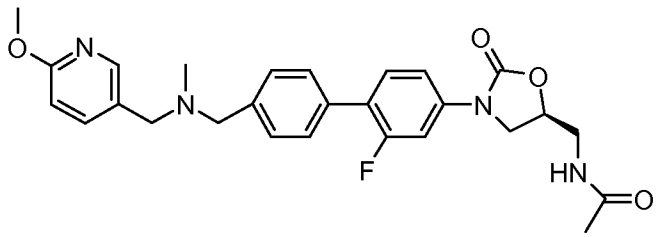
4031		2
	N-[3-(2-Fluoro-4'-{2-hydroxy-1-(R)-[(quinolin-4-ylmethyl)-amino]-ethyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4032		1
	N-(3-{2-Fluoro-4'-[(methyl-quinolin-4-ylmethyl-amino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4033		8
	N-(3-{2-Fluoro-2'-methoxy-4'-[(methyl-pyridin-4-ylmethyl-amino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4034		32
	N-(3-{2-Fluoro-4'-[(furan-3-ylmethyl-methyl-amino)-methyl]-2'-methoxy-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4035		2

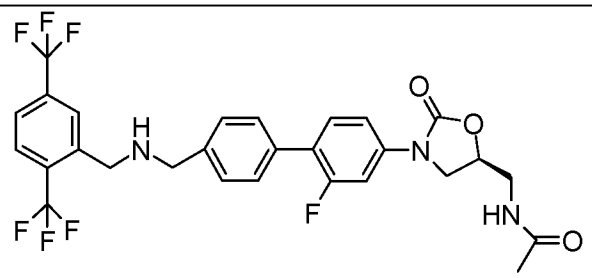
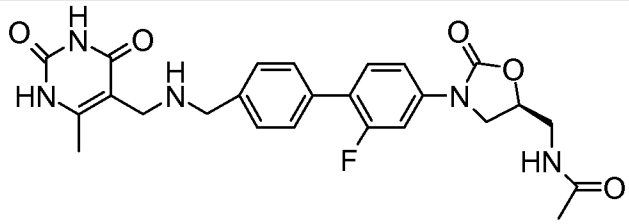
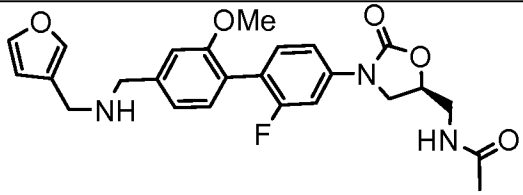
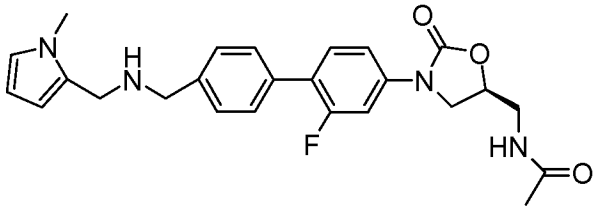
	N-(3-{4'-[(Ethyl-pyridin-4-ylmethyl-amino)-methyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4036		4
	N-[3-(4'-{[(2,4-Dihydroxy-6-methyl-pyrimidin-5-ylmethyl)-methyl-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4037		2
	N-[3-(4'-{[Bis-(4-hydroxy-3-methoxy-benzyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4038		0.25
	N-[3-(2-Fluoro-4'-{[(isoxazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4039		8
	N-(3-{2-Fluoro-2'-methoxy-4'-[(methyl-pyridin-4-ylmethyl-amino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	

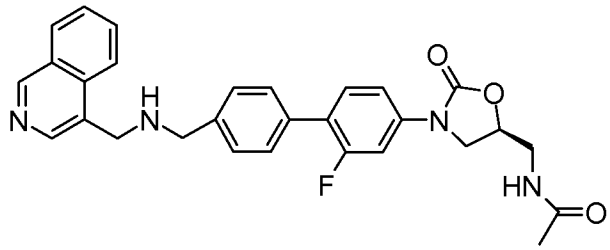
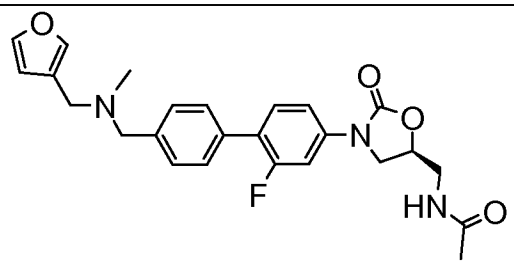
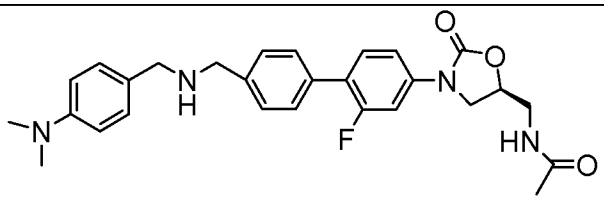
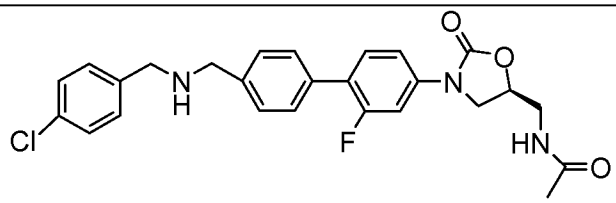
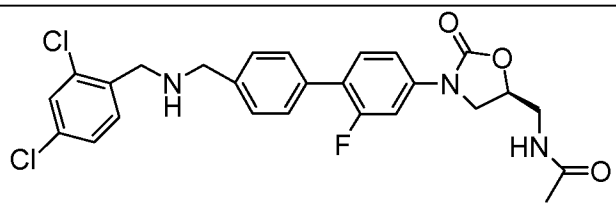
4040		8
	N-[3-(2-Fluoro-2'-methoxy-4'-{[(pyridin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4041		8
	N-(3-{2-Fluoro-2'-methoxy-4'-[(methyl-pyridin-4-ylmethyl-amino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4042		8
	N-[3-(2-Fluoro-4'-{[(furan-3-ylmethyl)-amino]-methyl}-2'-methoxy-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4043		32
	N-(3-{2-Fluoro-4'-[(furan-3-ylmethyl-methyl-amino)-methyl]-2'-methoxy-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	

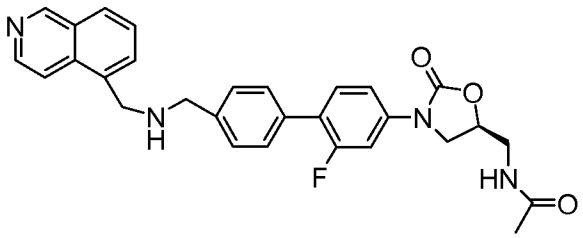
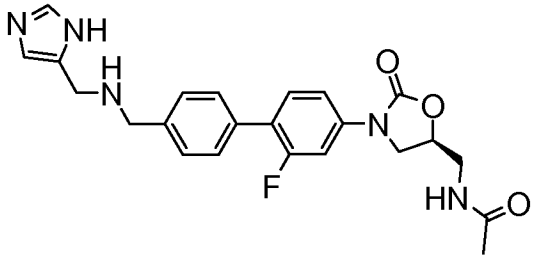
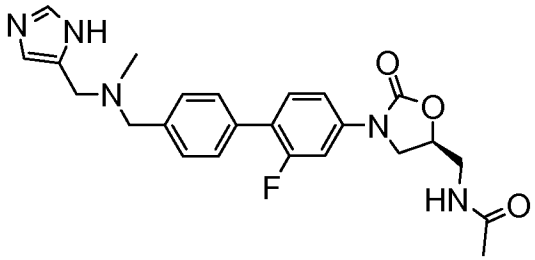
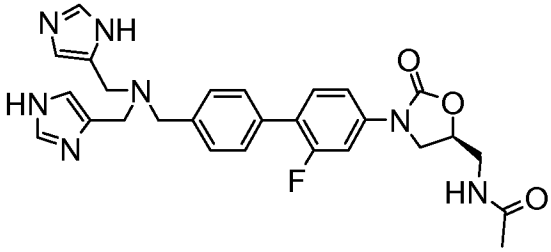
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	N-(3-{2-Fluoro-4'-[(methyl-pyridin-4-ylmethyl-amino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4045		2
	N-(3-{2-Fluoro-4'-[(methyl-pyridin-2-ylmethyl-amino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4046		4
	N-[3-(4'-{[(3,5-Dichloro-benzyl)-methyl-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4047		2
	N-(3-{2-Fluoro-4'-[(methyl-pyridin-3-ylmethyl-amino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	

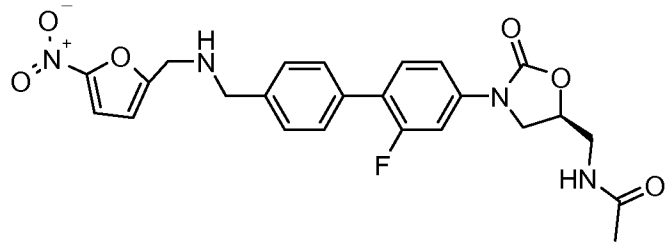
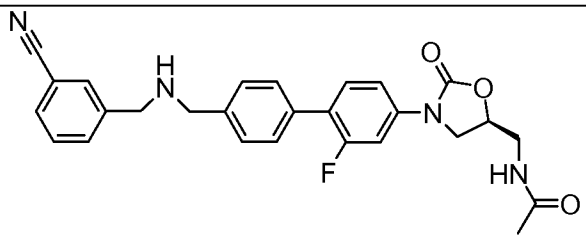
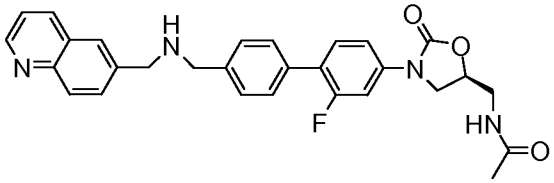
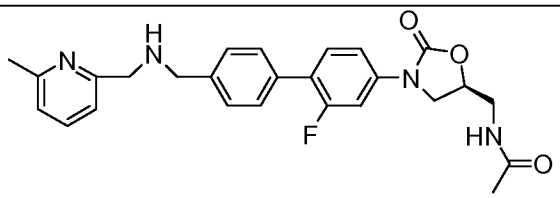
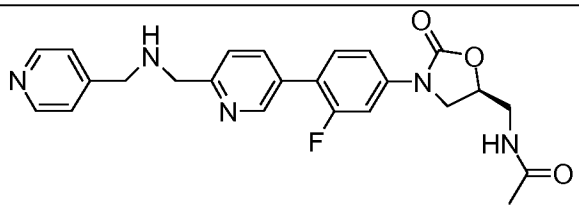
4048		2
	N-[3-(2-Fluoro-4'-{[(1H-pyrrol-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4049		1
	N-[3-(2-Fluoro-4'-{[(1-methyl-1H-indol-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4050		1
	1H-Indole-6-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-methyl-amide	
4051		4
	1-Methyl-1H-pyrrole-2-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-methyl-amide	

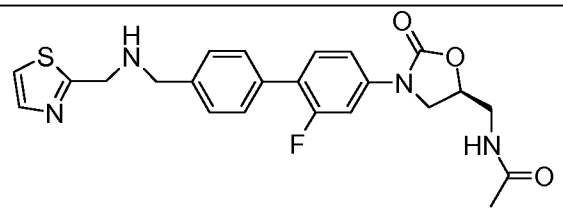
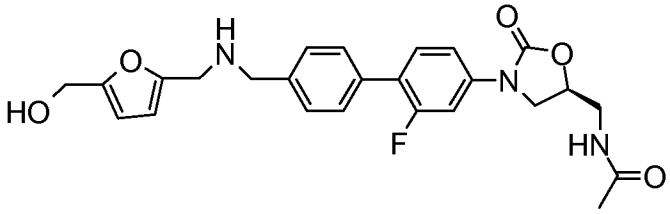
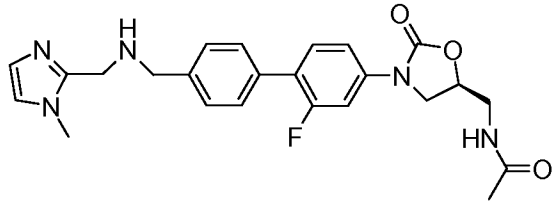
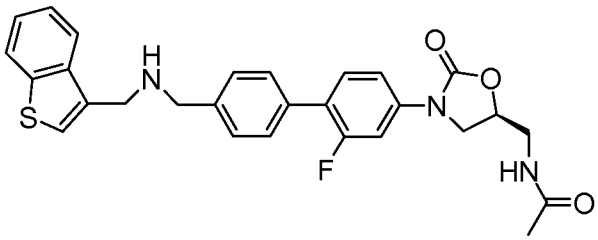
4052		64
	N-{3-[3-Fluoro-4-(5-{[(pyridin-4-ylmethyl)-amino]-methyl}-pyridin-2-yl)-phenyl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4053		4
	N-{3-[3-Fluoro-4-(5-{[(furan-3-ylmethyl)-amino]-methyl}-pyridin-2-yl)-phenyl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4054		1
	N-[3-(2-Fluoro-4'-{[(6-methoxy-pyridin-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4055		2
	N-[3-(2-Fluoro-4'-{[(6-methoxy-pyridin-3-ylmethyl)-methyl-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

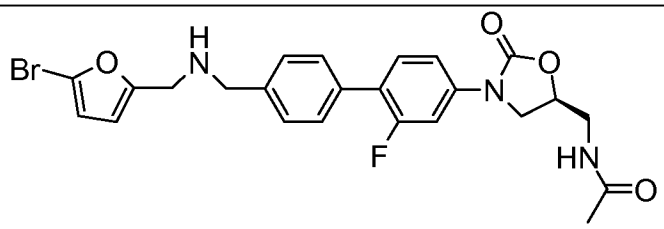
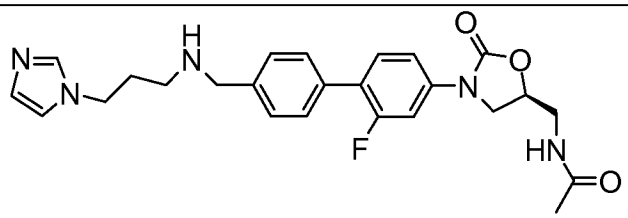
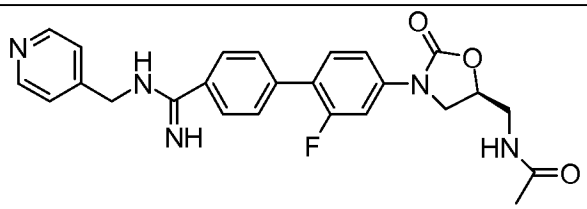
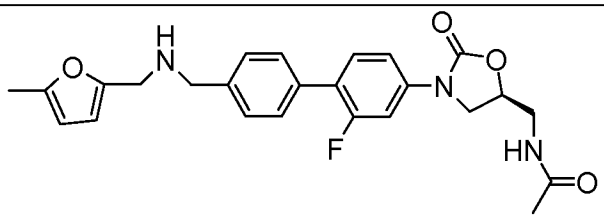
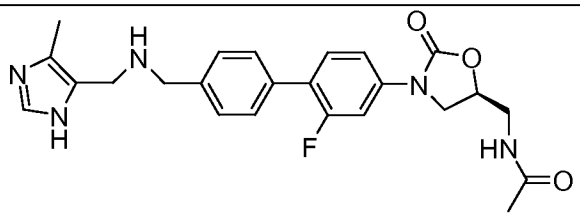
4056		2
	N-(3-{4'-[(2,5-Bis-trifluoromethyl-benzylamino)-methyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4057		16
	N-[3-(2-Fluoro-4'-{[(6-methyl-2,4-dioxo-1,2,3,4-tetrahydro-pyrimidin-5-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4058		8
	N-[3-(2-Fluoro-4'-{[(furan-3-ylmethyl)-amino]-methyl}-2'-methoxy-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4059		2
	N-[3-(2-Fluoro-4'-{[(1-methyl-1H-pyrrol-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

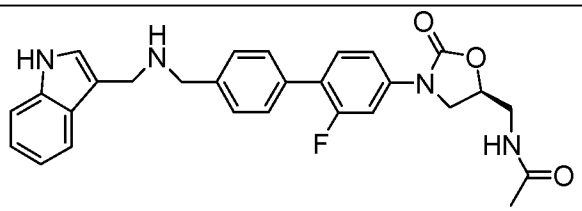
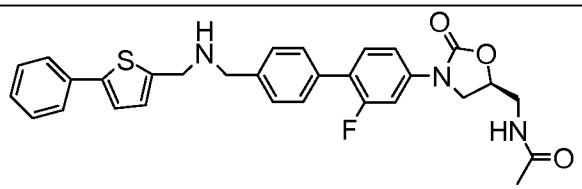
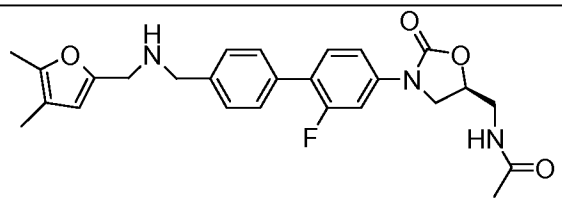
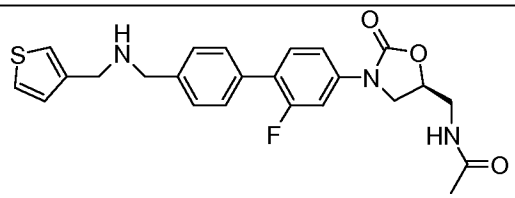
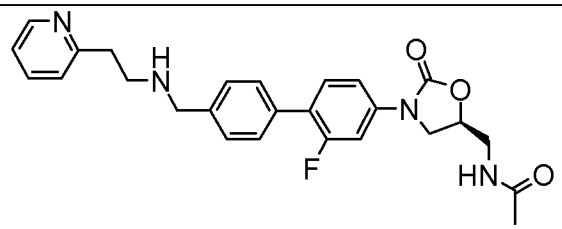
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	N-[3-(2-Fluoro-4'-{[(isoquinolin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4061		4
	N-(3-{2-Fluoro-4'-[(furan-3-ylmethyl-methyl-amino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4062		2
	N-(3-{4'-[(4-Dimethylamino-benzylamino)-methyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4063		2
	N-(3-{4'-[(4-Chloro-benzylamino)-methyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4064		2
	N-(3-{4'-[(2,4-Dichloro-benzylamino)-methyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	

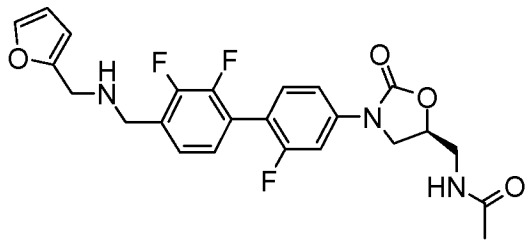
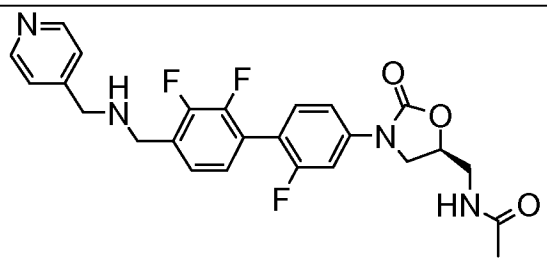
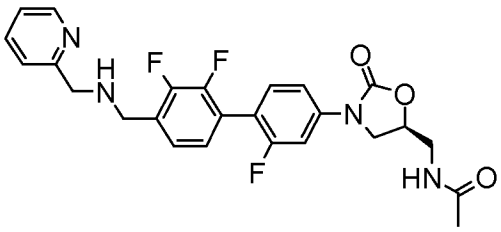
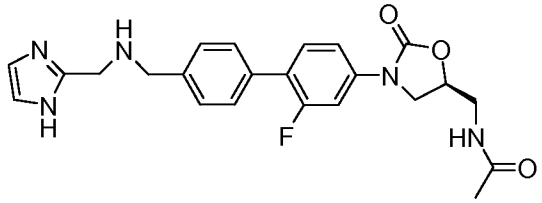
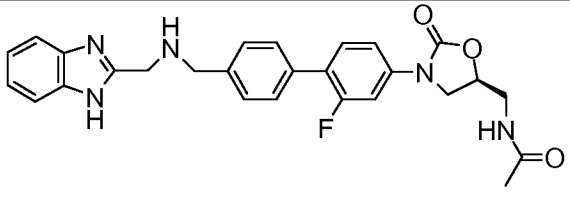
4065		2
	N-[3-(2-Fluoro-4'-{[(isoquinolin-5-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4066		8
	N-[3-(2-Fluoro-4'-{[(3H-imidazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4067		4
	N-[3-(2-Fluoro-4'-{[(3H-imidazol-4-ylmethyl)-methyl-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4068		128
	N-[3-(2-Fluoro-4'-{[(1H-imidazol-4-ylmethyl)-(3H-imidazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

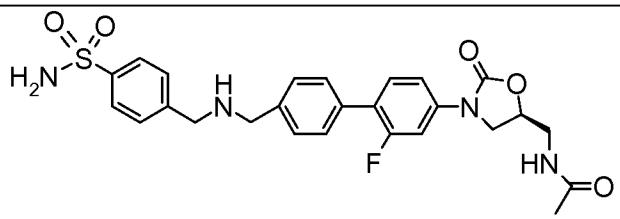
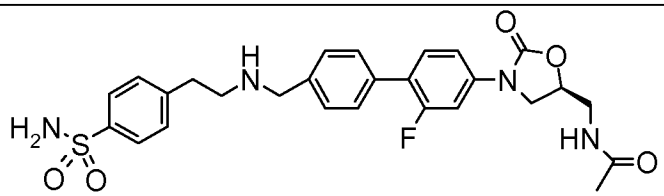
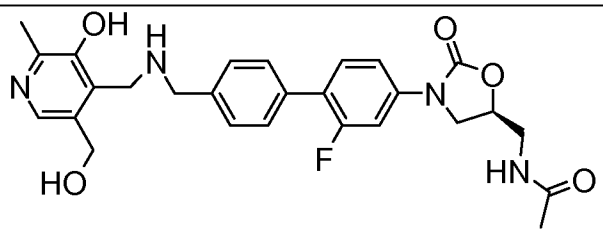
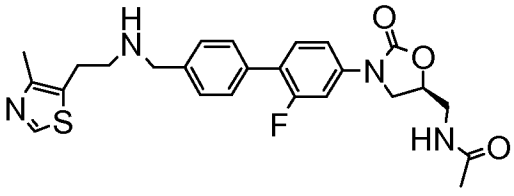
4069		1
	N-[3-(2-Fluoro-4'-{[(5-nitro-furan-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4070		1
	N-(3-{4'-[(3-Cyano-benzylamino)-methyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4071		2
	N-[3-(2-Fluoro-4'-{[(quinolin-6-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4072		2
	N-[3-(2-Fluoro-4'-{[(6-methyl-pyridin-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4073		2
	N-{3-[3-Fluoro-4-(6-{[(pyridin-4-ylmethyl)-amino]-methyl}-	

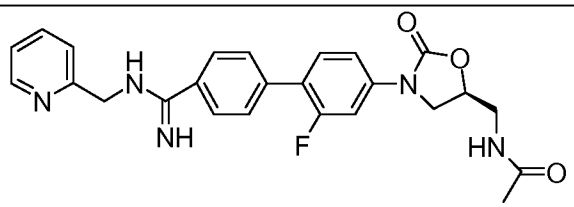
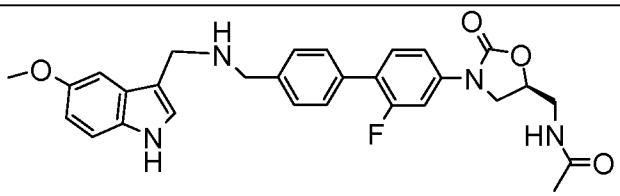
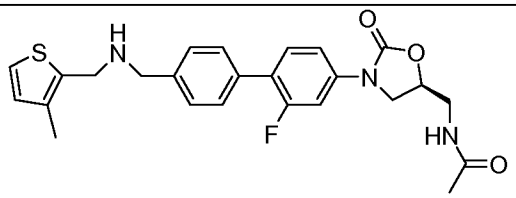
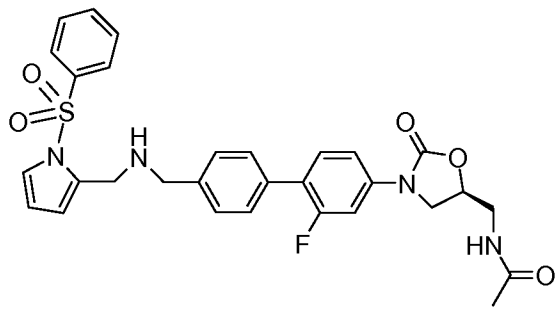
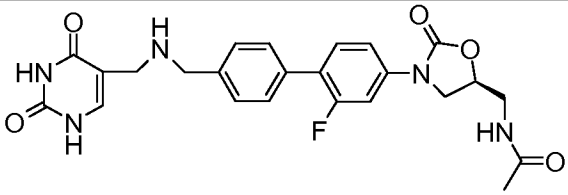
	pyridin-3-yl)-phenyl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4074		1
	N-[3-(2-Fluoro-4'-{[(thiazol-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4075		2
	N-[3-(2-Fluoro-4'-{[(5-hydroxymethyl-furan-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4076		4
	N-[3-(2-Fluoro-4'-{[(1-methyl-1H-imidazol-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4077		16
	N-[3-(4'-{[(Benzo[b]thiophen-3-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

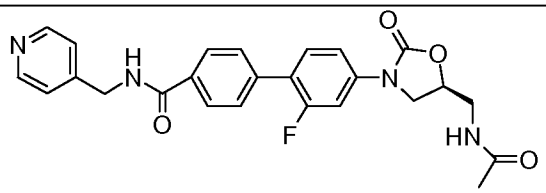
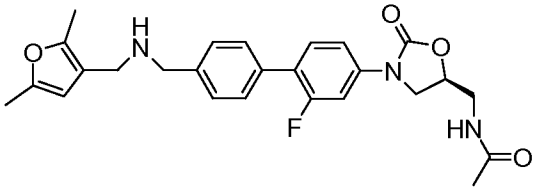
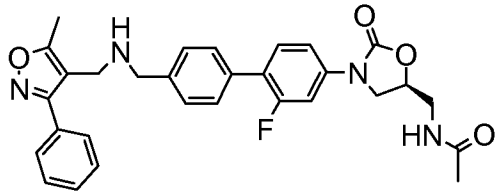
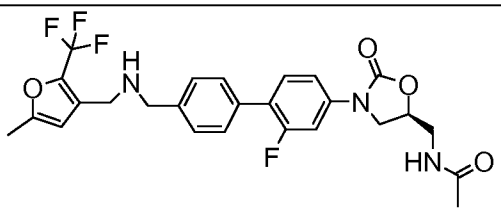
4078		2
	N-[3-(4'-{[(5-Bromo-furan-2-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4079		32
	N-(3-{2-Fluoro-4'-[(3-imidazol-1-yl-propylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4080		128
	N-{3-[2-Fluoro-4'-(N-pyridin-4-ylmethyl-carbamimidoyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4081		2
	N-[3-(2-Fluoro-4'-{[(5-methyl-furan-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4082		32
	N-[3-(2-Fluoro-4'-{[(5-methyl-3H-imidazol-4-ylmethyl)-	

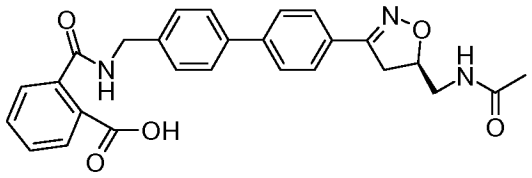
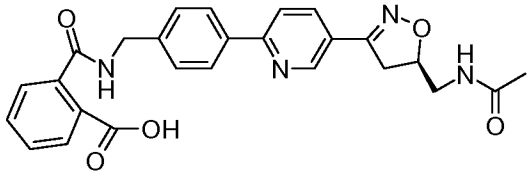
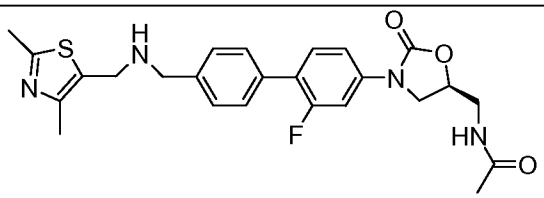
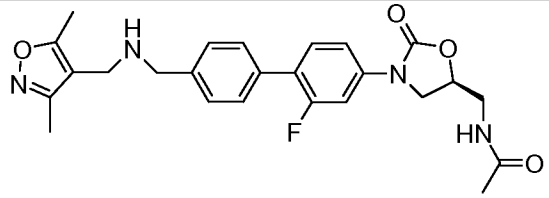
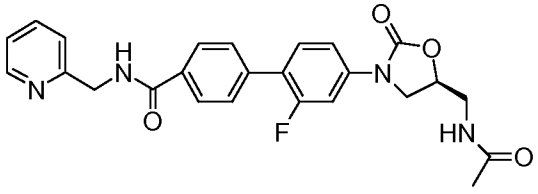
	amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4083		2
	N-[3-(2-Fluoro-4'-{[(1H-indol-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4084		128
	N-[3-(2-Fluoro-4'-{[(5-phenyl-thiophen-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4085		4
	N-[3-(4'-{[(4,5-Dimethyl-furan-2-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4086		4
	N-[3-(2-Fluoro-4'-{[(thiophen-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4087		4

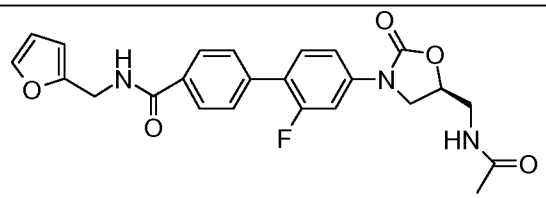
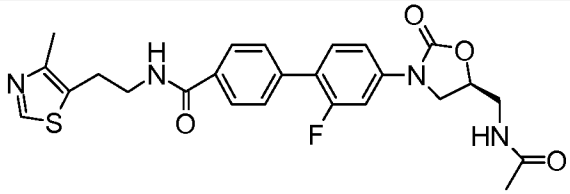
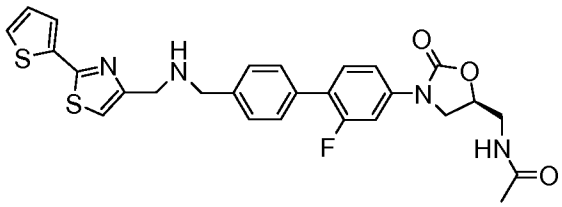
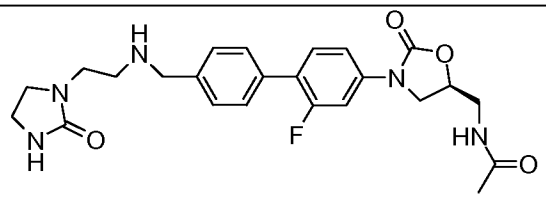
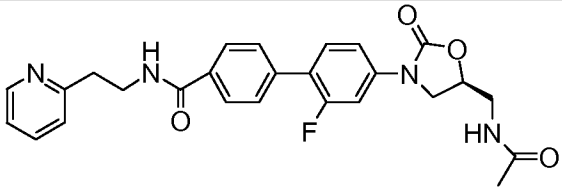
	N-(3-{2-Fluoro-4'-[(2-pyridin-2-yl-ethylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4088		2
	N-[2-Oxo-3-(2,2',3'-trifluoro-4'-{[(furan-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-oxazolidin-5-(S)-ylmethyl]-acetamide	
4089		2
	N-[2-Oxo-3-(2,2',3'-trifluoro-4'-{[(pyridin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-oxazolidin-5-(S)-ylmethyl]-acetamide	
4090		4
	N-[2-Oxo-3-(2,2',3'-trifluoro-4'-{[(pyridin-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-oxazolidin-5-(S)-ylmethyl]-acetamide	
4091		8
	N-[3-(2-Fluoro-4'-{[(1H-imidazol-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4092		4

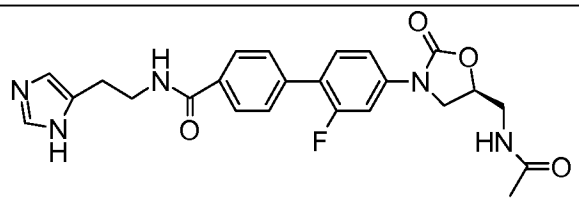
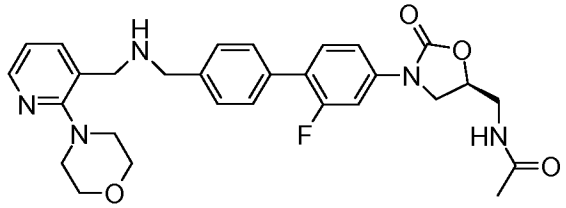
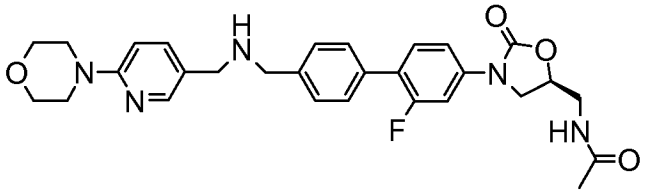
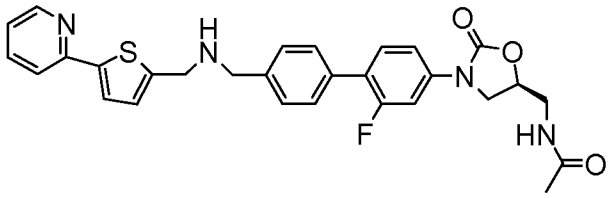
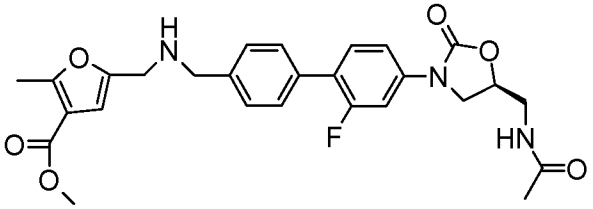
	N-[3-(4'-{[(1H-Benzoimidazol-2-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4093		8
	N-(3-{2-Fluoro-4'-[(4-sulfamoyl-benzylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4094		2
	N-[3-(2-Fluoro-4'-{[2-(4-sulfamoyl-phenyl)-ethylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4095		4
	N-[3-(2-Fluoro-4'-{[(3-hydroxy-5-hydroxymethyl-2-methyl-pyridin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4096		4
	N-[3-(2-Fluoro-4'-{[2-(4-methyl-thiazol-5-yl)-ethylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

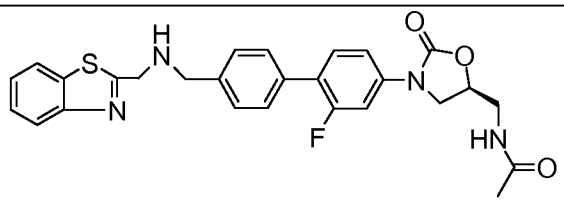
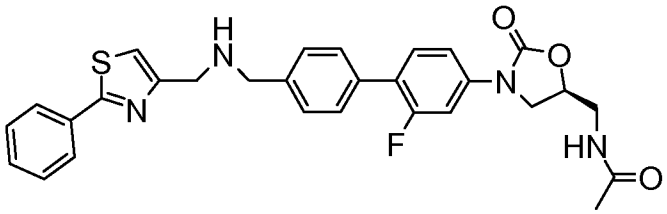
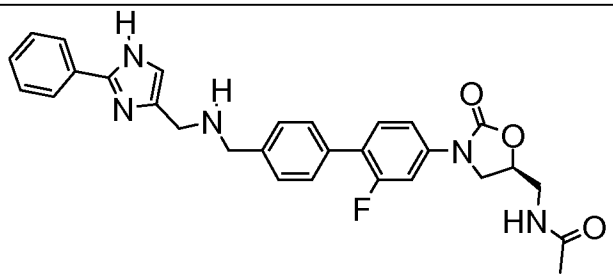
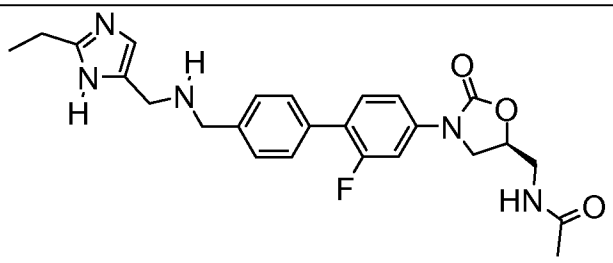
4097		16
	N-{3-[2-Fluoro-4'-(N-pyridin-2-ylmethyl-carbamimidoyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4098		2
	N-[3-(2-Fluoro-4'-{[(5-methoxy-1H-indol-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4099		4
	N-[3-(2-Fluoro-4'-{[(3-methyl-thiophen-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4100		4
	N-[3-(4'-{[(1-Benzenesulfonyl-1H-pyrrol-2-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4101		1

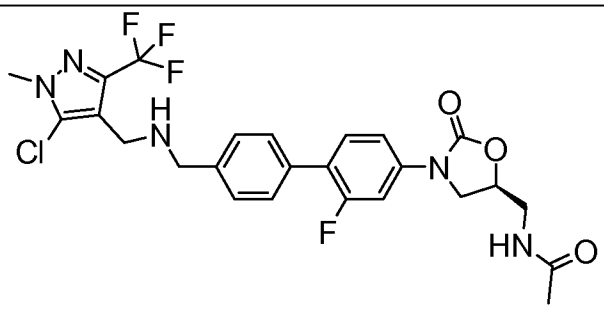
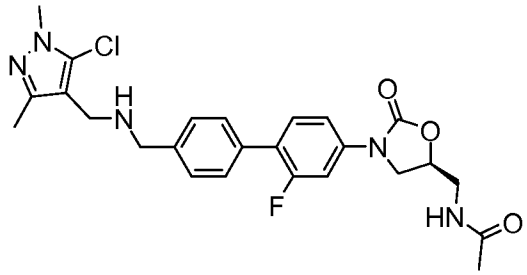
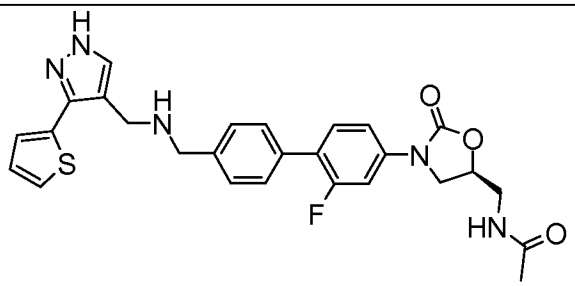
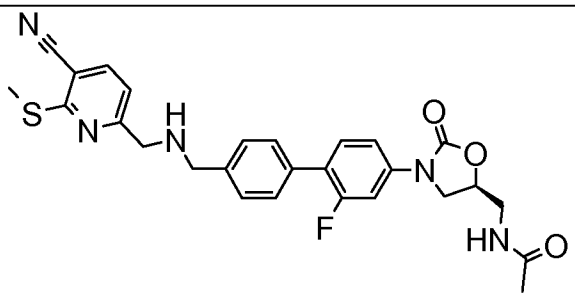
	N-[3-(4'-{[(2,4-Dioxo-1,2,3,4-tetrahydro-pyrimidin-5-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4102		2
	4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-carboxylic acid (pyridin-4-ylmethyl)-amide	
4103		8
	N-[3-(4'-{[(2,5-Dimethyl-furan-3-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4104		0.25
	N-[3-(2-Fluoro-4'-{[(5-methyl-3-phenyl-isoxazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4105		0.5
	N-[3-(2-Fluoro-4'-{[(5-methyl-2-trifluoromethyl-furan-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

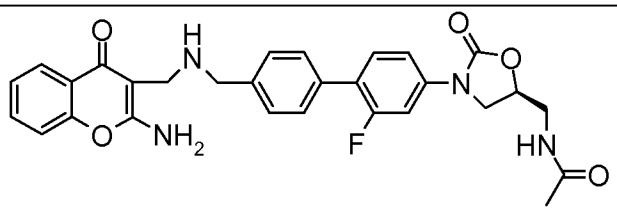
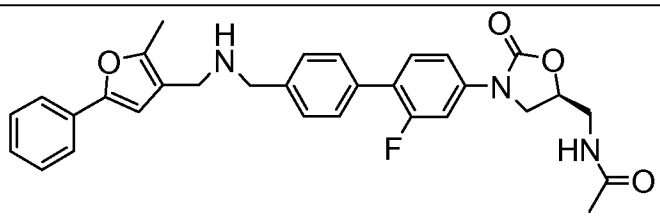
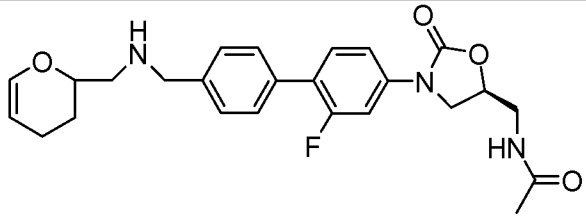
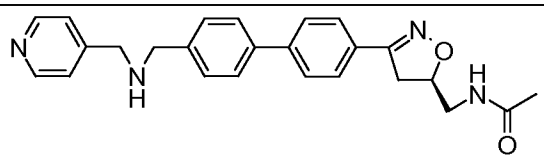
4106		128
	N-{4'-[5-(R)-(Acetylamino-methyl)-4,5-dihydro-isoxazol-3-yl]-biphenyl-4-ylmethyl}-phthalamic acid	
4107		128
	N-(4-{5-[5-(R)-(Acetylamino-methyl)-4,5-(S)-dihydro-isoxazol-3-yl]-pyridin-2-yl}-benzyl)-phthalamic acid	
4108		4
	N-[3-(4'-{[(2,4-Dimethyl-thiazol-5-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4109		1
	N-[3-(4'-{[(3,5-Dimethyl-isoxazol-4-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4110		0.25
	4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-carboxylic acid (pyridin-2-ylmethyl)-amide	

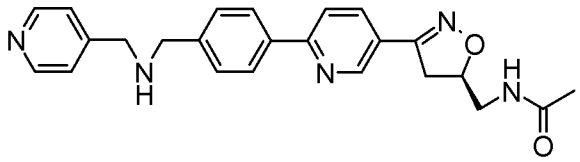
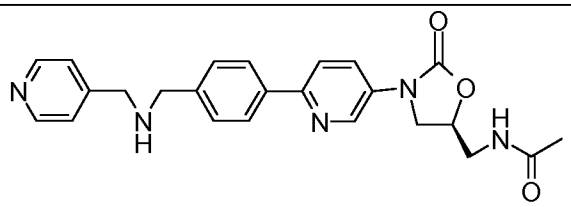
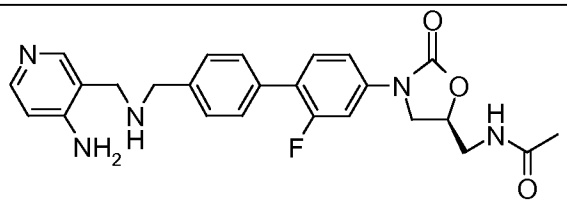
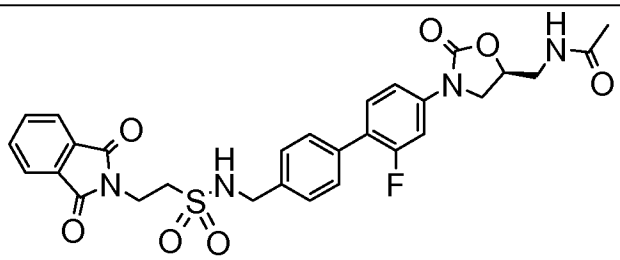
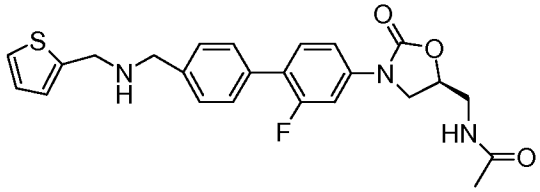
4111		2
	4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-carboxylic acid (furan-2-ylmethyl)-amide	
4112		0.25
	4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-carboxylic acid [2-(4-methyl-thiazol-5-yl)-ethyl]-amide	
4113		0.25
	N-[3-(2-Fluoro-4'-{[(2-thiophen-2-yl-thiazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4114		16
	N-[3-(2-Fluoro-4'-{[2-(2-oxo-imidazolidin-1-yl)-ethylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4115		0.5
	4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-carboxylic acid (2-pyridin-2-yl-ethyl)-amide	

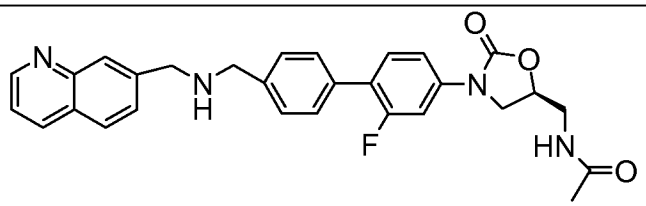
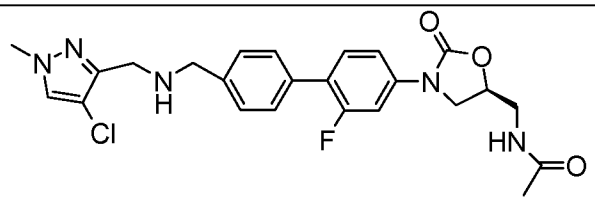
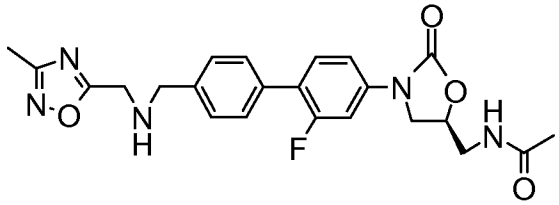
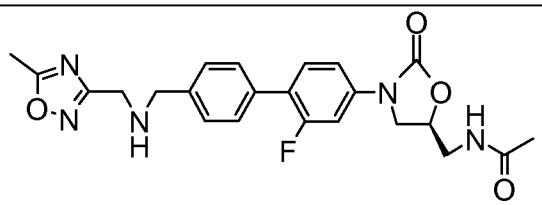
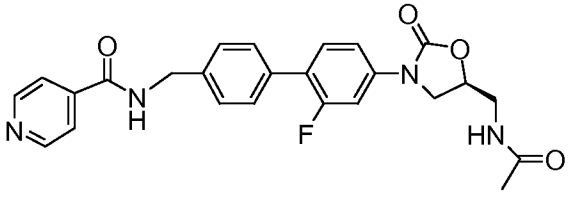
4116		1
	4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-carboxylic acid [2-(3H-imidazol-4-yl)-ethyl]-amide	
4117		8
	N-[3-(2-Fluoro-4'-{[(2-morpholin-4-yl-pyridin-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4118		8
	N-[3-(2-Fluoro-4'-{[(6-morpholin-4-yl-pyridin-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4119		1
	N-[3-(2-Fluoro-4'-{[(5-pyridin-2-yl-thiophen-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4120		1

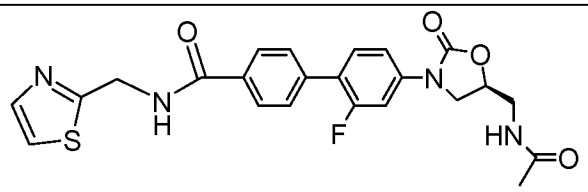
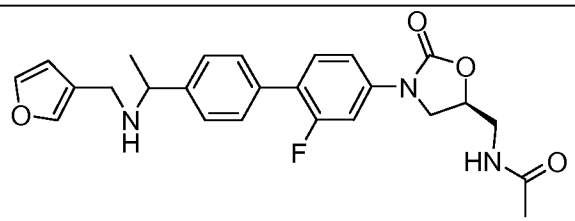
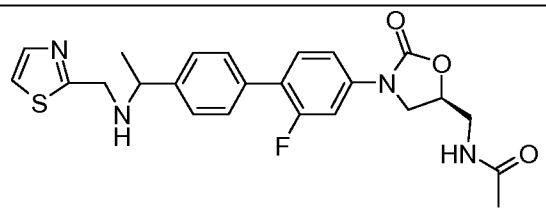
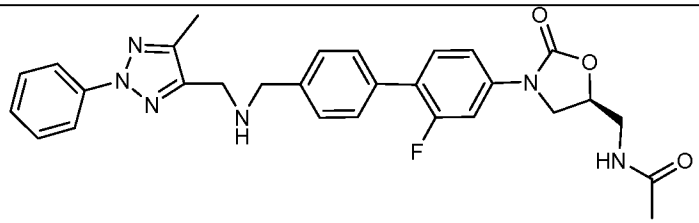
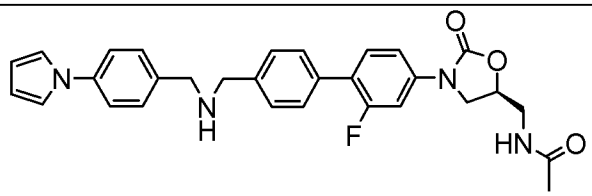
	5-[({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-methyl]-2-methyl-furan-3-carboxylic acid methyl ester	
4121		0.5
	N-[3-(4'-{[(Benzothiazol-2-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4122		1
	N-[3-(2-Fluoro-4'-{[(2-phenyl-thiazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4123		16
	N-[3-(2-Fluoro-4'-{[(2-phenyl-1H-imidazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4124		16
	N-[3-(4'-{[(2-Ethyl-3H-imidazol-4-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

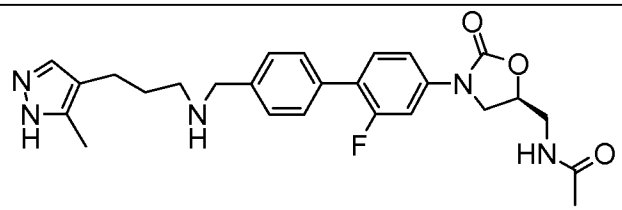
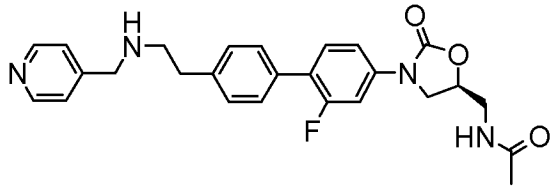
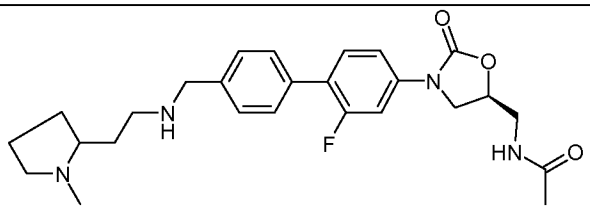
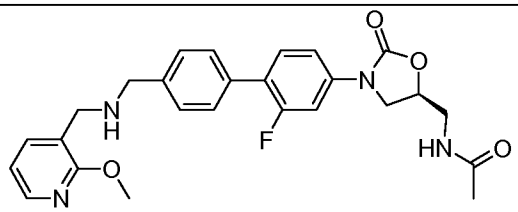
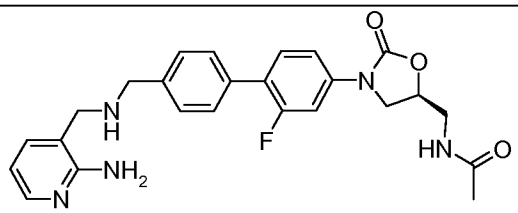
4125		0.5
	N-[3-(4'-{[(5-Chloro-1-methyl-3-trifluoromethyl-1H-pyrazol-4-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4126		0.5
	N-[3-(4'-{[(5-Chloro-1,3-dimethyl-1H-pyrazol-4-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4127		0.5
	N-[3-(2-Fluoro-4'-{[(3-thiophen-2-yl-1H-pyrazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4128		0.5

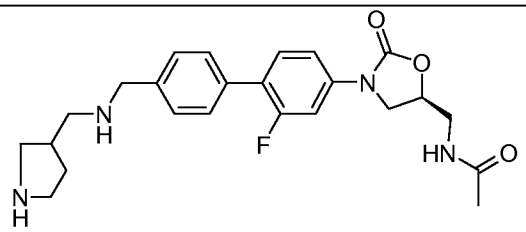
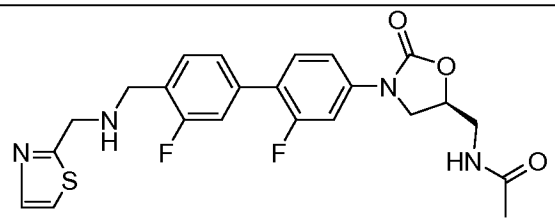
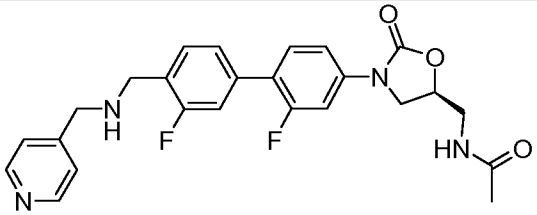
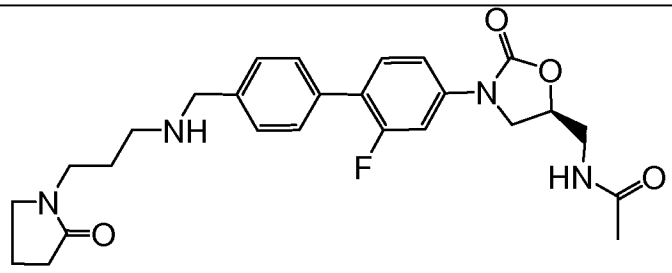
	N-[3-(4'-{[(5-Cyano-6-methylsulfanyl-pyridin-2-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4129		4
	N-[3-(4'-{[(2-Amino-4-oxo-4H-chromen-3-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4130		2
	N-[3-(2-Fluoro-4'-{[(2-methyl-5-phenyl-furan-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4131		1
	N-[3-(4'-{[(3,4-Dihydro-2H-pyran-2-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4132		4
	N-[3-(4'-{[(Pyridin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-4,5-dihydro-isoxazol-5-(R)-ylmethyl]-acetamide	

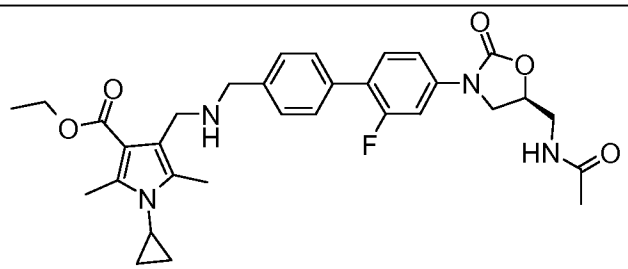
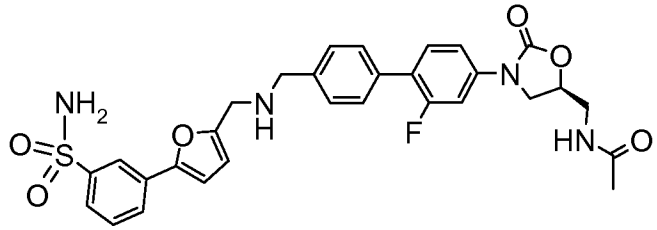
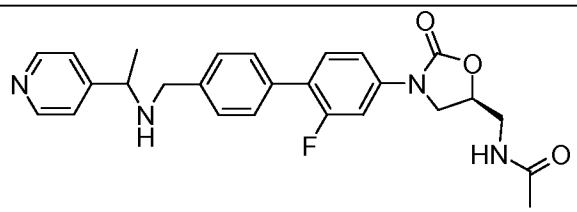
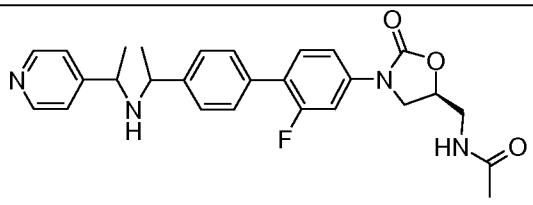
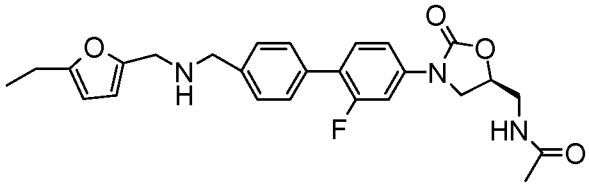
4133		128
	N-{3-[6-(4-{[(Pyridin-4-ylmethyl)-amino]-methyl}-phenyl)-pyridin-3-yl]-4,5-dihydro-isoxazol-5-(R)-ylmethyl}-acetamide	
4134		16
	N-{2-Oxo-3-[6-(4-{[(pyridin-4-ylmethyl)-amino]-methyl}-phenyl)-pyridin-3-yl]-oxazolidin-5-(S)-ylmethyl}-acetamide	
4135		4
	N-[3-(4'-{[(4-Amino-pyridin-3-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4136		8
	N-[3-(4'-{[2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-ethanesulfonylamino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4137		0.5
	N-[3-(2-Fluoro-4'-{[(thiophen-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

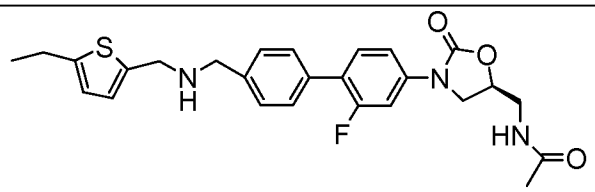
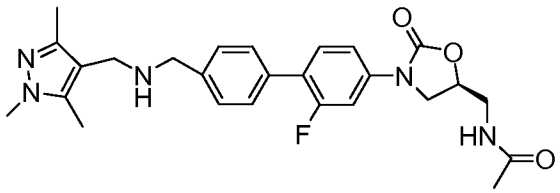
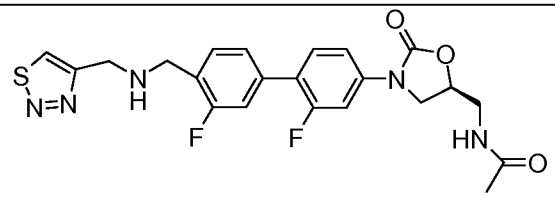
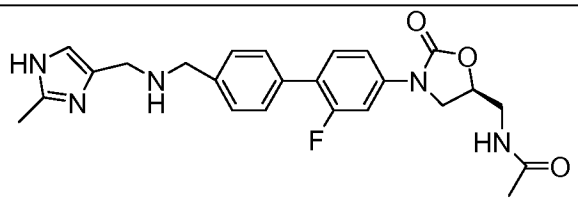
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	N-[3-(2-Fluoro-4'-{[(quinolin-7-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4139		2
	N-[3-(4'-{[(4-Chloro-1-methyl-1H-pyrazol-3-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4140		2
	N-[3-(2-Fluoro-4'-{[(3-methyl-[1,2,4]oxadiazol-5-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4141		2
	N-[3-(2-Fluoro-4'-{[(5-methyl-[1,2,4]oxadiazol-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4142		2
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-	

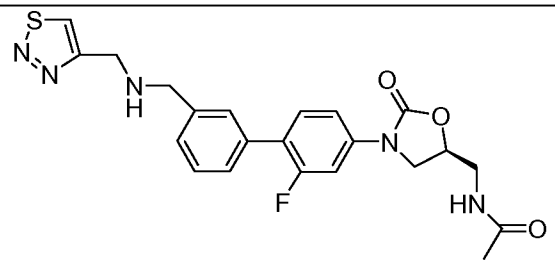
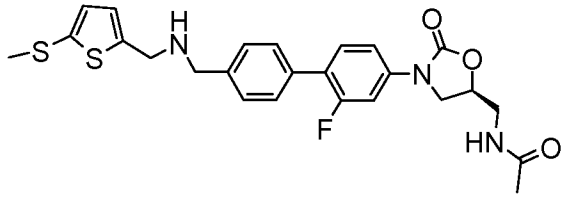
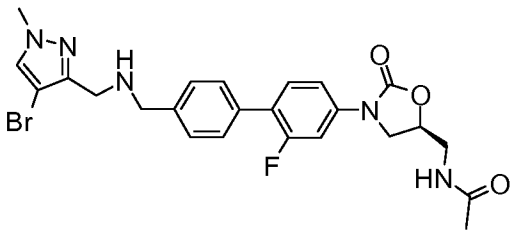
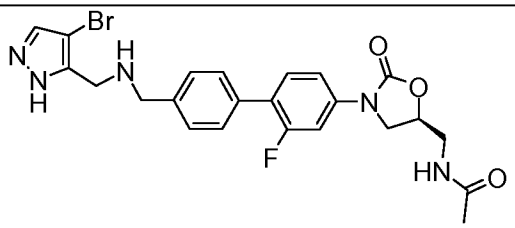
	fluoro-biphenyl-4-ylmethyl}-isonicotinamide	
4143		1
	4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-carboxylic acid (thiazol-2-ylmethyl)-amide	
4144		4
	N-[3-(2-Fluoro-4'-{1-(R/S)-[(furan-3-ylmethyl)-amino]-ethyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4145		2
	N-[3-(2-Fluoro-4'-{1-(R/S)-[(thiazol-2-ylmethyl)-amino]-ethyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4146		4
	N-[3-(2-Fluoro-4'-{[(5-methyl-2-phenyl-2H-[1,2,3]triazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4147		4
	N-(3-{2-Fluoro-4'-[(4-pyrrol-1-yl-benzylamino)-methyl]-	

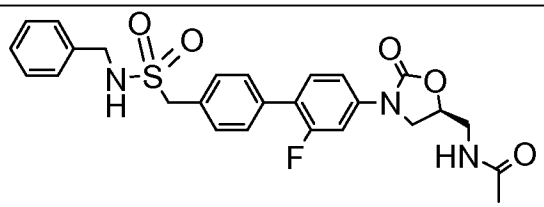
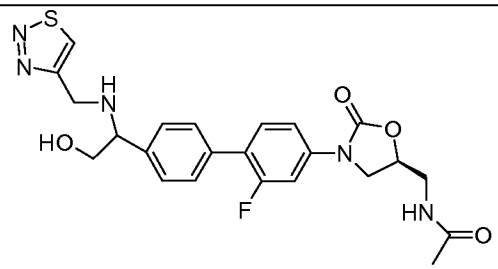
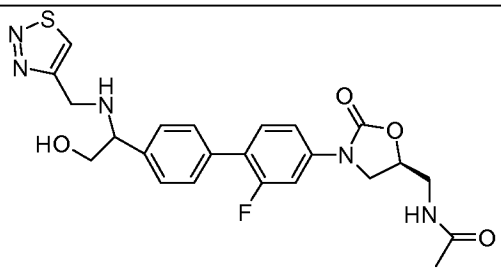
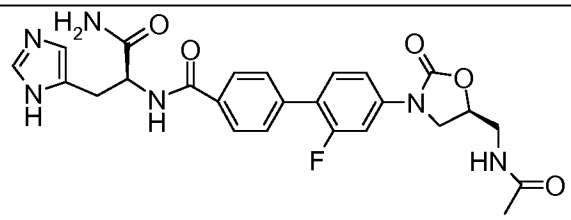
	biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4148		2
	N-[3-(2-Fluoro-4'-{[3-(5-methyl-1H-pyrazol-4-yl)-propylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4149		1
	N-[3-(2-Fluoro-4'-{2-[(pyridin-4-ylmethyl)-amino]-ethyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4150		16
	N-[3-(2-Fluoro-4'-{[2-(R/S)-(1-methyl-pyrrolidin-2-yl)-ethylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4151		2
	N-[3-(2-Fluoro-4'-{[(2-methoxy-pyridin-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4152		2

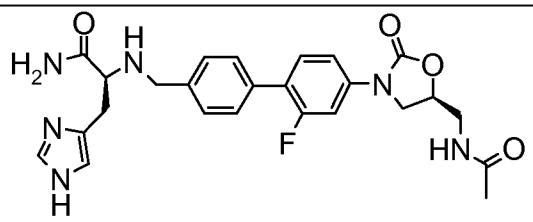
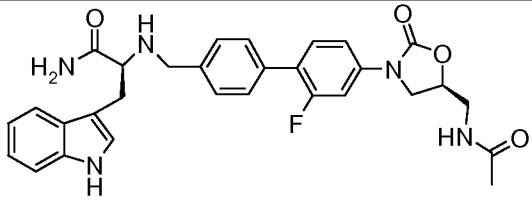
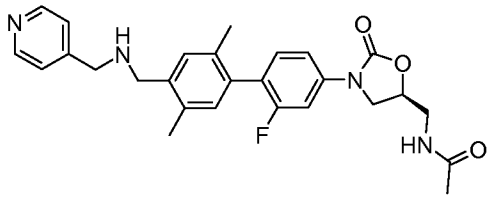
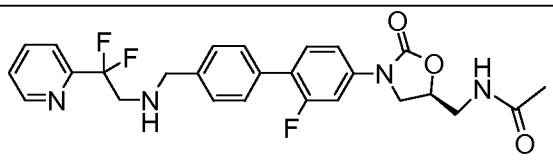
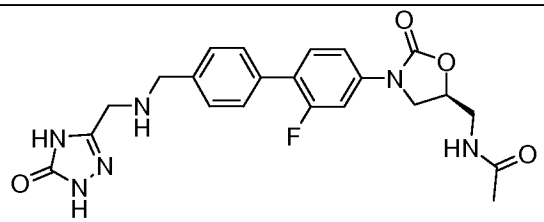
	N-[3-(4'-{[(2-Amino-pyridin-3-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4153		4
	N-[3-(2-Fluoro-4'-{[(pyrrolidin-3-(R/S)-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4154		1
	N-[3-(2,3'-Difluoro-4'-{[(thiazol-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4155		2
	N-[3-(2,3'-Difluoro-4'-{[(pyridin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4156		16
	N-[3-(2-Fluoro-4'-{[3-(2-oxo-pyrrolidin-1-yl)-propylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

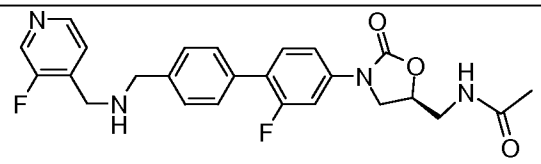
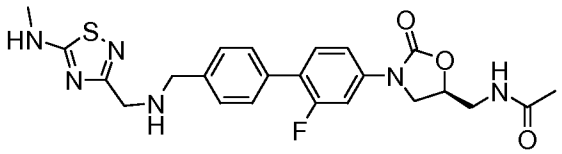
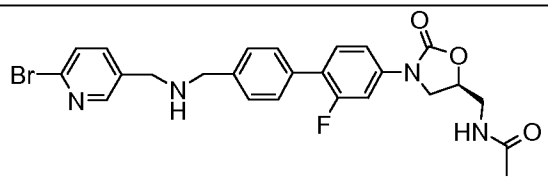
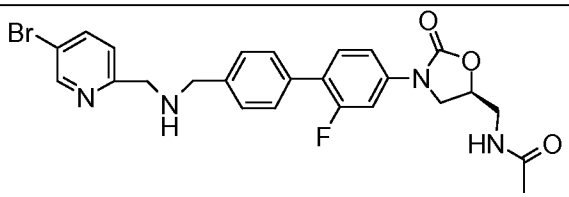
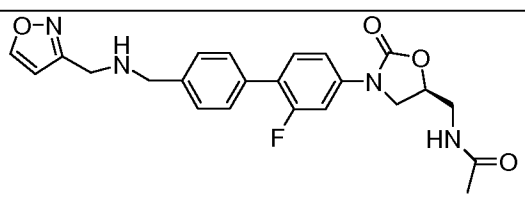
4157		8
	4-[({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-methyl]-1-cyclopropyl-2,5-dimethyl-1H-pyrrole-3-carboxylic acid ethyl ester	
4158		2
	N-{3-[2-Fluoro-4'-({[5-(3-sulfamoyl-phenyl)-furan-2-ylmethyl]-amino}-methyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4159		2
	N-(3-{2-Fluoro-4'-[(1-pyridin-4-(R/S)-yl-ethylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4160		8
	N-(3-{2-Fluoro-4'-[1-(R/S)-(1-pyridin-4-(R/S)-yl-ethylamino)-ethyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4161		2

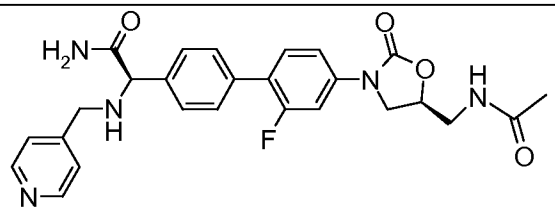
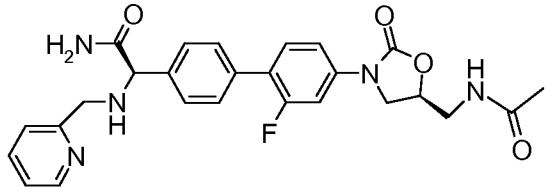
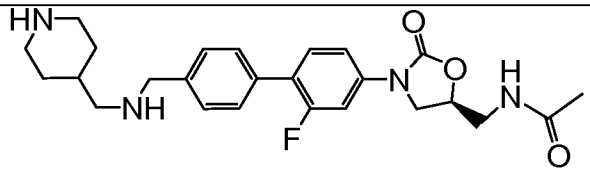
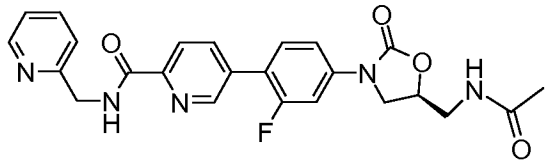
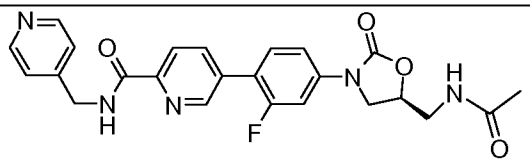
	N-[3-(4'-{[(5-Ethyl-furan-2-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4162		2
	N-[3-(4'-{[(5-Ethyl-thiophen-2-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4163		8
	N-[3-(2-Fluoro-4'-{[(1,3,5-trimethyl-1H-pyrazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4164		1
	N-[3-(2,3'-Difluoro-4'-{[([1,2,3]thiadiazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4165		4
	N-[3-(2-Fluoro-4'-{[(2-methyl-1H-imidazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

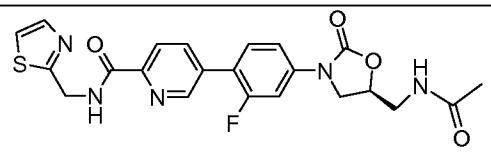
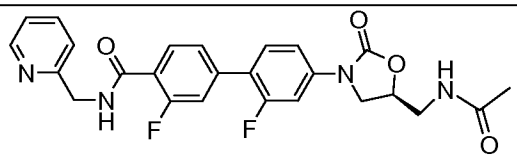
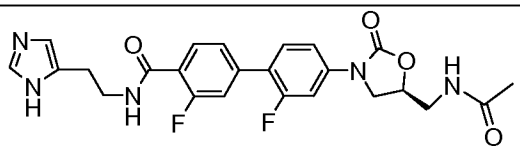
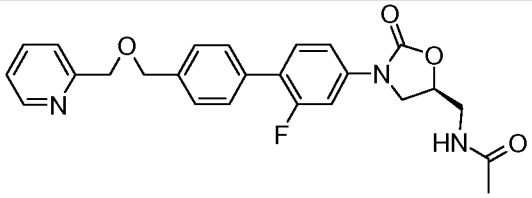
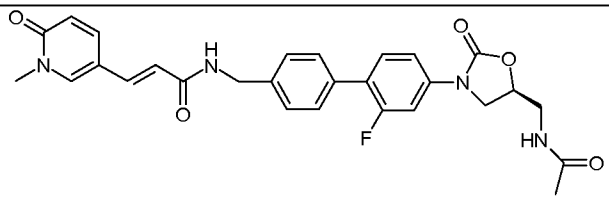
4166		8
	N-[3-(2-Fluoro-3'-{[([1,2,3]thiadiazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4167		2
	N-[3-(2-Fluoro-4'-{[(5-methylsulfanyl-thiophen-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4168		2
	N-[3-(4'-{[(4-Bromo-1-methyl-1H-pyrazol-3-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4169		2
	N-[3-(4'-{[(4-Bromo-2H-pyrazol-3-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

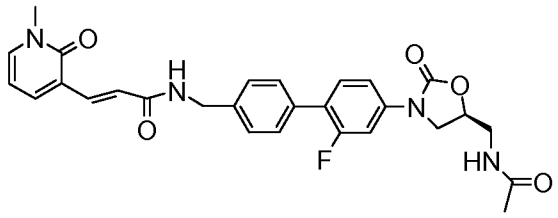
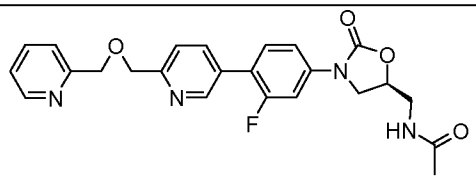
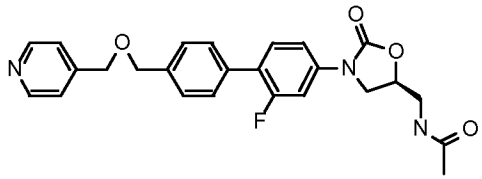
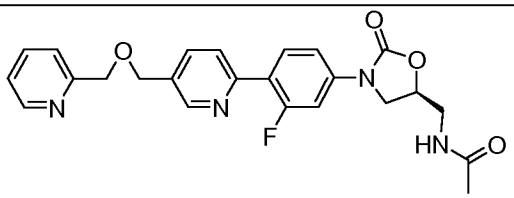
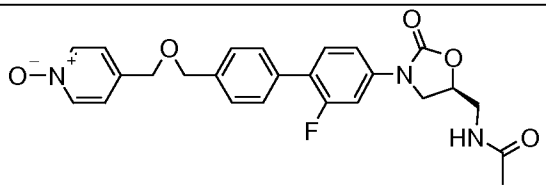
4170		128
	N-{3-[4'-(Benzylsulfamoyl-methyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4171		4
	N-[3-(2-Fluoro-4'-{2-hydroxy-1-[([1,2,3]thiadiazol-4-(R/S)-ylmethyl)-amino]-ethyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4172		8
	N-[3-(2-Fluoro-4'-{2-hydroxy-1-[([1,2,3]thiadiazol-4-(R/S)-ylmethyl)-amino]-ethyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4173		32
	4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-carboxylic acid [1-carbamoyl-2-(S)-(3H-imidazol-4-yl)-ethyl]-amide	

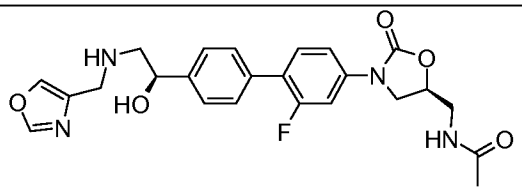
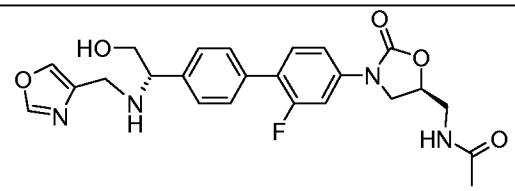
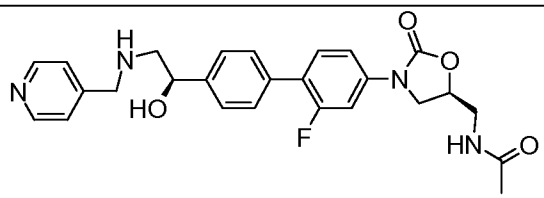
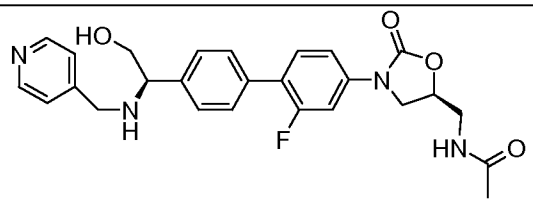
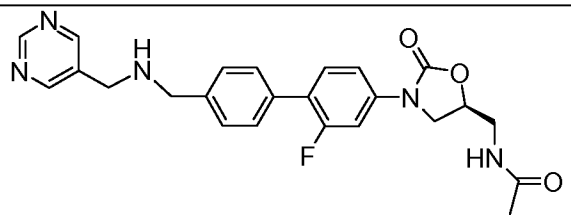
4174		
	2-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-3-(S)-(1H-imidazol-4-yl)-propionamide	
4175		2
	2-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-3-(S)-(1H-indol-3-yl)-propionamide	
4176		128
	N-[3-(2-Fluoro-2',5'-dimethyl-4'-{[(pyridin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4177		4
	N-(3-{4'-[(2,2-Difluoro-2-pyridin-2-yl-ethylamino)-methyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4178		8
	N-[3-(2-Fluoro-4'-{[(5-(S)-oxo-4,5-dihydro-1H-[1,2,4]triazol-3-	

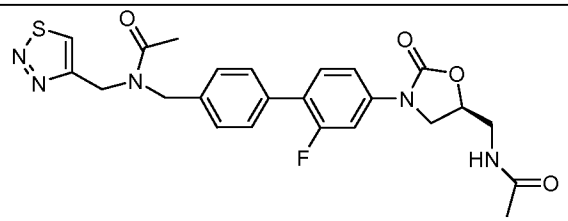
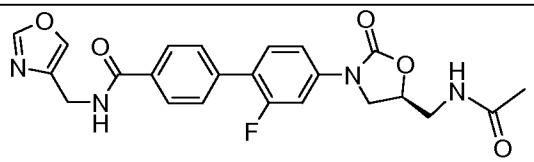
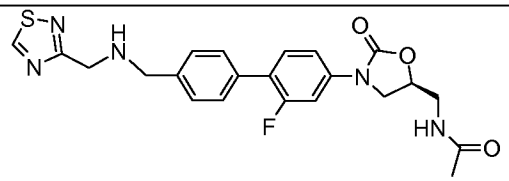
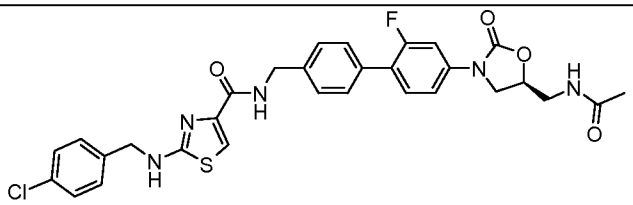
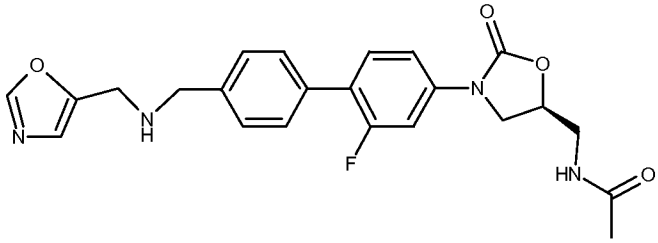
	ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4179		2
	N-[3-(2-Fluoro-4'-{[(3-fluoro-pyridin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4180		1
	N-[3-(2-Fluoro-4'-{[(5-methylamino-[1,2,4]thiadiazol-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4181		1
	N-[3-(4'-{[(6-Bromo-pyridin-3-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4182		2
	N-[3-(4'-{[(5-Bromo-pyridin-2-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4183		1
	N-[3-(2-Fluoro-4'-{[(isoxazol-3-ylmethyl)-amino]-methyl}-	

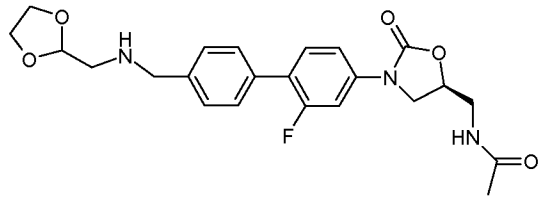
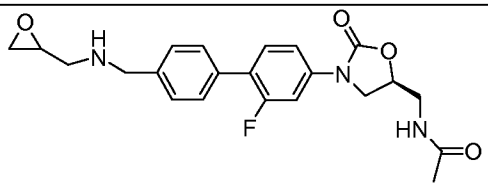
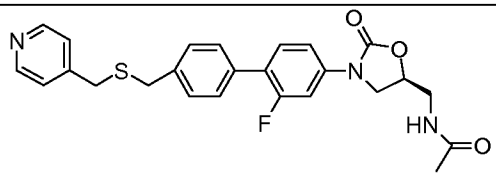
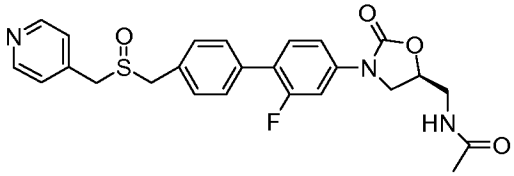
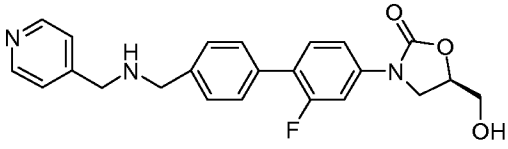
	biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4184		16
	2-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-yl}-2-(R)-[(pyridin-4-ylmethyl)-amino]-acetamide	
4185		16
	2-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-yl}-2-(R)-[(pyridin-2-ylmethyl)-amino]-acetamide	
4186		64
	N-[3-(2-Fluoro-4'-{[(piperidin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4187		1
	5-{4-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2-fluoro-phenyl}-pyridine-2-carboxylic acid (pyridin-2-ylmethyl)-amide	
4188		1
	5-{4-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2-fluoro-phenyl}-pyridine-2-carboxylic acid (pyridin-4-ylmethyl)-amide	

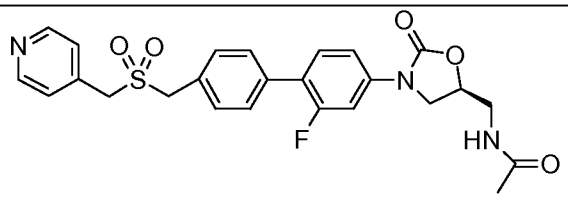
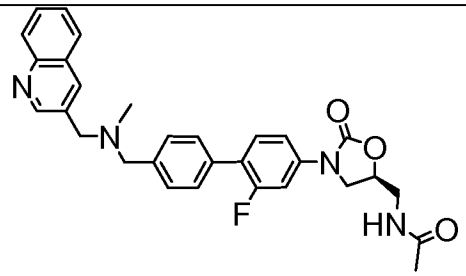
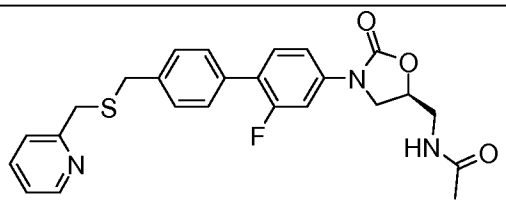
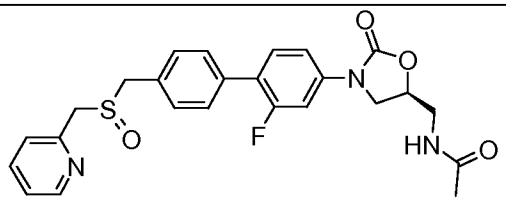
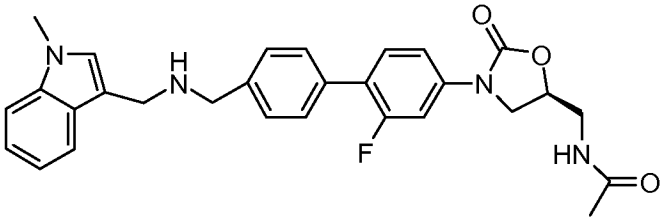
4189		1
	5-{4-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2-fluoro-phenyl}-pyridine-2-carboxylic acid (thiazol-2-ylmethyl)-amide	
4190		1
	4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-3,2'-difluoro-biphenyl-4-carboxylic acid (pyridin-2-ylmethyl)-amide	
4191		1
	4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-3,2'-difluoro-biphenyl-4-carboxylic acid [2-(3H-imidazol-4-yl)-ethyl]-amide	
4192		1
	N-{3-[2-Fluoro-4'-(pyridin-2-ylmethoxymethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4193		8
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-3-(1-methyl-6-oxo-1,6-dihydro-pyridin-3-yl)-acrylamide	

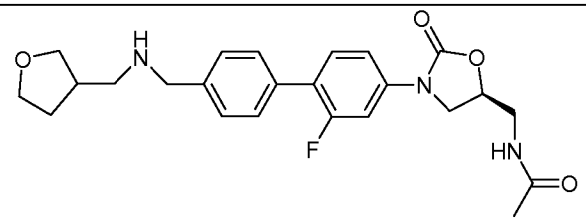
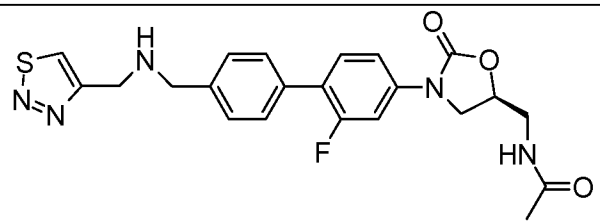
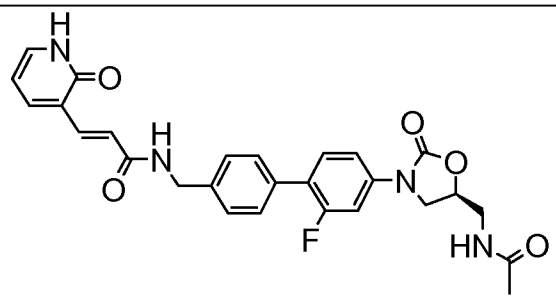
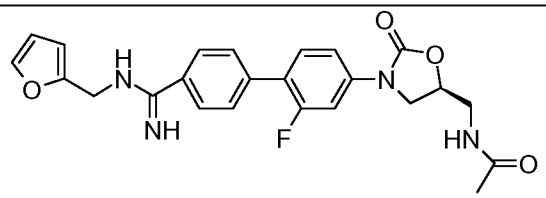
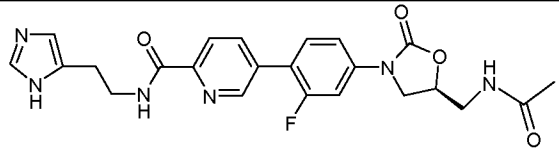
4194		2
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-3-(1-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)-acrylamide	
4195		1
	N-(3-{3-Fluoro-4-[6-(pyridin-2-ylmethoxymethyl)-pyridin-3-yl]-phenyl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4196		1
	N-{3-[2-Fluoro-4'-(pyridin-4-ylmethoxymethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4197		4
	N-(3-{3-Fluoro-4-[5-(pyridin-2-ylmethoxymethyl)-pyridin-2-yl]-phenyl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4198		2
	N-{3-[2-Fluoro-4'-(1-oxy-pyridin-4-ylmethoxymethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

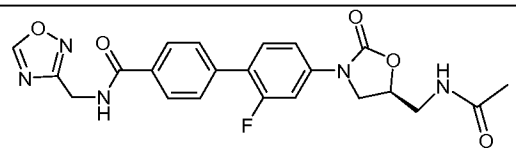
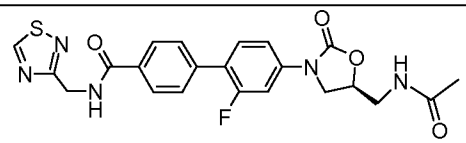
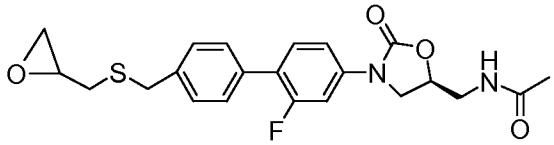
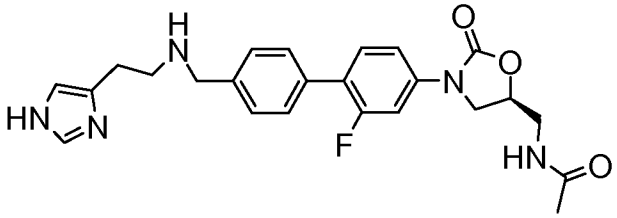
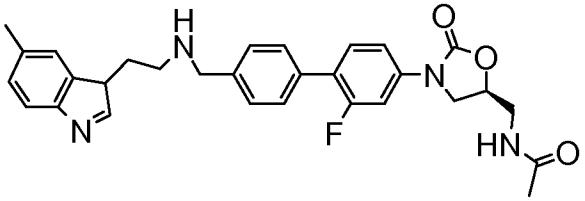
4199		4
	N-[3-(2-Fluoro-4'-{1-(R)-hydroxy-2-[(oxazol-4-ylmethyl)-amino]-ethyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4200		4
	N-[3-(2-Fluoro-4'-{2-hydroxy-1-(S)-[(oxazol-4-ylmethyl)-amino]-ethyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4201		2
	N-[3-(2-Fluoro-4'-{1-(R)-hydroxy-2-[(pyridin-4-ylmethyl)-amino]-ethyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4202		4
	N-[3-(2-Fluoro-4'-{2-hydroxy-1-(R)-[(pyridin-4-ylmethyl)-amino]-ethyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4203		1
	N-[3-(2-Fluoro-4'-{[(pyrimidin-5-ylmethyl)-amino]-methyl}-	

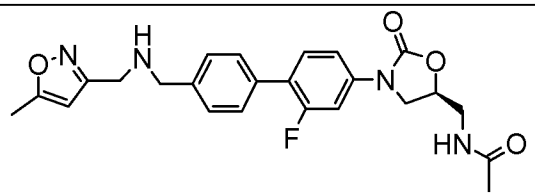
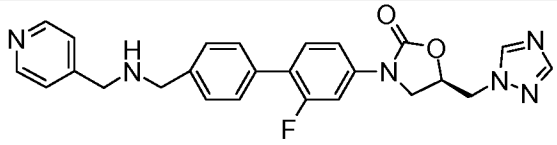
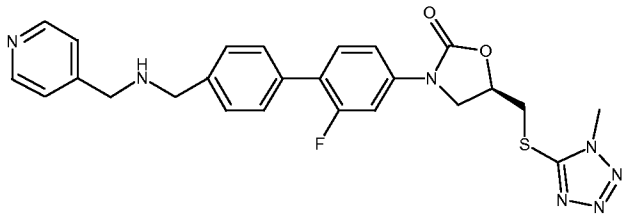
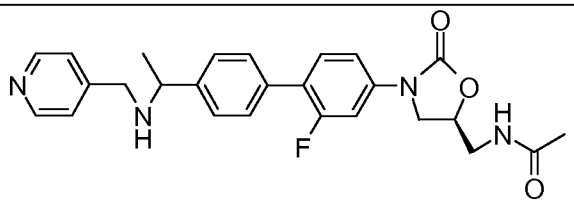
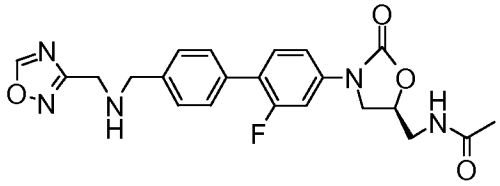
	biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4204		2
	N-(3-{4'-[(Acetyl-[1,2,3]thiadiazol-4-ylmethyl-amino)-methyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4205		1
	4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-carboxylic acid (oxazol-4-ylmethyl)-amide	
4206		1
	N-[3-(2-Fluoro-4'-{[([1,2,4]thiadiazol-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4207		2
	2-(4-Chloro-benzylamino)-thiazole-4-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	
4208		1

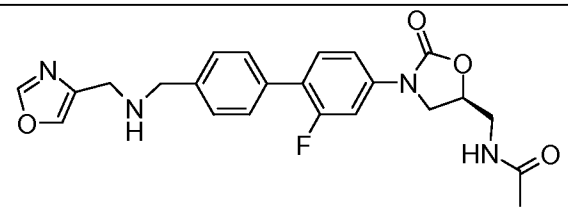
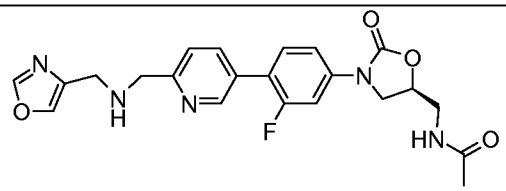
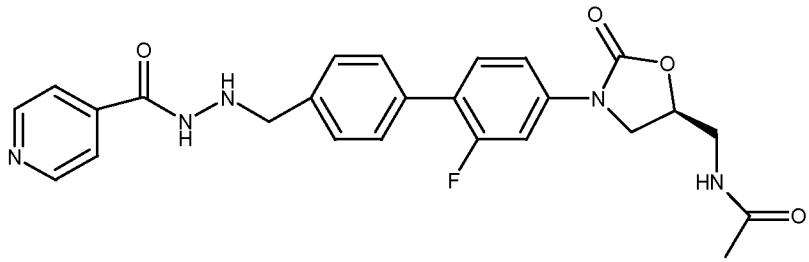
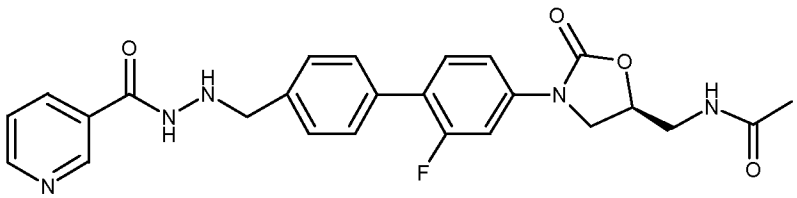
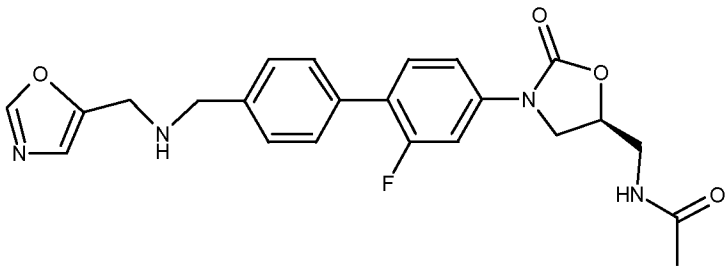
	N-[3-(2-Fluoro-4'-{[(oxazol-5-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4209		0.5
	N-[3-(4'-{[([1,3]Dioxolan-2-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4210		4
	N-(3-{2-Fluoro-4'-[(oxiranylmethyl-amino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4211		0.25
	N-{3-[2-Fluoro-4'-(pyridin-4-ylmethylsulfanylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4212		0.25
	N-{3-[2-Fluoro-4'-(pyridin-4-ylmethanesulfinylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4213		4
	3-(2-Fluoro-4'-{[(pyridin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-5-(R)-hydroxymethyl-oxazolidin-2-one	

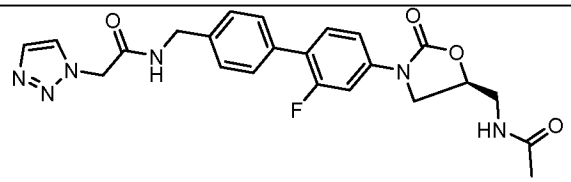
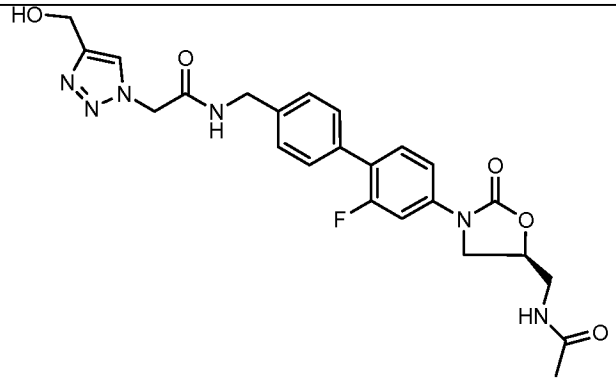
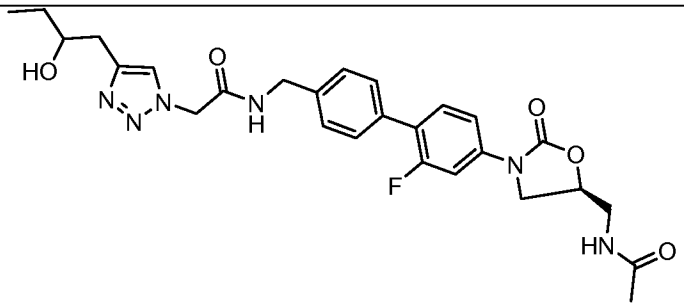
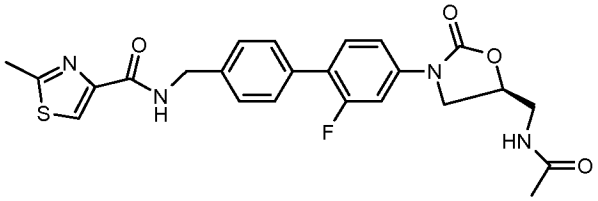
4214		1
	N-{3-[2-Fluoro-4'-(pyridin-4-ylmethanesulfonylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4215		0.25
	N-(3-{2-Fluoro-4'-[(methyl-quinolin-3-ylmethyl-amino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4216		0.5
	N-{3-[2-Fluoro-4'-(pyridin-2-ylmethylsulfanylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4217		1
	N-{3-[2-Fluoro-4'-(pyridin-2-ylmethanesulfinylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4218		2
	N-[3-(2-Fluoro-4'-{[(1-methyl-1H-indol-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-	

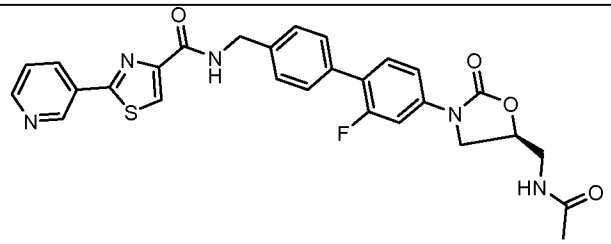
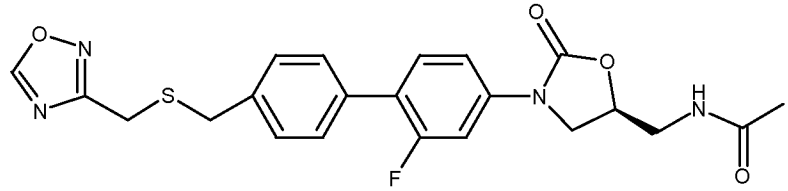
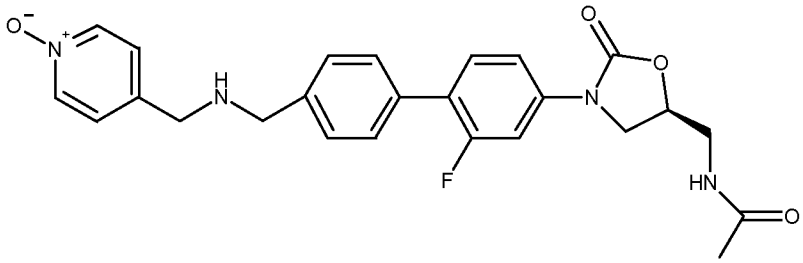
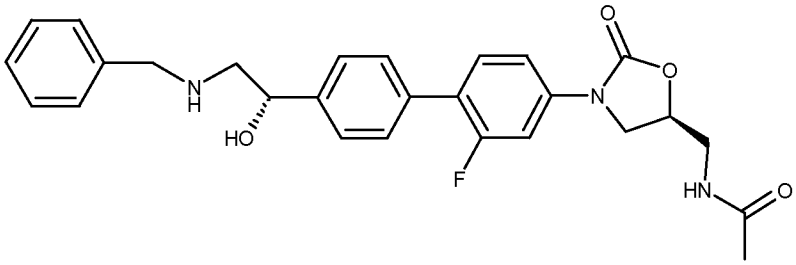
	acetamide	
4219		8
	N-[3-(2-Fluoro-4'-{[(tetrahydro-furan-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4220		0.25
	N-[3-(2-Fluoro-4'-{[(tetrahydro-furan-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4221		2
	N-[3-(2-Fluoro-4'-{[(thiophen-2-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4222		16
	N-{3-[2-Fluoro-4'-(N-furan-2-ylmethyl-carbamimidoyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4223		2

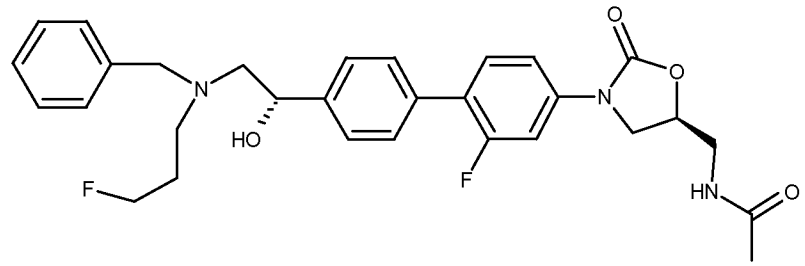
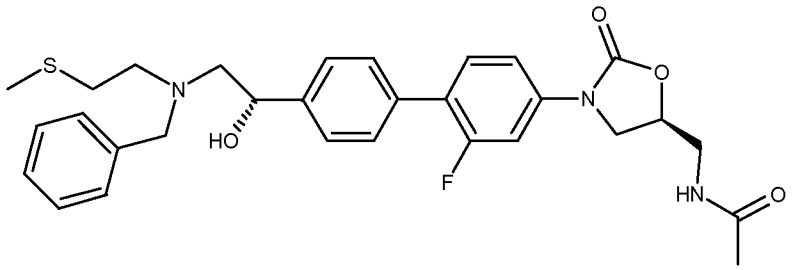
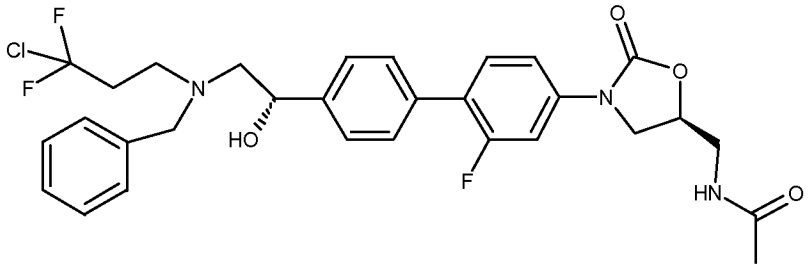
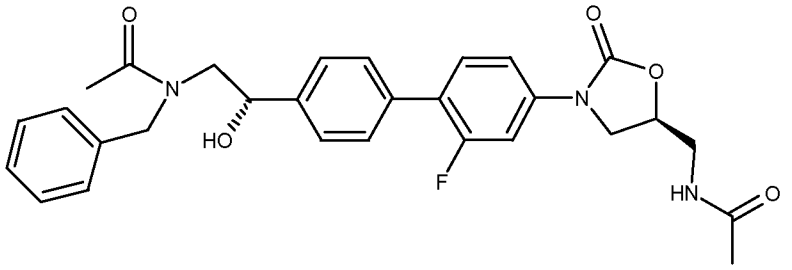
	5-{4-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2-fluoro-phenyl}-pyridine-2-carboxylic acid [2-(3H-imidazol-4-yl)-ethyl]-amide	
4224		0.5
	4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-carboxylic acid ([1,2,4]oxadiazol-3-ylmethyl)-amide	
4225		1
	4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-carboxylic acid ([1,2,4]thiadiazol-3-ylmethyl)-amide	
4226		1
	N-[3-(2-Fluoro-4'-oxiranylmethylsulfanylmethyl-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4227		4
	N-[3-(2-Fluoro-4'-{[2-(1H-imidazol-4-yl)-ethylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4228		2
	N-[3-(2-Fluoro-4'-{[2-(5-methyl-3H-indol-3-yl)-ethylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-	

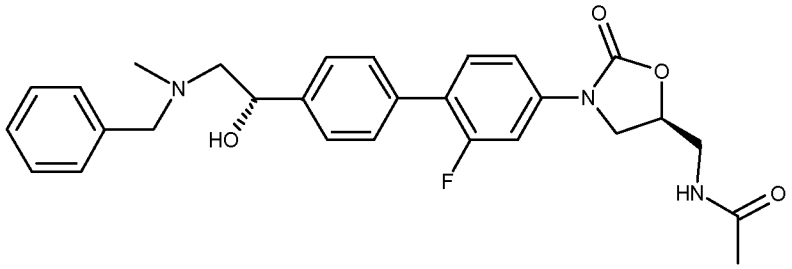
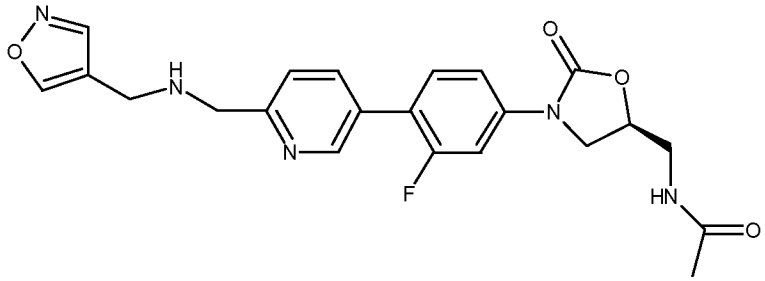
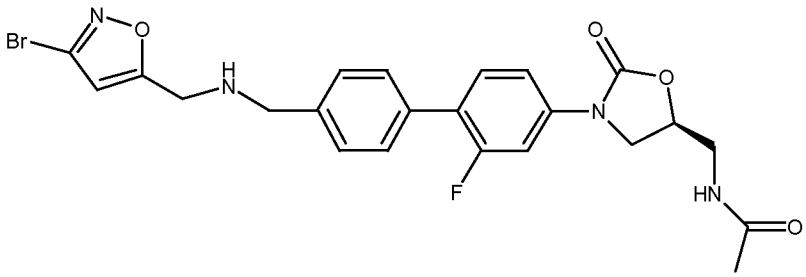
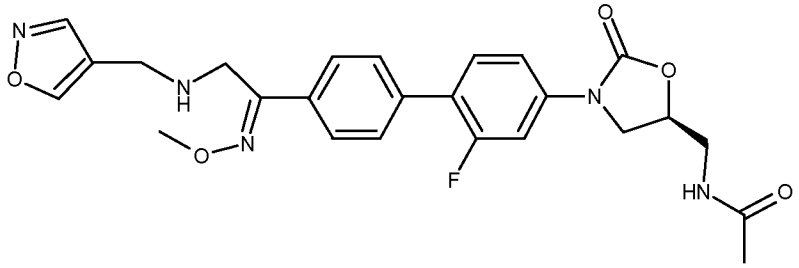
	acetamide	
4229		0.25
	N-[3-(2-Fluoro-4'-{[(5-methyl-isoxazol-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4230		32
	3-(2-Fluoro-4'-{[(pyridin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-5-(R)-[1,2,4]triazol-1-ylmethyl-oxazolidin-2-one	
4231		32
	3-(2-Fluoro-4'-{[(pyridin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-5-(R)-(1-methyl-1H-tetrazol-5-ylsulfanylmethyl)-oxazolidin-2-one	
4232		8
	N-[3-(2-Fluoro-4'-{1-(R/S)-[(pyridin-4-ylmethyl)-amino]-ethyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4233		0.5
	N-[3-(2-Fluoro-4'-{[([1,2,4]oxadiazol-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-	

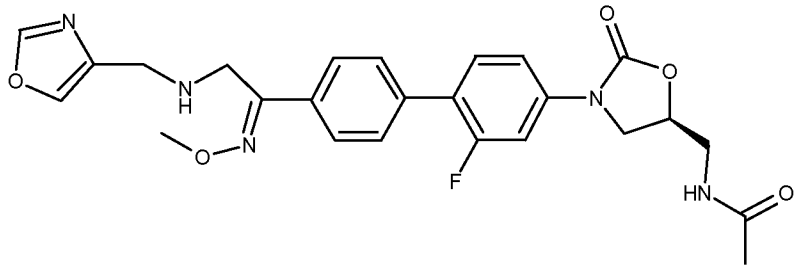
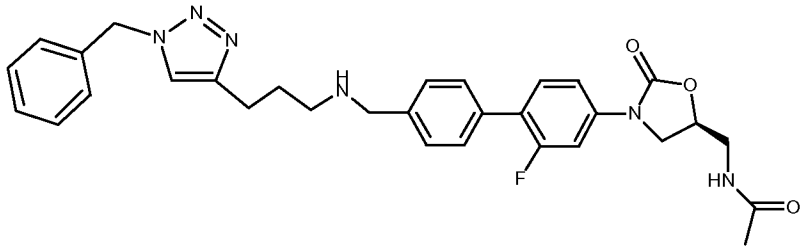
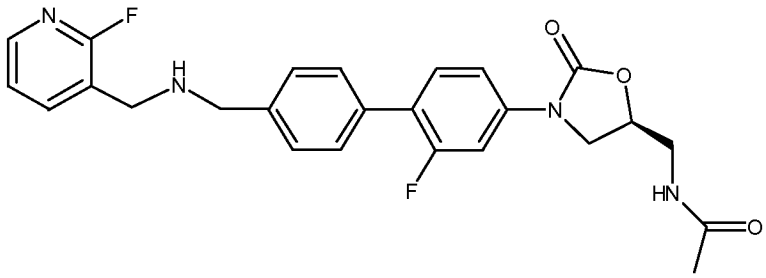
	acetamide	
4234		2
	N-[3-(2-Fluoro-4'-{[(oxazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4235		2
	N-{3-[3-Fluoro-4-(6-{[(oxazol-4-ylmethyl)-amino]-methyl}-pyridin-3-yl)-phenyl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4236		0.25
	N-(3-{2-Fluoro-4'-[N'-(pyridine-4-carbonyl)-hydrazinomethyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4237		0.25
	N-(3-{2-Fluoro-4'-[N'-(pyridine-3-carbonyl)-hydrazinomethyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4238		1

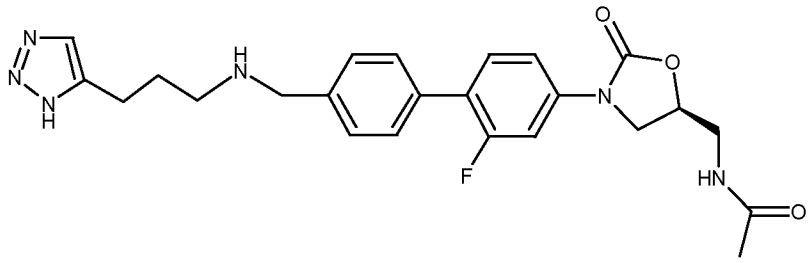
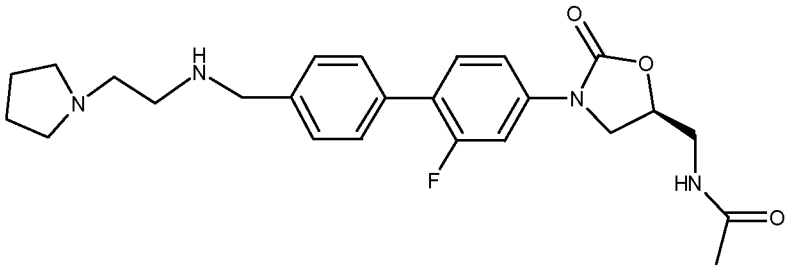
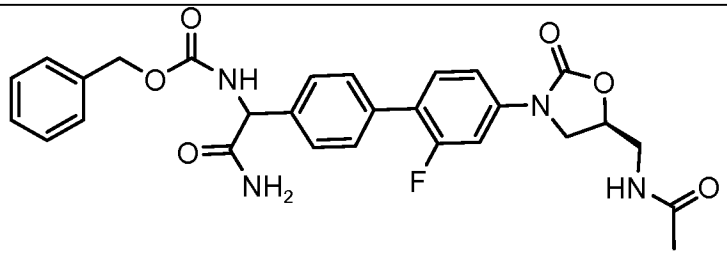
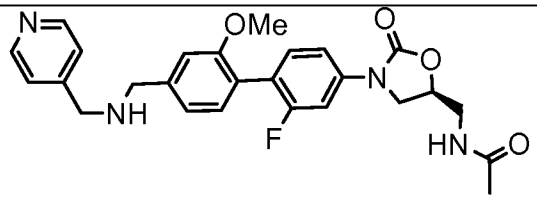
	N-[3-(2-Fluoro-4'-{[(oxazol-5-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4239		2
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-2-[1,2,3]triazol-1-yl-acetamide	
4240		16
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-2-(4-hydroxymethyl-[1,2,3]triazol-1-yl)-acetamide	
4241		4
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-2-[4-(2-hydroxy-butyl)-[1,2,3]triazol-1-yl]-acetamide	
4242		2
	2-Methyl-thiazole-4-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-	

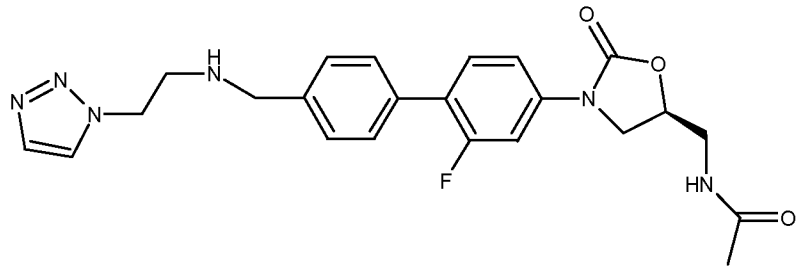
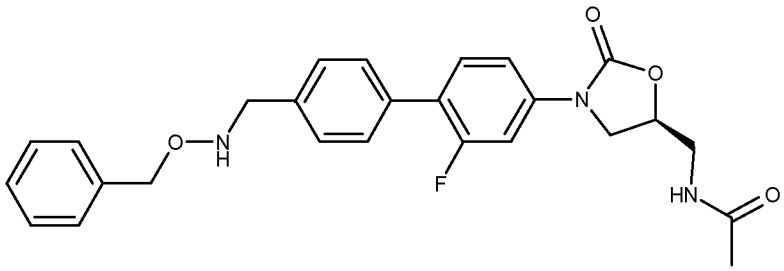
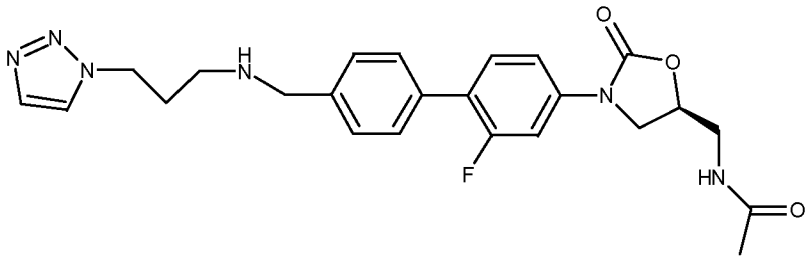
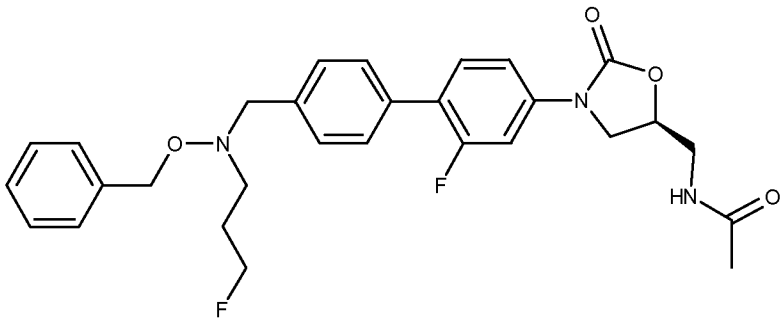
	amide	
4243		4
	2-Methyl-thiazole-4-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	
4244		0.5
	N-{3-[2-Fluoro-4'-([1,2,4]oxadiazol-3-ylmethylsulfanylmethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4245		2
	N-[3-(2-Fluoro-4'-{[(1-oxy-pyridin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4246		4
	N-{3-[4'-(2-Benzylamino-1-(S)-hydroxy-ethyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

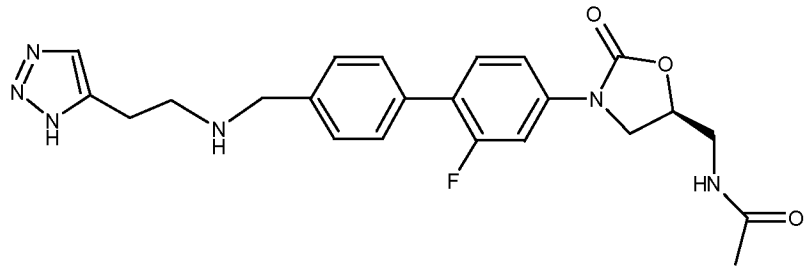
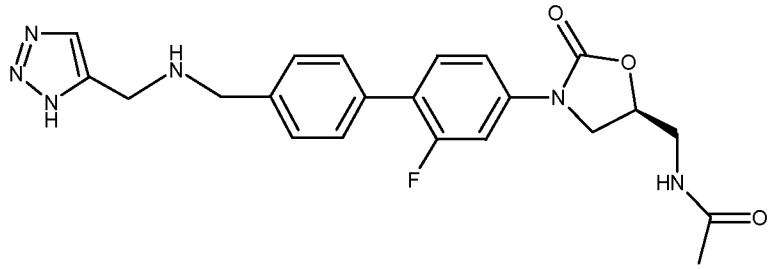
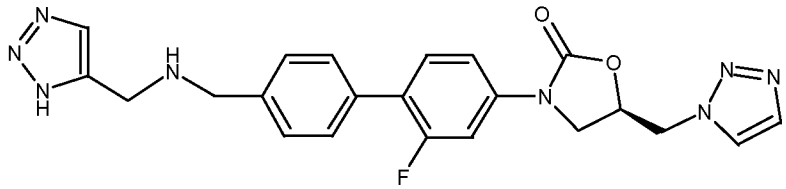
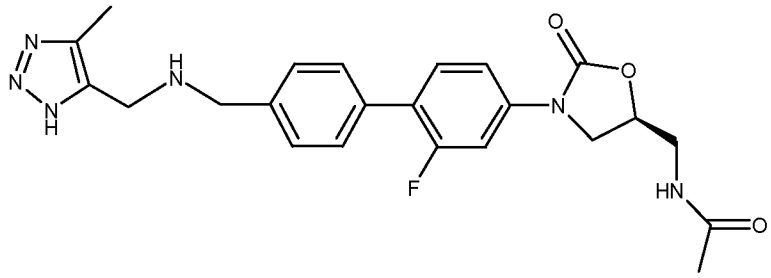
4247		8
	N-[3-(4'-{2-[Benzyl-(3-fluoro-propyl)-amino]-1-(S)-hydroxy-ethyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4248		4
	N-[3-(4'-{2-[Benzyl-(2-methylsulfanyl-ethyl)-amino]-1-(S)-hydroxy-ethyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4249		8
	N-[3-(4'-{2-[Benzyl-(3-chloro-3,3-difluoro-propyl)-amino]-1-(S)-hydroxy-ethyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4250		2
	N-(2-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-yl}-2-(S)-hydroxy-ethyl)-N-benzyl-	

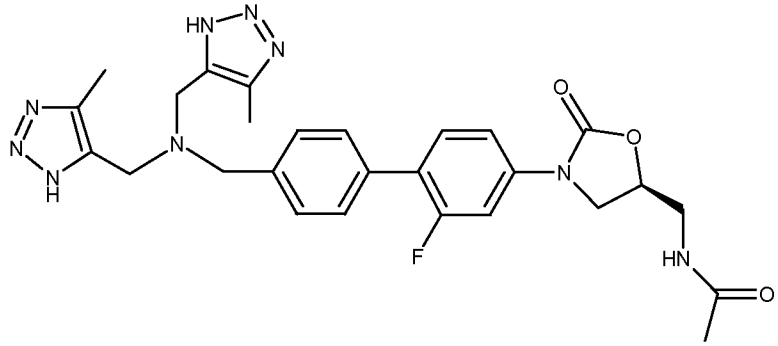
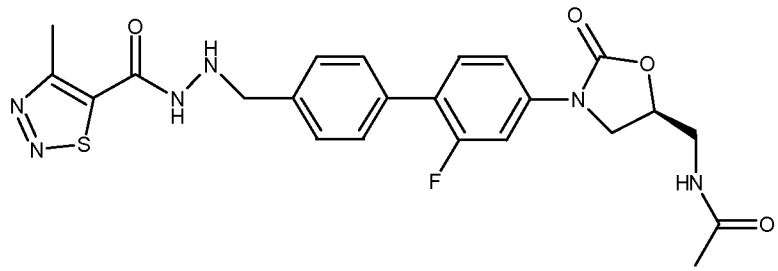
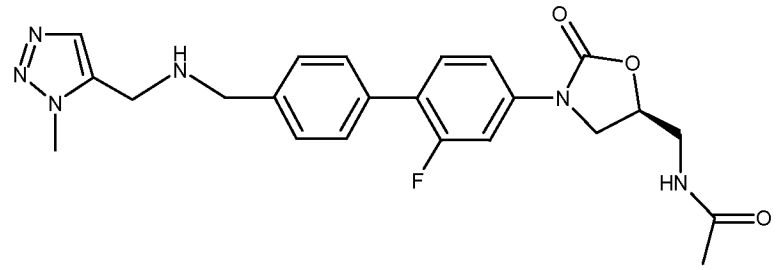
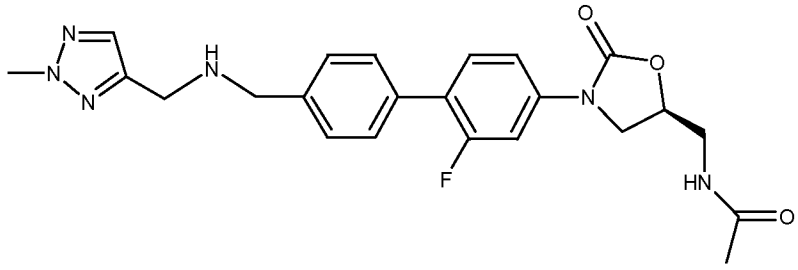
	acetamide	
4251		2
	N-(3-{4'-[2-(Benzyl-methyl-amino)-1-(S)-hydroxy-ethyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4252		2
	N-{3-[3-Fluoro-4-(6-{[(isoxazol-4-ylmethyl)-amino]-methyl}-pyridin-3-yl)-phenyl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4253		0.5
	N-[3-(4'-{[(3-Bromo-isoxazol-5-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4254		2

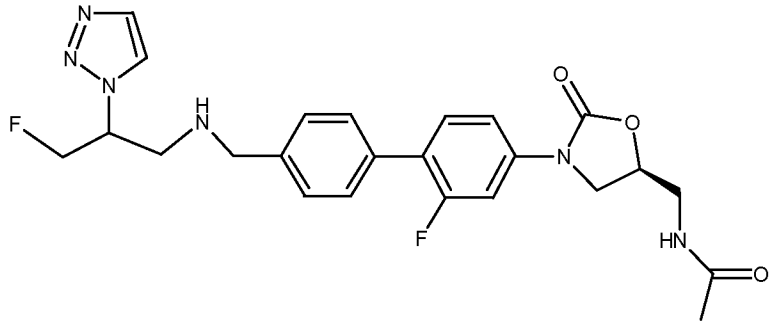
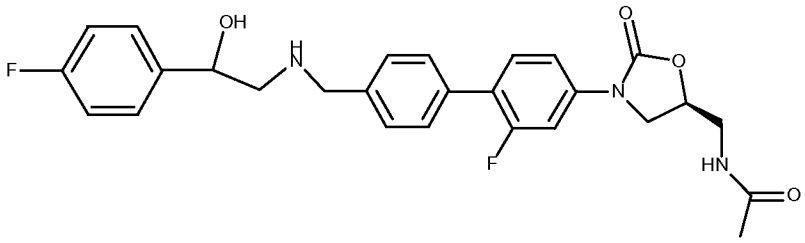
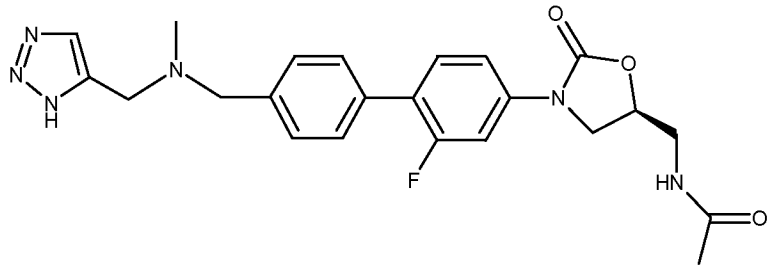
	N-[3-(2-Fluoro-4'-{2-[(isoxazol-4-ylmethyl)-amino]-1-methoxyimino-ethyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4255		2
	N-[3-(2-Fluoro-4'-{1-methoxyimino-2-[(oxazol-4-ylmethyl)-amino]-ethyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4256		4
	N-[3-(4'-{[3-(1-Benzyl-1H-[1,2,3]triazol-4-yl)-propylamino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4257		0.5
	N-[3-(2-Fluoro-4'-{[(2-fluoro-pyridin-3-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

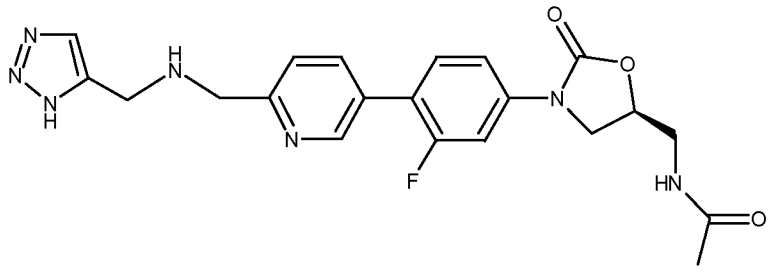
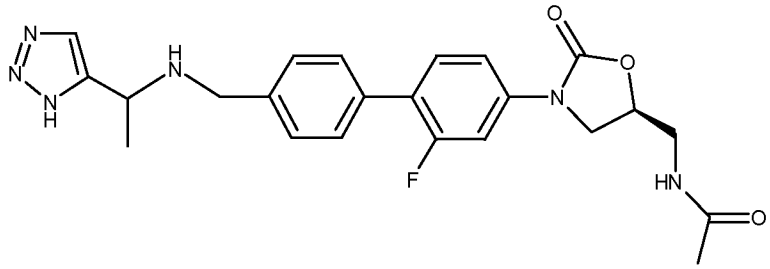
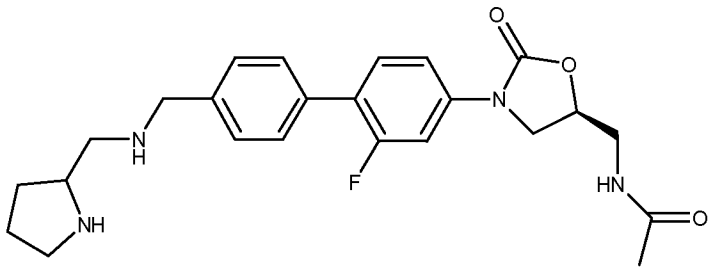
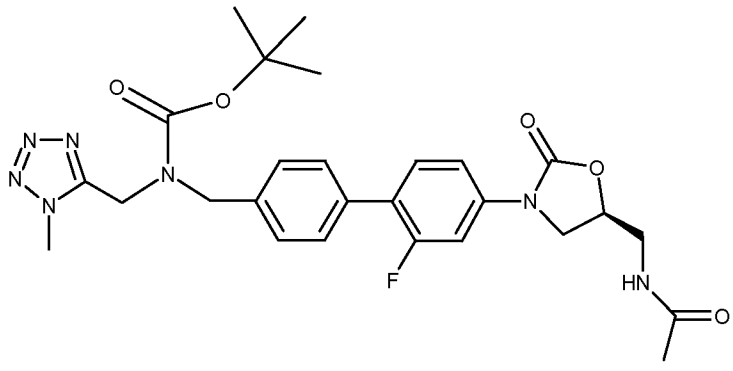
4258		4
	N-[3-(2-Fluoro-4'-{[3-(3H-[1,2,3]triazol-4-yl)-propylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4259		4
	N-(3-{2-Fluoro-4'-[(2-pyrrolidin-1-yl-ethylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4260		4
	N-[3-(3-Fluoro-4-morpholin-4-yl-phenyl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-3-(5-pyrimidin-2-yl-pyridin-2-yl)-propionamide	
4261		8
	N-[3-(2-Fluoro-2'-methoxy-4'-{[(pyridin-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

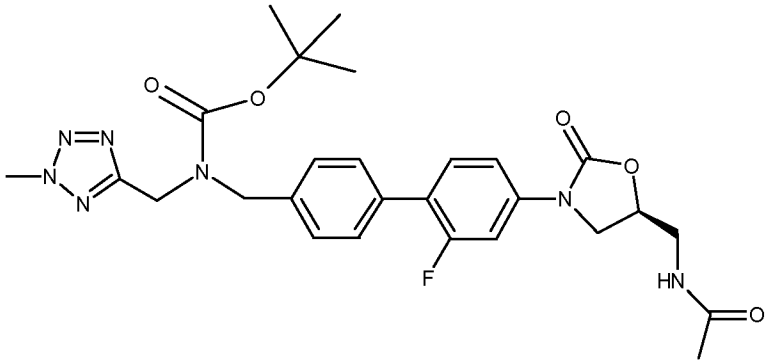
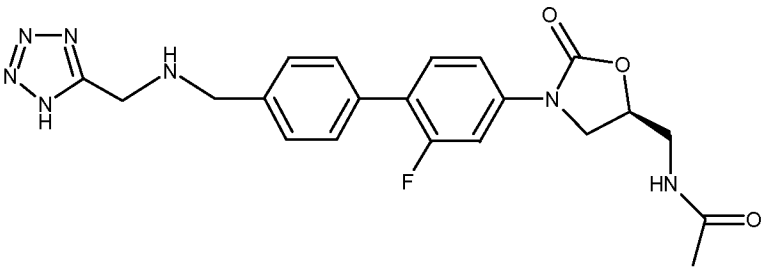
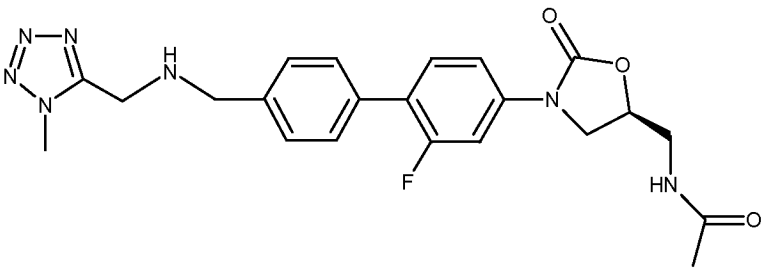
4262		2
	N-(3-{2-Fluoro-4'-[(2-[1,2,3]triazol-1-yl-ethylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4263		2
	N-{3-[4'-(Benzyloxyamino-methyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4264		4
	N-(3-{2-Fluoro-4'-[(3-[1,2,3]triazol-1-yl-propylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4265		4
	N-[3-(4'-{[Benzyloxy-(3-fluoro-propyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

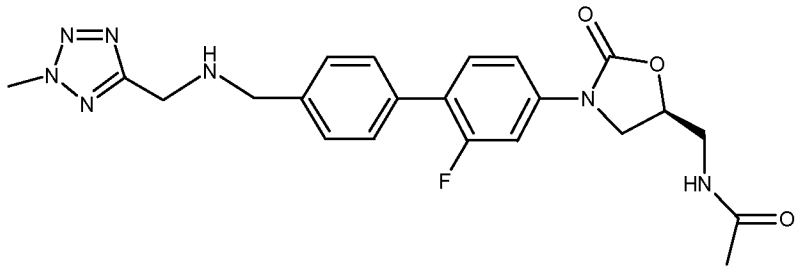
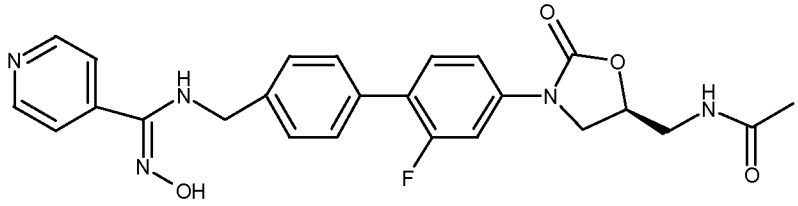
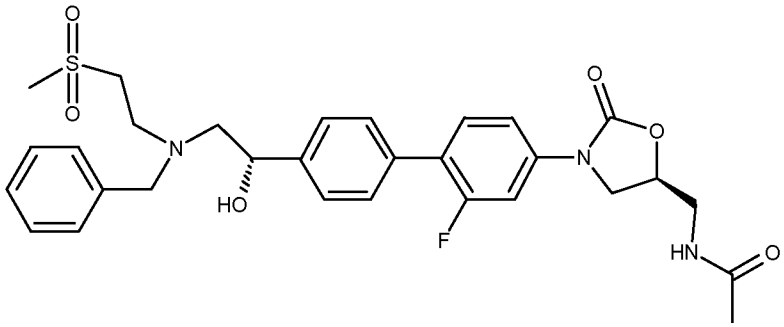
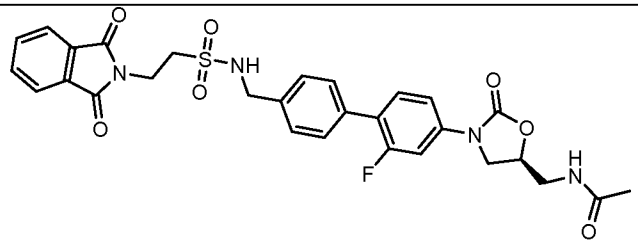
4266		4
	N-[3-(2-Fluoro-4'-{[2-(3H-[1,2,3]triazol-4-yl)-ethylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4267		0.25
	N-[3-(2-Fluoro-4'-{[(3H-[1,2,3]triazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4268		0.25
	3-(2-Fluoro-4'-{[(3H-[1,2,3]triazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-5-(R)-[1,2,3]triazol-1-ylmethyl-oxazolidin-2-one	
4269		2
	N-[3-(2-Fluoro-4'-{[(5-methyl-3H-[1,2,3]triazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

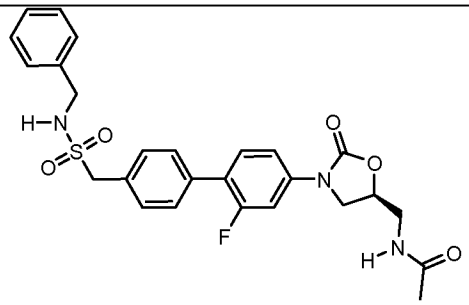
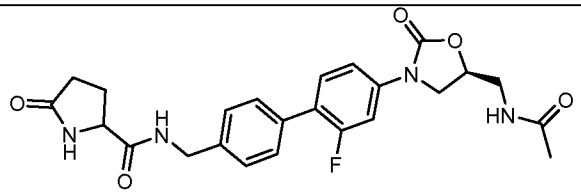
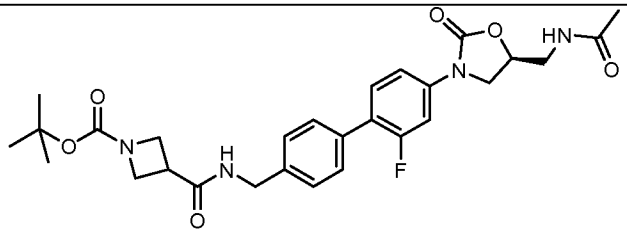
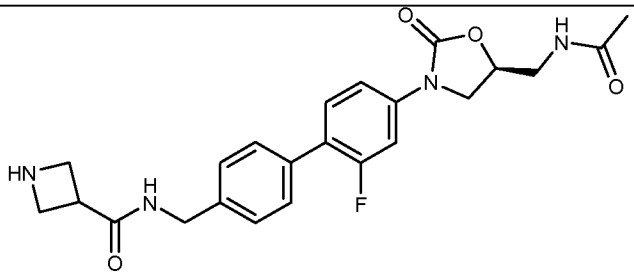
4270		4
	N-[3-(4'-{[Bis-(5-methyl-3H-[1,2,3]triazol-4-ylmethyl)-amino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4271		0.25
	N-(3-{2-Fluoro-4'-[N'-(4-methyl-[1,2,3]thiadiazole-carbonyl)-hydrazinomethyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4272		0.25
	N-[3-(2-Fluoro-4'-{[(3-methyl-3H-[1,2,3]triazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4273		0.25

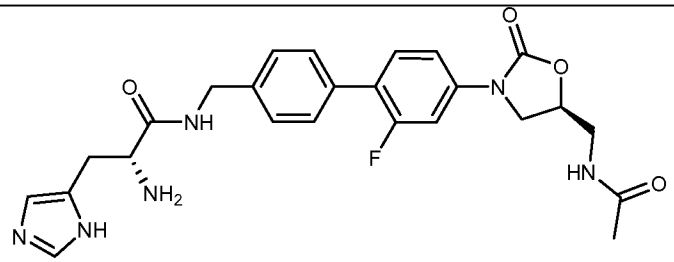
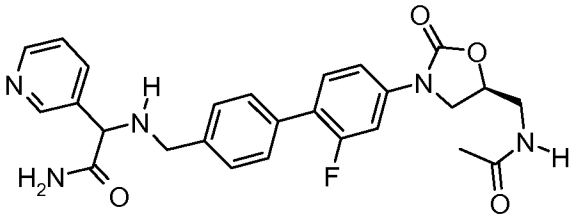
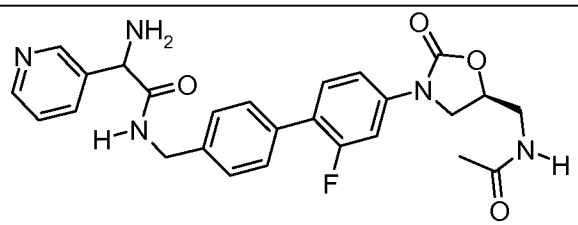
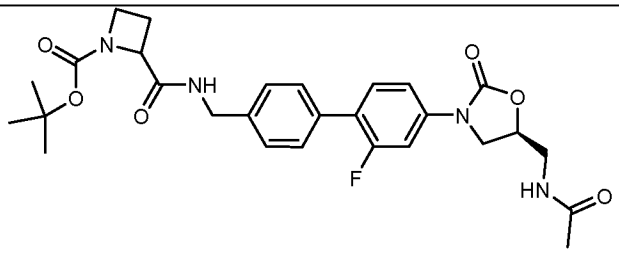
	N-[3-(2-Fluoro-4'-{[(2-methyl-2H-[1,2,3]triazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4274		2
	N-(3-{2-Fluoro-4'-[(3-fluoro-2-[1,2,3]triazol-1-yl-propylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4275		0.5
	N-[3-(2-Fluoro-4'-{[2-(4-fluoro-phenyl)-2-(R/S)-hydroxy-ethylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4276		0.25
	N-[3-(2-Fluoro-4'-{[methyl-(3H-[1,2,3]triazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

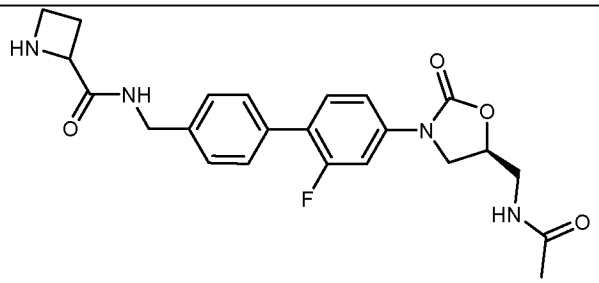
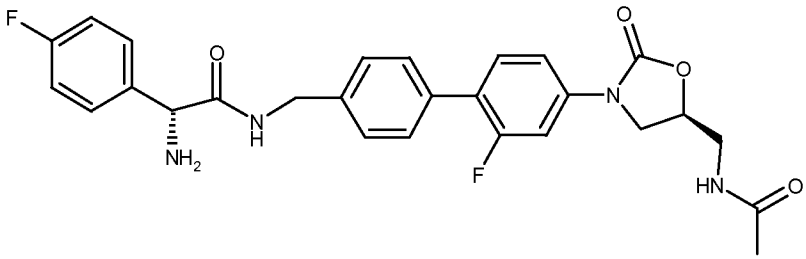
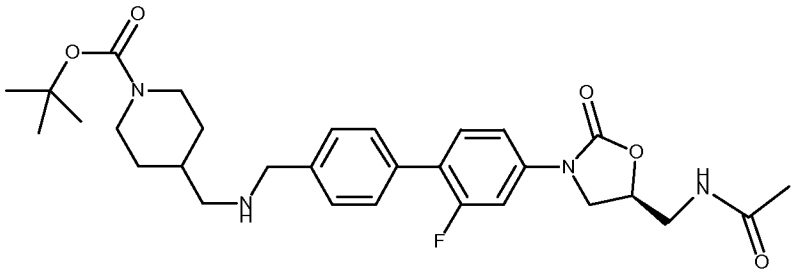
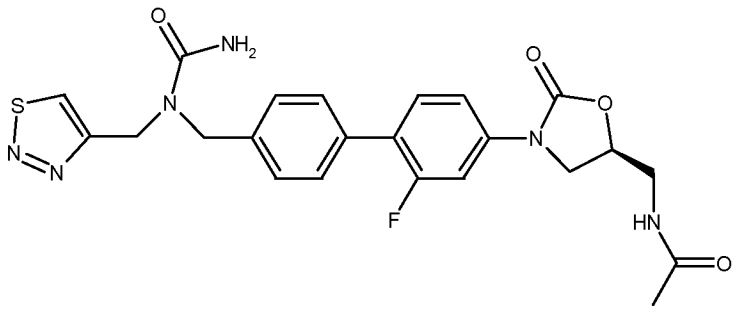
4277		4
	N-{3-[3-Fluoro-4-(6-{[(3H-[1,2,3]triazol-4-ylmethyl)-amino]-methyl}-pyridin-3-yl)-phenyl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4278		2
	N-[3-(2-Fluoro-4'-{[1-(R/S)-(3H-[1,2,3]triazol-4-yl)-ethylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4279		4
	N-[3-(2-Fluoro-4'-{[(pyrrolidin-2-(R/S)-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
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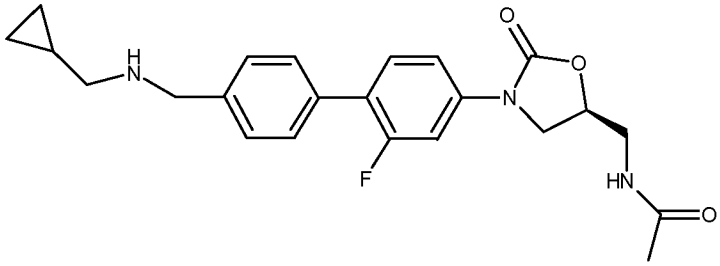
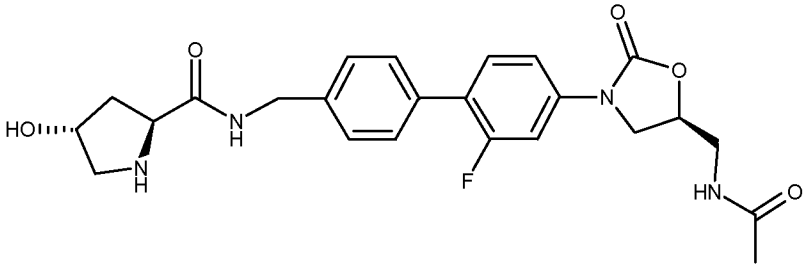
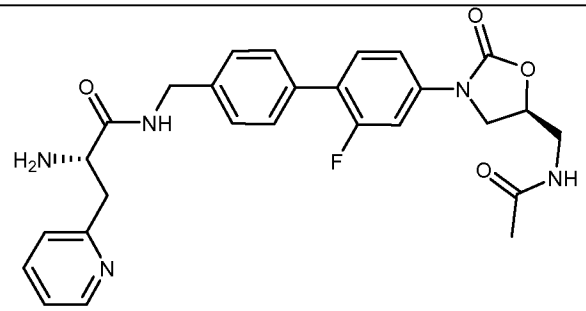
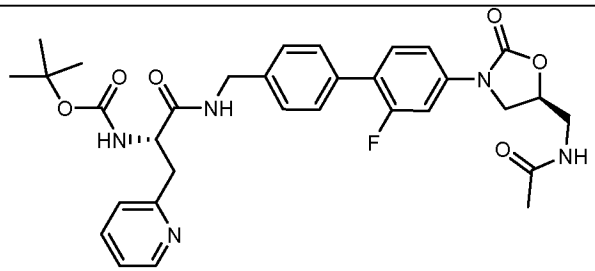
	{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro biphenyl-4-ylmethyl}-(1-methyl-1H-tetrazol-5-ylmethyl)-carbamic acid tert-butyl ester	
4281		2
	{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-(2-methyl-2H-tetrazol-5-ylmethyl)-carbamic acid tert-butyl ester	
4282		16
	N-[3-(2-Fluoro-4'-{[(1H-tetrazol-5-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4283		0.25
	N-[3-(2-Fluoro-4'-{[(1-methyl-1H-tetrazol-5-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

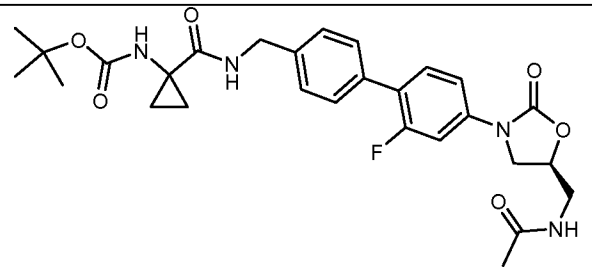
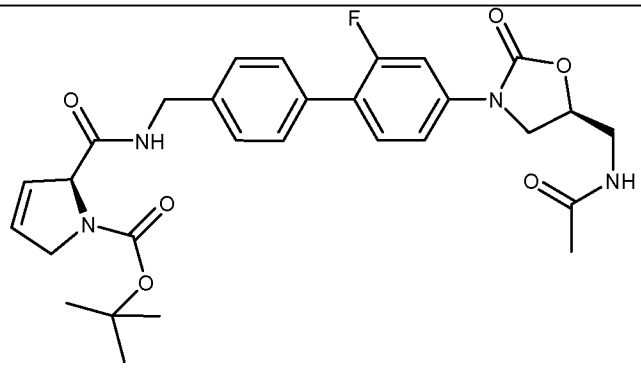
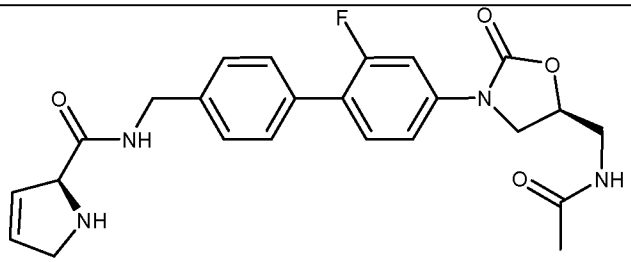
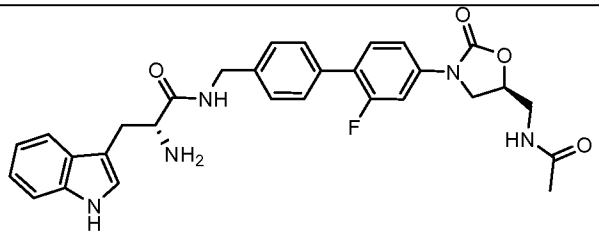
4284		0.25
	N-[3-(2-Fluoro-4'-{[(2-methyl-2H-tetrazol-5-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4285		8
	N-[3-(2-Fluoro-4'-{[(N-hydroxy-pyridine-4-carboximidoyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4286		2
	N-[3-(4'-{2-[Benzyl-(2-methanesulfonyl-ethyl)-amino]-1-(S)-hydroxy-ethyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
4287		8
	N-[3-(4'-{[2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-ethanesulfonylamino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

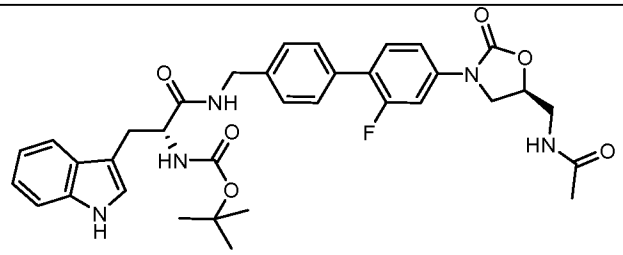
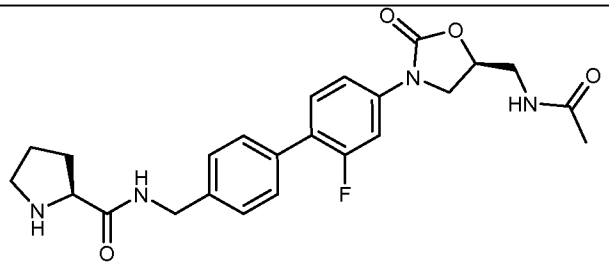
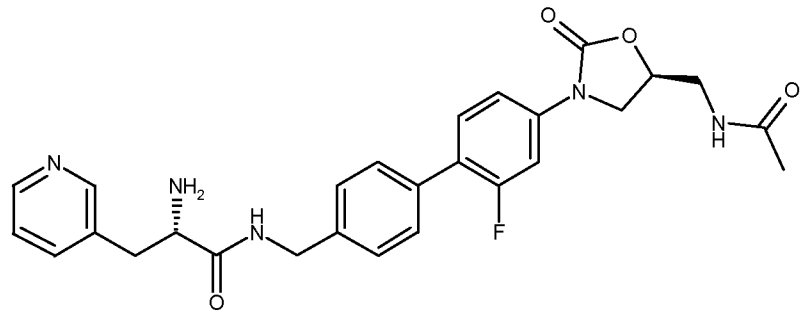
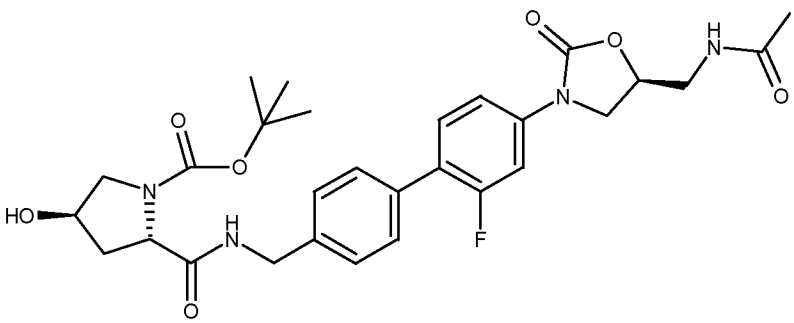
4288		128
	N-{3-[4'-(Benzylsulfamoyl-methyl)-2-fluoro-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
4289		8
	5-Oxo-pyrrolidine-2-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	
4290		16
	3-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-carbamoyl)-azetidine-1-carboxylic acid tert-butyl ester	
4291		8
	Azetidine-3-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	

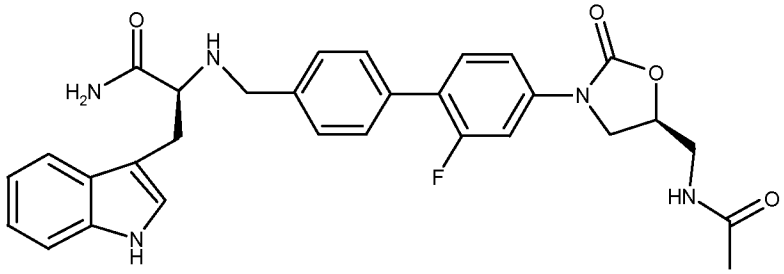
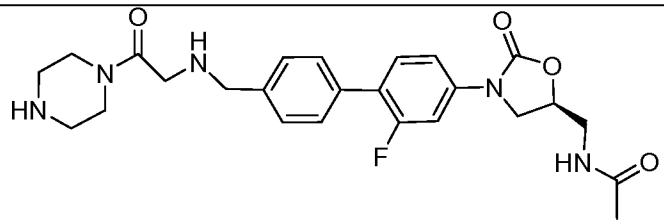
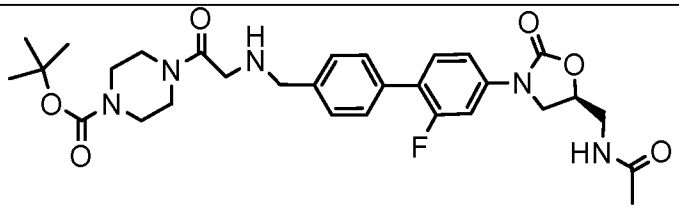
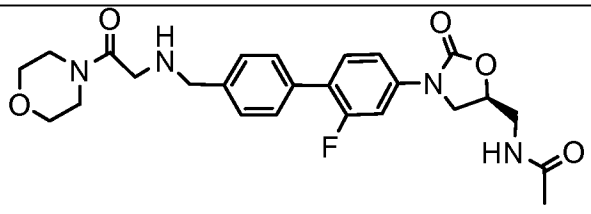
4292		16
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-2-(R)-amino-3-(3H-imidazol-4-yl)-propionamide	
4293		4
	2-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-2-pyridin-3-yl-acetamide	
4294		4
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-2-amino-2-pyridin-3-yl-acetamide	
4295		8
	2-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-carbamoyl)-azetidine-1-carboxylic acid tert-butyl ester	

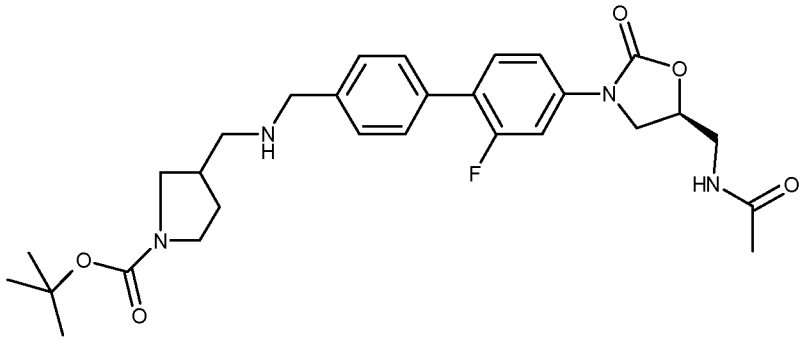
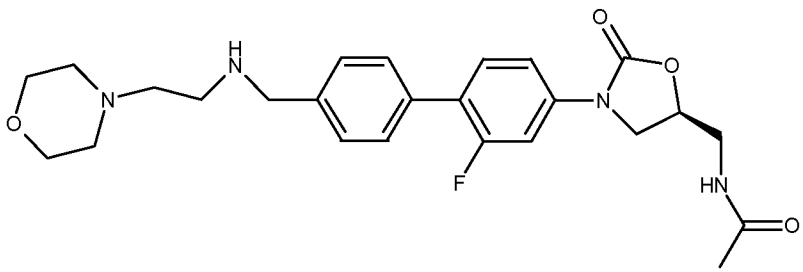
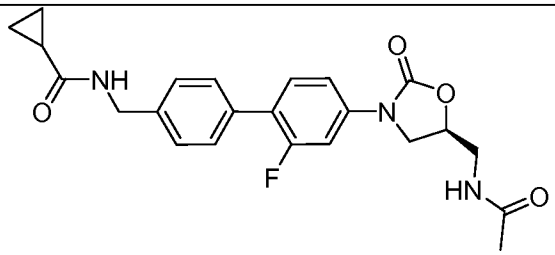
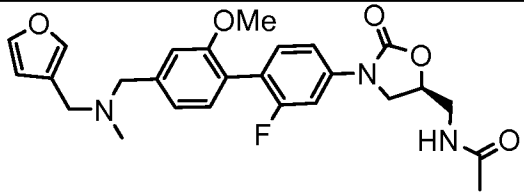
4296		2
	Azetidine-2-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	
4297		2
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-2-(R)-amino-2-(4-fluoro-phenyl)-acetamide	
4298		8
	4-[({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-methyl]-piperidine-1-carboxylic acid tert-butylester	
4299		2
	N-{3-[2-Fluoro-4'-(1-[1,2,3]thiadiazol-4-ylmethyl-ureidomethyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-	

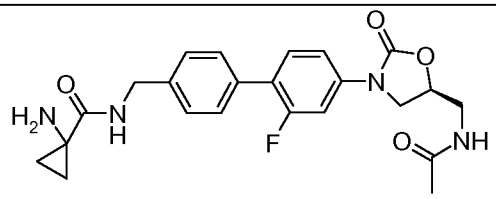
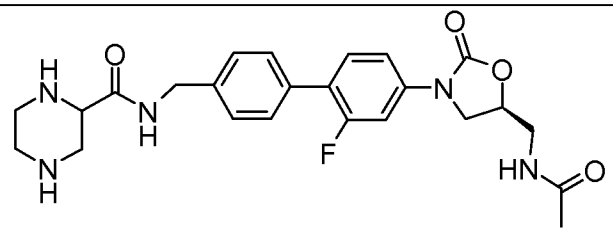
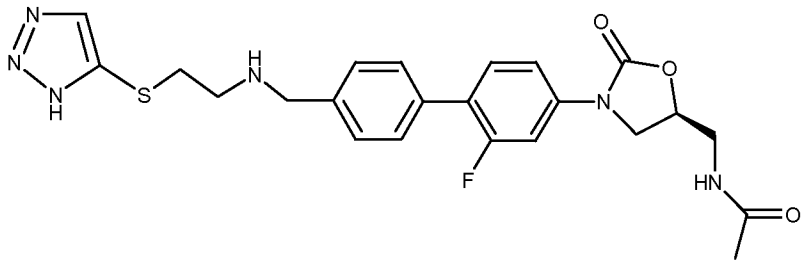
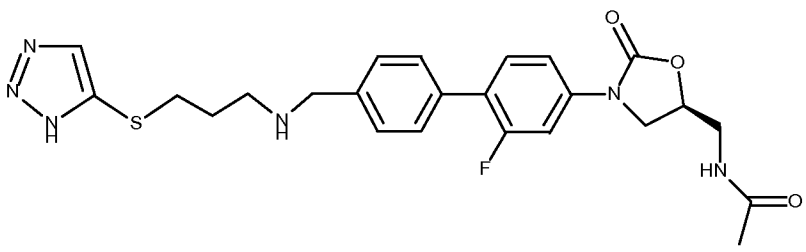
	ylmethyl}-acetamide	
4300		4
	N-(3-{4'-[(Cyclopropylmethyl-amino)-methyl]-2-fluoro-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4301		8
	4-(R)-Hydroxy-pyrrolidine-2-(S)-carboxylicacid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	
4302		8
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-2-(S)-amino-3-pyridin-2-yl-propionamide	
4303		8
	[1-(S)-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-carbamoyl)-2-pyridin-2-yl-	

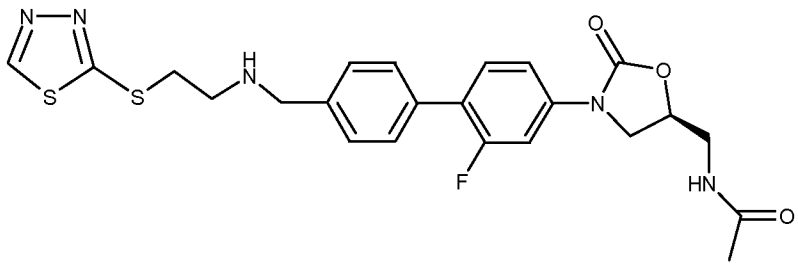
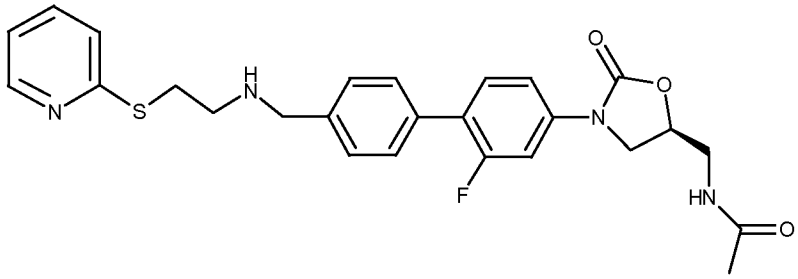
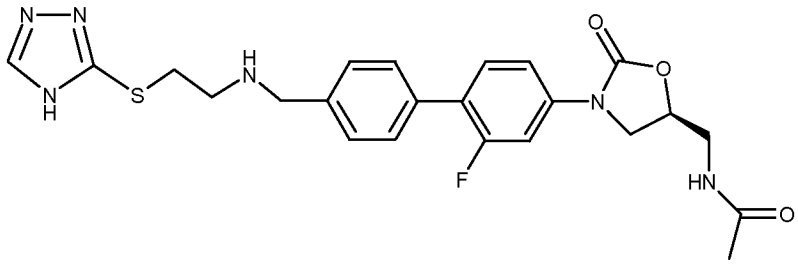
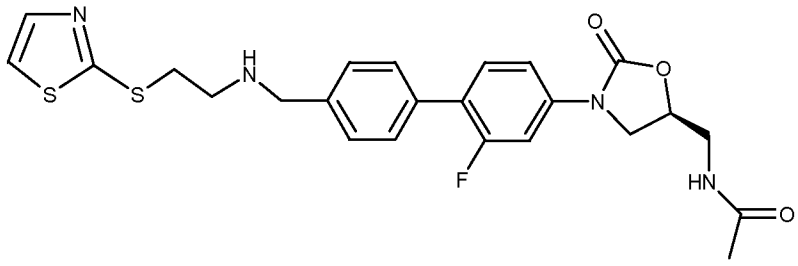
	ethyl]-carbamic acid tert-butyl ester	
4304		16
	[1-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-carbamoyl)-cyclopropyl]-carbamic acid tert-butyl ester	
4305		16
	2-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-carbamoyl)-2,5-dihydro-pyrrole-1-(S)-carboxylic acid tert-butylester	
4306		2
	2,5-Dihydro-1H-pyrrole-2-(S)-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	
4307		2
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-2-(R)-amino-3-(1H-indol-3-yl)-	

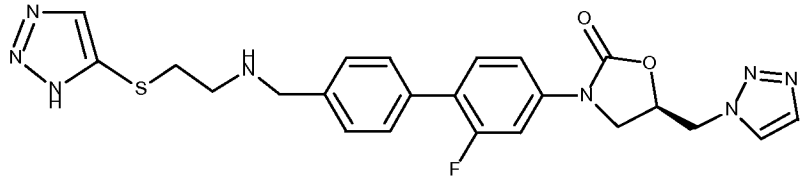
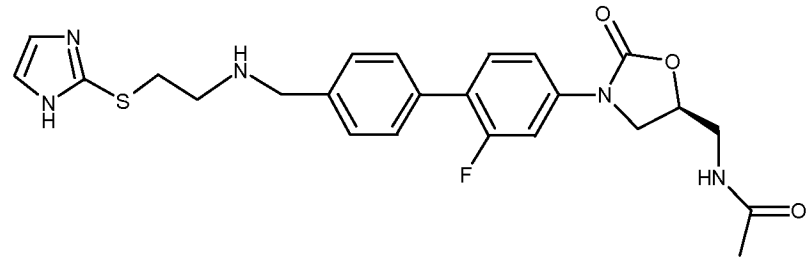
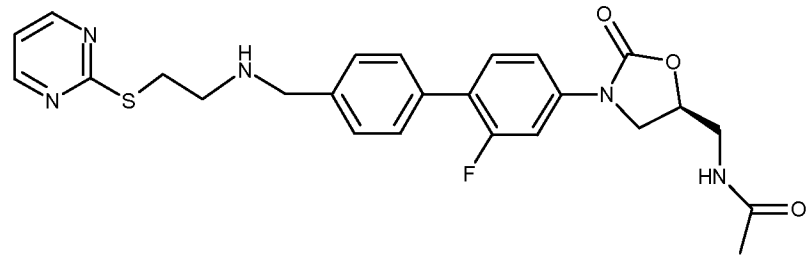
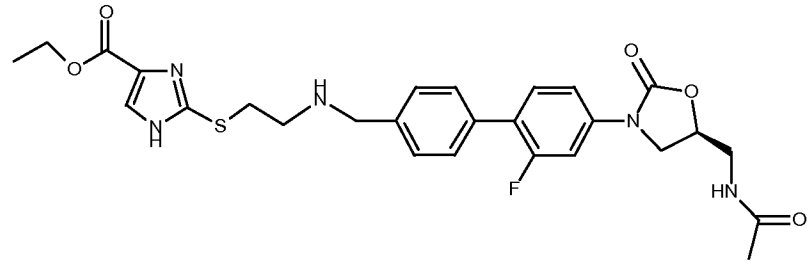
	propionamide	
4308		128
	[1-(R)-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-carbamoyl)-2-(1H-indol-3-yl)-ethyl]-carbamic acid tert-butyl ester	
4309		8
	Pyrrolidine-2-(S)-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	
4310		4
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-2-(R)-amino-3-pyridin-3-yl-propionamide	
4311		16

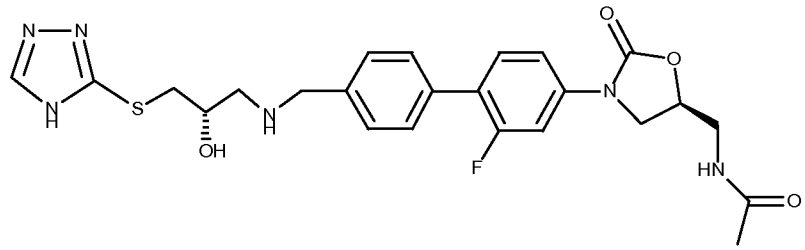
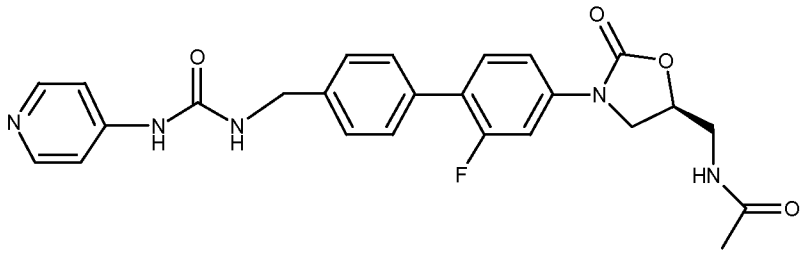
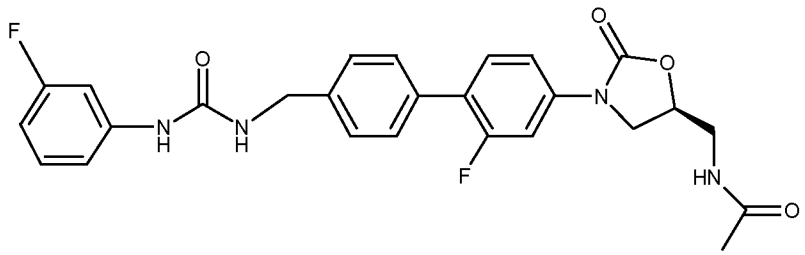
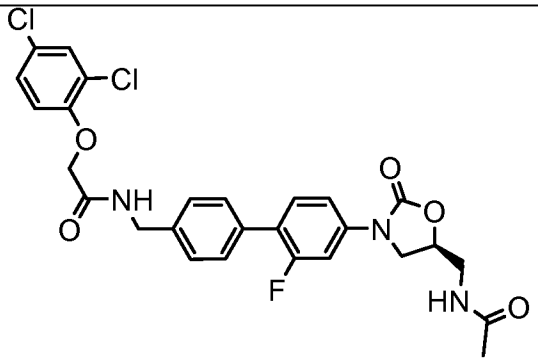
	2-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-carbamoyl)-4-(R)-hydroxy-pyrrolidine-1-(S)-carboxylic acid tert-butyl ester	
4312		2
	2-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-3-(S)-(1H-indol-3-yl)-propionamide	
	2-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-3-(1H-imidazol-4-yl)-propionamide	
4314		4
	N-(3-{2-Fluoro-4'-[(2-oxo-2-piperazin-1-yl-ethylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4315		4
	4-[2-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-acetyl]-piperazine-1-carboxylic acid tert-butyl ester	
4316		4

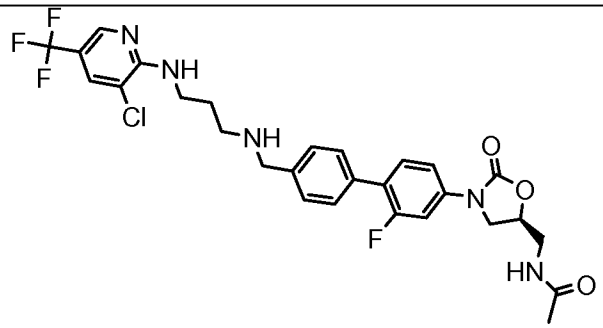
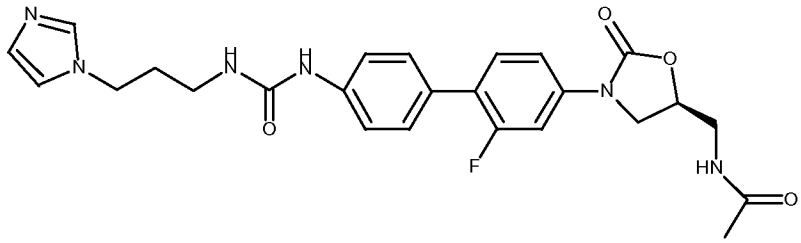
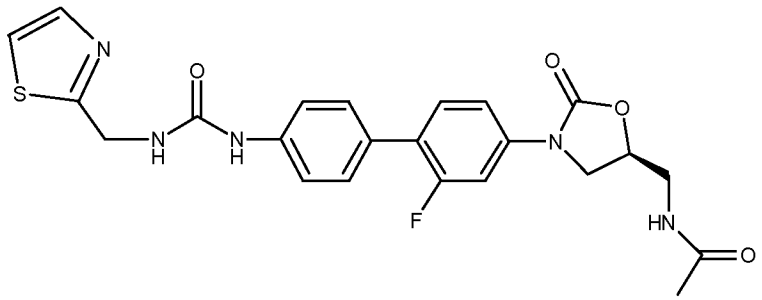
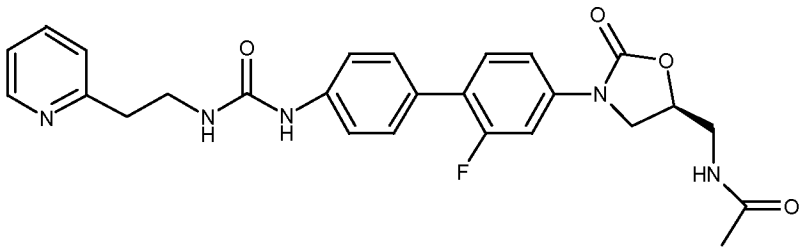
	N-(3-{2-Fluoro-4'-[(2-morpholin-4-yl-2-oxo-ethylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4317		16
	3-[({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-methyl]-pyrrolidine-1-carboxylic acid tert-butyl ester	
4318		16
	N-(3-{2-Fluoro-4'-[(2-morpholin-4-yl-ethylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
4319		16
	Cyclopropanecarboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	
4320		32
	N-(3-{2-Fluoro-4'-[(furan-3-ylmethyl-methyl-amino)-methyl]-2'-methoxy-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-	

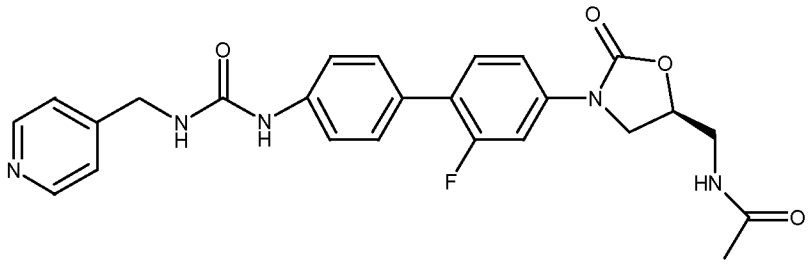
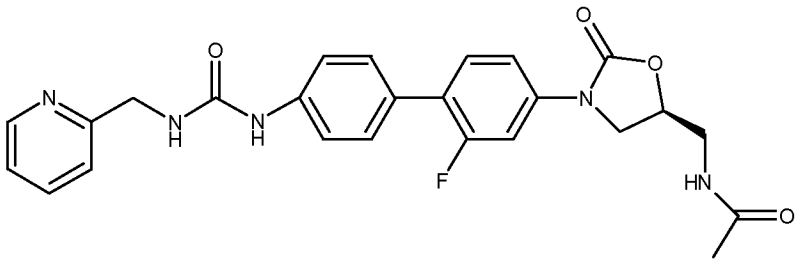
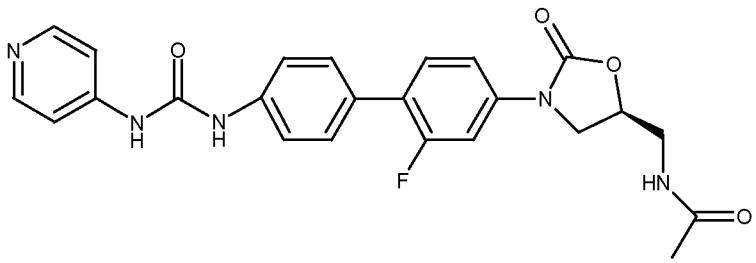
	acetamide	
4321		2
	1-Amino-cyclopropanecarboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	
4322		2
	Piperazine-2-(R/S)-carboxylic acid {4'-[5-(S)-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amide	
5001		1
	N-[3-(2-Fluoro-4'-{[2-(3H-[1,2,3]triazol-4-ylsulfanyl)-ethylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
5002		0.25
	N-[3-(2-Fluoro-4'-{[3-(3H-[1,2,3]triazol-4-ylsulfanyl)-propylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	

5003		1
	N-[3-(2-Fluoro-4'-{[2-([1,3,4]thiadiazol-2-ylsulfanyl)-ethylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
5004		1
	N-[3-(2-Fluoro-4'-{[2-(pyridin-2-ylsulfanyl)-ethylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
5005		0.5
	N-[3-(2-Fluoro-4'-{[2-(4H-[1,2,4]triazol-3-ylsulfanyl)-ethylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
5006		1
	N-[3-(2-Fluoro-4'-{[2-(thiazol-2-ylsulfanyl)-ethylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-	

	acetamide	
5007		0.25
	3-(2-Fluoro-4'-{[2-(3H-[1,2,3]triazol-4-ylsulfanyl)-ethylamino]-methyl}-biphenyl-4-yl)-5-(R)-[1,2,3]triazol-1-ylmethyl-oxazolidin-2-one	
5008		2
	N-[3-(2-Fluoro-4'-{[2-(1H-imidazol-2-ylsulfanyl)-ethylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
5009		1
	N-[3-(2-Fluoro-4'-{[2-(pyrimidin-2-ylsulfanyl)-ethylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
5010		4
	2-[2-({4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-amino)-ethylsulfanyl]-1H-imidazole-4-carboxylic acid ethyl ester	

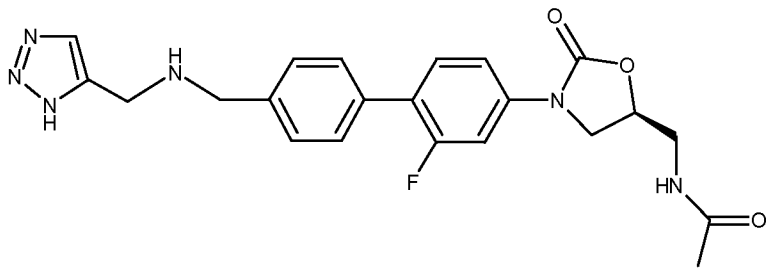
5011		4
	N-[3-(2-Fluoro-4'-{[2-(S)-(hydroxy-3-(4H-[1,2,4]triazol-3-ylsulfanyl)-propylamino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
5012		2
	N-(3-{2-Fluoro-4'-[(3-pyridin-4-yl-ureido)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
5013		32
	N-(3-{2-Fluoro-4'-[3-(3-fluoro-phenyl)-ureidomethyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
5014		16
	N-{4'-[5-(S)-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-2-(2,4-dichloro-phenoxy)-acetamide	

5015		4
	N-[3-(4'-{[3-(3-Chloro-5-trifluoromethyl-pyridin-2-ylamino)-propylamino]-methyl}-2-fluoro-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide	
6001		16
	N-(3-{2-Fluoro-4'-[3-(3-imidazol-1-yl-propyl)-ureido]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	
6002		2
	N-{3-[2-Fluoro-4'-(3-thiazol-2-ylmethyl-ureido)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
6003		2
	N-(3-{2-Fluoro-4'-[3-(2-pyridin-2-yl-ethyl)-ureido]-biphenyl-4-yl}-2-oxo-oxazolidin-5-(S)-ylmethyl)-acetamide	

6004		1
	N-{3-[2-Fluoro-4'-(3-pyridin-4-ylmethyl-ureido)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
6005		1
	N-{3-[2-Fluoro-4'-(3-pyridin-2-ylmethyl-ureido)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	
6006		128
	N-{3-[2-Fluoro-4'-(3-pyridin-4-yl-ureido)-biphenyl-4-yl]-2-oxo-oxazolidin-5-(S)-ylmethyl}-acetamide	

or a pharmaceutically, acceptable salt, ester, or prodrug thereof.

[0077] An antibiotic compound particularly useful in the invention is radezolid (compound 4267, structure shown below), or a pharmaceutically acceptable salt, ester, tautomer, or prodrug thereof:



[0078] Other names for the compound radezolid include:

RX-1741;

N-[3-(2-Fluoro-4'-{[(3H-[1,2,3]triazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide;

N-[3-(2-Fluoro-4'-{[(1H-[1,2,3]triazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-(S)-ylmethyl]-acetamide;

N-{[(5S)-3-(2-fluoro-4′-{[(1H-1,2,3-triazol-5-ylmethyl)amino]methyl}biphenyl-4-yl)-2-oxo-1,3-oxazolidin-5-yl]methyl}acetamide;

869884-78-6;

UNII-53PC6LO35W; and

(S)-N-((3-(4'-((((1H-1,2,3-triazol-5-yl)methyl)amino)methyl)-2-fluoro-[1,1'-biphenyl]-4-yl)-2-oxooxazolidin-5-yl)methyl)acetamide.

[0079] As used herein, the term radezolid can also be used to refer to tautomers of radezolid, for example, the compound (S)-N-((3-(4'-((((1H-1,2,3-triazol-4-yl)methyl)amino)methyl)-2-fluoro-[1,1'-biphenyl]-4-yl)-2-oxooxazolidin-5-yl)methyl)acetamide

Other Aspects of the Compounds of the Present Invention

[0080] Antibiotic compounds designed, selected and/or optimized for use in the present invention, after being produced, can be characterized using a variety of assays known to those skilled in the art to determine whether the compounds have biological activity. For example, the antibiotic compounds can be characterized by conventional assays, including but not limited to those assays described below, to determine whether the compounds have a predicted activity, binding activity and/or binding specificity.

[0081] Furthermore, high-throughput screening can be used to speed up analysis using such assays. As a result, it can be possible to screen rapidly the molecules described herein for activity, for example as anti-bacterial. Also, it can be possible to assay how the compounds interact with a ribosome or ribosomal subunit and/or are effective as modulators (for example, inhibitors) of protein synthesis using techniques known in the art. General methodologies for performing high-throughput screening are described, for example, in Devlin, *High Throughput Screening*, (Marcel Dekker, 1998); and U.S. Patent No. 5,763,263. High-throughput assays can use one or more different assay techniques including, but not limited to, those described below.

[0082] (1) *Surface Binding Studies*. A variety of binding assays can be useful in screening new molecules for their binding activity. One approach includes surface plasmon resonance

(SPR) that can be used to evaluate the binding properties of molecules of interest with respect to a ribosome, ribosomal subunit or a fragment thereof.

[0083] SPR methodologies measure the interaction between two or more macromolecules in real-time through the generation of a quantum-mechanical surface plasmon. One device, (BIAcore Biosensor RTM from Pharmacia Biosensor, Piscataway, N.J.) provides a focused beam of polychromatic light to the interface between a gold film (provided as a disposable biosensor "chip") and a buffer compartment that can be regulated by the user. A 100 nm thick "hydrogel" composed of carboxylated dextran that provides a matrix for the covalent immobilization of analytes of interest is attached to the gold film. When the focused light interacts with the free electron cloud of the gold film, plasmon resonance is enhanced. The resulting reflected light is spectrally depleted in wavelengths that optimally evolved the resonance. By separating the reflected polychromatic light into its component wavelengths (by means of a prism), and determining the frequencies that are depleted, the BIAcore establishes an optical interface which accurately reports the behavior of the generated surface plasmon resonance. When designed as above, the plasmon resonance (and thus the depletion spectrum) is sensitive to mass in the evanescent field (which corresponds roughly to the thickness of the hydrogel). If one component of an interacting pair is immobilized to the hydrogel, and the interacting partner is provided through the buffer compartment, the interaction between the two components can be measured in real time based on the accumulation of mass in the evanescent field and its corresponding effects of the plasmon resonance as measured by the depletion spectrum. This system permits rapid and sensitive real-time measurement of the molecular interactions without the need to label either component.

[0084] (2) *Fluorescence Polarization*. Fluorescence polarization (FP) is a measurement technique that can readily be applied to protein-protein, protein-ligand, or RNA-ligand interactions in order to derive IC_{50}s and K_ds of the association reaction between two molecules. In this technique one of the molecules of interest is conjugated with a fluorophore. This is generally the smaller molecule in the system (in this case, the compound of interest). The sample mixture, containing both the ligand-probe conjugate and the ribosome, ribosomal subunit or fragment thereof, is excited with vertically polarized light. Light is absorbed by the probe fluorophores, and re-emitted a short time later. The degree of polarization of the emitted light is measured. Polarization of the emitted light is dependent on several factors, but most importantly on viscosity of the solution and on the apparent molecular weight of the fluorophore. With proper controls, changes in the degree of polarization of the emitted light depends only on changes in

the apparent molecular weight of the fluorophore, which in-turn depends on whether the probe-ligand conjugate is free in solution, or is bound to a receptor. Binding assays based on FP have a number of important advantages, including the measurement of IC_{50}s and Kds under true homogenous equilibrium conditions, speed of analysis and amenity to automation, and ability to screen in cloudy suspensions and colored solutions.

[0085] (3) *Protein Synthesis*. It is contemplated that, in addition to characterization by the foregoing biochemical assays, the compound of interest can also be characterized as a modulator (for example, an inhibitor of protein synthesis) of the functional activity of the ribosome or ribosomal subunit.

[0086] Furthermore, more specific protein synthesis inhibition assays can be performed by administering the compound to a whole organism, tissue, organ, organelle, cell, a cellular or subcellular extract, or a purified ribosome preparation and observing its pharmacological and inhibitory properties by determining, for example, its inhibition constant (IC_{50}) for inhibiting protein synthesis. Incorporation of ^{3}H leucine or ^{35}S methionine, or similar experiments can be performed to investigate protein synthesis activity. A change in the amount or the rate of protein synthesis in the cell in the presence of a molecule of interest indicates that the molecule is a modulator of protein synthesis. A decrease in the rate or the amount of protein synthesis indicates that the molecule is an inhibitor of protein synthesis.

[0087] Furthermore, the antibiotic compounds can be assayed for anti-proliferative or anti-infective properties on a cellular level. For example, where the target organism is a microorganism, the activity of compounds of interest can be assayed by growing the microorganisms of interest in media either containing or lacking the compound. Growth inhibition can be indicative that the molecule could be acting as a protein synthesis inhibitor. More specifically, the activity of the compounds of interest against bacterial pathogens can be demonstrated by the ability of the compound to inhibit growth of defined strains of human pathogens, particularly *Propionibacterium acnes* and *Propionibacterium granulosum* and resistant strains thereof. For this purpose, a panel of bacterial strains can be assembled to include a variety of target pathogenic species, some containing resistance mechanisms that have been characterized. Use of such a panel of organisms permits the determination of structure-activity relationships not only in regards to potency and spectrum, but also with a view to obviating resistance mechanisms. The assays can be performed in microtiter trays according to conventional methodologies as published by The National Committee for Clinical Laboratory Standards (NCCLS) guidelines (NCCLS. M7-A5-Methods for Dilution Antimicrobial

Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard-Fifth Edition. NCCLS Document M100-S12/M7 (ISBN 1-56238-394-9)).

4. Formulation and Administration

[0088] The methods of the present invention can be practiced by delivering the antibiotic compounds of the present invention using any suitable carrier. The dose of antibiotic compound, mode of administration and use of suitable carrier will depend upon the intended patient or subject and the targeted microorganism, *e.g.*, the target bacterial organism. The formulations, both for human medical use and veterinary use, of the antibiotic compounds according to the present invention typically include such antibiotic compounds in association with a pharmaceutically acceptable carrier.

[0089] The carrier(s) should be "acceptable" in the sense of being compatible with compounds of the present invention and not deleterious to the recipient. Pharmaceutically acceptable carriers, in this regard, are intended to include any and all solvents, dispersion media, coatings, absorption delaying agents, and the like, compatible with pharmaceutical administration. The use of such media and agents for pharmaceutically active substances is known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds (identified or designed according to the invention and/or known in the art) also can be incorporated into the compositions. The formulations can conveniently be presented in dosage unit form and can be prepared by any of the methods well known in the art of pharmacy/microbiology. In general, some formulations are prepared by bringing the compound into association with a liquid carrier or a finely divided solid carrier or both, and then, if necessary, shaping the product into the desired formulation.

[0090] In some embodiments, the methods, uses and compositions for use disclosed herein can further include an additional active agent. In some embodiments, the additional active agent is selected from the group consisting of salicylic acid, benzoyl peroxide, glycolic acid, lactic acid, citric acid, lactobionic acid, triclosan, triclocarban and combinations thereof. Other exemplary agents which can be used in accordance with the present disclosure include those discussed in Decker, A.; Graber, E. M. *J. Clin. Aesthet. Dermatol.* **2012,** *5*(5), 32-40, the contents of which are hereby incorporated by reference in their entirety.

[0091] A pharmaceutical composition of the invention can be formulated to be compatible with its intended route of administration. These can include solids and semisolids. Solutions or

suspensions can include the following components: a sterile diluent such as water, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. The pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide.

[0092] A wide variety of formulations and administration methods can be found in S.K. Niazi, ed., Handbook of Pharmaceutical Formulations, Vols. 1-6 [Vol. 1 Compressed Solid Products, Vol. 2 Uncompressed Drug Products, Vol. 3 Liquid Products, Vol. 4 Semi-Solid Products, Vol. 5 Over the Counter Products, and Vol. 6 Sterile Products], CRC Press, April 27, 2004.

[0093] Useful solutions for oral or parenteral administration can be prepared by any of the methods well known in the pharmaceutical art, described, for example, in *Remington's Pharmaceutical Sciences*, 18th ed. (Mack Publishing Company, 1990). Formulations for parenteral administration can also include glycocholate for buccal administration, methoxysalicylate for rectal administration, or citric acid for vaginal administration. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic. Suppositories for rectal administration also can be prepared by mixing the drug with a non-irritating excipient such as cocoa butter, other glycerides, or other compositions which are solid at room temperature and liquid at body temperatures. Formulations also can include, for example, polyalkylene glycols such as polyethylene glycol, oils of vegetable origin, and hydrogenated naphthalenes. Formulations for direct administration can include glycerol and other compositions of high viscosity. Other potentially useful parenteral carriers for these drugs include ethylene-vinyl acetate copolymer particles, osmotic pumps, implantable infusion systems, and liposomes. Formulations for inhalation administration can contain as excipients, for example, lactose, or can be aqueous solutions containing, for example, polyoxyethylene-9-lauryl ether, glycocholate and deoxycholate, or oily solutions for administration in the form of nasal drops, or as a gel to be applied intranasally. Retention enemas also can be used for rectal delivery.

[0094] Formulations of the present invention suitable for oral administration can be in the form of: discrete units such as capsules, gelatin capsules, sachets, tablets, troches, or lozenges, each containing a predetermined amount of the drug; a powder or granular composition; a

solution or a suspension in an aqueous liquid or non-aqueous liquid; or an oil-in-water emulsion or a water-in-oil emulsion. The drug can also be administered in the form of a bolus, electuary or paste. A tablet can be made by compressing or molding the drug optionally with one or more accessory ingredients. Compressed tablets can be prepared by compressing, in a suitable machine, the drug in a free-flowing form such as a powder or granules, optionally mixed by a binder, lubricant, inert diluent, surface active or dispersing agent. Molded tablets can be made by molding, in a suitable machine, a mixture of the powdered drug and suitable carrier moistened with an inert liquid diluent.

[0095] Oral compositions generally include an inert diluent or an edible carrier. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients. Oral compositions prepared using a fluid carrier for use as a mouthwash include the compound in the fluid carrier and are applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose; a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

[0096] Formulations suitable for topical administration, including eye treatment, include liquid or semi-liquid preparations such as liniments, lotions, gels, applicants, oil-in-water or water-in-oil emulsions such as creams, ointments or pastes; foams; or solutions or suspensions such as drops. Formulations for topical administration to the skin surface can be prepared by dispersing the drug with a dermatologically acceptable carrier such as a lotion, cream, ointment or soap. Useful are carriers capable of forming a film or layer over the skin to localize application and inhibit removal. For topical administration to internal tissue surfaces, the agent can be dispersed in a liquid tissue adhesive or other substance known to enhance adsorption to a tissue surface. For example, hydroxypropylcellulose or fibrinogen/thrombin solutions can be used to advantage. Alternatively, tissue-coating solutions, such as pectin-containing formulations can be used.

[0097] Additionally, the carrier for a topical formulation can be in the form of a hydroalcoholic system (*e.g.* liquids and gels), an anhydrous oil or silicone based system, or an emulsion system, including, but not limited to, oil-in-water, water-in-oil, water-in-oil-in-water,

and oil-in-water-in-silicone emulsions. The emulsions can cover a broad range of consistencies including thin lotions (which can also be suitable for spray or aerosol delivery), creamy lotions, light creams, heavy creams, and the like. The emulsions can also include microemulsion systems. Other suitable topical carriers include anhydrous solids and semisolids (such as gels and sticks); and aqueous based mousse systems. Nonlimiting examples of the topical carrier systems useful in the present invention are described in the following four references, all of which are incorporated herein by reference in their entirety: "Sun Products Formulary", Cosmetics & Toiletries, vol. 105, pp. 122-139 (December 1990); "Sun Products Formulary", Cosmetics & Toiletries, vol. 102, pp. 117-136 (March 1987); U.S. Pat. No. 4,960,764 to Figueroa et al., issued Oct. 2, 1990; and U.S. Pat. No. 4,254,105 to Fukuda et al., issued Mar. 3, 1981.

[0098] The pharmaceutically-acceptable topical carriers, in total, typically comprise from about 0.1% to about 99.8% by weight of the compositions useful in the present invention, alternatively from about 0.1% to about 99.9%, alternatively from about 0.1% to about 99%, alternatively from about 5% to about 99%, alternatively from about 10% to about 99%, alternatively from about 20% to about 99%, alternatively about 50% to about 99%, alternatively from about 80% to about 99%, and alternatively from about 85% to about 95%.

[0099] For inhalation treatments, inhalation of powder (self-propelling or spray formulations) dispensed with a spray can, a nebulizer, or an atomizer can be used. Such formulations can be in the form of a fine powder for pulmonary administration from a powder inhalation device or self-propelling powder-dispensing formulations. In the case of self-propelling solution and spray formulations, the effect can be achieved either by choice of a valve having the desired spray characteristics (*i.e.,* being capable of producing a spray having the desired particle size) or by incorporating the active ingredient as a suspended powder in controlled particle size. For administration by inhalation, the compounds also can be delivered in the form of an aerosol spray from pressured container or dispenser which contains a suitable propellant, *e.g.,* a gas such as carbon dioxide, or a nebulizer.

[0100] Systemic administration also can be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants generally are known in the art, and include, for example, for transmucosal administration, detergents and bile salts. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds typically are formulated into ointments, salves, gels, or creams as generally known in the art.

[0101] The active compounds can be prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. Liposomal suspensions can also be used as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

[0102] Oral or parenteral compositions can be formulated in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound and the therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

[0103] Where adhesion to a tissue surface is desired the composition can include the drug dispersed in a fibrinogen-thrombin composition or other bioadhesive. The compound then can be painted, sprayed or otherwise applied to the desired tissue surface. Alternatively, the drugs can be formulated for parenteral or oral administration to humans or other mammals, for example, in effective amounts, *e.g.,* amounts that provide appropriate concentrations of the drug to target tissue for a time sufficient to induce the desired effect.

[0104] In conjunction with the methods of the present invention, pharmacogenomics (*i.e.,* the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) can be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, a physician or clinician can consider applying knowledge obtained in relevant pharmacogenomics studies in determining whether to administer a drug as well as tailoring the dosage and/or therapeutic regimen of treatment with the drug.

[0105] Generally, an effective amount of dosage of active compound will be in the range of from about 0.01 to about 1500, depending on the mode of administration. The amount administered will also likely depend on such variables as the condition to be treated, the severity

of the condition, the age and overall health status of the patient, the relative biological efficacy of the compound delivered, the formulation of the compound, the presence and types of excipients in the formulation, and the route of administration. Also, it is to be understood that the initial dosage administered can be increased beyond the above upper level in order to rapidly achieve the desired tissue level or blood level, or the initial dosage can be smaller than the optimum.

[0106] Nonlimiting doses of active compound comprise from about 0.1 to about 1500 mg per dose. Nonlimiting examples of doses, which can be formulated as a unit dose for convenient administration to a patient include: about 0.10 mg, about 0.15 mg, about 0.20 mg, about 0.25 mg, about 0.30 mg, about 0.35 mg, about 0.40 mg, about 0.45 mg, about 0.50 mg, about 0.75 mg, about 1 mg, about 2 mg, about 2.5 mg, about 3 mg, about 4 mg, about 5 mg, about 7.5 mg, about 10 mg, about 12.5 mg, about 15, mg, about 20 mg, about 25 mg, about 30 mg, about 35 mg, about 40 mg, about 45 mg, about 50 mg, about 60 mg, about 70 mg, about 75 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 125 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 175 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 225 mg, about 230 mg, about 240 mg, about 250 mg, about 275 mg, about 300 mg, about 325, about 350 mg, about 375 mg, about 400 mg, about 425 mg, about 450 mg, about 475 mg, about 500 mg, about 525 mg, about 550 mg, about 575 mg, about 600 mg, about 625 mg, about 650 mg, about 675 mg about 700 mg, about 725 mg, about 750 mg, about 775 mg, about 800 mg, about 825 mg, about 850 mg, about 875 mg, about 900 mg, about 925 mg, about 950 mg, about 975 mg, about 1000 mg, about 1025 mg, about 1050, mg, about 1075 mg, about 1100 mg, about 1125 mg, about 1150 mg, about 1175 mg, about 1200 mg, about 1225 mg, about 1250 mg, about 1275 mg, about 1300 mg, about 1325 mg, about 1350 mg, about 1375 mg, about 1400 mg, about 1425 mg, about 1450 mg, about 1475 mg, and about 1500 mg. The foregoing doses are useful for administering the compounds of the present invention according to the methods of the present invention.

[0107] Alternatively, the amount of active ingredient in the compositions useful in the methods of the present invention can be described on a weight percentage basis. Nonlimiting amounts of active ingredients include about 0.01%, about 0.015%, about 0.02%, about 0.025% about 0.03%, about 0.035% about 0.04%, about 0.045%, about 0.05%, about 0.055%, about 0.06%, about 0.065%, about 0.07%, about 0.075%, about 0.080%, about 0.085%, about 0.090%, about 0.095%, about 0.1%, about 0.15%, about 0.2%, about 0.25%, about 0.3%, about 0.35%, about 0.4%, about 0.45%, about 0.5%, about 0.55%, about 0.6%, about 0.65%, about 0.7%, about 0.75%, about 0.8%, about 0.85%, about 0.9%, about 0.95%, about 1%, about 1.25%, about 1.5%,

about 1.75%, about 2%, about 2.5%, about 3%, about 3.5%, about 4%, about 4.5%, about 5%, about 5.5%, about 6%, about 6.5%, about 7%, about 7.5%, about 8%, about 8.5%, about 9%, about 9.5%, about 10%, about 10.5%, about 11%, about 11.5%, about 12%, about 12.5%, about 13%, about 13.5%, about 14%, about 14.5%, about 15%, about 15.5%, about 16%, about 16.5%, about 17%, about 17.5%, about 18%, about 18.5%, about 19%, about 19.5%, about 20%, about 21%, about 22%, about 23%, about 24%, about 25%, about 26%, about 27%, about 28%, about 29%, about 30%, about 31%, about 32%, about 33%, about 34%, about 35%, about 36%, about 37%, about 38%, about 39%, about 40%, about 41%, about 42%, about 43%, about 44%, about 45%, about 46%, about 47%, about 48%, about 49%, about 50%, about 51%, about 52%, about 53%, about 54%, about 55%, about 56%, about 57%, about 58%, about 59%, about 60%, about 61%, about 62%, about 63%, about 64%, about 65%, about 66%, about 67%, about 68%, about 69%, about 70%, about 71%, about 72%, about 73%, about 74%, about 75%, about 76%, about 77%, about 78%, about 79%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, about 99.1%, about 99.2%, about 99.3%, about 99.4%, about 99.5%, about 99.6%, about 99.7%, about 99.8%, and about 99.9%.

[0108] *See, e.g.,* PCT Application No. WO 2005/019211 A2, published, March 3, 2005, which describes various aspects useful in the present invention.

Optional Components

[0109] In addition to the required components of the compositions useful in the present invention, a variety of optional components can also be incorporated.

Anti-Acne Agents

[0110] The compositions useful in the present invention can also contain anti-acne agents in addition to the antibiotics. These other anti-acne agents can comprise from about 0.01% to about 20% by weight of the compositions useful herein, or alternatively from about 0.01% to about 10%, and yet alternatively from about 0.1% to about 5%. Mixtures of these additional anti-acne actives may also be used. Examples of these other anti-acne agents, particularly for oral compositions include conventional antibiotic agents such as erythromycin, agents such as tretinoin, etc. Examples of these other anti-acne agents, particularly for topical compositions include keratolytics such as sulfur, lactic acid, glycolic, pyruvic acid, urea, resorcinol, and N-

acetylcysteine; retinoids such as retinoic acid and its derivatives (*e.g.*, cis and trans); antibiotics, antimicrobials, antibacterials, antifungals, antiprotozoals, and antivirals (*e.g.*, benzoyl peroxide, octopirox, erythromycin, tetracycline, triclosan, azelaic acid and its derivatives, phenoxy ethanol and phenoxy propanol, ethyl acetate, clindamycin and meclocycline, triclosan, chlorhexidine, tetracycline, neomycin, miconazole hydrochloride, octopirox, parachlorometaxylenol, nystatin, tolnaftate, clotrimazole, and the like); sebostats such as flavonoids; hydroxy acids; antipruritic drugs including, for example, pharmaceutically-acceptable salts of methdilizine and trimeprazine; and bile salts such as scymnol sulfate and its derivatives, deoxycholate, and cholate. Other exemplary agents which can be used in accordance with the present disclosure include those discussed in Decker, A.; Graber, E. M. *J. Clin. Aesthet. Dermatol.* **2012,** *5*(5), 32-40, the contents of which are hereby incorporated by reference in their entirety.

[0111] Also useful, particularly for oral and topical compositions are non-steroidal anti-inflammatory drugs (NSAIDS). The NSAIDS can be selected from the following categories: propionic acid derivatives; acetic acid derivatives; fenamic acid derivatives; biphenylcarboxylic acid derivatives; and oxicams. All of these NSAIDS are fully described in the U.S. Pat. No. 4,985,459 to Sunshine et al., issued Jan. 15, 1991, incorporated by reference herein. Most preferred are the propionic NSAIDS including but not limited to aspirin, acetaminophen, ibuprofen, naproxen, benoxaprofen, flurbiprofen, fenoprofen, fenbufen, ketoprofen, indoprofen, pirprofen, carprofen, oxaprozin, pranoprofen, miroprofen, tioxaprofen, suprofen, alminoprofen, tiaprofenic acid, fluprofen and bucloxic acid. Also useful are the steroidal anti-inflammatory drugs including hydrocortisone and the like.

Other Components for Topical Compositions

[0112] The following components are especially useful for topical compositions.

Humectants, Moisturizers, and Skin Conditioners

[0113] Particularly for topical compositions, optional component of the compositions useful in the instant invention is at least one humectant/moisturizer/skin conditioner. A variety of these materials can be employed and each can be present at a level of from about 0.1% to about 20%, alternatively from about 1% to about 10% and yet alternatively from about 2% to about 5%. These materials include urea; guanidine; glycolic acid and glycolate salts (*e.g.* ammonium and quaternary alkyl ammonium); lactic acid and lactate salts (*e.g.* ammonium and quaternary alkyl ammonium); aloe vera in any of its variety of forms (*e.g.*, aloe vera gel); polyhydroxy alcohols such as sorbitol, glycerol, hexanetriol, propylene glycol, hexylene glycol and the like;

polyethylene glycol; sugars and starches; sugar and starch derivatives (*e.g.*, alkoxylated glucose); hyaluronic acid; lactamide monoethanolamine; acetamide monoethanolamine; and mixtures thereof.

[0114] In certain embodiments for topical compositions, humectants/moisturizers/skin conditioners useful herein are the C_3 -C_6 diols and triols, and also aloe vera gel. Especially preferred is the triol, glycerol, and also aloe vera gel.

Surfactants

[0115] The compositions useful in the methods of the present invention, particularly the topical compositions, can optionally comprise one or more surfactants. The surfactants can be present at a level from about 0.1% to about 10%, alternatively from about 0.2% to about 5%, and yet alternatively from about 0.2% to about 2.5%. Suitable surfactants include, but are not limited to, nonionic surfactants such as polyalkylene glycol ethers of fatty alcohols, and anionic surfactants such as taurates and alkyl sulfates. Nonlimiting examples of these surfactants include isoceteth-20, sodium methyl cocoyl taurate, sodium methyl oleoyl taurate, and sodium lauryl sulfate. See U.S. Pat. No. 4,800,197, to Kowcz et al., issued Jan. 24, 1989, which is incorporated herein by reference in its entirety. Examples of a broad variety of additional surfactants useful herein are described in McCutcheon's, Detergents and Emulsifiers, North American Edition (1986), published by Allured Publishing Corporation, which is incorporated herein by reference in its entirety.

Emollients

[0116] The compositions useful in the methods of the present invention, particularly topical compositions, can also optionally comprise at least one emollient. Examples of suitable emollients include, but are not limited to, volatile and non-volatile silicone oils, highly branched hydrocarbons, and non-polar carboxylic acid and alcohol esters, and mixtures thereof. Emollients useful in the instant invention are further described in U.S. Pat. No. 4,919,934, to Deckner et al., issued Apr. 24, 1990, which is incorporated herein by reference in its entirety.

[0117] The emollients can typically comprise in total from about 1% to about 50%, preferably from about 1% to about 25%, and more preferably from about 1% to about 10% by weight of the compositions useful in the present invention.

Sunscreens

[0118] The compositions useful in the methods of the present invention for topical administration can also optionally comprise at least one sun screening agent. A wide variety of one or more sun screening agents are suitable for use in the present invention and are described in U.S. Pat. No. 5,087,445, to Haffey et al., issued Feb. 11, 1992; U.S. Pat. No. 5,073,372, to Turner et al., issued Dec. 17, 1991; U.S. Pat. No. 5,073,371, to Turner et al. issued Dec. 17, 1991; and Segarin, et al., at Chapter VIII, pages 189 et seq., of Cosmetics Science and Technology, all of which are incorporated herein by reference in their entirety.

[0119] Preferred among those sunscreens which are useful in the compositions of the instant invention are those selected from the group consisting of ethy1Hexyl p-methoxycinnamate, octocrylene, octyl salicylate, oxybenzone, and mixtures thereof.

[0120] Other useful sunscreens include the solid physical sunblocks such as titanium dioxide (micronized titanium dioxide, 0.03 microns), zinc oxide, silica, iron oxide and the like. Without being limited by theory, it is believed that these inorganic materials provide a sun screening benefit through reflecting, scattering, and absorbing harmful UV, visible, and infrared radiation.

[0121] Still other useful sunscreens are those disclosed in U.S. Pat. No. 4,937,370, to Sabatelli, issued Jun. 26, 1990; and U.S. Pat. No. 4,999,186, to Sabatelli et al., issued Mar. 12, 1991; these two references are incorporated by reference herein in their entirety. The sun screening agents disclosed therein have, in a single molecule, two distinct chromophore moieties which exhibit different ultra-violet radiation absorption spectra. One of the chromophore moieties absorbs predominantly in the UVB radiation range and the other absorbs strongly in the UVA radiation range. These sun screening agents provide higher efficacy, broader UV absorption, lower skin penetration and longer lasting efficacy relative to conventional sunscreens.

[0122] Generally, the sunscreens can comprise from about 0.5% to about 20% of the compositions useful herein. Exact amounts will vary depending upon the sunscreen chosen and the desired Sun Protection Factor (SPF). SPF is a commonly used measure of photoprotection of a sunscreen against erythema. See Federal Register, Vol. 43, No. 166, pp. 38206-38269, Aug. 25, 1978, which is incorporated herein by reference in its entirety.

Delivery Methods for Topical Compositions

[0123] The topical compositions useful for the methods of the instant invention can also be delivered from a variety of delivery devices. The following are two nonlimiting examples.

Medicated Cleansing Pads

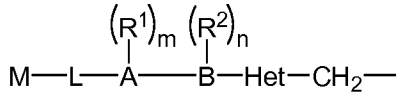
[0124] The compositions useful herein can be incorporated into a medicated cleansing pad. Preferably, these pads comprise from about 50% to about 75% by weight of one or more layers of nonwoven fabric material and from about 20% to about 75% by weight (on dry solids basis) of a water soluble polymeric resin. These pads are described in detail in U.S. Pat. No. 4,891,228, to Thaman et al., issued Jan. 2, 1990 and U.S. Pat. No. 4,891,227, to Thaman et al., issued Jan. 2, 1990; both of which are incorporated by reference herein in their entirety.

Dispensing Devices

[0125] The compositions useful herein can also be incorporated into and delivered from a soft-tipped or flexible dispensing device. These devices are useful for the controlled delivery of the compositions to the skin surface and have the advantage that the treatment composition itself never need be directly handled by the user. Nonlimiting examples of these devices comprise a fluid container including a mouth, an applicator, means for holding the applicator in the mouth of the container, and a normally closed pressure-responsive valve for permitting the flow of fluid from the container to the applicator upon the application of pressure to the valve. The valve can include a diaphragm formed from an elastically fluid impermeable material with a plurality of non-intersecting arcuate slits therein, where each slit has a base which is intersected by at least one other slit, and where each slit is out of intersecting relation with its own base, and wherein there is a means for disposing the valve in the container inside of the applicator. Examples of these applicator devices are described in U.S. Pat. No. 4,693,623, to Schwartzman, issued Sep. 15, 1987; U.S. Pat. No. 4,620,648, to Schwartzman, issued Sep. 15, 1987; U.S. Pat. No. 3,669,323, to Harker et al., issued Jun. 13, 1972; U.S. Pat. No. 3,418,055, to Schwartzman, issued Dec. 24, 1968; and U.S. Pat. No. 3,410,645, to Schwartzman, issued Nov. 12, 1968; all of which are incorporated herein by reference in their entirety. Examples of applicators useful herein are commercially available from Dab-O-Matic, Mount Vernon, N.Y.

4. Embodiments

[0126] In one aspect, disclosed herein is a method of treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes, Gardnerella vaginalis,* or *Staphylococcus aureus* in a patient, the method comprising administering a pharmaceutically effective amount of a compound having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, wherein:

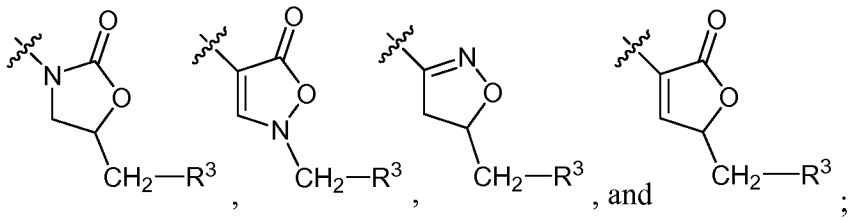
A is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

B is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

Het-CH_2-R^3 is selected from the group consisting of:



, and ;

M is selected from the group consisting of:

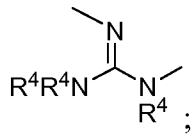
a) saturated, unsaturated, or aromatic C_{3-14} carbocycle, and b) saturated, unsaturated, or aromatic 3-14 membered heterocycle containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, wherein a) or b) optionally is substituted with one or more R^5 groups;

M-L is selected from the group consisting of:

a) M-X, b) M-L^1, c) M-L^1-X, d) M-X-L^2, e) M-L^1-X-L^2, f) M-X-L^1-X-L^2, g) M-L^1-X-L^2-X, h) M-X-X-, i) M-L^1-X-X-, j) M-X-X-L^2, and k) M-L^1-X-X-L^2, wherein

X, at each occurrence, independently is selected from the group consisting of:

a) -O-, b) -NR^4-, c) –N(O)-, d) –N(OR^4)-, e) -$S(O)_p$-, f) -SO_2NR^4-, g) -NR^4SO_2-, h) -NR^4-N=, i) =N-NR^4-, j) -O-N=, k) =N-O-, l) -N=, m) =N-, n) -NR^4-NR^4-, o) -$NR^4C(O)O$-, p) -$OC(O)NR^4$-, q) -$NR^4C(O)NR^4$- r) -$NR^4C(NR^4)NR^4$-, and s)



;

L^1 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups; and

L^2 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups;

R^1, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) $-CF_3$, f) $-OR^4$, g) -CN, h) $-NO_2$, i) $-NR^4R^4$, j) $-C(O)R^4$, k) $-C(O)OR^4$, l) $-OC(O)R^4$, m) $-C(O)NR^4R^4$, n) $-NR^4C(O)R^4$, o) $-OC(O)NR^4R^4$, p) $-NR^4C(O)OR^4$, q) $-NR^4C(O)NR^4R^4$, r) $-C(S)R^4$, s) $-C(S)OR^4$, t) $-OC(S)R^4$, u) $-C(S)NR^4R^4$, v) $-NR^4C(S)R^4$, w) $-OC(S)NR^4R^4$, x) $-NR^4C(S)OR^4$, y) $-NR^4C(S)NR^4R^4$, z) $-NR^4C(NR^4)NR^4R^4$, aa) $-S(O)_pR^4$, bb) $-SO_2NR^4R^4$, and cc) R^4;

R^2, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) $-CF_3$, f) $-OR^4$, g) -CN, h) $-NO_2$, i) $-NR^4R^4$, j) $-C(O)R^4$, k) $-C(O)OR^4$, l) $-OC(O)R^4$, m) $-C(O)NR^4R^4$, n) $-NR^4C(O)R^4$, o) $-OC(O)NR^4R^4$, p) $-NR^4C(O)OR^4$, q) $-NR^4C(O)NR^4R^4$, r) $-C(S)R^4$, s) $-C(S)OR^4$, t) $-OC(S)R^4$, u) $-C(S)NR^4R^4$, v) $-NR^4C(S)R^4$, w) $-OC(S)NR^4R^4$, x) $-NR^4C(S)OR^4$, y) $-NR^4C(S)NR^4R^4$, z) $-NR^4C(NR^4)NR^4R^4$, aa) $-S(O)_pR^4$, bb) $-SO_2NR^4R^4$, and cc) R^4;

R^3 is selected from the group consisting of:

a) $-OR^4$, b) $-NR^4R^4$, c) $-C(O)R^4$, d) $-C(O)OR^4$, e) $-OC(O)R^4$, f) $-C(O)NR^4R^4$, g) $-NR^4C(O)R^4$, h) $-OC(O)NR^4R^4$, i) $-NR^4C(O)OR^4$, j) $-NR^4C(O)NR^4R^4$, k) $-C(S)R^4$, l) $-C(S)OR^4$, m) $-OC(S)R^4$, n) $-C(S)NR^4R^4$, o) $-NR^4C(S)R^4$, p) $-OC(S)NR^4R^4$, q) $-NR^4C(S)OR^4$, r) $-NR^4C(S)NR^4R^4$, s) $-NR^4C(NR^4)NR^4R^4$, t) $-S(O)_pR^4$, u) $-SO_2NR^4R^4$, and v) R^4;

R^4, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) $-C(O)-C_{1-6}$ alkyl, h) $-C(O)-C_{2-6}$ alkenyl, i) –C(O)-

C_{2-6} alkynyl, j) -C(O)-C_{3-14} saturated,
unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^5 groups;

R^5, at each occurrence, is independently selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) =NR^6, h) =NOR^6, i) =N-NR^6R^6, j) -CF_3, k) -OR^6, l) -CN, m) -NO_2, n) –NR^6R^6, o) -C(O)R^6, p) -C(O)OR^6, q) -OC(O)R^6, r) -C(O)NR^6R^6, s) –NR^6C(O)R^6, t) -OC(O)NR^6R^6, u) -NR^6C(O)OR^6, v) -NR^6C(O)NR^6R^6, w) -C(S)R^6, x) -C(S)OR^6, y) -OC(S)R^6, z) -C(S)NR^6R^6, aa) -NR^6C(S)R^6, bb) -OC(S)NR^6R^6, cc) -NR^6C(S)OR^6, dd) –NR^6C(S)NR^6R^6, ee) –NR^6C(NR^6)NR^6R^6, ff) -$S(O)_pR^6$, gg) -$SO_2NR^6R^6$, and hh) R^6;

R^6, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) -C(O)-C_{1-6} alkyl, h) -C(O)-C_{2-6} alkenyl, i) –C(O)-C_{2-6} alkynyl, j) -C(O)-C_{3-14} saturated,
unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^7 groups;

R^7, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) =NR^8, h) =NOR^8, i) =N-NR^8R^8, j) -CF_3, k) -OR^8, l) -CN, m) -NO_2, n) –NR^8R^8, o) -C(O)R^8, p) -C(O)OR^8, q) -OC(O)R^8,

r) -C(O)NR^8R^8, s) –$NR^8C(O)R^8$, t) -OC(O)NR^8R^8, u) -$NR^8C(O)OR^8$, v) -$NR^8C(O)NR^8R^8$, w) -C(S)R^8, x) -C(S)OR^8, y) -OC(S)R^8, z) -C(S)NR^8R^8, aa) -$NR^8C(S)R^8$, bb) -OC(S)NR^8R^8, cc) -$NR^8C(S)OR^8$, dd) –$NR^8C(S)NR^8R^8$, ee) -$NR^8C(NR^8)NR^8R^8$, ff) -$S(O)_pR^8$, gg) -$SO_2NR^8R^8$, hh) C_{1-6} alkyl, ii) C_{2-6} alkenyl, jj) C_{2-6} alkynyl, kk) C_{3-14} saturated, unsaturated, or aromatic carbocycle, and ll) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of hh) – ll) optionally is substituted with one or more moieties selected from the group consisting of R^8, F, Cl, Br, I, -CF_3, –OR^8, –SR^8, -CN, -NO_2, –NR^8R^8, -C(O)R^8, -C(O)OR^8, -OC(O)R^8, -C(O)NR^8R^8, -$NR^8C(O)R^8$, -OC(O)NR^8R^8, -$NR^8C(O)OR^8$, -$NR^8C(O)NR^8R^8$, -C(S)R^8, -C(S)OR^8, -OC(S)R^8, -C(S)NR^8R^8, -$NR^8C(S)R^8$, -OC(S)NR^8R^8, -$NR^8C(S)OR^8$, -$NR^8C(S)NR^8R^8$, -$NR^8C(NR^8)NR^8R^8$, -$SO_2NR^8R^8$, and-$S(O)_pR^8$;

R^8, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) -C(O)-C_{1-6} alkyl, h) -C(O)-C_{2-6} alkenyl, i) –C(O)-C_{2-6} alkynyl, j) -C(O)-C_{3-14} saturated, unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

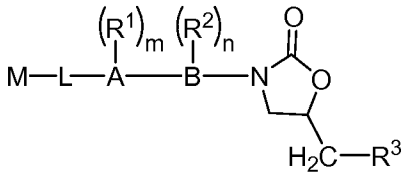
wherein any of b) – p) optionally is substituted with one or more moieties selected from the group consisting of F, Cl, Br, I, -CF_3, -OH, -OCH_3, -SH, -SCH_3, -CN, -NO_2, –NH_2, -$NHCH_3$, -$N(CH_3)_2$, -C(O)CH_3, -C(O)OCH_3, -C(O)NH_2, –$NHC(O)CH_3$, -SO_2NH_2, -SO_2NHCH_3, -$SO_2N(CH_3)_2$, and-$S(O)_pCH_3$;

m, at each occurrence, independently is 0, 1, 2, 3, or 4;

n, at each occurrence, independently is 0, 1, 2, 3, or 4; and

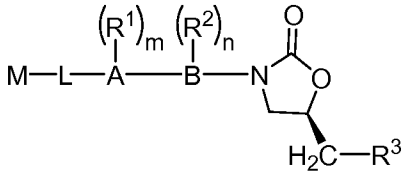
p, at each occurrence, independently is 0, 1, or 2.

[0127] In some embodiments, the compound has the formula:



or a pharmaceutically acceptable salt, ester or prodrug thereof.

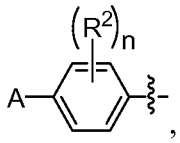
[0128] In some embodiments, the compound has the formula:



or a pharmaceutically acceptable salt, ester or prodrug thereof.

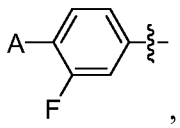
[0129] In some embodiments, A is selected from the group consisting of phenyl and pyridyl. In some embodiments, B is selected from the group consisting of phenyl and pyridyl. In some embodiments, m is 0, 1, or 2. In some embodiments, n is 0, 1, or 2. In some embodiments, A is selected from the group consisting of phenyl and pyridyl, B is selected from the group consisting of phenyl and pyridyl, m is 0, 1, or 2 and n is 0, 1, or 2.

[0130] In some embodiments, A-B is:



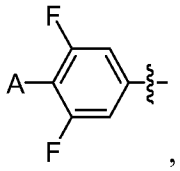
,

[0131] In some embodiments, A-B is:



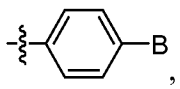
,

[0132] In some embodiments, A-B is:



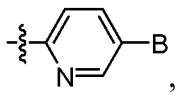
,

[0133] In some embodiments, A-B is:



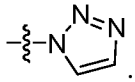
,

[0134] In some embodiments, A-B is:



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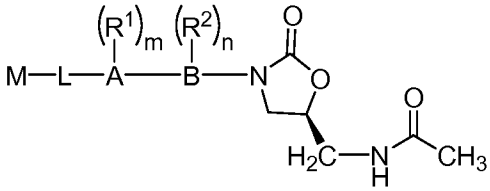
[0135] In some embodiments, R^3 is $-NHC(O)R^4$. In some embodiments, R^3 is:



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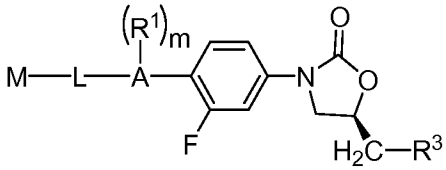
[0136] In some embodiments, R^4 is $-CH_3$.

[0137] In some embodiments, the compound has the formula:



or a pharmaceutically acceptable salt, ester or prodrug thereof.

[0138] In some embodiments, the compound has the formula:



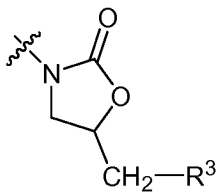
or a pharmaceutically acceptable salt, ester or prodrug thereof.

[0139] In some embodiments:

A is a phenyl;

B is a phenyl;

Het-CH_2-R^3 is:



;

M is a 5-membered unsaturated heterocycle containing one or more nitrogen heteroatoms optionally substituted with one or more R^5 groups, wherein the heterocycle contains only nitrogen atoms;

M-L is M-L^1-X-L^2, wherein

X, at each occurrence, independently is selected from the group consisting of:

a) $-NR^4-$, b) $-SO_2NR^4-$

L^1 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups; and

L^2 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups;

R^1, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) ;

R^2, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d);

R^3 is $-NR^4C(O)R^4$;

R^4, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl;

R^5, at each occurrence, is independently selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) $-CF_3$, h) -CN, i) $-NO_2$, j) $-NR^6R^6$, k) $-C(O)R^6$, l) $-C(O)NR^6R^6$, m) $-S(O)_pR^6$, and n) R^6;

R^6, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl,

wherein any of b) – d) optionally is substituted with one or more R^7 groups;

R^7, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) $=NR^8$, f) $-CF_3$, g) $-OR^8$, h) -CN, i) $-NO_2$, j) $-NR^8R^8$, k) $-C(O)R^8$, and l) $-C(O)OR^8$;

R^8, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl,

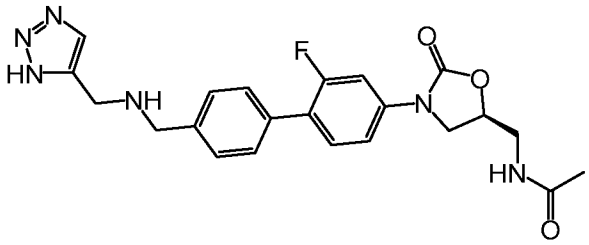
wherein any of b) – d) optionally is substituted with one or more moieties selected from the group consisting of F, Cl, Br, I, $-CF_3$, and -OH;

m is 0, 1, 2, 3, or 4;

n is 0, 1, 2, 3, or 4; and

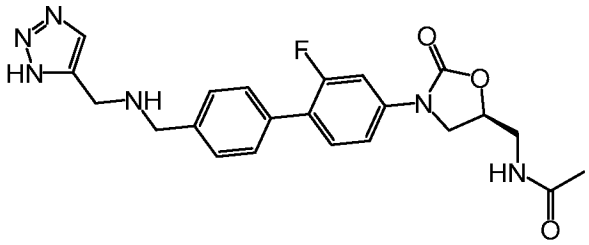
p, at each occurrence, independently is 0, 1, or 2.

[0140] In some embodiments, the compound has the formula:



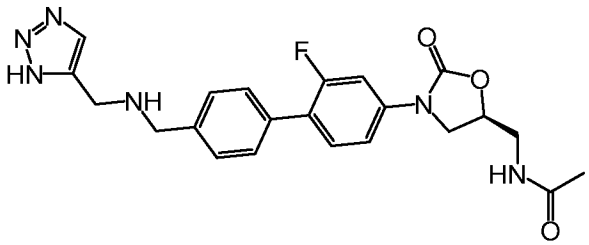
or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof.

[0141] In some embodiments, the compound has the formula:



wherein the compound is a pharmaceutically acceptable salt selected from the group consisting of acetate, ascorbate, benzoate, citrate, esylate, ethanedisulfonate, fumarate, hydrochloride, lactate, maleate, mesylate, phosphate, pyroglutamate, salicylate, succinate, sulfate, tartrate, and tosylate.

[0142] In another aspect, disclosed herein is a method of treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient, the method comprising administering a pharmaceutically effective amount of a compound having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof.

[0143] In some embodiments, the compound is a pharmaceutically acceptable salt selected from the group consisting of acetate, ascorbate, benzoate, citrate, esylate, ethanedisulfonate, fumarate, hydrochloride, lactate, maleate, mesylate, phosphate, pyroglutamate, salicylate, succinate, sulfate, tartrate, and tosylate.

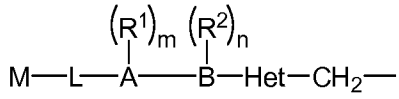
[0144] In some embodiments, the skin infection is treated in the patient. In some embodiments, the skin infection is prevented in the patient. In some embodiments, the method reduces the risk of the skin infection in the patient.

[0145] In some embodiments, the skin infection is caused or mediated by *Propionibacterium acnes*. In some embodiments, the skin infection is caused or mediated by *Staphylococcus aureus*. In some embodiments, the skin infection is caused or mediated by *Gardnerella vaginalis*.

[0146] In some embodiments, the skin infection is selected from acne vulgaris, rosacea, impetigo, otitis externa, bacterial conjunctivitis, and bacterial vaginosis. In some embodiments, the skin infection is acne vulgaris. In some embodiments, the skin infection is bacterial vaginosis.

[0147] In some embodiments, the compound, composition or medicament is administered orally, parentally, or topically. In some embodiments, the compound, composition or medicament is administered topically.

[0148] In some embodiments, the compound is administered in a topical formulation comprising one or more dermatologically acceptable carriers and one or more compounds having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, wherein:

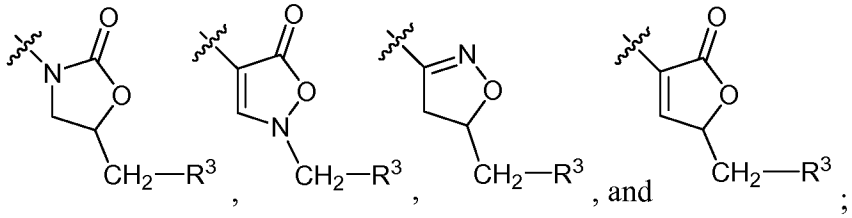
A is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

B is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

Het-CH_2-R^3 is selected from the group consisting of:



, and ;

M is selected from the group consisting of:

a) saturated, unsaturated, or aromatic C_{3-14} carbocycle, and b) saturated, unsaturated, or aromatic 3-14 membered heterocycle containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

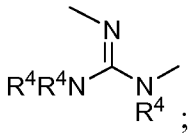
wherein a) or b) optionally is substituted with one or more R^5 groups;

M-L is selected from the group consisting of:

a) M-X, b) M-L^1, c) M-L^1-X, d) M-X-L^2, e) M-L^1-X-L^2, f) M-X-L^1-X-L^2, g) M-L^1-X-L^2-X, h) M-X-X-, i) M-L^1-X-X-, j) M-X-X-L^2, and k) M-L^1-X-X-L^2, wherein

X, at each occurrence, independently is selected from the group consisting of:

a) -O-, b) -NR^4-, c) –N(O)-, d) –N(OR^4)-, e) -$S(O)_p$-, f) -SO_2NR^4-, g) -NR^4SO_2-, h) -NR^4-N=, i) =N-NR^4-, j) -O-N=, k) =N-O-, l) -N=, m) =N-, n) -NR^4-NR^4-, o) -$NR^4C(O)O$-, p) -$OC(O)NR^4$-, q) -$NR^4C(O)NR^4$- r) -$NR^4C(NR^4)NR^4$-, and s)



;

L^1 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups; and

L^2 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups;

R^1, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) -CF_3, f) –OR^4, g) -CN, h) -NO_2, i) -NR^4R^4, j) -$C(O)R^4$, k) -$C(O)OR^4$, l) -$OC(O)R^4$, m) -$C(O)NR^4R^4$, n) -$NR^4C(O)R^4$, o) -$OC(O)NR^4R^4$, p) -$NR^4C(O)OR^4$, q) –$NR^4C(O)NR^4R^4$, r) -$C(S)R^4$, s) -$C(S)OR^4$, t) -$OC(S)R^4$, u) -$C(S)NR^4R^4$, v) –$NR^4C(S)R^4$, w) -$OC(S)NR^4R^4$, x) –$NR^4C(S)OR^4$, y) -$NR^4C(S)NR^4R^4$, z) -$NR^4C(NR^4)NR^4R^4$, aa) -$S(O)_pR^4$, bb) -$SO_2NR^4R^4$, and cc) R^4;

R^2, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) -CF_3, f) –OR^4, g) -CN, h) -NO_2, i) -NR^4R^4, j) -$C(O)R^4$, k) -$C(O)OR^4$, l) -$OC(O)R^4$, m) -$C(O)NR^4R^4$, n) -$NR^4C(O)R^4$, o) -$OC(O)NR^4R^4$, p) -$NR^4C(O)OR^4$, q) –$NR^4C(O)NR^4R^4$, r) -$C(S)R^4$, s) -$C(S)OR^4$, t) -$OC(S)R^4$, u) -$C(S)NR^4R^4$, v) –$NR^4C(S)R^4$, w) -$OC(S)NR^4R^4$, x) –$NR^4C(S)OR^4$, y) -$NR^4C(S)NR^4R^4$, z) -$NR^4C(NR^4)NR^4R^4$, aa) -$S(O)_pR^4$, bb) -$SO_2NR^4R^4$, and cc) R^4;

R^3 is selected from the group consisting of:

a) $-OR^4$, b) $-NR^4R^4$, c) $-C(O)R^4$, d) $-C(O)OR^4$, e) $-OC(O)R^4$, f) $-C(O)NR^4R^4$, g) $-NR^4C(O)R^4$, h) $-OC(O)NR^4R^4$, i) $-NR^4C(O)OR^4$, j) $-NR^4C(O)NR^4R^4$, k) $-C(S)R^4$, l) $-C(S)OR^4$, m) $-OC(S)R^4$, n) $-C(S)NR^4R^4$, o) $-NR^4C(S)R^4$, p) $-OC(S)NR^4R^4$, q) $-NR^4C(S)OR^4$, r) $-NR^4C(S)NR^4R^4$, s) $-NR^4C(NR^4)NR^4R^4$, t) $-S(O)_pR^4$, u) $-SO_2NR^4R^4$, and v) R^4;

R^4, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) $-C(O)-C_{1-6}$ alkyl, h) $-C(O)-C_{2-6}$ alkenyl, i) $-C(O)-C_{2-6}$ alkynyl, j) $-C(O)-C_{3-14}$ saturated,

unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) $-C(O)O-C_{1-6}$ alkyl, m) $-C(O)O-C_{2-6}$ alkenyl, n) $-C(O)O-C_{2-6}$ alkynyl, o) $-C(O)O-C_{3-14}$ saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^5 groups;

R^5, at each occurrence, is independently selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) $=NR^6$, h) $=NOR^6$, i) $=N-NR^6R^6$, j) $-CF_3$, k) $-OR^6$, l) -CN, m) $-NO_2$, n) $-NR^6R^6$, o) $-C(O)R^6$, p) $-C(O)OR^6$, q) $-OC(O)R^6$, r) $-C(O)NR^6R^6$, s) $-NR^6C(O)R^6$, t) $-OC(O)NR^6R^6$, u) $-NR^6C(O)OR^6$, v) $-NR^6C(O)NR^6R^6$, w) $-C(S)R^6$, x) $-C(S)OR^6$, y) $-OC(S)R^6$, z) $-C(S)NR^6R^6$, aa) $-NR^6C(S)R^6$, bb) $-OC(S)NR^6R^6$, cc) $-NR^6C(S)OR^6$, dd) $-NR^6C(S)NR^6R^6$, ee) $-NR^6C(NR^6)NR^6R^6$, ff) $-S(O)_pR^6$, gg) $-SO_2NR^6R^6$, and hh) R^6;

R^6, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) $-C(O)-C_{1-6}$ alkyl, h) $-C(O)-C_{2-6}$ alkenyl, i) $-C(O)-C_{2-6}$ alkynyl, j) $-C(O)-C_{3-14}$ saturated,

unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated,

unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^7 groups;

R^7, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) =NR^8, h) =NOR^8, i) =N-NR^8R^8, j) -CF_3, k) -OR^8, l) -CN, m) -NO_2, n) –NR^8R^8, o) -C(O)R^8, p) -C(O)OR^8, q) -OC(O)R^8, r) -C(O)NR^8R^8, s) –NR^8C(O)R^8, t) -OC(O)NR^8R^8, u) -NR^8C(O)OR^8, v) -NR^8C(O)NR^8R^8, w) -C(S)R^8, x) -C(S)OR^8, y) -OC(S)R^8, z) -C(S)NR^8R^8, aa) -NR^8C(S)R^8, bb) -OC(S)NR^8R^8, cc) -NR^8C(S)OR^8, dd) –NR^8C(S)NR^8R^8, ee) -NR^8C(NR^8)NR^8R^8, ff) -$S(O)_pR^8$, gg) -$SO_2NR^8R^8$, hh) C_{1-6} alkyl, ii) C_{2-6} alkenyl, jj) C_{2-6} alkynyl, kk) C_{3-14} saturated, unsaturated, or aromatic carbocycle, and ll) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of hh) – ll) optionally is substituted with one or more moieties selected from the group consisting of R^8, F, Cl, Br, I, -CF_3, –OR^8, –SR^8, -CN, -NO_2, –NR^8R^8, -C(O)R^8, -C(O)OR^8, -OC(O)R^8, -C(O)NR^8R^8, –NR^8C(O)R^8, -OC(O)NR^8R^8, –NR^8C(O)OR^8, -NR^8C(O)NR^8R^8, -C(S)R^8, -C(S)OR^8, -OC(S)R^8, -C(S)NR^8R^8, -NR^8C(S)R^8, -OC(S)NR^8R^8, -NR^8C(S)OR^8, –NR^8C(S)NR^8R^8, -NR^8C(NR^8)NR^8R^8, -$SO_2NR^8R^8$, and-$S(O)_pR^8$;

R^8, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) -C(O)-C_{1-6} alkyl, h) -C(O)-C_{2-6} alkenyl, i) –C(O)-C_{2-6} alkynyl, j) -C(O)-C_{3-14} saturated, unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected

from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

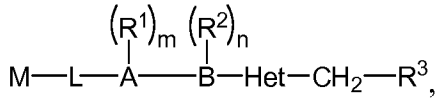
wherein any of b) – p) optionally is substituted with one or more moieties selected from the group consisting of F, Cl, Br, I, -CF_3, -OH, -OCH_3, -SH, -SCH_3, -CN, -NO_2, –NH_2, -$NHCH_3$, -$N(CH_3)_2$, -C(O)CH_3, -C(O)OCH_3, -C(O)NH_2, –$NHC(O)CH_3$, -SO_2NH_2, -SO_2NHCH_3, -$SO_2N(CH_3)_2$, and-$S(O)_pCH_3$;

m, at each occurrence, independently is 0, 1, 2, 3, or 4;

n, at each occurrence, independently is 0, 1, 2, 3, or 4; and

p, at each occurrence, independently is 0, 1, or 2.

[0149] In another aspect, disclosed herein is a topical formulation for use in treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes, Gardnerella vaginalis,* or *Staphylococcus aureus* in a patient, the formulation comprising one or more dermatologically acceptable carriers and one or more compounds having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, wherein:

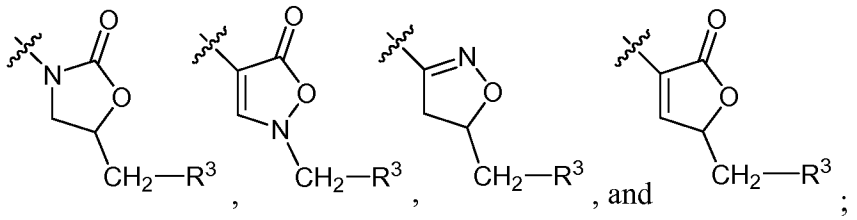
A is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

B is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

Het-CH_2-R^3 is selected from the group consisting of:



M is selected from the group consisting of:

a) saturated, unsaturated, or aromatic C_{3-14} carbocycle, and b) saturated, unsaturated, or aromatic 3-14 membered heterocycle containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

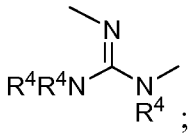
wherein a) or b) optionally is substituted with one or more R^5 groups;

M-L is selected from the group consisting of:

a) M-X, b) M-L^1, c) M-L^1-X, d) M-X-L^2, e) M-L^1-X-L^2, f) M-X-L^1-X-L^2, g) M-L^1-X-L^2-X, h) M-X-X-, i) M-L^1-X-X-, j) M-X-X-L^2, and k) M-L^1-X-X-L^2, wherein

X, at each occurrence, independently is selected from the group consisting of:

a) -O-, b) -NR^4-, c) –N(O)-, d) –N(OR^4)-, e) -$S(O)_p$-, f) -SO_2NR^4-, g) -NR^4SO_2-, h) -NR^4-N=, i) =N-NR^4-, j) -O-N=, k) =N-O-, l) -N=, m) =N-, n) -NR^4-NR^4-, o) -$NR^4C(O)O$-, p) -$OC(O)NR^4$-, q) -$NR^4C(O)NR^4$- r) -$NR^4C(NR^4)NR^4$-, and s)



;

L^1 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups; and

L^2 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups;

R^1, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) -CF_3, f) –OR^4, g) -CN, h) -NO_2, i) -NR^4R^4, j) -$C(O)R^4$, k) -$C(O)OR^4$, l) -$OC(O)R^4$, m) -$C(O)NR^4R^4$, n) -$NR^4C(O)R^4$, o) -$OC(O)NR^4R^4$, p -$NR^4C(O)OR^4$, q) –$NR^4C(O)NR^4R^4$, r) -$C(S)R^4$, s) -$C(S)OR^4$, t) -$OC(S)R^4$, u) -$C(S)NR^4R^4$, v) –$NR^4C(S)R^4$, w) -$OC(S)NR^4R^4$, x) –$NR^4C(S)OR^4$, y) -$NR^4C(S)NR^4R^4$, z) -$NR^4C(NR^4)NR^4R^4$, aa) -$S(O)_pR^4$, bb) -$SO_2NR^4R^4$, and cc) R^4;

R^2, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) -CF_3, f) –OR^4, g) -CN, h) -NO_2, i) -NR^4R^4, j) -$C(O)R^4$, k) -$C(O)OR^4$, l) -$OC(O)R^4$, m) -$C(O)NR^4R^4$, n) -$NR^4C(O)R^4$, o) -$OC(O)NR^4R^4$,

p) -$NR^4C(O)OR^4$, q) –$NR^4C(O)NR^4R^4$, r) -$C(S)R^4$, s) -$C(S)OR^4$, t) -$OC(S)R^4$, u) -$C(S)NR^4R^4$, v) –$NR^4C(S)R^4$, w) -$OC(S)NR^4R^4$, x) –$NR^4C(S)OR^4$, y) -$NR^4C(S)NR^4R^4$, z) -$NR^4C(NR^4)NR^4R^4$, aa) -$S(O)_pR^4$, bb) -$SO_2NR^4R^4$, and cc) R^4;

R^3 is selected from the group consisting of:

a) –OR^4, b) –NR^4R^4, c) -$C(O)R^4$, d) -$C(O)OR^4$, e) -$OC(O)R^4$, f) -$C(O)NR^4R^4$, g) -$NR^4C(O)R^4$, h) -$OC(O)NR^4R^4$, i) –$NR^4C(O)OR^4$, j) -$NR^4C(O)NR^4R^4$, k) -$C(S)R^4$, l) -$C(S)OR^4$, m) -$OC(S)R^4$, n) -$C(S)NR^4R^4$, o) –$NR^4C(S)R^4$, p) -$OC(S)NR^4R^4$, q -$NR^4C(S)OR^4$, r) –$NR^4C(S)NR^4R^4$, s) –$NR^4C(NR^4)NR^4R^4$, t) -$S(O)_pR^4$, u) -$SO_2NR^4R^4$, and v) R^4;

R^4, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) -C(O)-C_{1-6} alkyl, h) -C(O)-C_{2-6} alkenyl, i) –C(O)-C_{2-6} alkynyl, j) -C(O)-C_{3-14} saturated,
unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^5 groups;

R^5, at each occurrence, is independently selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) =NR^6, h) =NOR^6, i) =N-NR^6R^6, j) -CF_3, k) -OR^6, l) -CN, m) -NO_2, n) –NR^6R^6, o) -$C(O)R^6$, p) -$C(O)OR^6$, q) -$OC(O)R^6$, r) -$C(O)NR^6R^6$, s) –$NR^6C(O)R^6$, t) -$OC(O)NR^6R^6$, u) -$NR^6C(O)OR^6$, v) -$NR^6C(O)NR^6R^6$, w) -$C(S)R^6$, x) -$C(S)OR^6$, y) -$OC(S)R^6$, z) -$C(S)NR^6R^6$, aa) -$NR^6C(S)R^6$, bb) -$OC(S)NR^6R^6$, cc) -$NR^6C(S)OR^6$, dd) –$NR^6C(S)NR^6R^6$, ee) –$NR^6C(NR^6)NR^6R^6$, ff) -$S(O)_pR^6$, gg) -$SO_2NR^6R^6$, and hh) R^6;

R^6, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) -C(O)-C_{1-6} alkyl, h) -C(O)-C_{2-6} alkenyl, i) –C(O)-C_{2-6} alkynyl, j) -C(O)-C_{3-14} saturated,
unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^7 groups;

R^7, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) =NR^8, h) =NOR^8, i) =N-NR^8R^8, j) -CF_3, k) -OR^8, l) -CN, m) -NO_2, n) –NR^8R^8, o) -C(O)R^8, p) -C(O)OR^8, q) -OC(O)R^8, r) -C(O)NR^8R^8, s) –NR^8C(O)R^8, t) -OC(O)NR^8R^8, u) -NR^8C(O)OR^8, v) -NR^8C(O)NR^8R^8, w) -C(S)R^8, x) -C(S)OR^8, y) -OC(S)R^8, z) -C(S)NR^8R^8, aa) -NR^8C(S)R^8, bb) -OC(S)NR^8R^8, cc) -NR^8C(S)OR^8, dd) –NR^8C(S)NR^8R^8, ee) -NR^8C(NR^8)NR^8R^8, ff) -$S(O)_pR^8$, gg) -$SO_2NR^8R^8$, hh) C_{1-6} alkyl, ii) C_{2-6} alkenyl, jj) C_{2-6} alkynyl, kk) C_{3-14} saturated, unsaturated, or aromatic carbocycle, and ll) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of hh) – ll) optionally is substituted with one or more moieties selected from the group consisting of R^8, F, Cl, Br, I, -CF_3, –OR^8, –SR^8, -CN, -NO_2, –NR^8R^8, -C(O)R^8, -C(O)OR^8, -OC(O)R^8, -C(O)NR^8R^8, –NR^8C(O)R^8, -OC(O)NR^8R^8, –NR^8C(O)OR^8, -NR^8C(O)NR^8R^8, -C(S)R^8, -C(S)OR^8, -OC(S)R^8, -C(S)NR^8R^8, -NR^8C(S)R^8, -OC(S)NR^8R^8, -NR^8C(S)OR^8, -NR^8C(S)NR^8R^8, -NR^8C(NR^8)NR^8R^8, -$SO_2NR^8R^8$, and-$S(O)_pR^8$;

R^8, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) -C(O)-C_{1-6} alkyl, h) -C(O)-C_{2-6} alkenyl, i) –C(O)-C_{2-6} alkynyl, j) -C(O)-C_{3-14} saturated,

unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

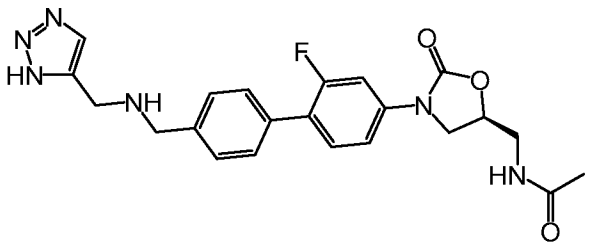
wherein any of b) – p) optionally is substituted with one or more moieties selected from the group consisting of F, Cl, Br, I, -CF_3, -OH, -OCH_3, -SH, -SCH_3, -CN, -NO_2, –NH_2, -$NHCH_3$, -$N(CH_3)_2$, -C(O)CH_3, -C(O)OCH_3, -C(O)NH_2, –$NHC(O)CH_3$, -SO_2NH_2, -SO_2NHCH_3, -$SO_2N(CH_3)_2$, and-$S(O)_pCH_3$;

m, at each occurrence, independently is 0, 1, 2, 3, or 4;

n, at each occurrence, independently is 0, 1, 2, 3, or 4; and

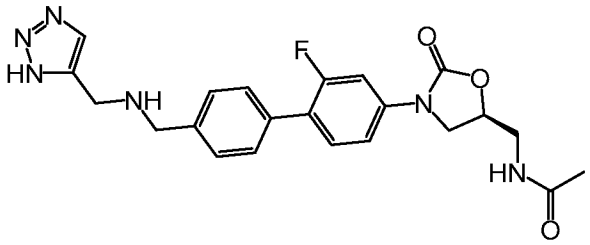
p, at each occurrence, independently is 0, 1, or 2.

[0150] In some embodiments, the compound has the formula:



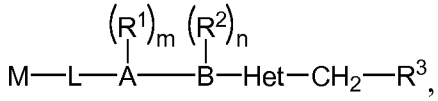
or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof.

[0151] In some embodiments, the compound has the formula:



wherein the compound is a pharmaceutically acceptable salt selected from the group consisting of acetate, ascorbate, benzoate, citrate, esylate, ethanedisulfonate, fumarate, hydrochloride, lactate, maleate, mesylate, phosphate, pyroglutamate, salicylate, succinate, sulfate, tartrate, and tosylate.

[0152] In another aspect, disclosed herein is a topical formulation for use in treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes, Gardnerella vaginalis,* or *Staphylococcus aureus* in a patient, the formulation comprising one or more dermatologically acceptable carriers and one or more compounds having the formula:

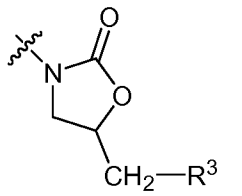


or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, wherein:

A is a phenyl;

B is a phenyl;

Het-CH_2-R^3 is:



M is a 5-membered unsaturated heterocycle containing one or more nitrogen heteroatoms optionally substituted with one or more R^5 groups, wherein the heterocycle contains only nitrogen atoms;

M-L is M-L^1-X-L^2, wherein

X, at each occurrence, independently is selected from the group consisting of:

a) -NR^4-, b) -SO_2NR^4-

L^1 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups; and

L^2 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups;

R^1, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) ;

R^2, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d);

R^3 is $-NR^4C(O)R^4$;

R^4, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl;

R^5, at each occurrence, is independently selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) $-CF_3$, h) -CN, i) $-NO_2$, j) $-NR^6R^6$, k) $-C(O)R^6$, l) $-C(O)NR^6R^6$, m) $-S(O)_pR^6$, and n) R^6;

R^6, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl,

wherein any of b) – d) optionally is substituted with one or more R^7 groups;

R^7, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) $=NR^8$, f) $-CF_3$, g) $-OR^8$, h) -CN, i) $-NO_2$, j) $-NR^8R^8$, k) $-C(O)R^8$, and l) $-C(O)OR^8$;

R^8, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl,

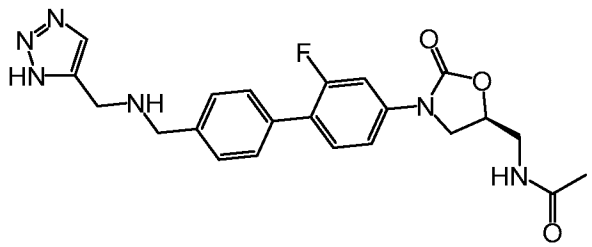
wherein any of b) – d) optionally is substituted with one or more moieties selected from the group consisting of F, Cl, Br, I, $-CF_3$, and -OH;

m is 0, 1, 2, 3, or 4;

n is 0, 1, 2, 3, or 4; and

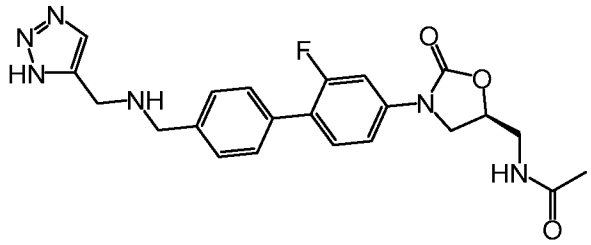
p, at each occurrence, independently is 0, 1, or 2.

[0153] In some embodiments, the compound has the formula:



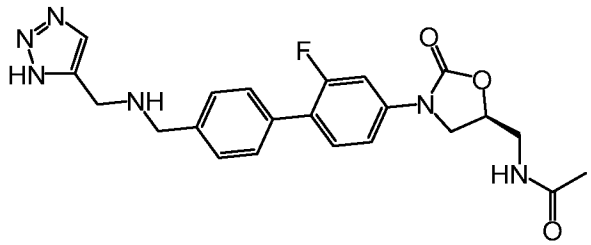
or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof.

[0154] In some embodiments, the compound has the formula:



wherein the compound is a pharmaceutically acceptable salt selected from the group consisting of acetate, ascorbate, benzoate, citrate, esylate, ethanedisulfonate, fumarate, hydrochloride, lactate, maleate, mesylate, phosphate, pyroglutamate, salicylate, succinate, sulfate, tartrate, and tosylate.

[0155] In another aspect, disclosed herein is a topical formulation for use in treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes, Gardnerella vaginalis,* or *Staphylococcus aureus* in a patient, the formulation comprising one or more dermatologically acceptable carriers and a compound having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof.

[0156] In some embodiments, the compound is a pharmaceutically acceptable salt selected from the group consisting of acetate, ascorbate, benzoate, citrate, esylate, ethanedisulfonate, fumarate, hydrochloride, lactate, maleate, mesylate, phosphate, pyroglutamate, salicylate, succinate, sulfate, tartrate, and tosylate.

[0157] In some embodiments, disclosed herein is a method of treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient, the method comprising administering a pharmaceutically effective amount of the topical formulation disclosed herein.

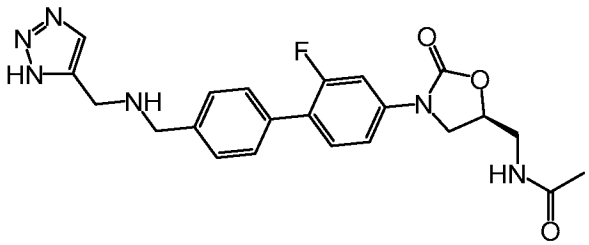
[0158] In some embodiments, the method is a method of treating a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient. In some embodiments, the method is a method of preventing a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient. In some embodiments, the method is a method of reducing the risk of a skin infection

caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient.

[0159] In some embodiments, the skin infection is caused or mediated by *Propionibacterium acnes*. In some embodiments, the skin infection is caused or mediated by *Staphylococcus aureus*. In some embodiments, the skin infection is caused or mediated by *Gardnerella vaginalis*.

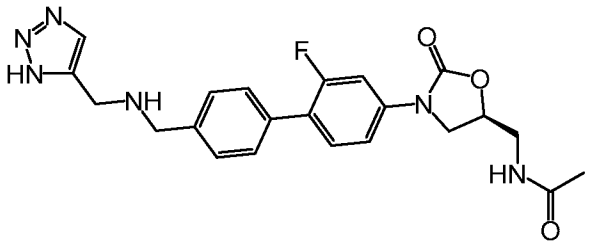
[0160] In some embodiments, the skin infection is selected from acne vulgaris, rosacea, impetigo, otitis externa, bacterial conjunctivitis, and bacterial vaginosis. In some embodiments, the skin infection is acne vulgaris. In some embodiments, the skin infection is bacterial vaginosis.

[0161] In some embodiments, the compound has the formula:



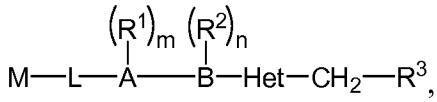
or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof.

[0162] In some embodiments, the compound has the formula:



wherein the compound is a pharmaceutically acceptable salt selected from the group consisting of acetate, ascorbate, benzoate, citrate, esylate, ethanedisulfonate, fumarate, hydrochloride, lactate, maleate, mesylate, phosphate, pyroglutamate, salicylate, succinate, sulfate, tartrate, and tosylate.

[0163] In another aspect, disclosed herein is a use of a compound having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, wherein:

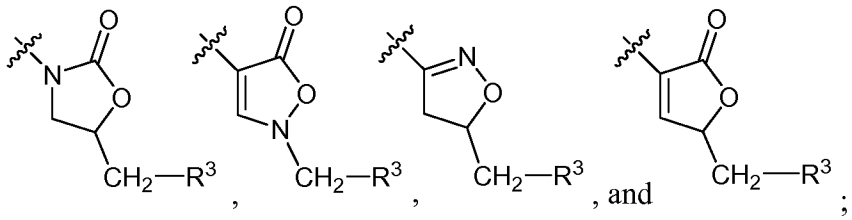
A is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

B is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

Het-CH_2-R^3 is selected from the group consisting of:



;

M is selected from the group consisting of:

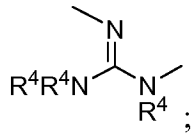
a) saturated, unsaturated, or aromatic C_{3-14} carbocycle, and b) saturated, unsaturated, or aromatic 3-14 membered heterocycle containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, wherein a) or b) optionally is substituted with one or more R^5 groups;

M-L is selected from the group consisting of:

a) M-X, b) M-L^1, c) M-L^1-X, d) M-X-L^2, e) M-L^1-X-L^2, f) M-X-L^1-X-L^2, g) M-L^1-X-L^2-X, h) M-X-X-, i) M-L^1-X-X-, j) M-X-X-L^2, and k) M-L^1-X-X-L^2, wherein

X, at each occurrence, independently is selected from the group consisting of:

a) -O-, b) -NR^4-, c) –N(O)-, d) –N(OR^4)-, e) -$S(O)_p$-, f) -SO_2NR^4-, g) -NR^4SO_2-, h) -NR^4-N=, i) =N-NR^4-, j) -O-N=, k) =N-O-, l) -N=, m) =N-, n) -NR^4-NR^4-, o) -$NR^4C(O)O$-, p) -$OC(O)NR^4$-, q) -$NR^4C(O)NR^4$- r) -$NR^4C(NR^4)NR^4$-, and s)



;

L^1 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups; and

L^2 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups;

R^1, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) -CF_3, f) –OR^4, g) -CN, h) -NO_2, i) -NR^4R^4, j) -$C(O)R^4$, k) -$C(O)OR^4$, l) -$OC(O)R^4$, m) -$C(O)NR^4R^4$, n) -$NR^4C(O)R^4$, o) -$OC(O)NR^4R^4$, p) -$NR^4C(O)OR^4$, q) –$NR^4C(O)NR^4R^4$, r) -$C(S)R^4$, s) -$C(S)OR^4$, t) -$OC(S)R^4$,

u) -C(S)NR^4R^4, v) –$NR^4C(S)R^4$, w) -OC(S)NR^4R^4, x) –$NR^4C(S)OR^4$,
y) -$NR^4C(S)NR^4R^4$, z) -$NR^4C(NR^4)NR^4R^4$, aa) -$S(O)_pR^4$, bb) -$SO_2NR^4R^4$, and
cc) R^4;

R^2, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) -CF_3, f) –OR^4, g) -CN, h) -NO_2, i) -NR^4R^4, j) -C(O)R^4,
k) -C(O)OR^4, l) -OC(O)R^4, m) -C(O)NR^4R^4, n) -$NR^4C(O)R^4$, o) -OC(O)NR^4R^4,
p) -$NR^4C(O)OR^4$, q) –$NR^4C(O)NR^4R^4$, r) -C(S)R^4, s) -C(S)OR^4, t) -OC(S)R^4,
u) -C(S)NR^4R^4, v) –$NR^4C(S)R^4$, w) -OC(S)NR^4R^4, x) –$NR^4C(S)OR^4$,
y) -$NR^4C(S)NR^4R^4$, z) -$NR^4C(NR^4)NR^4R^4$, aa) -$S(O)_pR^4$, bb) -$SO_2NR^4R^4$, and
cc) R^4;

R^3 is selected from the group consisting of:

a) –OR^4, b) –NR^4R^4, c) -C(O)R^4, d) -C(O)OR^4, e) -OC(O)R^4, f) -C(O)NR^4R^4,
g) -$NR^4C(O)R^4$, h) -OC(O)NR^4R^4, i) –$NR^4C(O)OR^4$, j) -$NR^4C(O)NR^4R^4$,
k) -C(S)R^4, l) -C(S)OR^4, m) -OC(S)R^4, n) -C(S)NR^4R^4, o) –$NR^4C(S)R^4$,
p) -OC(S)NR^4R^4, q) –$NR^4C(S)OR^4$, r) –$NR^4C(S)NR^4R^4$, s) –$NR^4C(NR^4)NR^4R^4$,
t) -$S(O)_pR^4$, u) -$SO_2NR^4R^4$, and v) R^4;

R^4, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) -C(O)-C_{1-6} alkyl, h) -C(O)-C_{2-6} alkenyl, i) –C(O)-C_{2-6} alkynyl, j) -C(O)-C_{3-14} saturated,
unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^5 groups;

R^5, at each occurrence, is independently selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) =NR^6, h) =NOR^6, i) =N-NR^6R^6, j) -CF_3,
k) -OR^6, l) -CN, m) -NO_2, n) –NR^6R^6, o) -C(O)R^6, p) -C(O)OR^6, q) -OC(O)R^6,

r) -C(O)NR^6R^6, s) –$NR^6C(O)R^6$, t) -OC(O)NR^6R^6, u) -$NR^6C(O)OR^6$, v) -$NR^6C(O)NR^6R^6$, w) -C(S)R^6, x) -C(S)OR^6, y) -OC(S)R^6, z) -C(S)NR^6R^6, aa) -$NR^6C(S)R^6$, bb) -OC(S)NR^6R^6, cc) -$NR^6C(S)OR^6$, dd) –$NR^6C(S)NR^6R^6$, ee) –$NR^6C(NR^6)NR^6R^6$, ff) -$S(O)_pR^6$, gg) -$SO_2NR^6R^6$, and hh) R^6;

R^6, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) -C(O)-C_{1-6} alkyl, h) -C(O)-C_{2-6} alkenyl, i) –C(O)-C_{2-6} alkynyl, j) -C(O)-C_{3-14} saturated,

unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^7 groups;

R^7, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) =NR^8, h) =NOR^8, i) =N-NR^8R^8, j) -CF_3, k) -OR^8, l) -CN, m) -NO_2, n) –NR^8R^8, o) -C(O)R^8, p) -C(O)OR^8, q) -OC(O)R^8, r) -C(O)NR^8R^8, s) –$NR^8C(O)R^8$, t) -OC(O)NR^8R^8, u) -$NR^8C(O)OR^8$, v) -$NR^8C(O)NR^8R^8$, w) -C(S)R^8, x) -C(S)OR^8, y) -OC(S)R^8, z) -C(S)NR^8R^8, aa) -$NR^8C(S)R^8$, bb) -OC(S)NR^8R^8, cc) -$NR^8C(S)OR^8$, dd) –$NR^8C(S)NR^8R^8$, ee) -$NR^8C(NR^8)NR^8R^8$, ff) -$S(O)_pR^8$, gg) -$SO_2NR^8R^8$, hh) C_{1-6} alkyl, ii) C_{2-6} alkenyl, jj) C_{2-6} alkynyl, kk) C_{3-14} saturated, unsaturated, or aromatic carbocycle, and ll) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of hh) – ll) optionally is substituted with one or more moieties selected from the group consisting of R^8, F, Cl, Br, I, -CF_3, –OR^8, –SR^8, -CN, -NO_2, –NR^8R^8, -C(O)R^8, -C(O)OR^8, -OC(O)R^8, -C(O)NR^8R^8, -$NR^8C(O)R^8$, -OC(O)NR^8R^8, –

$NR^8C(O)OR^8$, $-NR^8C(O)NR^8R^8$, $-C(S)R^8$, $-C(S)OR^8$, $-OC(S)R^8$, $-C(S)NR^8R^8$, $-NR^8C(S)R^8$, $-OC(S)NR^8R^8$, $-NR^8C(S)OR^8$, $-NR^8C(S)NR^8R^8$, $-NR^8C(NR^8)NR^8R^8$, $-SO_2NR^8R^8$, and $-S(O)_pR^8$;

R^8, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) $-C(O)-C_{1-6}$ alkyl, h) $-C(O)-C_{2-6}$ alkenyl, i) $-C(O)-C_{2-6}$ alkynyl, j) $-C(O)-C_{3-14}$ saturated, unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) $-C(O)O-C_{1-6}$ alkyl, m) $-C(O)O-C_{2-6}$ alkenyl, n) $-C(O)O-C_{2-6}$ alkynyl, o) $-C(O)O-C_{3-14}$ saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more moieties selected from the group consisting of F, Cl, Br, I, $-CF_3$, -OH, $-OCH_3$, -SH, $-SCH_3$, -CN, $-NO_2$, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)CH_3$, $-C(O)OCH_3$, $-C(O)NH_2$, $-NHC(O)CH_3$, $-SO_2NH_2$, $-SO_2NHCH_3$, $-SO_2N(CH_3)_2$, and $-S(O)_pCH_3$;

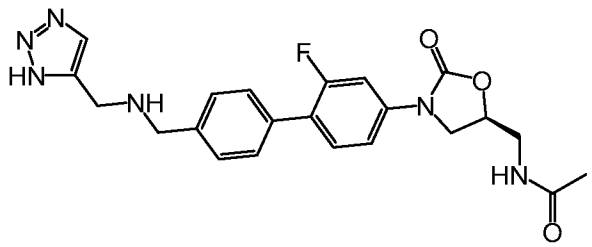
m, at each occurrence, independently is 0, 1, 2, 3, or 4;

n, at each occurrence, independently is 0, 1, 2, 3, or 4; and

p, at each occurrence, independently is 0, 1, or 2,

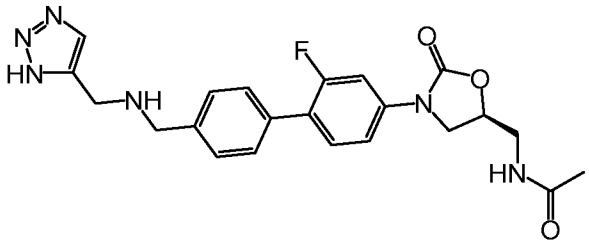
in the manufacture of a medicament for treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient.

[0164] In some embodiments, the compound has the formula:



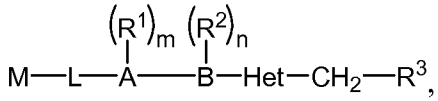
or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof.

[0165] In some embodiments, the compound has the formula:



wherein the compound is a pharmaceutically acceptable salt selected from the group consisting of acetate, ascorbate, benzoate, citrate, esylate, ethanedisulfonate, fumarate, hydrochloride, lactate, maleate, mesylate, phosphate, pyroglutamate, salicylate, succinate, sulfate, tartrate, and tosylate.

[0166] In another aspect, disclosed herein is a use of a compound having the formula:

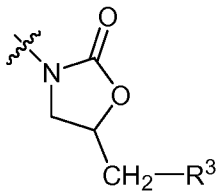


or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, wherein:

A is a phenyl;

B is a phenyl;

Het-CH_2-R^3 is:



;

M is a 5-membered unsaturated heterocycle containing one or more nitrogen heteroatoms optionally substituted with one or more R^5 groups, wherein the heterocycle contains only nitrogen atoms;

M-L is M-L^1-X-L^2, wherein

X, at each occurrence, independently is selected from the group consisting of:

a) -NR^4-, b) -SO_2NR^4-

L^1 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups; and

L^2 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups;

R^1, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) ;

R^2, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d);

R^3 is $-NR^4C(O)R^4$;

R^4, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl;

R^5, at each occurrence, is independently selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) $-CF_3$, h) -CN, i) $-NO_2$, j) $-NR^6R^6$, k) $-C(O)R^6$, l) $-C(O)NR^6R^6$, m) $-S(O)_pR^6$, and n) R^6;

R^6, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl,

wherein any of b) – d) optionally is substituted with one or more R^7 groups;

R^7, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) $=NR^8$, f) $-CF_3$, g) $-OR^8$, h) -CN, i) $-NO_2$, j) $-NR^8R^8$, k) $-C(O)R^8$, and l) $-C(O)OR^8$;

R^8, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl,

wherein any of b) – d) optionally is substituted with one or more moieties selected from the group consisting of F, Cl, Br, I, $-CF_3$, and -OH;

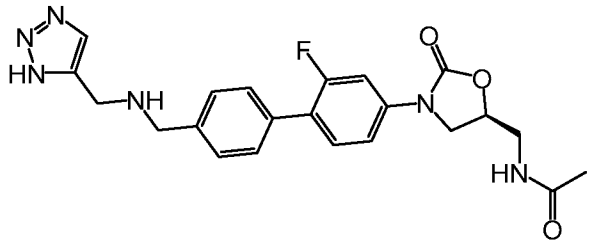
m is 0, 1, 2, 3, or 4;

n is 0, 1, 2, 3, or 4; and

p, at each occurrence, independently is 0, 1, or 2,

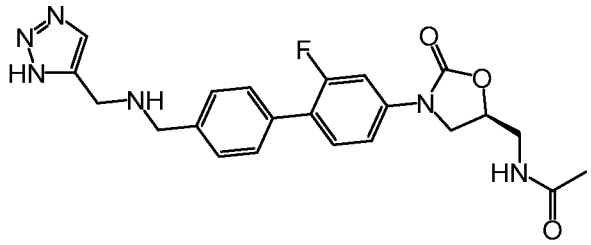
in the manufacture of a medicament for treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient comprising.

[0167] In some embodiments, the compound has the formula:



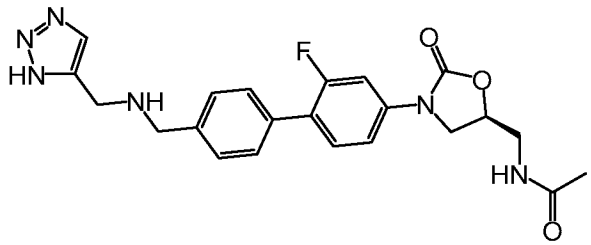
or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof.

[0168] In some embodiments, the compound has the formula:



wherein the compound is a pharmaceutically acceptable salt selected from the group consisting of acetate, ascorbate, benzoate, citrate, esylate, ethanedisulfonate, fumarate, hydrochloride, lactate, maleate, mesylate, phosphate, pyroglutamate, salicylate, succinate, sulfate, tartrate, and tosylate.

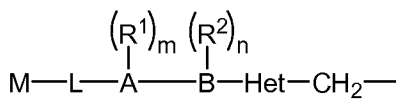
[0169] In another aspect, disclosed herein is a use of a compound having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, in the manufacture of a medicament for treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient.

[0170] In some embodiments, the compound is a pharmaceutically acceptable salt selected from the group consisting of acetate, ascorbate, benzoate, citrate, esylate, ethanedisulfonate, fumarate, hydrochloride, lactate, maleate, mesylate, phosphate, pyroglutamate, salicylate, succinate, sulfate, tartrate, and tosylate.

[0171] In another aspect, disclosed herein is a use of a compound having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, wherein:

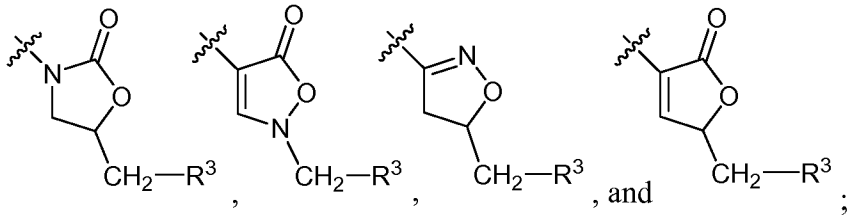
A is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

B is selected from the group consisting of:

phenyl, pyridyl, pyrazinyl, pyrimidinyl, and pyridazinyl;

Het-CH_2-R^3 is selected from the group consisting of:



, and ;

M is selected from the group consisting of:

a) saturated, unsaturated, or aromatic C_{3-14} carbocycle, and b) saturated, unsaturated, or aromatic 3-14 membered heterocycle containing one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

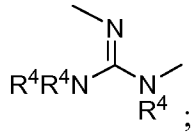
wherein a) or b) optionally is substituted with one or more R^5 groups;

M-L is selected from the group consisting of:

a) M-X, b) M-L^1, c) M-L^1-X, d) M-X-L^2, e) M-L^1-X-L^2, f) M-X-L^1-X-L^2, g) M-L^1-X-L^2-X, h) M-X-X-, i) M-L^1-X-X-, j) M-X-X-L^2, and k) M-L^1-X-X-L^2, wherein

X, at each occurrence, independently is selected from the group consisting of:

a) -O-, b) -NR^4-, c) –N(O)-, d) –N(OR^4)-, e) -$S(O)_p$-, f) -SO_2NR^4-, g) -NR^4SO_2-, h) -NR^4-N=, i) =N-NR^4-, j) -O-N=, k) =N-O-, l) -N=, m) =N-, n) -NR^4-NR^4-, o) -$NR^4C(O)O$-, p) -$OC(O)NR^4$-, q) -$NR^4C(O)NR^4$- r) -$NR^4C(NR^4)NR^4$-, and s)



;

L^1 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups; and

L^2 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups;

R^1, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) $-CF_3$, f) $-OR^4$, g) -CN, h) $-NO_2$, i) $-NR^4R^4$, j) $-C(O)R^4$, k) $-C(O)OR^4$, l) $-OC(O)R^4$, m) $-C(O)NR^4R^4$, n) $-NR^4C(O)R^4$, o) $-OC(O)NR^4R^4$, p) $-NR^4C(O)OR^4$, q) $-NR^4C(O)NR^4R^4$, r) $-C(S)R^4$, s) $-C(S)OR^4$, t) $-OC(S)R^4$, u) $-C(S)NR^4R^4$, v) $-NR^4C(S)R^4$, w) $-OC(S)NR^4R^4$, x) $-NR^4C(S)OR^4$, y) $-NR^4C(S)NR^4R^4$, z) $-NR^4C(NR^4)NR^4R^4$, aa) $-S(O)_pR^4$, bb) $-SO_2NR^4R^4$, and cc) R^4;

R^2, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) $-CF_3$, f) $-OR^4$, g) -CN, h) $-NO_2$, i) $-NR^4R^4$, j) $-C(O)R^4$, k) $-C(O)OR^4$, l) $-OC(O)R^4$, m) $-C(O)NR^4R^4$, n) $-NR^4C(O)R^4$, o) $-OC(O)NR^4R^4$, p) $-NR^4C(O)OR^4$, q) $-NR^4C(O)NR^4R^4$, r) $-C(S)R^4$, s) $-C(S)OR^4$, t) $-OC(S)R^4$, u) $-C(S)NR^4R^4$, v) $-NR^4C(S)R^4$, w) $-OC(S)NR^4R^4$, x) $-NR^4C(S)OR^4$, y) $-NR^4C(S)NR^4R^4$, z) $-NR^4C(NR^4)NR^4R^4$, aa) $-S(O)_pR^4$, bb) $-SO_2NR^4R^4$, and cc) R^4;

R^3 is selected from the group consisting of:

a) $-OR^4$, b) $-NR^4R^4$, c) $-C(O)R^4$, d) $-C(O)OR^4$, e) $-OC(O)R^4$, f) $-C(O)NR^4R^4$, g) $-NR^4C(O)R^4$, h) $-OC(O)NR^4R^4$, i) $-NR^4C(O)OR^4$, j) $-NR^4C(O)NR^4R^4$, k) $-C(S)R^4$, l) $-C(S)OR^4$, m) $-OC(S)R^4$, n) $-C(S)NR^4R^4$, o) $-NR^4C(S)R^4$, p) $-OC(S)NR^4R^4$, q) $-NR^4C(S)OR^4$, r) $-NR^4C(S)NR^4R^4$, s) $-NR^4C(NR^4)NR^4R^4$, t) $-S(O)_pR^4$, u) $-SO_2NR^4R^4$, and v) R^4;

R^4, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) $-C(O)-C_{1-6}$ alkyl, h) $-C(O)-C_{2-6}$ alkenyl, i) $-C(O)-C_{2-6}$ alkynyl, j) $-C(O)-C_{3-14}$ saturated,

unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) $-C(O)O-C_{1-6}$ alkyl, m) $-C(O)O-C_{2-6}$ alkenyl, n) $-C(O)O-C_{2-6}$ alkynyl, o) $-C(O)O-C_{3-14}$ saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^5 groups;

R^5, at each occurrence, is independently selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) =NR^6, h) =NOR^6, i) =N-NR^6R^6, j) -CF_3, k) -OR^6, l) -CN, m) -NO_2, n) –NR^6R^6, o) -$C(O)R^6$, p) -$C(O)OR^6$, q) -$OC(O)R^6$, r) -$C(O)NR^6R^6$, s) –$NR^6C(O)R^6$, t) -$OC(O)NR^6R^6$, u) -$NR^6C(O)OR^6$, v) -$NR^6C(O)NR^6R^6$, w) -$C(S)R^6$, x) -$C(S)OR^6$, y) -$OC(S)R^6$, z) -$C(S)NR^6R^6$, aa) -$NR^6C(S)R^6$, bb) -$OC(S)NR^6R^6$, cc) -$NR^6C(S)OR^6$, dd) –$NR^6C(S)NR^6R^6$, ee) –$NR^6C(NR^6)NR^6R^6$, ff) -$S(O)_pR^6$, gg) -$SO_2NR^6R^6$, and hh) R^6;

R^6, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) -C(O)-C_{1-6} alkyl, h) -C(O)-C_{2-6} alkenyl, i) –C(O)-C_{2-6} alkynyl, j) -C(O)-C_{3-14} saturated,
unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) -C(O)O-C_{1-6} alkyl, m) -C(O)O-C_{2-6} alkenyl, n) –C(O)O-C_{2-6} alkynyl, o) -C(O)O-C_{3-14} saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more R^7 groups;

R^7, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) =NR^8, h) =NOR^8, i) =N-NR^8R^8, j) -CF_3, k) -OR^8, l) -CN, m) -NO_2, n) –NR^8R^8, o) -$C(O)R^8$, p) -$C(O)OR^8$, q) -$OC(O)R^8$, r) -$C(O)NR^8R^8$, s) –$NR^8C(O)R^8$, t) -$OC(O)NR^8R^8$, u) -$NR^8C(O)OR^8$, v) -$NR^8C(O)NR^8R^8$, w) -$C(S)R^8$, x) -$C(S)OR^8$, y) -$OC(S)R^8$, z) -$C(S)NR^8R^8$, aa) -$NR^8C(S)R^8$, bb) -$OC(S)NR^8R^8$, cc) -$NR^8C(S)OR^8$, dd) –$NR^8C(S)NR^8R^8$, ee) -$NR^8C(NR^8)NR^8R^8$, ff) -$S(O)_pR^8$, gg) -$SO_2NR^8R^8$, hh) C_{1-6} alkyl,
ii) C_{2-6} alkenyl, jj) C_{2-6} alkynyl, kk) C_{3-14} saturated, unsaturated, or aromatic carbocycle, and ll) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of hh) – ll) optionally is substituted with one or more moieties selected from the group consisting of R^8, F, Cl, Br, I, $-CF_3$, $-OR^8$, $-SR^8$, -CN, $-NO_2$, $-NR^8R^8$, $-C(O)R^8$, $-C(O)OR^8$, $-OC(O)R^8$, $-C(O)NR^8R^8$, $-NR^8C(O)R^8$, $-OC(O)NR^8R^8$, $-NR^8C(O)OR^8$, $-NR^8C(O)NR^8R^8$, $-C(S)R^8$, $-C(S)OR^8$, $-OC(S)R^8$, $-C(S)NR^8R^8$, $-NR^8C(S)R^8$, $-OC(S)NR^8R^8$, $-NR^8C(S)OR^8$, $-NR^8C(S)NR^8R^8$, $-NR^8C(NR^8)NR^8R^8$, $-SO_2NR^8R^8$, and-$S(O)_pR^8$;

R^8, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl, e) C_{3-14} saturated, unsaturated, or aromatic carbocycle, f) 3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, g) $-C(O)-C_{1-6}$ alkyl, h) $-C(O)-C_{2-6}$ alkenyl, i) $-C(O)-C_{2-6}$ alkynyl, j) $-C(O)-C_{3-14}$ saturated, unsaturated, or aromatic carbocycle, k) -C(O)-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, l) $-C(O)O-C_{1-6}$ alkyl, m) $-C(O)O-C_{2-6}$ alkenyl, n) $-C(O)O-C_{2-6}$ alkynyl, o) $-C(O)O-C_{3-14}$ saturated, unsaturated, or aromatic carbocycle, and p) -C(O)O-3-14 membered saturated, unsaturated, or aromatic heterocycle comprising one or more heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur,

wherein any of b) – p) optionally is substituted with one or more moieties selected from the group consisting of F, Cl, Br, I, $-CF_3$, -OH, $-OCH_3$, -SH, $-SCH_3$, -CN, $-NO_2$, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$, $-C(O)CH_3$, $-C(O)OCH_3$, $-C(O)NH_2$, $-NHC(O)CH_3$, $-SO_2NH_2$, $-SO_2NHCH_3$, $-SO_2N(CH_3)_2$, and-$S(O)_pCH_3$;

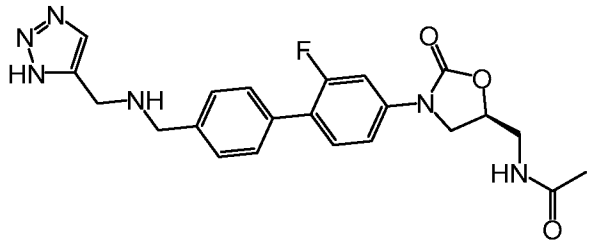
m, at each occurrence, independently is 0, 1, 2, 3, or 4;

n, at each occurrence, independently is 0, 1, 2, 3, or 4; and

p, at each occurrence, independently is 0, 1, or 2,

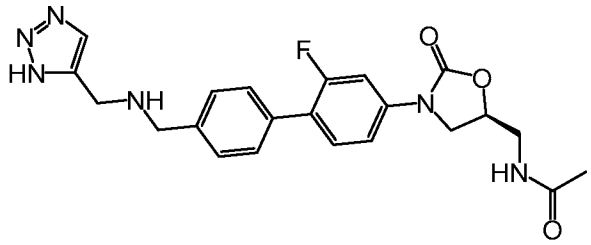
for treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient.

[0172] In some embodiments, the compound has the formula:



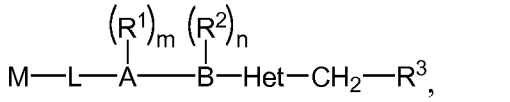
or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof.

[0173] In some embodiments, the compound has the formula:



wherein the compound is a pharmaceutically acceptable salt selected from the group consisting of acetate, ascorbate, benzoate, citrate, esylate, ethanedisulfonate, fumarate, hydrochloride, lactate, maleate, mesylate, phosphate, pyroglutamate, salicylate, succinate, sulfate, tartrate, and tosylate.

[0174] In another aspect, disclosed herein is a use of a compound having the formula:

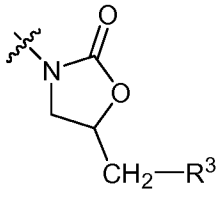


or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, wherein:

A is a phenyl;

B is a phenyl;

Het-CH_2-R^3 is:



;

M is a 5-membered unsaturated heterocycle containing one or more nitrogen heteroatoms optionally substituted with one or more R^5 groups, wherein the heterocycle contains only nitrogen atoms;

M-L is M-L^1-X-L^2, wherein

X, at each occurrence, independently is selected from the group consisting of:

a) -NR^4-, b) -SO_2NR^4-

L^1 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups; and

L^2 is selected from the group consisting of:

a) C_{1-6} alkyl, b) C_{2-6} alkenyl, and c) C_{2-6} alkynyl,

wherein any of a) – c) optionally is substituted with one or more R^5 groups;

R^1, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) ;

R^2, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d);

R^3 is $-NR^4C(O)R^4$;

R^4, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl;

R^5, at each occurrence, is independently selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) =O, f) =S, g) $-CF_3$, h) -CN, i) $-NO_2$, j) $-NR^6R^6$, k) $-C(O)R^6$, l) $-C(O)NR^6R^6$, m) $-S(O)_pR^6$, and n) R^6;

R^6, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl,

wherein any of b) – d) optionally is substituted with one or more R^7 groups;

R^7, at each occurrence, independently is selected from the group consisting of:

a) F, b) Cl, c) Br, d) I, e) $=NR^8$, f) $-CF_3$, g) $-OR^8$, h) -CN, i) $-NO_2$, j) $-NR^8R^8$, k) $-C(O)R^8$, and l) $-C(O)OR^8$;

R^8, at each occurrence, independently is selected from the group consisting of:

a) H, b) C_{1-6} alkyl, c) C_{2-6} alkenyl, d) C_{2-6} alkynyl,

wherein any of b) – d) optionally is substituted with one or more moieties selected from the group consisting of F, Cl, Br, I, $-CF_3$, and -OH;

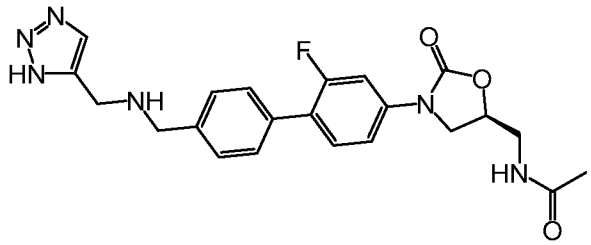
m is 0, 1, 2, 3, or 4;

n is 0, 1, 2, 3, or 4; and

p, at each occurrence, independently is 0, 1, or 2,

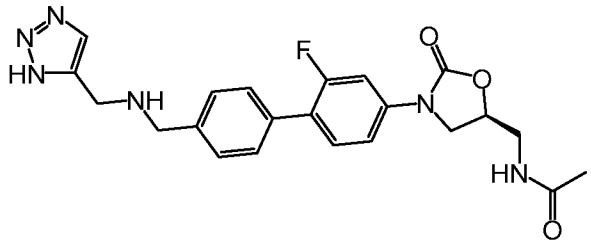
for treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient.

[0175] In some embodiments, the compound has the formula:



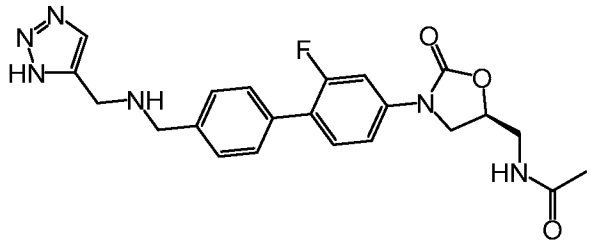
or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof.

[0176] In some embodiments, the compound has the formula:



wherein the compound is a pharmaceutically acceptable salt selected from the group consisting of acetate, ascorbate, benzoate, citrate, esylate, ethanedisulfonate, fumarate, hydrochloride, lactate, maleate, mesylate, phosphate, pyroglutamate, salicylate, succinate, sulfate, tartrate, and tosylate.

[0177] In another aspect, disclosed herein is a use of a compound having the formula:



or a pharmaceutically acceptable tautomer, salt, ester, or prodrug thereof, for treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient.

[0178] In some embodiments, the compound is a pharmaceutically acceptable salt selected from the group consisting of acetate, ascorbate, benzoate, citrate, esylate, ethanedisulfonate, fumarate, hydrochloride, lactate, maleate, mesylate, phosphate, pyroglutamate, salicylate, succinate, sulfate, tartrate, and tosylate.

[0179] In some embodiments, the use is a use in the manufacture of a medicament for treating a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or

Staphylococcus aureus in a patient. In some embodiments, the use is a use in the manufacture of a medicament for preventing a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus* in a patient. In some embodiments, the use is a use in the manufacture of a medicament for reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis* or *Staphylococcus aureus* in a patient.

[0180] In some embodiments, the skin infection is caused or mediated by *Propionibacterium acnes*. In some embodiments, the skin infection is caused or mediated by *Staphylococcus aureus*. In some embodiments, the skin infection is caused or mediated by *Gardnerella vaginalis*.

[0181] In some embodiments, the skin infection is selected from acne vulgaris, rosacea, impetigo, otitis externa, bacterial conjunctivitis, and bacterial vaginosis. In some embodiments, the skin infection is acne vulgaris. In some embodiments, the skin infection is bacterial vaginosis.

[0182] In some embodiments, the medicament is administered orally, parentally, or topically. In some embodiments, the medicament is administered topically.

[0183] In some embodiments, the patient is a mammal or domestic animal. In some embodiments, the patient is a human.

[0184] In some embodiments, the compound is administered once daily or twice daily. In some embodiments, the compound is administered once daily. In some embodiments, the compound is administered twice daily.

EXAMPLES

[0185] The following examples further describe and demonstrate embodiments within the scope of the present invention. The examples are given solely for the purpose of illustration and are not to be construed as limitations of the present invention, as many variations thereof are possible without departing from the spirit and scope of the invention. Ingredients are identified by chemical or CTFA name.

EXAMPLE 1: Anti-Microbial Activity of Radezolid and Comparator Agents

[0186] The in vitro antimicrobial activity of radezolid (compound 4267) and comparator antimicrobial agents were evaluated against several different types of bacteria. Bacterial isolates were obtained from the American Type Culture Collection (ATCC), Manassas, VA.

[0187] Susceptibility testing was performed by the agar dilution reference method (radezolid, linezolid, and clindamycin) and broth microdilution method (all agents) as described by the Clinical and Laboratory Standards Institute (CLSI).

[0188] For the agar dilution method, Brucella agar (BBL, 211086) was prepared according to the manufacturer's instructions and cooled to 48-50 °C in a water bath. Once the agar was cooled, it was supplemented with 10 mL of hemin + vitamin K1 Solution (Remel, R450951), 1 mL of 1 mg/mL vitamin K1 working solution (Sigma, V3501), and 50 mL laked sheep blood (Remel, R54004). The media was dispensed into 50 mL centrifuge tubes and held at 48-50 °C. The antimicrobial agents were reconstituted and prepared at 200X the desired concentrations for ranges of 0.03-8 μg/mL (radezolid and linezolid) and 0.06-16 μg/mL (clindamycin). The diluted antimicrobial agents were added to the dispensed media, gently mixed, and poured into sterile petri dishes. Once hardened, the plates were held in anaerobic jars at room temperature and used the following day.

[0189] For broth microdilution testing a master 96-well tray at 100X the highest desired concentration was prepared by adding compound to an appropriate well in the first column and serially diluting through the 10th column. DMSO or water was added to the 11th and 12th columns for growth and sterility controls. A 1:10 dilution was made into a 96-well tray containing Brucella Broth (BBL, 211088) supplemented with hemin + vitamin K1, and 5% lysed horse blood (1HB) (Remel, R54092). Daughter plates containing 10 μL of each well of the 10X tray were dispensed.

[0190] The anaerobic bacterial isolates were removed from frozen stocks and placed into thioglycollate broth with hemin and vitamin K1 and without indicator (THIO) (Anaerobe Systems, AS-805). The *G. vaginalis* isolates were reconstituted from the ATCC vials using Brucella Broth (BRU-Broth) (Anaerobe Systems, AS-105) and plated onto Brucella Blood Agar plates (BRU) (Anaerobe Systems, AS-141) and chocolate agar plates (CA) (BD BBL, 221169). THIO and BRU were incubated for 48 hours in an anaerobic jar at 35 °C; CA plates were incubated at 35 °C for 48 hours in 5% CO_2. The *S. aureus* isolate was removed from a frozen stock, streaked onto TSA with 5% sheep blood (BA) (BD BBL, 221261), and incubated overnight at 35 °C in ambient air. The day before testing the anaerobes and *G. vaginalis* were subcultured to fresh BRU and THIO and *S. aureus* was subcultured to BA; all were incubated as required.

[0191] On the day of testing, a 0.5 McFarland equivalent of each isolate was prepared in Brucella broth with hemin + vitamin K1. For the agar dilution method, 2 μL spots were inoculated onto each agar plate containing antibiotic in ascending concentration order, as well as

BRU and CA plates before and after each set of compound as growth control (beginning) and to assess any drug carryover (end). BRU plates and those containing compound were incubated at 35 °C in an anaerobic environment for 24 hours, read, and re-incubated for an additional 24 hours followed by a final reading. CA plates were incubated at 35 °C in 5% CO_2 for 48 hours as a negative control (note that some anaerobes are aerotolerant and may grow in CO_2). Following incubation, MICs were determined as the lowest concentration showing a marked reduction in growth or no growth compared to the growth control plate.

[0192] For the broth microdilution method, 0.5 mL of the 0.5 McFarland equivalent was placed into 4.5 mL of Brucella Broth with hemin, vitamin K1, and 5% 1HB. This intermediate suspension was diluted further (1.1 mL into 8.9 mL) in Brucella Broth with hemin, vitamin K1, and 5% 1HB for a final concentration of ~10^5 CFU/well. Trays were incubated at 35 °C in an anaerobic environment for 24 hours, read, and re-incubated for an additional 24 hours followed by a final reading. To confirm the inoculum, a sample from a growth control well was diluted and spread onto BRU and CA. The plates were incubated for 48 hours at 35 °C in an anaerobic (BRU) or 5% CO_2 (CA) environment; colonies were counted and the inoculum was determined. Following incubation, the MIC endpoint was determined as the lowest concentration showing no growth or significantly reduced growth. If growth was poor, the MIC endpoint was not determined.

[0193] Agar and broth microdilution MICs for radezolid, linezolid, and clindamycin against the ten isolates are shown below in Table 3, and broth microdilution MICs for the remaining comparators are shown in Table 4. The "reference" agar dilution method is recommended by CLSI for anaerobic susceptibility testing. Due to limited space, only three compounds were tested by this method: radezolid, linezolid, and clindamycin, and all isolates grew well.

[0194] The broth microdilution method is recommended by CLSI for *B. fragilis* group isolates only, but all isolates were tested by this method. Of the three *P. acnes* isolates, two did not grow in broth, and a third isolate grew poorly. The remaining isolates grew well in broth.

[0195] Comparing broth and agar dilution MICs when values were obtained for both methods, MICs were mostly identical or within 2-fold for each antimicrobial agent. Only *F. magna* had MICs that differed by 4-fold, for radezolid.

Table 3. Agar Dilution and Broth Microdilution MICs for Radezolid, Linezolid, and Clindamycin

		Radezolid		Linezolid		Clindamycin	
Organism	**ATCC No.**	**Agar**	**Broth**	**Agar**	**Broth**	**Agar**	**Broth**
B. fragilis	25285	4	2	4	2	2	1
B. thetaiotaomicron	29741	>8	8	4	4	8	8
F. magna	15794	0.5	0.125	2	1	1	0.5
P. acnes	11828	0.125	No growth	0.5	No growth	0.125	No growth
P. acnes	29399	0.125	Poor growth	0.5	Poor growth	≤0.06	Poor growth
P. acnes	11827	0.125	No growth	0.5	No growth	≤0.06	No growth
P. granulosum	25746	0.25	0.125	2	1	1	1
G. vaginalis	14018	0.06	0.125	0.5	0.5	0.25	0.125
G. vaginalis	49145	0.06	0.06	0.5	0.5	0.125	≤0.06
S. aureus	29213	1	2	2	4	0.25	0.25

[0196] Agar dilution MICs for radezolid were more potent than those of linezolid by 4-fold for *P. acnes* and *F. magna*, and by 8-fold for *P. granulosum* and *G. vaginalis*. Radezolid and linezolid demonstrated similar activity against *S. aureus*. Clindamycin and radezolid MICs were within 2 - 4-fold of each other for most of the isolates.

Table 4. Broth Microdilution MICs for Radezolid and Comparator Agents

Organism	ATCC No.	RDZ	ERY	MET	TET	DOX
B. fragilis	25285	2	16	0.5	0.25	≤0.06
B. thetaiotaomicron	29741	8	16	4	8	2
F. magna	15794	0.125	4	0.125	0.25	0.125
P. acnes	11828	No growth	No growth	No growth	No growth	No growth
P. acnes	29399	Poor growth	Poor growth	Poor growth	Poor growth	Poor growth
P. acnes	11827	No growth	No growth	No growth	No growth	No growth
P. granulosum	25746	0.125	16	1	0.25	0.25
G. vaginalis	14018	0.125	≤0.06	8	0.5	0.5
G. vaginalis	49145	0.06	≤0.06	4	>32	32
S. aureus	29213	2	1	>32	1	0.5

Abbreviations: RDZ, radezolid; ERY, erythromycin; MET, metronidazole; TET, tetracycline; DOX, doxycycline

[0197] In broth microdilution testing, radezolid was 8-fold more active than linezolid against *P. granulosum* and *G. vaginalis* 49145. Radezolid was also more active than clindamycin, erythromycin, and metronidazole against *P. granulosum*, and more active than metronidazole, tetracycline, and doxycycline against *G. vaginalis*.

[0198] The oxazolidinones and clindamycin demonstrated similar potency against *B. fragilis*. MICs for most agents were within 2-fold of radezolid MICs against *B. thetaiotaomicron*; doxycycline was 4-fold more potent.

[0199] Against *F. magna*, radezolid was more active than linezolid, clindamycin, and erythromycin; the other agents were similar in activity to radezolid. Metronidazole MICs were significantly higher than radezolid against *S. aureus*; doxycycline and clindamycin MICs were 4-fold and 8-fold lower, respectively. The MICs for the remaining comparator compounds were within 2-fold of radezolid for *S. aureus*.

[0200] In this study, radezolid demonstrated robust antimicrobial activity against most of the isolates tested, with agar dilution MICs of 0.06-1 μg/mL for all organisms. Radezolid demonstrated enhanced activity compared to the other oxazolidinones against several of the isolates.

[0201] Table 5 shows MICs for radezolid and comparator agents against ribosome-based resistance phenotypes. As shown in Table 5, radezolid exhibited similar or superior results to linezolid and azithromycin across all phenotypes tested.

Table 5. Minimum Inhibitory Concentrations (MICs) (μg/mL) for Radezolid and Comparator Agents Against Ribosome-Based Resistance Phenotypes

Bacterial Strain	Resistance Phenotype	Linezolid	Azithromycin	Radezolid
Enterococcus faecalis ATCC29212	QC	4	8	0.25
Enterococcus faecalis ATCC29212-P5	Lin-R (G2576U)	32	8	1
Enterococcus faecalis 1069	VanB	4	128	0.25
Enterococcus faecium A6349	VanA+Lin-R (G2576U)	16	128	0.5
Staphylococcus aureus ATCC29213	QC	4	1	1
Staphylococcus aureus A7820	Lin-R (G2576U) +Mac-R (ErmC)	64	128	16
Staphylococcus aureus *01A1095*	Mac-R	4	128	1

EXAMPLE 2: Safety of Radezolid Versus Comparator Agent

[0202] Safety of radezolid versus comparator linezolid were tested in long-term rat studies (*see* **FIGs. 1-2**). Radezolid showed good safety. As shown in Figure 1, the male rats generally had higher body weights than the females, with similar body weights within each of the dose groups. There was 100% survival in all dose groups. No test article-related changes were observed in hematology, coagulation, clinical chemistry, or urinalysis. An unscheduled euthanization on day 75 for high-dose linezolid groups showed decreased red cell mass, absolute

reticulocyte and neutrophil counts in rats dosed with 100 mg/kg/day linezolid. This is correlated with decreased cellularity of sternal and femoral bone marrow. Table 6 shows the calculated safety margin of radezolid based on these data.

Table 6. Calculated Safety Margin of Radezolid

Exposure (AUC 0 – 24): male rats at 200 mg/kg on Day 29	101.9 μg*hr/mL
Exposure (AUC 0 – 24): human @ 300 mg dose	3.33 μg*hr/mL
Safety margin (Rat NOAEL AUC / Human efficacious AUC)	30.8x

EXAMPLE 3: Uptake of Radezolid Versus Comparator Agent

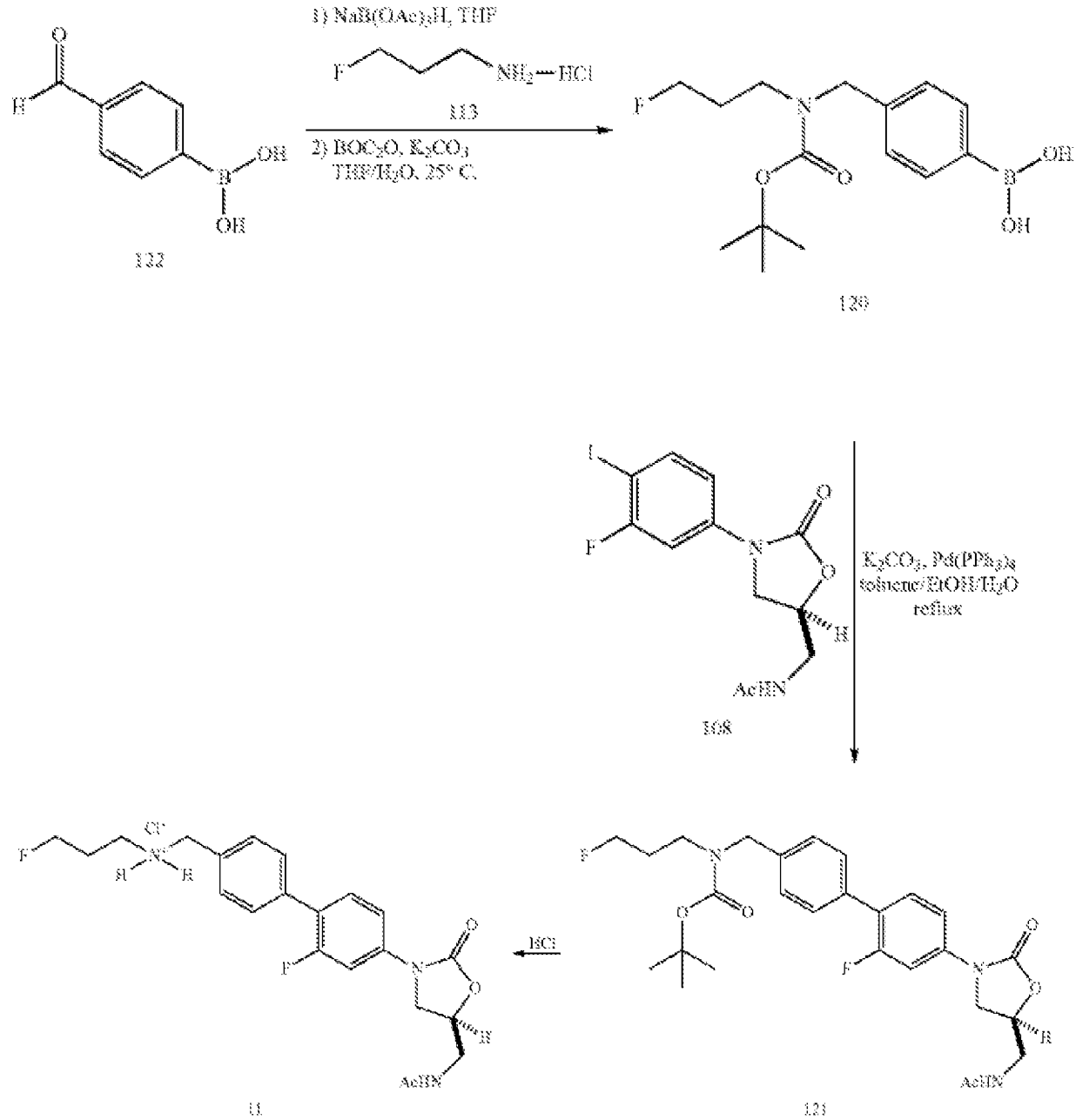
[0203] Approximately 60% of the radezolid accumulates in the cytosol of cells while approximately 40% accumulates in the lysosome. Radezolid accumulates in mammalian cells (*e.g.*, defense cells, macrophages, lung cells, and non-phagocytic cells) to a 17-fold greater extent than linezolid. Radezolid kills intracellular *S. aureus* (including linezolid-resistant), *Listeria monocytogenes* and *Legionella pneumophila*, organisms that reside in different cellular compartments. Accumulation affords once-daily dosing at doses lower than those predicted by plasma levels. Accumulation offers a wider safety window for radezolid as compared to linezolid. *See* Lemaire *et al.* AAC 2010, 54(6): 6549-59.

[0204] Levels of radezolid remain high in granuloma pouch even as they decline in the plasma, contributing to efficacy at the site of infection (*see* **FIGs. 3-4**).

EXAMPLE 4: Synthesis of (5*S*)-N-(3-{2-fluoro-4'- [(3-fluoro-propylamino)-methyl]-biphenyl-4-yl}-2-oxo-oxazolidin-5-ylmethyl)-acetamide mono hydrochloride salt (Compound 11)

[0205] Scheme 1 below depicts synthesis of aryl boronic acid **120**, which is coupled to aryl iodide **108** to yield compound **11**.

Scheme 1. Synthesis of Compound 11



[0206] A solution of 4-formylphenyl boronic acid **122** (10.0 g, 66.69 mmol) in anhydrous DMF (150 mL) was treated with 3-fluoropropylamine hydrochloride salt **113** (8.70 g, 76.70 mmol, 1.15 equiv) at room temperature. The resulting mixture was treated with $NaB(OAc)_3H$ (28.30 g, 133.39 mmol, 2.0 equiv) at room temperature and stirred for 3 h. When TLC and HPLC/MS showed the reaction was complete, the reaction mixture was treated with water (150 mL), solid Na_2CO_3 (14.14 g, 133.39 mmol, 2.0 equiv), and BOC_2O (22.05 g, 100.04 mmol, 1.5 equiv). The resulting reaction mixture was stirred at room temperature for 3 h. When TLC and HPLC/MS showed the reaction was complete, the reaction mixture was poured into water (500

mL) and EtOAc (500 mL). The two layers were separated and the aqueous layer was treated with a 2 N aqueous HCl (130 mL) to pH 4. The aqueous layer was then extracted with EtOAc (160 mL), and the combined organic layers were washed with water (2x100 mL) and saturated aqueous NaCl (2x 100 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The residue was further dried *in vacuo* to afford the desired 4-(N-tert-butylcarbonyl-3-fluoropropylaminomethyl) phenyl boronic acid **120** (25.0 g) as a pale yellow oil. This product was directly used in the subsequent reaction without further purification.

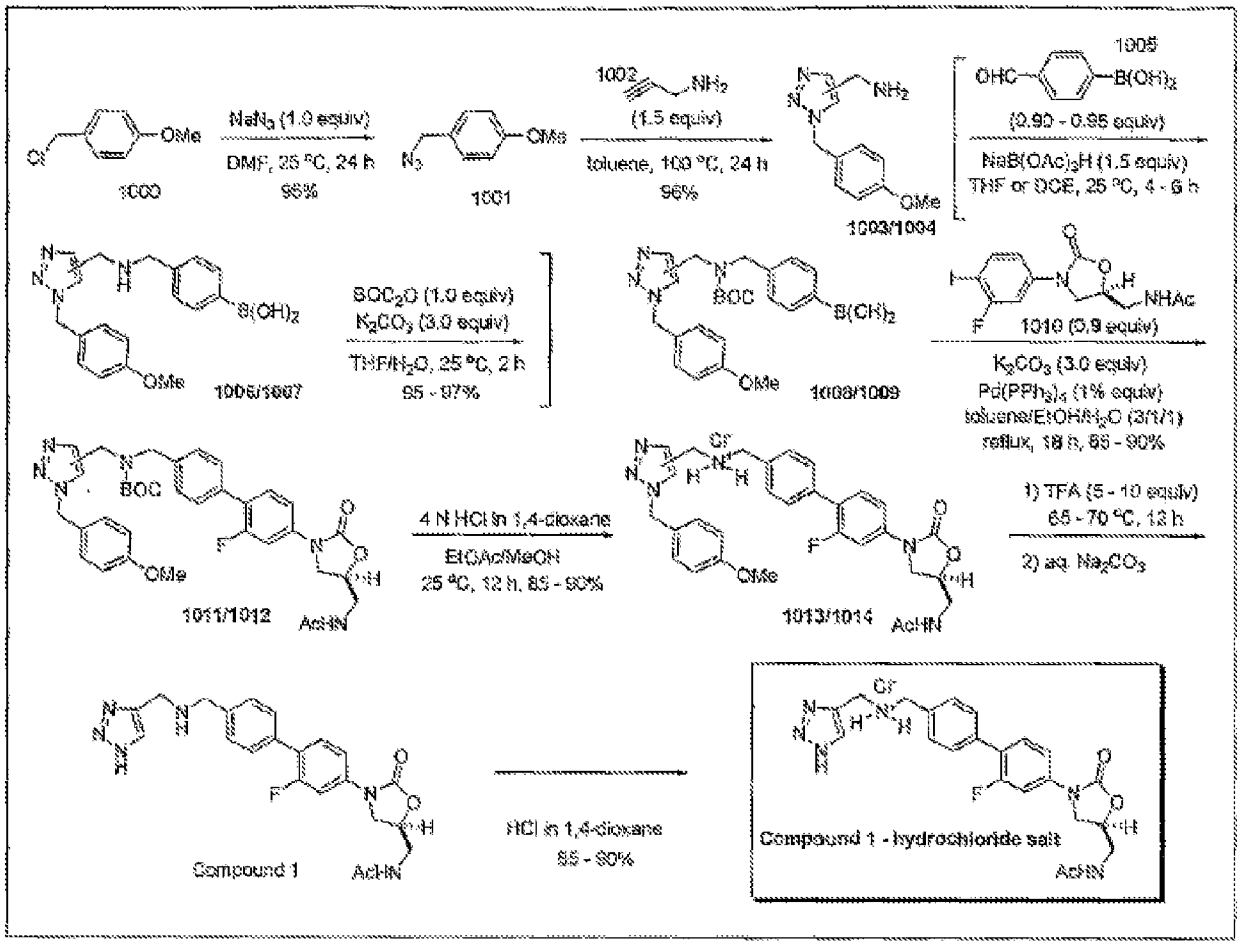
[0207] A suspension of aryl boronic acid **120** (25.0 g, 64.30 mmol, 1.45 equiv) in a mixture of toluene (120 mL), EtOH (40 mL), and water (40 mL) was treated with (5*S*)-N-[3-(3-fluoro-4-iodo-phenyl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide **108** (16.80 g, 44.44 mmol) and solid K_2CO_3 (18.40 g, 133.4 mmol, 3.0 equiv) at room temperature. The resulting reaction mixture was degassed three times under a steady stream of argon before being treated with $Pd(PPh_3)_4$ (2.57 g, 2.23 mmol, 0.05 equiv). The resulting reaction mixture was degassed three times under a steady stream of argon before being warmed to reflux for 8 h. When TLC and HPLC/MS showed the reaction was complete, the reaction mixture was cooled to room temperature before being poured into water (300 mL) and ethyl acetate (EtOAc, 300 mL). The two layers were separated, and the organic phase was washed with water (60 mL) and saturated aqueous NaCl (2x50 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The product was recrystallized from EtOAc/hexanes and dried *in vacuo* to afford the desired (5*S*)-{4'-[5-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro -biphenyl-4-ylmethyl}-(3-fluoro-propyl)-carbamic acid tert-butyl ester **121** (21.2 g, 61.5% yield for three steps) as an off-white powder.

[0208] BOC-protected amine **121** was subsequently treated with 4 N hydrogen chloride in 1,4-dioxane to afford compound **11**. ^1H NMR (300 MHz, DMSO-d_6) δ 1.90 (s, 3H, $COCH_3$), 2.11-2.20 (m, 2H), 3.10 (m, 2H), 3.50 (t, 2H, J = 5.4 Hz), 3.87 (dd, 1H, J = 6.4, 9.2 Hz), 4.24 (t, 1H, J = 9.1 Hz), 4.27 (s, 2H, $ARCH_2$), 4.54 (t, 1H, J = 5.8 Hz), 4.70 (t, 1H, J = 5.8 Hz), 4.83 (m, 1H), 7.50 (dd, 1H, J = 2.2, 8.6 Hz), 7.65-7.74 (m, 6H, aromatic-H), 8.37 (t, 1H, J = 5.8 Hz, $NHCOCH_3$), 9.43 (br. s, 2H, $RArN^+H_2$). $C_{22}H_{25}F_2N_3O_3HCl$, LCMS (EI) *m/e* 418 (M^++H).

EXAMPLE 5: Synthesis of Radezolid

[0209] Radezolid (shown as Compound 1) and its hydrochloride salt are synthesized according to Scheme 2 below.

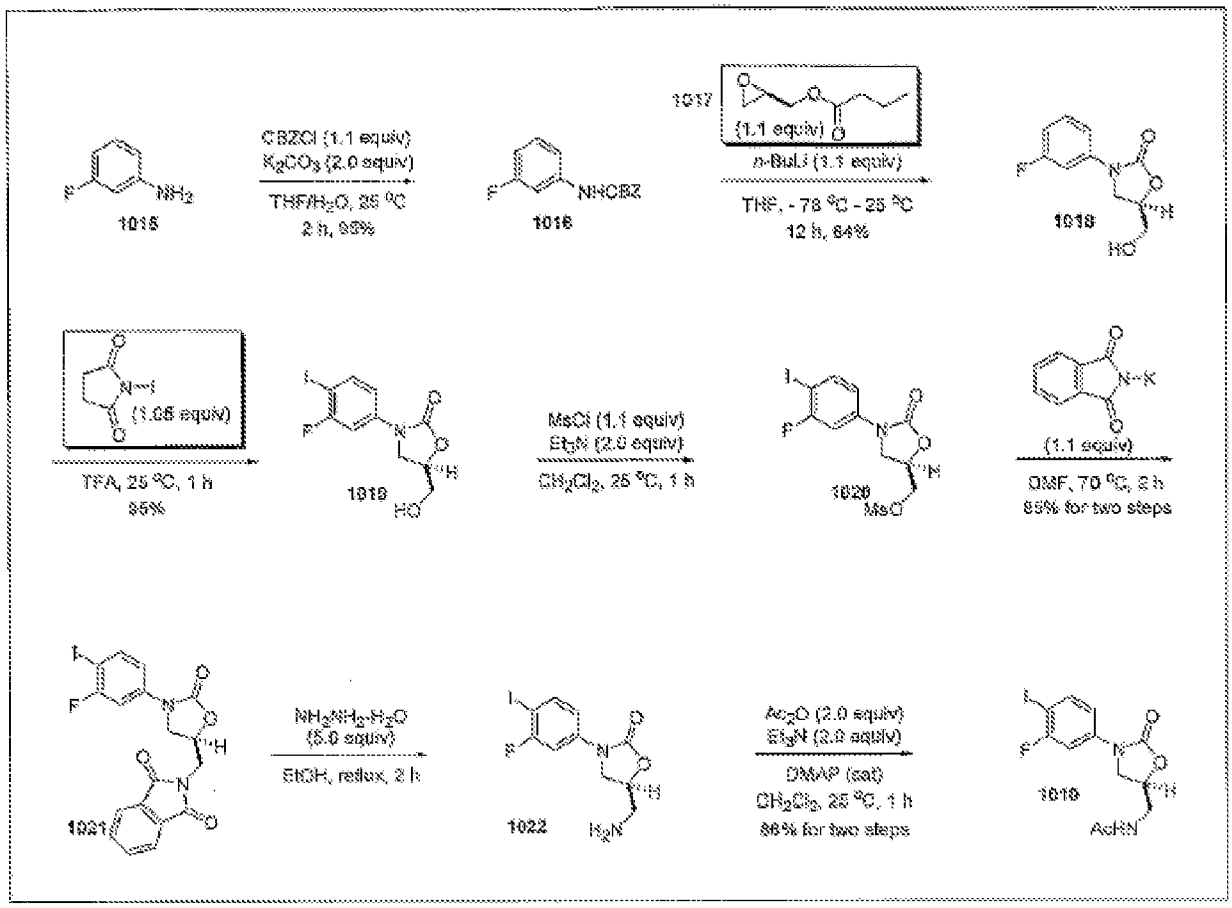
Scheme 2. Synthesis of Radezolid (Compound 1) and its Hydrochloride Salt



Synthesis of Oxazolidinone Compound 1010

[0210] Oxazolidinone compound **1010** is prepared according to Scheme 3 below.

Scheme 3. Synthesis of Oxazolidinone Compound 1010



[0211] (3-Fluoro-phenyl)-carbamic acid benzyl ester (1016). A solution of the 3-fluoro-phenylamine (**1015**, which is commercially available under the names 3-fluoroaniline or 1-amino-3-fluorobenzene, 18.7 g, 168.3 mmol) in tetrahydrofuran (THF, 150 mL) was treated with potassium carbonate (K_2CO_3, 46.45 g, 336.6 mmol, 2.0 equiv) and water (150 mL) before a solution of benzyl chloroformate (CBZCl, 31.58 g, 185.1 mmol, 26.1 mL, 1.1 equiv) in THF (50 mL) was dropwise added into the reaction mixture at room temperature under nitrogen. The resulting reaction mixture was stirred at room temperature for 2 h. When TLC showed that the reaction was complete, the reaction mixture was treated with water (100 mL) and ethyl acetate (EtOAc, 100 mL). The two layers were separated, and the aqueous layer was extracted with EtOAc (2 x 100 mL). The combined organic extracts were washed with water (2 x l00 mL) and saturated NaCl aqueous solution (100 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was further dried *in vacuo* to afford the crude, (3-fluoro-phenyl)-carbamic acid benzyl ester (2, 39.2 g, 41.23 g theoretical, 95%) as pale-yellow oil, which was found to be essentially pure and was directly used in the subsequent reactions without further purifications. For **1016**: ^{1}H

NMR (300 MHz, $CDCl_3$) δ 5.23 (s, 2H, OCH_2Ph), 6.75 - 6.82 (m, 2H), 7.05 (dd, 1H, J= 1.4, 8.2 Hz), 7.22 - 7.45 (m, 6H); $C_{14}H_{12}FNO_2$, LCMS (EI) *m/e* 246 (M^+ + H).

[0212] **(5*R*)-3-(3-Fluoro-phenyl)-5-hydroxymethyl-oxazolidin-2-one (1018)**. A solution of (3-fluorophenyl)-carbamic acid benzyl ester (**1016**, 39.2 g, 160.0 mmol) in anhydrous tetrahydrofuran (THF, 300 mL) was cooled dowel to -78 °C in a dry-ice-acetone bath before a solution of *n*-butyllithium (*n*-BuLi, 2.5 M solution in hexane, 70.4 mL, 176 mmol, 1.1 equiv) in hexane was dropwise added at -78 °C under nitrogen. The resulting reaction mixture was subsequently stirred at -78 °C for 1 h before a solution of (*R*)-(-)-glycidyl butyrate 1017 (25.37 g, 24.6 mL, 176 mmol, 1.1 equiv) in anhydrous THF (100 mL) was dropwise added into the reaction mixture at-78 °C under nitrogen. The resulting reaction mixture was stirred at -78 °C for 30 min before being gradually warmed up to room temperature for 12 h under nitrogen. When TLC and HPLC/MS showed that the reaction was complete, the reaction mixture was quenched with water (200 mL), and the resulting mixture was stirred at room temperature for 1 h before ethyl acetate (EtOAc, 200 mL) was added. The two layers were separated, and the aqueous layer was extracted with EtOAc (2 x 100 mL). The combined organic extracts were washed with water (2 x 100 mL) and saturated NaCl aqueous solution (100 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The white crystals were precipitated out from the concentrated solution when most of the solvents were evaporated. The residue was then treated with 20% EtOAc-hexane (100 mL) and the resulting slurry was further stirred at room temperature for 30 min. The solids were then collected by filtration and washed with 20% EtOAc-hexane (2 x 50 mL) to afford the crude, (5*R*)-(3-(3-fluoro-phenyl)-5-hydroxymethyl-oxazolidin-2-one (**1018**, 24.4 g, 33.76 g theoretical, 72.3%) as white crystals, which were found to be essentially pure and was directly used in the subsequent reactions without further purifications. For **1018**: ^1H NMR (300 MHz, DMSO-d_6) δ 3.34 - 3.72 (m, 2H), 3.83 (dd, 1H, J= 6.2, 9.0 Hz), 4.09 (t, 1H, J= 12.0 Hz), 4.68 -4.75 (m, 1H), 5.23 (t, 1H, J = 5.6 Hz, OH), 6.96 (m, 1H), 7.32 - 7.56 (m, 3H); $C_{10}H_{10}FNO_3$, LCMS (EI) *m/e* 212 (M^+ + H).

[0213] **(5*R*)-3-(3-Fluoro-4-iodo-phenyl)-5-hydroxymethyl-oxazolidin-2-one (1019)**. A solution of (5*R*)-(3-(3-fluoro-phenyl)-5-hydroxymethyl-oxazolidin-2-one (**1018**, 10.74 g, 50.9 mmol) in trifluoroacetic acid (TFA, 50 mL) was treated with N-iodosuccinimide (NIS, 12.03 g, 53.45 mmol, 1.05 equiv) at 25 °C, and the resulting reaction mixture was stirred at 25 °C for 2 h. When TLC and HPLC/MS showed that the reaction was complete, the reaction mixture was concentrated *in vacuo*. The residue was then treated with water (100 mL) and 20% EtOAc-hexane (100 mL) at 25 °C, and the resulting mixture was stirred at 25 °C for 30 min before being cooled down to 0 – 5 °C for 2 h. The white solids were collected by filtration, washed with water

(2 x 25 mL) and 20% EtOAc-hexane (2 x 25 mL), and dried *in vacuo* to afford the crude, (5*R*)-3-(3-fluoro-4-iodo-phenyl)-5-hydroxymethyl-oxazolidin-2-one (**1019**, 15.1 g, 17.15 g theoretical, 88%) as off-white powders, which were found to be essentially pure and were directly used in the subsequent reactions without further purifications. For **1019**: ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.58 (dd, 1H, J= 4.2, 12.6 Hz), 3.67 (dd, 1H, J= 3.0, 12.6 Hz), 3.67 (dd, 1H, J= 6.3, 9.0 Hz), 4.07 (t, 1H, J = 9.0 Hz), 4.72 (m, 1H), 5.21 (br. s, 1H, OH), 7.22 (dd, 1H, J= 2.4, 8.4 Hz), 7.58 (dd, 1H, J= 2.4, 11.1 Hz), 7.81 (dd, 1H, J= 7.8, 8.7 Hz); $C_{10}H_9FINO_3$, LCMS (EI) *m/e* 338 (M^+ + H).

[0214] (5*R*)-Methanesulfonic acid 3-(3-fluoro-4-iodo-phenyl)-2-oxo-oxazolidin-5-ylmethyl ester (1020). A solution of (5*R*)-3-(3-fluoro-4-iodo-phenyl)-5-hydroxymethyl-oxazolidin-2-one (**1019**, 25.2 g, 74.8 mmol) in methylene chloride (CH_2Cl_2, 150 mL) was treated with trimethylamine (TEA, 15.15 g, 20.9 mL, 150 mmol, 2.0 equiv) at 25 °C, and the resulting mixture was cooled down to 0 – 5 °C before methanesulfonyl chloride (MsCl, 10.28 g, 6.95 mL, 89.7 mmol, 1.2 equiv) was dropwise introduced into the reaction mixture at 0 – 5 °C under nitrogen. The resulting reaction mixture was subsequently stirred at 0 – 5 °C for 1 h under nitrogen. When TLC and HPLC/MS showed that the reaction was complete, the reaction mixture was quenched with water (100 mL) and CH_2Cl_2 (100 mL). The two layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (100 mL). The combined organic extracts were washed with water (2 x 100 mL) and saturated NaCl aqueous solution (100 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was further dried *in vacuo* to afford the crude, (5*R*)-methanesulfonic acid 3-(3-fluoro-4-iodo-phenyl)-2-oxo-oxazolidin-5-ylmethyl ester (**1020**, 30.71 g, 31.04 g theoretical, 98.9%) as an off-white powder, which was found to be essentially pure and was directly used in the subsequent reactions without further purifications. For **1020**: $C_{11}H_{11}FINO_5S$, LCMS (EI) *m/e* 416 (M^+ + H).

[0215] (5*R*)-2-[3-(3-Fluoro-4-iodo-phenyl)-2-oxo-oxazolidin-5-ylmethyl]-isoindole-1,3-dione (1021). A solution of (5*R*)-methanesulfonic acid 3-(3-fluoro-4-iodo-phenyl)-2-oxo-oxazolidin-5-ylmethyl ester (**1020**, 26.38 g, 63.57 mmol) in anhydrous N,N-dimethylformamide (DMF, 120 mL) was treated with solid potassium phthalimide (12.95 g, 70.0 mmol, 1.1 equiv) at 25 °C, and the resulting reaction mixture was warmed up to 70 °C for 2 h. When TLC and HPLC showed that the reaction was complete, the reaction mixture was cooled down to room temperature before being quenched with water (400 mL), and the resulting mixture was stirred at room temperature for 10 min before being cooled down to 0 – 5 °C for 1 h. The white precipitates were then collected by filtration, washed with water (3 x 100 mL), and dried *in vacuo* to afford the crude, (5*R*)-2-[3-(3-fluoro-4-iodo-phenyl)-2-oxo-oxazolidin-5-ylmethyl]-isoindole-1,3-dione (**1021**, 27.85 g, 29.64 g theoretical, 94%) as an off-white powder, which was found to

be essentially pure and was directly used in the subsequent reactions without further purifications. For **1021**: $C_{18}H_{12}FIN_2O_4$, LCMS (EI) *m/e* 467 (M^+ + H).

[0216] (5*S*)-5-Aminomethyl-3-(3-fluoro-4-iodo-phenyl)-oxazolidin-2-one (1022). A solution of (5*R*)-2-[3-(3-fiuoro-4-iodo-phenyl)-2-oxo-oxazolidin-5-ylmethyl]-isoindole-l,3-dione (**1021**, 23.3 g, 50.0 mmol) in ethanol (EtOH, 150 mL) was treated with hydrazine monohydrate (12.52 g, 12.1 mL, 250 mmol, 5.0 equiv) at 25 °C, and the resulting reaction mixture was warmed up to reflux for 2 h. White precipitates were formed while the reaction mixture was refluxed. When TLC and HPLC showed that the reaction was complete, the reaction mixture was cooled down to room temperature before being quenched with water (100 mL). The white precipitates were totally dissolved when water was introduced into the reaction mixture and a homogeneous solution was generated. The aqueous solution was then extracted with CH_2Cl_2 (3 x 200 mL), and the combined organic extracts were washed with water (2 x 100 mL) and saturated NaCl aqueous solution (100 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was further dried *in vacuo* to afford the crude (5*S*)-5-aminomethyl-3-(3-fluoro-4-iodo-phenyl)-oxazolidin-2-one (**1022**, 16.0 g, 16.8 g theoretical, 95.2%) as a white powder, which was found to be essentially pure and was directly used in the subsequent reactions without further purifications. For **1022**: $C_{10}H_{10}FIN_2O_2$, LCMS (EI) *m/e* 337 (M^+ + H).

[0217] (5*S*)-N-[3-(3-Fluoro-4-iodo-phenyl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide (1010). A suspension of (5*S*)-5-aminomethyl-3-(3-fluoro-4-iodo-phenyl)-oxazolidin-2-one (**1022**, 16.0 g, 47.6 mmol) in CH_2Cl_2 (150 mL) was treated with triethylamine (TEA, 9.62 g, 13.2 mL, 95.2 mmol, 2.0 equiv) at 25 °C, and the resulting reaction mixture was cooled down to 0 – 5 °C before being treated with acetic anhydride (Ac_2O, 7.29 g, 6.75 mL, 71.4 mmol, 1.5 equiv) and 4-N,N-dimethylaminopyridine (DMAP, 58 mg, 0.5 mmol, 0.01 equiv) at 0 – 5 °C under nitrogen. The resulting reaction mixture was subsequently stirred at 0 – 5 °C for 2 h. When TLC and HPLC showed that the reaction was complete, the reaction mixture was quenched with water (100 mL). The two layers were separated, and the aqueous layer was then extracted with CH_2Cl_2 (2 x 50 mL), and the combined organic extracts were washed with water (2 x 100 mL) and saturated NaCl aqueous solution (100 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was further dried *in vacuo* to afford the crude, (5*S*)-N-[3-(3-fluoro-4-iodo-phenyl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide (**1010**, 17.36 g, 17.99 g theoretical, 96.5%) as white powders, which were found to be essentially pure and were directly used in the subsequent reactions without further purifications. For **1010**: ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.63 (s, 3H, $NHCOCH_3$), 3.25 (t, 2H, J= 5.4 Hz), 3.56 (dd, 1H, J= 6.4, 9.2 Hz), 3.95 (t, 1H, J= 9.1 Hz), 4.58 (m, 1H), 5.16 (t, 1H, J= 5.7 Hz, OH), 7.02 (dd, 1H, J= 2.4, 8.2 Hz), 7.38 (dd, 1H, J= 2.4, 10.8

Hz), 7.66 (t, 1H, J= 7.5, 8.4 Hz), 8.08 (t, 1H, J= 5.8 Hz, $NHCOCH_3$); $C_{12}H_{12}FIN_2O_3$, LCMS (EI) *m/e* 379 (M^+ + H).

[0218] Synthesis of Radezolid (Compound 1)

[0219] 4-Methoxybenzyl Azide 1001. A solution of 4-methoxybenzyl chloride **1000** (51.8 g, 331.0 mmol) in anhydrous DMF (200 mL) was treated with solid sodium azide (21.5 g, 331.0 mmol, 1.0 equiv) at 25 °C, and the resulting mixture was stirred at 25 °C for 24 h. When TLC and HPLC/MS showed that the reaction was complete, the reaction mixture was quenched with water (400 mL) and ethyl acetate (EtOAc, 400 mL) at room temperature. The two layers were separated, and the aqueous layer was extracted with EtOAc (200 mL). The combined organic extracts were washed with water (2 x 200 mL) and saturated NaCl aqueous solution (100 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The crude 4-methoxybenzyl amide (51.2 g, 53.95 g theoretical, 94.9% yield) was obtained as a colorless oil, which by HPLC and ^{1}H NMR was found to be essentially pure and was directly used in the subsequent reaction without further purifications. For 4-methoxybenzyl azide **1001**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.84 (s, 3H, $ArOCH_3$), 4.29 (s, 2H, Ar-CH_2), 6.96 (d, 2H, J = 8.7 Hz), 7.28 (d, 2H, J= 7.8 Hz).

[0220] C-[1-(4-Methoxy-benzyl)-1H-[1,2,3ltriazol-4-yl]-methylamine and C-[3-(4-Methoxybenzyl)-3*H*-[1,2,3]triazol-4-yl]-methylamine (1003 and 1004). A solution of 4-methoxybenzylamide **1001** (61.2 g, 375.5 mmol) in toluene (188 mL) was treated with propargylamine **1002** (commercially available, 30.97 g, 38.6 mL, 563.0 mmol, 1.5 equiv) at 25 °C, and the resulting reaction mixture was warmed up to gentle reflux at 100 – 110 °C for 21 h. When TLC and HPLC/MS showed that the reaction was complete, the reaction mixture was cooled down to room temperature before being concentrated *in vacuo* to remove the excess amount of propargylamine and solvent. The oily residue was then treated with 30% ethyl acetate – hexane (v/v, 260 mL), and the resulting mixture was warmed up to reflux and stirred at reflux for 30 min before being cooled down to room temperature for 1 h. The pale-yellow solids were then collected by filtration, washed with 30% ethyl acetate – hexane (v/v, 2 x 100 mL), and dried *in vacuo* at 40 °C for overnight to afford the crude, cycloaddition product (78.8 g, 81.75 g theoretical, 96.4%) as a mixture of two regioisomers, C-[1-(4-methoxy-benzyl)-1H-[1,2,3]triazol-4-yl]-methylamine and C-[3-(4-methoxy-benzyl)-3*H*-[1,2,3]triazol-4-yl]-methylamine (**1003** and **1004**), in a ratio of 1.2 to 1 by ^{1}H NMR. The crude cycloaddition product was found to be essentially pure and the two regioisomers were not separated before being used directly in the subsequent reaction without further purification. For **1003** and **1004**: ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.82 (br. s, 2H, NH_2), 3.72 and 3.73 (two s, 3H, Ar-OCH_3), 5.47 and 5.53 (two s, 2H, $ArCH_2$), 6.89 and 6.94 (two d, 2H, J= 8.7Hz, Ar-H), 7.17 and 7.29 (two d, 2H,

J= 8.7 Hz, Ar-H), 7.58 and 7.87 (two br. s, 1H, triazole-CH); $C_{11}H_{14}N_40$, LCMS (EI) *m/e* 219 (M^+ + H) and 241 (M^+ + Na).

[0221] 4-({*tert*-Butoxycarbonyl- [1-(4-methoxy-benzyl)-1H-[1,2,3]triazol-4-ylmethyl]-amino}-methyl)-phenylboronic acid and 4-({*tert*-Butoxycarbonyl-[3-(4-methoxy-benzyl)-3*H*-[1,2,3]triazol-4-ylmethyl]-amino}-methyl)-phenylboronic acid (1008 and **1009)**. *Method A*. A solution of the regioisomeric C-[1-(4-methoxy-benzyl)-1H-[1,2,3]triazol-4-yl]-methylamine and C-[3-(4-methoxy-benzyl)-3*H*-[1,2,3]triazol-4-yl]-methylamine (**1003** and **1004**, 20.0 g, 91.74 mmol) in 1,2-dichloroethane (DCE, 280 mL) was treated with 4-formylphenylboronic acid **1005** (commercially available, 12.39 g, 82.57 mmol, 0.9 equiv) at room temperature, and the resulting reaction mixture was stirred at room temperature for 10 min. Sodium triacetoxyborohydride ($NaB(OAc)_3H$, 29.2 g, 137.6 mmol, 1.5 equiv) was then added to the reaction mixture in three portions over the period of 1.5 h at room temperature, and the resulting reaction mixture was stirred at room temperature for an additional 3.5 h. When TLC and HPLC/MS showed that the reductive amination reaction was complete, the reaction mixture was concentrated *in vacuo*. The residue, which contained a regioisomeric mixture of 4-({[1-(4-methoxy-benzyl)- 1H-[1,2,3]triazol-4-ylmethyl]-amino}-methyl)-phenylboronic acid and 4-({[3-(4-methoxy-benzyl)-3*H*-[1,2,3]triazol-4-ylmethyl]-amino}-methyl)-phenylboronic acid as the reductive amination products (**1006** and **1007**), was then treated with tetrahydrofuran (THF, 100 mL) and water (water, 100 mL). The resulting solution was subsequently treated with solid potassium carbonate (K_2CO_3, 37.98 g, 275.2 mmol, 3.0 equiv) and di-*tert*-butyl dicarbonate (BOC_2O, 20.02 g, 91.74 mmol, 1.0 equiv) at room temperature and the reaction mixture was stirred at room temperature for 2 h. When TLC and HPLC/MS showed that the N-BOC protection reaction was complete, the reaction mixture was treated with ethyl acetate (EtOAc, 150 mL) and water (water, 100 mL). The two layers were separated, and the aqueous layer was extracted with ethyl acetate (50 mL). The combined organic extracts were washed with water (50 mL), 1.5 N aqueous HCl solution (2 x 100 mL), water (100 mL), and saturated aqueous NaCl solution (100 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The crude, regioisomeric 4- ({*tert*-butoxycarbonyl-[1-(4-methoxy-benzyl)-1*H*-[1,2,3]triazol-4-ylmethyl]-amino}-methyl)-phenylboronic acid and 4-({*tert*-butoxycarbonyl-[3-(4-methoxy-benzyl)-3*H*-[1,2,3]triazol-4-ylmethyl]-amino}-methyl)-phenylboronic acid (**1008** and **1009**, 35.98 g, 37.32 g, 96.4%) was obtained as a pale-yellow oil, which solidified upon standing at room temperature *in vacuo*. This crude material was directly used in the subsequent reaction without further purification. For **1008** and **1009**: ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.32 and 1.37 (two br. s, 9H, $COOC(CH_3)_3$), 3.70, 3.73 and 3.74 (three s, 3H,

Ar-OCH_3), 4.07 - 4.39 (m, 4H), 5.49 and 5.52 (two s, 2H), 6.70 -8.04 (m, 9H, Ar-H and triazole-CH); $C_{23}H_{29}BN_4O_5$, LCMS (EI) *m/e* 453 (M^+ + H) and 475 (M^++ Na).

[0222] *Method B*. A solution of the regioisomeric C-[1-(4-methoxy-benzyl)-1*H*-[1,2,3]triazol-4-yl]-methylamine and C-[3-(4-methoxy-benzyl)-3*H*-[1,2,3]triazol-4-yl]-methylamine (**1003** and **1004**, 20.06 g, 92.0 mmol) in tetrahydrofuran (THF, 300 mL) was treated with 4-formylphenylboronic acid (13.11 g, 87.4 mmol, 0.95 equiv) at room temperature, and the resulting reaction mixture was stirred at room temperature for 10 min. Sodium triacetoxyborohydride ($NaB(OAc)_3H$, 29.25 g, 138.0 mmol, 1.5 equiv) was then added to the reaction mixture in three portions over the period of 1.5 h at room temperature, and the resulting reaction mixture was stirred at room temperature for an additional 3.5 h. When TLC and HPLC/MS showed that the reductive amination reaction was complete, the reaction mixture, which contained a regioisomeric mixture of 4-({[1-(4-methoxy-benzyl)-1H-[1,2,3]triazol-4-ylmethyl]-amino}-methyl)-phenylboronic acid and 4-({[3-(4-methoxy-benzyl)-3*H*-[1,2,3]triazol-4-ylmethyl]-amino}-methyl)-phenylboronic acid as the reductive amination products (1006 and 1007), was then treated with water (water, 200 mL). The resulting aqueous solution was subsequently treated with solid potassium carbonate (K_2CO_3, 38.0 g, 276 mmol, 3.0 equiv) and di-*tert*-butyl dicarbonate (BOC_2O, 20.08 g, 92 mmol, 1.0 equiv) at room temperature and the reaction mixture was stirred at room temperature for 2 h. When TLC and HPLC/MS showed that the N-BOC protection reaction was complete, the reaction mixture was treated with ethyl acetate (EtOAc, 150 mL) and water (water, 100 mL). The two layers were separated, and the aqueous layer was extracted with ethyl acetate (50 mL). The combined organic extracts were washed with water (50 mL), 1.5 N aqueous HCl solution (2 x 100 mL), water (100 mL), and saturated aqueous NaCl solution (100 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The crude, 4-({*tert*-butoxycarbonyl-[1 -(4-methoxy-benzyl)-1*H*-[1,2,3]triazol-4-ylmethyl]-amino}-methyl)-phenylboronic acid and 4-({*tert*-butoxycarbonyl-[3-(4-methoxy-benzyl)-3*H*-[1,2,3]triazol-4-ylmethyl]-amino}-methyl)-phenylboronic acid (**1008** and **1009**, 38.45 g, 39.50 g, 97.3%) was obtained as a pale-yellow oil, which solidified upon standing at room temperature *in vacuo*. This crude material was found to be essentially identical in every comparable aspect as the material obtained from *Method A* and was directly used in the subsequent reaction without further purification.

[0223] **(5*S*)-{4'-[5-(Acertylamino-methyl)-2-oxo-oxazolidin-3-yl-2'-fluoro-biphenyl-4-ylmethyl}-[1-(4-methoxy-benzyl)-1H-[1,2,3]triazol-4-ylmethyl]-carbamic acid *tert*-butyl ester and (5*S*)-{4'-[5-(Acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluoro-biphenyl-4-ylmethyl}-[1-(4-methoxy-benzyl)-1H-[1,2,3]triazol-5-ylmethyl]-carbamic acid *tert*-butyl**

ester (1011 and **1012)**. A suspension of the crude regioisomeric mixture of 4-({*tert*-butoxycarbonyl-[1-(4-methoxybenzyl)-1*H*-[1,2,3]triazol-4-ylmethyl]-amino}-methyl)-phenylboronic acid and 4-({*tert*-butoxycarbonyl-[3-(4-methoxy-benzyl)-3*H*-[1,2,3]triazol-4-ylmethyl]-amino}-methyl)-phenylboronic acid (**1008** and **1009**, 37.62 g, 83.23 mmol) and N-[3-(3-fluoro-4-iodo-phenyl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide (**1010**, 28.32 g, 74.9 mmol, 0.90 equiv) in toluene (150 mL) was treated with powder K_2CO_3 (34.45 g, 249.7 mol, 3.0 equiv), EtOH (50 mL), and water (50 mL) at 25 °C, and the resulting mixture was degassed three times under a steady stream of Argon at 25 °C. $Pd(PPh_3)_4$ (866 mg, 0.749 mmol, 0.01 equiv) was subsequently added to the reaction mixture, and the resulting reaction mixture was degassed three times again under a steady stream of Argon at 25 °C before being warmed up to gentle reflux for 18 h. When TLC and HPLC/MS showed the coupling reaction was complete, the reaction mixture was cooled down to room temperature before being treated with water (100 mL) and ethyl acetate (100 mL). The two layers were then separated, and the aqueous layer was extracted with EtOAc (100 mL). The combined organic extracts were washed with water (50 mL), 1.5 N aqueous HCl solution (2 x 150 mL), water (100 mL), and the saturated aqueous NaCl solution (100 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residual oil was solidified upon standing at room temperature *in vacuo* to afford the crude, (5*S*)-{4'-[5-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluorobiphenyl-4-ylmethyl}-[1-(4-methoxy-benzyl)-1*H*-[1,2,3]triazol-4-ylmethyl]-carbamic acid *tert*-butylester (1011) and (5*S*)-{4'-[5-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluorobiphenyl-4-ylmethyl} -[1-(4-methoxy-benzyl)-1H-[1,2,3]triazol-5-ylmethyl]-carbamic acid *tert*-butylester (**1012**) as a regioisomeric mixture. This crude product (43.36 g, 49.28 g theoretical, 88%) was used directly in the subsequent reaction without further purification. For the mixture of **1011** and **1012**: ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.35 and 1.38 (two br. s, 9H, $COO(CH_3)_3$), 1.85 (s, 3H, $COCH_3$), 3.45 (t, 2H, J= 5.4 Hz), 3.73 and 3.76 (two s, 3H, Ar-OCH_3), 3.79 (dd, 1H, J= 6.6, 9.1 Hz), 4.18 (t, 1H, J= 9.1 Hz), 4.35 - 4.43 (m, 4H), 4.73 - 4.81 (m, 1H), 5.50 (br. s, 2H), 6.90 and 6.98 (two d, 2H, J= 8.7 Hz), 7.28 and 7.32 (two d, 2H, J= 8.7 Hz), 7.35 (dd, 2H, J= 2.2, 8.6 Hz), 7.42 (dd, 1H, J= 2.2, 8.6 Hz), 7.49 - 7.63 (m, 4H, aromatic-H), 7.90 and 7.99 (two br. s, 1H, triazole-CH), 8.29 (t, 1H, J= 5.8 Hz, $NHCOCH_3$); $C_{35}H_{39}FN_6O_6$, LCMS (EI) $_{m/e}$ 659 (M^+ + H) and 681 (M^+ + Na).

[0224] (5*S*)-N-{3-[2-Fluoro-4'-({[1-(4-methoxy-benzyl)-1*H*-[1,2,3]triazol-4-ylmethyl]-amino}-methyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide Hydrochloride (1013) and (5*S*)-N-{3-[2-Fluoro-4'-({[1-(4-methoxy-benzyl)-1H-[1,2,3]triazol-5-ylmethyl] -amino}-methyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide Hydrochloride (1014). A solution of a regioisomeric mixture of (5*S*)-{4'-[5-(acetylamino-methyl)-2-oxo-

oxazolidin-3-yl]-2'-fluoro-biphenyl-4-methyl}-[1-(4-methoxy-benzyl)-1*H*-[1,2,3]triazol-4-ylmethyl]-carbamic acid *tert*-butyl ester and (5*S*)-{4'-[5-(acetylamino-methyl)-2-oxo-oxazolidin-3-yl]-2'-fluorobiphenyl-4-ylmethyl}-[1-(4-methoxy-benzyl)-1*H*-[1,2,3]triazol-5-ylmethyl]-carbamic acid *tert*-butyl ester (**1011** and **1012**, 37.28 g, 56.65 mmol) in ethyl acetate (EtOAc, 150 mL) and methanol (MeOH, 30 mL) was treated with a solution of 4 N hydrogen chloride in 1,4-dioxane (113.3 mL, 453.2 mmol, 8.0 equiv) at room temperature, and the resulting reaction mixture was stirred at room temperature for 12 h. When TLC and HPLC/MS showed that the N-BOC deprotection reaction was complete, the solvents were removed *in vacuo*. The residue was then suspended in 250 mL of 5% methanol (MeOH) in acetonitrile (CH_3CN), and the resulting slurry was stirred at room temperature for 1 h. The solids were then collected by filtration, washed with toluene (2 x 100 mL) and 5% methanol in acetonitrile (2 x 50 mL), and dried *in vacuo* to afford a regioisomeric mixture of the crude, (5*S*)-N-{3-[2-fluoro-4'-({[1-(4-methoxy-benzyl)-1H-[1,2,3]triazol-4-ylmethyl]-amino}-methyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide hydrochloride and (5*S*)-N-{3-[2-fluoro-4'-({[1-(4-methoxy-benzyl)-1*H*-[1,2,3]triazol-5-ylmethyl]-amino}-methyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide hydrochloride (**1013** and **1014**, 30.0 g, 33.68 g theoretical, 89.1% yield) as off-white crystals in a ratio of 1.2 to 1. This material was found by ^{1}H NMR and HPLC/MS to be essentially pure and was directly used in the subsequent reactions without further purification. For the regioisomeric mixture of **1013** and **1014**: ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.84 (s, 3H, $COCH_3$), 3.44 (t, 2H, J = 5.4 Hz), 3.71 and 3.74 (two s, 3H, Ar-OCH_3), 3.80 (dd, 1H, J= 6.6, 9.1 Hz), 4.17 (t, 1H, J= 9.1 Hz), 4.23 -4.30 (m, 4H), 4.73 -4.80 (m, 1H), 5.58 and 5.70 (two s, 2H), 6.88 and 6.93 (two d, 2H, J= 8.7 Hz), 7.15 and 7.32 (two d, 2H, J = 8.7 Hz), 7.43 (dd, 2H, J= 2.2, 8.6 Hz), 7.52 - 7.62 (m, 6H, aromatic-H), 8.28 (s, 1H, triazole-CH), 8.32 (t, 1H, J= 5.8 Hz, $NHCOCH_3$), 9.91 and 10.32 (two br. s, 2H, $ArCH_2N^+H_2$) ; $C_{30}H_{31}FN_6O_4$, LCMS (El) *m/e* 559 (M^+ + H) and 581 (M^+ + Na).

[0225] (5*S*)-N-[3-(2-Fluoro-4'-{[(1H-[1,2,3]triazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide (1) (radezolid). A solution of the crude regioisomeric mixture of (5*S*)-N-{3-[2-fluoro-4'-({[1-(4-methoxy-benzyl)-1H-[1,2,3]triazol-4-ylmethyl]-amino}-methyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide hydrochloride and (5*S*)-N-{3-[2-fluoro-4'({[1-(4-methoxy-benzyl)-1H-[1,2,3]triazol-5-ylmethyl]-amino}-methyl)-biphenyl-4-yl]-2-oxo-oxazolidin-5-ylmethyl}-acetamide hydrochloride (**1013** and **1014**, 29.17 g, 49.07 mmol) in trifluoroacetic acid (TFA, 150 mL) was warmed up to 65 – 70 °C, and the resulting reaction mixture was stirred at 65 – 70 °C for 12 h. When TLC and HPLC/MS showed that the deprotection reaction was complete, the solvents

were removed *in vacuo*. The residual solids were then treated with ethyl acetate (EtOAc, 100 mL) and water (150 mL) before being treated with a saturated aqueous solution of sodium carbonate (30 mL) at room temperature. The resulting mixture was then stirred at room temperature for 1 h before the solids were collected by filtration, washed with EtOAc (2 x 50 mL) and water (2 x 50 mL), and dried *in vacuo* at 40 – 45 °C to afford the crude, (5S)-N-[3-(2-fluoro-4'-{[(1*H*-[1,2,3]triazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide (**1** as the free base, 18.9 g, 21.49 g theoretical, 87.9%) as an off-white powder, which by HPLC/MS and ^{1}H NMR was found to be one pure regioisomer and this regioisomer was found to be identical to the material obtained from deprotection of **1013** alone by the same method. For **1** as the free base: ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.85 (s, 3H, $COCH_3$), 3.44 (t, 2H, J= 5.4 Hz), 3.74 (s, 2H), 3.77 (s, 2H), 3.79 (dd, 1H, J= 6.4, 9.2 Hz), 4.17 (t, 1H, J= 9.1 Hz), 4.72-4.81 (m, 1H), 7.39- 7.62 (m, 7H, aromatic-H), 7.73 (s, 1H, triazole-CH), 8.29 (t, 1H, J= 5.8 Hz, $NHCOCH_3$), 9.72 (br. s, 2H, $ArCH_2N^+H_2$), 15.20 (hr. s, 1H, triazole-NH); $C_{22}H_{23}FN_6O_3$, LCMS (EI) *m/e* 439 (M^+ + H) and 461 (M^+ +Na); DSC onset melt at 208.4 °C.

[0226] (5*S*)-N-[3-(2-Fluoro-4'-{[(1H-[1,2,3]triazol-4-ylmethyl)-amino]-methyl}-biphenyl-4-yl)-2-oxo-oxazolidin-5-ylmethyl]-acetamide chloride (1 hydrochloride salt). A suspension of **1** free base (18.0 g, 41.1 mmol) in ethyl acetate (EtOAc, 80 mL), and methanol (MeOH, 20 mL) was treated with a solution of 4.0 N hydrogen chloride in 1,4-dioxane (41.1 mL, 164.4 mmol, 4.0 equiv) at room temperature, and the resulting mixture was stirred at room temperature for 8 h. The solvents were then removed *in vacuo*, and the residue was further dried *in vacuo* before being treated with a mixture of 10% methanol in acetonitrile (80 mL). The solids were collected by filtration, washed with 10% MeOH/acetonitrile (2 x 40 mL), and dried *in vacuo* to afford **1** hydrochloride salt (18.13 g, 19.50 g theoretical, 93% yield) as off-white crystals; DSC endotherm at 266 °C; onset melt at 261 °C.

[0227] Recrystallization of Radezolid Hydrochloride. The crude **1** hydrochloride salt was recrystallized from acetonitrile and water according to the following procedure: A suspension of the crude **1** hydrochloride salt (50.0 g) in acetonitrile (1250 mL) was warmed up to reflux before the distilled water (water, 280 mL) was gradually introduced to the mixture. The resulting clear yellow to light brown solution was then stirred at reflux for 10 min before being cooled down to 45 – 55 °C. The solution was then filtered through a Celite bed at 45 – 55 °C, and the filtrates were gradually cooled down to room temperature before being further cooled down to 0 – 5 °C in an ice bath for 1 h. The solids were then collected by filtration, washed with acetonitrile (2 x 50 mL), and dried *in vacuo* at 40 °C for 24 h to afford the recrystallized **1** hydrochloride salt (42.5 g, 50.0 g theoretical, 85% recovery) as off-white crystals. For **1**: ^{1}H NMR (300 MHz, DMSO-d_6) δ

1.86 (s, 3H, $COCH_3$), 3.45 (t, 2H, J= 5.4 Hz), 3.84 (dd, 1H, J= 6.4, 9.2 Hz), 4.19 (t, 1H, J= 9.1 Hz), 4.24 (br. s, 2H), 4.31(br. s, 2H), 4.74-4.79 (m, 1H), 7.44(dd, 1H, J= 2.2, 8.6 Hz), 7.57 - 7.66 (m, 6H, aromatic-H), 8.17 (s, 1H, triazole-CH), 8.30 (t, 1H, J= 5.8 Hz, $NHCOCH_3$), 9.72 (br. s, 2H, $ArCH_2N^+H_2$), 15.20 (br. s, 1H, triazole-NH); ^{13}C NMR (75 MHz, DMSO-d_6) δ 22.57, 40.69, 41.50, 47.36, 49.23, 71.85, 105.70 (d, J= 28.5 Hz), 114.14 (d, J = 2.9 Hz), 122.29 (d, J = 13.3 Hz), 128.82 (d, J= 3.0 Hz), 130.70, 130.94, 131.0, 131.22, 135.30, 137.92 (br. s), 139.66 (d, J=11.2 Hz), 154.11,159.13 (d, J= 243.5 Hz), 170.19; $C_{22}H_{23}FN_6O_3$ - HCl, LCMS (EI) *m/e* 439 (M^+ + H) and 461 (M^+ + Na); FTIR cm^{-1} 3300, ~3400-~2300, 3003, 2933, 2810, 2779, 1730, 1654, 1552, 1502, and 807; DSC endotherm at 266 °C; onset melt at 261 °C.

[0228] Radezolid Sulfate Salt. To ~l g of radezolid free base was added 15 mL of acetonitrile/water (2/3 by volume) to generate a radezolid slurry. To the radezolid slurry was added 1 equivalent of sulfuric acid dissolved in water. The resulting clear solution was evaporated on a rotary evaporator with water bath setting at 50 °C. The solution formed a white wet gel. The wet gel was dried under a nitrogen stream. 10 mL of methanol was added to dissolve the gel. The gel remained undissolved. 35 mL of DCM was added subsequently, and the gel-like solid turned into a fluffy white solid. The mixture was further mixed on a slurry wheel overnight. The solid was collected by vacuum filtration on a paper filter, and dried under reduced pressure for ~30 min. Yielded ~0.7 g of crystalline (low crystallinity) salt. (Note: There was some loss during the rotary evaporation). DSC endotherm at 72 and 166 °C; onset melt at 158 °C.

[0229] Radezolid Tosylate Salt. To ~1 g of radezolid free base was added 20 mL of water to generate a radezolid slurry. To the radezolid slurry was added 1 equivalent of toluenesulfonic acid dissolved in methanol at ambient temperature. The radezolid dissolved upon mixing. Some tacky solid formed and attached to the wall of the glass vial. As another 0.5 equivalents of acid added to the mixture, more solid formed. Solid was scraped off the vial. The mixture was further mixed on a slurry wheel overnight. A white soft precipitation formed along the wall of the vial. A white chunky solid formed upon addition of 20 mL of acetone. A solid was collected by vacuum filtration. Yielded ~0.4 g of crystalline salt. DSC endotherm at 97 and 173°C; onset melt at 168 °C.

[0230] Radezolid Esylate Salt. To ~1.1 g of radezolid free base was added 15 mL of acetonitrile/water (2/3 by volume) to generate a radezolid slurry. To the radezolid slurry was added ~ 1.2 equivalents of acid dissolved in methanol. The resulting clear solution was evaporated on a rotary evaporator with water bath setting at 50 °C. Glassy gel was generated. The resulting white foamy gel was resuspended in 35 mL of acetone. The mixture was further

mixed on a slurry wheel overnight. A white solid was collected by vacuum filtration on a paper filter and dried under reduced pressure for ~15 min. Yielded ~1.3 g of crystalline salt. DSC endotherm at 57 and 222 °C; onset melt at 216 °C.

[0231] **Radezolid Ethanedisulfonate Salt**. To ~1.1 g of radezolid free base was added 15 mL of acetonitrile/water (2/3 by volume) to generate a radezolid slurry. To the radezolid slurry was added 0.74 equivalents of acid dissolved in methanol. The resulting clear solution was evaporated on a rotary evaporator with water bath setting at 50 °C. The resulting clear gel was resuspended in 8 mL of methanol, and sonicated. A white gel-like solid formed after sonication. 60 mL of DCM was added subsequently. A white solid formed. The mixture was further mixed on a slurry wheel overnight. A white precipitate was collected by vacuum filtration on a paper filter and dried under reduced pressure for ~ 20 min. Yielded ~ 1.4 g of crystalline salt. DSC endotherm at 204 °C; onset melt at 198 °C.

[0232] **Radezolid Pyroglutamate Salt.** To ~1.1 g of radezolid free base was added 15 mL of acetonitrile/water (2/3 by volume) to generate an API slurry. To the API slurry was added 1.5 equivalents of pyroglutamic acid dissolved in water. The resulting clear solution was evaporated on a rotary evaporator with water bath setting at 50 °C, resulted in a clear gel. The gel was resuspended in acetone in a final volume of ~35 mL. The mixture was further mixed on a slurry wheel overnight. The solid was collected by vacuum filtration on a paper filter, dried under reduced pressure for 30 min. Yielded ~ 1.3 g of amorphous salt. DSC endotherm at 80 and 118 °C; exotherm at 128 °C; T_g of 79 °C.

[0233] **Radezolid Mesylate Salt.** To ~1.1 g of radezolid free base was added 15 mL of acetonitrile/water (2/3 by volume) to generate a radezolid slurry. To the radezolid slurry was added 1.4 equivalents of acid dissolved in water. The resulting clear solution was evaporated on a rotary evaporator with water bath setting at 50 °C, resulted in a mixture of clear gel and white solid. To the mixture was added 30 mL of acetone. The suspension was further mixed on a slurry wheel overnight. Solid was collected by vacuum filtration on a paper filter, rinsed briefly with acetone, and dried under reduced pressure for ~5 min. Yielded ~1.3 g of crystalline salt. DSC endotherm at 82 and 203 °C; onset melt at 198 °C.

[0234] **Radezolid Mesylate Salt (25 g scale).** A sample of radezolid free base (23.5 g, 53.6 mmol) was suspended in a mixture of water (200 mL) and acetonitrile (20 mL) at room temperature. Neat methanesulfonic acid (3.56 mL, 54.9 mmol) was added. As the acid was added, the slurry thinned and became clear with a few solid particles. Stirring was continued at room temperature for 1 h until all particles had dissolved. The solution was transferred to a rotovap with the water bath set at 50 °C, and approximately 22 mL of solvent was stripped at 100

mBar. The warm solution was cooled in an ice bath and a white precipitate formed. After holding at 0 °C for approximately 1 h, the precipitate was collected by filtration, and the filter cake was washed with cold water (20 mL). The filter cake was then dried in a vacuum oven for 48 h (house vacuum ca. 100 mBar, 65 °C). The radezolid mesylate salt was obtained as a white powder in 90 % yield (25.7 g). An estimate of 0.75 mol % water content was made by ^{1}H NMR in d_6-DMSO, controlling for the amount of water present in the deuterated solvent. DSC endotherm at 82 and 203 °C; onset melt at 198 °C.

Characterization of Radezolid Salts

[0235] The thermal properties were evaluated by differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA) as shown in Tables 7-8 below.

[0236] DSC data were collected on a TA Instruments 2910 DSC. In general, samples in the mass range of 1 to 10 mg were crimped in aluminum sample pans and scanned from 25 to about 300 °C at 10 °C/minute using a nitrogen purge at 50 mL/min.

[0237] TGA data were collected on a TA Instruments 2950 TGA. In general, samples in the mass range of 5 to 15 mg were placed in an open, pre-tarred platinum sample pan and scanned from 25 to about 150 °C at 10 °C/minute using a nitrogen purge.

[0238] Dynamic vapor sorption/desorption (DVS) data were collected on a VTI SGA-100 Vapor Sorption Analyzer. Sorption and desorption data were collected over a range of 5% to 95% relative humidity (RH) at 10% RH intervals under a nitrogen purge. Samples were not dried prior to analysis. Equilibrium criteria used for analysis were less than 0.0100% weight change in 5 minutes, with a maximum equilibration time of 3 hours if the weight criterion was not met. Data were not corrected for the initial moisture content of the samples. Sodium chloride and polyvinylpyrrolidine (PVP) were used as calibration standards.

Thermal Characterization of Radezolid Salts

Table 7. Differential Scanning Calorimetry of Radezolid Salts

Salt Form	Appearance	DSC Peak Temperature (°C) Desolvation	DSC Onset Temperature (°C) Melt
Free base	White solids	N/A	208.4
Acetate	White solids	N/A	207.4
Ascorbate	Yellow clear	N/A	N/A
Benzoate	White solids	106.7	180.4
Citrate	White solids	N/A	N/A
Fumarate	White solids	155.7	217.5
Hydrochloride	White solids	N/A	245.8
Lactate	White solids	122.6	195.9
Maleate	White solids	N/A	147.3
Mesylate	White solids	100.6	189.3
Phosphate	White solids	N/A	178.4
Salicylate	White solids	82.1, 131.5	180.5
Succinate	White solids	N/A	166.7
Sulfate	White solids	N/A	180.5
Tartrate	White solids	88.7, 140.6	210.7

Table 8. Thermal Characterization of Radezolid Salts

Salt	DSC Results	TGA Results	DVS Results
Esylate	Endo: 57 and 222 °C (onset: 216 °C)	0.2933% weight loss up to 200 °C	Sorption: 0.22% weight loss upon equilibration at 5% RH; 2.930% weight gain from 5 to 95% RH Desorption: 2.999% weight loss from 95 to 5% RH
Ethane-1,2-disulfonate	Endo: 204 °C (onset: 198 °C)	0.5052% weight loss up to 200 °C	Sorption: 0.017% weight loss upon equilibration at 5% RH; 2.355% weight gain from 5 to 95% RH Desorption: 2.388% weight loss from 95 to 5% RH
Hydrochloride	Endo: 266 °C (onset: 261 °C)	0.1759% weight loss up to 220 °C	Sorption: 0.03% weight gain upon equilibration at 5% RH; 0.064% weight gain from 5 to 95% RH Desorption: 0.069% weight loss from 95 to 5% RH
Mesylate	Endo: 82 and 203 °C (onset 198 °C)	2.774% weight loss up to 200 °C (corresponding to 0.8 moles of water)	Sorption: 0.114% weight loss upon equilibration at 5% RH; 1.025% weight gain from 5 to 95% RH Desorption: 0.835% weight loss from 95 to 5% RH
Pyroglutamate	Endo: 80 and 118 °C; Exo: 128 °C;	3.262% weight loss up to 150 °C	Sorption: 2.801% weight loss upon equilibration at 5% RH; 23.962% weight gain from 5 to

	Tg: 79 °C		95% RH Desorption: 24.936% weight loss from 95 to 5% RH
Sulfate	Endo: 72 and 166 °C (onset: 158 °C)	1.915% weight loss up to 140 °C (corresponding to 0.6 moles of water)	Sorption: 0.654% weight loss upon equilibration at 5% RH; 11.527% weight gain from 5 to 95% RH Desorption: 11.504% weight loss from 95 to 5% RH
Tosylate	Endo: 97 and 173 °C (onset: 168 °C)	5.464% weight loss up to 100 °C (corresponding to 2 moles of water)	Sorption: 0.070% weight loss upon equilibration at 5% RH; 0.435% weight gain from 5 to 95% RH Desorption: 0.435% weight loss from 95 to 5% RH

Solubility of Radezolid Salts

[0239] The solubilities of the various radezolid salts was determined and are shown in Table 9 below. Approximately 2-3.5 mg of each salt was weighed into a glass vessel at ambient temperature. HPLC grade water, 200 μL, was added to each and stirred with a stir bar for two hours. Samples were inspected for solubility both visually and/or microscopically using a Carl Zeiss SV8 stereomicroscope. Additional solvent was added periodically until the solute completely dissolved or the solubility became <0.04 mg/mL.

Table 9. Solubility of Radezolid Primary Isolated Salts

Salt Form	Salt (mg)	Volume (mL)	Solubility (mg/mL)
Fumarate	3.13	1.20	2.6
Citrate	2.56	1.00	2.6
Maleate	3.61	1.60	2.3
Tartrate	2.88	1.60	1.8
Phosphate	3.58	3.40	1.1
Ascorbate	2.51	75.80	<0.03
Benzoate	2.47	82.20	<0.03
Salicylate	3.61	122.20	<0.03
Succinate	2.36	82.20	<0.03
Hydrochloride	2.38	82.20	<0.03
Acetate	2.21	118.20	<0.02
Lactate	2.61	118.20	<0.02
Free base	2.26	116.20	<0.02

[0240] Solubilities of the radezolid free base and radezolid HCl salt in various solvents were estimated and are shown in Tables 10 and 11, respectively, below. A weighed sample was treated with aliquots of test solvent at ambient temperature. Complete dissolution of the test material was determined by visual inspection. Solubility was estimated based on the total solvent used to provide complete dissolution. The actual solubility may be greater than the approximate solubility calculated because of the use of solvent aliquots that were too large or due to a slow rate of dissolution. The solubility is expressed as "less than" if dissolution did not occur during the experiment. If complete dissolution was achieved as a result of only one aliquot addition, the solubility is expressed as "greater than." The approximate solubilities were rounded to the nearest whole number.

Table 10. Approximate Solubilities of Radezolid Free Base

Solvent	Approximate Solubility (mg/mL)
Acetone	<1
Acetonitrile	<1
Dichloromethane	<1
Ethyl acetate	<1
Ethyl ether	<1
Hexafluoroisopropanol (HFIPA)	≥245
HFIPA/Methanol (1:3 by volume)	<1
Hexamethyl-phosphoramide	<26
Methanol	<1
2,2,2-trifluoroethanol (TFE)	≥54
Tetrahydrofuran (THF)	<1
Water	<1

Table 11. Approximate Solubilities of Radezolid HCl Salt

Solvent	Approximate Solubility (mg/mL)
1-Butanol[b]	<2
2-Butanone[b]	<2
Dioxane[b]	<2
Ethanol[b]	<2
Hexafluoroisopropanol (HFIPA)	≥225
Methanol[b]	<2
Propionitrile[b]	<2
2-Propanol[b]	<2
Tert-butanol[b]	<5
Tetrahydrofuran (THF)[b]	<2
2,2,2-trifluoroethanol (TFE)	≥6
HFIPA/Dioxane (9:1)	≥52
HFIPA/Ethanol (5:1)	≥80
HFIPA/THF	≥74

[b] Material never went into solution.

[0241] In another set of experiments, solubility of various radezolid salts was determined by HPLC. The results are provided in Table 12 below. Approximately 1 mL of saturated solution (with excess of solid in solution) of each salt was prepared in water. The mixture was further mixed overnight on a slurry wheel then centrifuged on a desktop centrifuge at maximum speed for ~5 min. The supernatant was collected, and pH was measured. Solubility was determined at the native pH. Then the pH was adjusted to ~3.5 with sodium hydroxide solution or an acid solution in which salt was generated. The supernatant was filtered through a 0.2 μm nylon syringe filter and diluted into 0.1% formic acid solution immediately after filtration for HPLC.

[0242] All HPLC analyses were performed using an Agilent 1100 series liquid chromatograph equipped with a diode array detector, degasser, quaternary pump, and an

autosampler. The chromatographic column was a 4.6 x 150 mm SymmetryShield RP18 column with 3.5 μm packing (Waters). The column temperature was set to 30 °C, and the detector wavelength was 270 nm with a bandwidth of 8 nm and a reference wavelength of 360 nm. The mobile phase A was 0.1% formic acid in water (HPLC grade), mobile phase B was 0.1 % formic acid in methanol (HPLC grade). Flow rate was 1.2 mL/min and the column was equilibrated with 85% mobile phase A and 15% mobile phase B. The injection volume was 5 μl. The elution program was as follows: After sample was injected, the initial gradient was run from 85% mobile phase A, 15 % mobile phase B to 100% mobile phase B in 25 min, followed by 3 min with 100% mobile phase B, then a reverse gradient was run from 100% mobile phase B to 15% mobile phase B in 2 min, then with another 10 min of equilibration run with 85% mobile phase A and 15% mobile phase B.

Table 12. Solubility Determination of Radezolid Salts in Water by HPLC at 23 °C

Salt	Solubility at Native pH (mg/mL)	Native pH	Solubility at Adjusted pH (mg/mL)	Adjusted pH
Esylate	53.8	4.0	61.7	3.5
Ethane-1,2-disulfonate[C]	>133.2	2.0	>116.9	3.6
HCl Salt	1.7	4.6	2.0	3.5
Mesylate	18.6	4.1	18.0	3.5
Pyroglutamate[C]	>250	N/A	N/A	N/A
Sulfate	4.0	1.9	3.3	3.6
Tosylate	0.9	5.1	0.4	3.4

[C] Solution was not saturated.

EXAMPLE 6: Topical Compositions of Radezolid

[0243] A topical composition is prepared by combining the following components utilizing conventional mixing techniques.

Ingredients	% Weight
Deionized Water	qs 100
Ethanol (SD 40B Alcohol)	35.0
Any Compounds in Table 2	0.5 - 10
Salicylic Acid (Optional)	2.0
Dexpanthenol (Optional)	3.0

[0244] In a suitable vessel the antibiotic compound is dissolved in ethanol with stirring. Next, if being added, the optional salicylic acid is dissolved in this ethanol mixture with stirring. If being used, the dexpanthenol is dissolved in a separate vessel in the water with stirring. The water, or if being used, the dexpanthenol solution is combined with the alcohol mixture with mixing.

Topical Gel

[0245] A topical composition is prepared by combining the following components utilizing conventional mixing techniques.

Ingredients	% Weight
Deionized Water	qs 100
Ethanol (SD 40B Alcohol)	35.0
Any Compounds in Table 2	0.5 - 10
Hydrophilic Gelling Agent	3.0

[0246] In a suitable vessel the antibiotic compound is dissolved in ethanol with stirring. Next, the hydrophilic gelling agent is dissolved in a separate vessel in the water with stirring. The hydrophilic gelling agent solution is combined with the alcohol mixture with mixing.

[0247] This composition is useful for topical application for the treatment of acne or other skin infections caused or mediated by *Propionibacterium acnes*, *Gardnerella vaginalis*, or *Staphylococcus aureus*.

EXAMPLE 7: Oral Formulations of Radezolid

Tablets

[0248] Tablet compositions are made using standard mixing techniques as shown below in Tables 13-15. Both wet and dry granulation methods can be used. The tablets useful herein can have both intragranular as well as extragranular components, and some of the same components can be used both in the intragranular and extragranular portions of the tablet. The tablets can be further coated with waxes, gelatins, shellacs, and other suitable materials, and can be imprinted or polished. All components in the following tables are on a weight basis of mg, unless otherwise indicated.

Table 13. Tablet Formulations

Ingredient	1	2	3	4	5	6	7
Radezolid	541.6	541.6	541.6	541.6	541.6	541.6	541.6
Emulsifier	70.00[2]	70.00[3]	115.00[2]	75.00[3]	85.00[2]	70.00[2]	70.00[3]
Hydroxypropylmethylcellulose	45.00	45.00	N/A	45.00	N/A	35.00	35.00
Sodium starch glycolate	45.00	45.00	45.00	45.00	45.00	35.00	35.00
Mannitol	54.40	54.40	54.40	54.40	54.40	54.40	54.40
Microcrystalline cellulose	32.00	32.00	32.00	32.00	32.00	32.00	32.00
Fumed silica	8.00	8.00	8.00	8.00	8.00	8.00	8.00
Magnesium stearate	4.00	4.00	4.00	4.00	4.00	4.00	4.00

[2] Gelucire 50/13

[3] Gelucire 44/14

Table 14. Tablet Formulations (continued)

Ingredient	8	9	10	11	12	13	14
Radezolid	541.6	541.6	541.6	541.6	541.6	541.1	541.6
Emulsifier	80.00[2]	65.00[3]	110.00[3]	80.00[2]	80.00[3]	120.00[2]	85.00[3]
Hydroxypropylmethylcellulose	N/A	45.00	N/A	40.00	40.00	N/A	40.00
Sodium starch glycolate	35.00	45.00	50.00	40.00	40.00	40.00	40.00
Mannitol	54.40	54.40	54.40	54.40	54.40	54.40	54.40
Microcrystalline cellulose	32.00	32.00	32.00	32.00	32.00	32.00	32.00
Fumed silica	8.00	8.00	8.00	8.00	8.00	8.00	8.00
Magnesium stearate	4.00	4.00	4.00	4.00	4.00	4.00	4.00

[2] Gelucire 50/13

[3] Gelucire 44/14

Table 15. Tablet Formulations (continued)

Ingredient	15	16	17	18	19	20
Radezolid	541.1	541.6	541.6	541.1	541.6	541.1
Emulsifier	90.00[2]	60.00[2]	60.00[3]	75.00[2]	75.00[3]	120.00[3]
Hydroxypropylmethylcellulose	N/A	40.00	40.00	N/A	40.00	N/A
Sodium starch glycolate	40.00	40.00	40.00	40.00	40.00	40.00
Mannitol	54.40	54.40	54.40	54.40	54.40	54.40
Microcrystalline cellulose	32.00	32.00	32.00	32.00	32.00	32.00
Fumed silica	8.00	8.00	8.00	8.00	8.00	8.00
Magnesium stearate	4.00	4.00	4.00	4.00	4.00	4.00

[2] Gelucire 50/13

[3] Gelucire 44/14

Capsules

[0249] The capsule compositions are made using standard mixing techniques and are shown below in Tables 16-19. Both wet and dry granulation methods can be used to make the granulation component which is then loaded into a gelatin capsule, such as a soft gelatin capsule or a hard two piece gelatin or starch capsule. All components are on a weight basis of mg per capsule.

Table 16. Capsule Formulations

Ingredient	1	2	3	4	5
Radezolid	324.93	324.93	324.93	324.93	324.93
Emulsifier	65.00[2]	125.00[2]	65.00[2]	65.00[2]	65.00[2]
Povidone	N/A	N/A	25.00	20.00	55.00
Hydroxypropylmethylcellulose	31.00	N/A	N/A	15.00	N/A
Sodium starch glycolate	30.00	25.00	30.00	30.00	30.00
Mannitol	78.00	66.00	78.00	78.00	63.00
Microcrystalline cellulose	58.57	46.57	64.57	64.57	49.57
Fumed silica	8.00	8.00	8.00	8.00	8.00
Magnesium stearate	4.50	4.50	4.50	4.50	4.50

[2] Gelucire 44/14

Table 17. Capsule Formulations (continued)

Ingredient	6	7	8	9	10
Radezolid	324.93	324.93	324.93	324.93	324.93
Emulsifier	55.00[2]	55.00[3]	115.00[3]	55.00[3]	55.00[3]
Povidone	30.00	N/A	N/A	35.00	15.00
Hydroxypropylmethylcellulose	N/A	36.00	N/A	N/A	20.00
Sodium starch glycolate	35.00	35.00	35.00	30.00	30.00
Mannitol	78.00	78.00	66.00	78.00	78.00
Microcrystalline cellulose	64.57	58.57	46.57	64.57	64.57
Fumed silica	8.00	8.00	8.00	8.00	8.00
Magnesium stearate	4.50	4.50	4.50	4.50	4.50

[2] Gelucire 44/14

[3] Gelucire 50/13

Table 18. Capsule Formulations (continued)

Ingredient	11	12	13	14	15
Radezolid	324.93	324.93	324.93	324.93	324.93
Emulsifier	60.00[2]	120.00[2]	60.00[2]	60.00[2]	60.00[2]
Povidone	N/A	N/A	30.00	15.00	60.00
Hydroxypropylmethylcellulose	36.00	N/A	N/A	15.00	N/A
Sodium starch glycolate	30.00	30.00	30.00	30.00	30.00
Mannitol	78.00	66.00	78.00	78.00	63.00
Microcrystalline cellulose	58.57	46.57	64.57	64.57	49.57
Fumed silica	8.00	8.00	8.00	8.00	8.00
Magnesium stearate	4.50	4.50	4.50	4.50	4.50

[2] Gelucire 44/14

Table 19. Capsule Formulations (continued)

Ingredient	16	17	18	19	20
Radezolid	324.93	324.93	324.93	324.93	324.93
Emulsifier	60.00[2]	60.00[3]	120.00[3]	60.00[3]	60.00[3]
Povidone	30.00	N/A	N/A	30.00	15.00
Hydroxypropylmethylcellulose	N/A	36.00	N/A	N/A	15.00
Sodium starch glycolate	30.00	30.00	30.00	30.00	30.00
Mannitol	78.00	78.00	66.00	78.00	78.00
Microcrystalline cellulose	64.57	58.57	46.57	64.57	64.57
Fumed silica	8.00	8.00	8.00	8.00	8.00
Magnesium stearate	4.50	4.50	4.50	4.50	4.50

[2] Gelucire 44/14

[3] Gelucire 50/13

Soft Gelatin Capsules

[0250] A soft gelatin mixture is first prepared from the following ingredients: gelatin (47.00 weight %), glycerin (15.00 weight %), and water (QS 100). The ingredients are combined in a suitable vessel and heated with mixing at about 65 °C. to form a uniform solution. Using standard encapsulation methodology, the resulting solution is used to prepare soft gelatin

capsules containing approximately 600 mg of the compositions of Capsules 1 to 20, above. The resulting soft gelatin capsules are suitable for oral administration.

Hard Gelatin Capsules

[0251] Hard gelatin capsules are purchased from any commercially available source. The capsules are filled manually or by capsule filling machine with approximately 600 mg of the compositions of Capsule 1 to 20 above. The resulting hard gelatin capsules are suitable for oral administration.

Solid Oral Formulation

[0252] The ingredients are combined using standard wet granulation procedures to form tablets, which are then optionally enteric coated. The resulting compositions as exemplified in Tables 20-21 are suitable for oral administration.

Table 20. Solid Oral Formulation Composition

Ingredient	Amount (mg)
Radezolid	162.5
Fumaric acid	75.00
Tartaric acid	75.00
Sodium Starch Glycolate	0-25.00
Polydextrose	25.00
Gelucire 44/14	25-50.00
Cyclodextrin (cavitron hydroxypropyl-β-cyclodextrin)	0-125.00
Mannitol	50-100
Colloidal silicon dioxide	4.00
Magnesium stearate	3.50
Purified Water[a]	
Enteric film coating	0-100

[a] Purified water is used as a granulating agent and is removed during the drying process.

Pharmaceutical Composition for Oral Administration

Table 21. Pharmaceutical Composition for Oral Administration

Ingredients	Percent by Weight	mg in Tablet
Intra Granular		
Radezolid hydrochloride	20.31	162.51
HPMCAS-M Spray Dried	13.28	106.24
HPMCAS-H Spray Dried	13.28	106.24
Croscarmellose Sodium	4.00	31.98
Microcrystalline cellulose	11.60	92.76
Lactose monohydrate	11.60	92.76
Colloidal silicon dioxide	0.75	6.00
Magnesium Stearate	0.9	1.50
Extra Granular		
Croscarmellose Sodium	1.50	12.00
Di-Cal Phosphate (DC Grade)	23.38	187.00
Colloidal silicon dioxide	0.06	0.50
Magnesium Stearate	0.06	0.50
Total	100.00	800.00

[**0253**] The procedure for making the pharmaceutical composition for oral administration is as follows:

1. Pass radezolid hydrochloride and colloidal silicon dioxide through a #20 Mesh screen together, not sequentially.
2. Bag blend 5 minutes. Sample approximately 0.25g to a glass vial.
3. Pass remaining intragranular ingredients, except the magnesium stearate, through a comill U5 at 1000 rpm with a 0.032R screen. Collect all in a single container.
4. Add to V-blender and blend for 1 minute at 24 rpm.
5. Remove approximately 100g of blend.
6. Add radezolid hydrochloride and colloidal silicon dioxide from step 2 to V-blender.
7. Add 100g of blend to container containing radezolid hydrochloride, hand shake, and add to blender, on the same side as the radezolid hydrochloride was added.
8. Blend for 15 min. at 24 rpm.

9. Pass Magnesium Stearate through a #20 Mesh Screen with the approximately 100g of blend from step 8.
10. Blend in V (Twin Shell) blender for 4 min. at 24 RPM. Collect 50g sample for bsv, tsv, etc.
11. Dry Granulate on TF Mini Roller compactor to a Solid Fraction of 0.6-0.7. Start with polished smooth rolls, switch to grooved if necessary.
12. Mill Dry Granulated ribbons on the Co-Mill U5 with 0.032"Conidur screen at 100 rpm. Stop after approximately 100-300 g and measure particle size.
13. If needed, change to different screen. Screen used: 0.032C and complete granulation.
14. Add granules from step 13 and extragranular croscarmellose sodium, colloidal silicon dioxide, and dicalciumphosphateto 4qt. V -Blender and blend for 15 min. at 24 RPM.
15. Pass the extragranular magnesium stearate through a #20 Mesh Screen with approximately 100g of blend from step 14 above.
16. Blend in V (Twin Shell) blender for 4 min. at 24 RPM. Save 100 g Final Blend for characterization.
17. Compress on Kilian T100 rotary tablet press with 0.3586 X 0.7174 " Modified Oval to a hardness of approximately 16-20 Kp. Sample using BRPPD stratified sampling plan.

[0254] The foregoing formulation is useful for treating, preventing, or reducing the risk of a microbial infection in a patient in need thereof, *e.g.*, a human patient.

Intravenous Formulations

[0255] Compositions for intravenous administration are made using standard techniques and are shown below in Tables 22-23.

Table 22. Intravenous Radezolid Hydrochloride Formulation with 2.778 mg/mL of free base

		Batch size, mL	1,000 gram batch
Ingredient	**Mg/mL**	**% (w/w)**	**Amt (g) / batch**
Radezolid hydrochloride	3.009	0.30%	3.009
Citric acid anhydrous	4.00	0.40%	4.000
Sodium citrate tribasic (dihydrate)	1.22	0.12%	1.220
5% dextrose solution (D5W)	q.s. volume	q.s.	q.s.
1 Normal Sodium hydroxide or phosphoric acid	q.s. pH	q.s.	q.s.
Total, mg	1007	100.00%	1007.000
Final pH is 3.5 (±0.1)			
Density of the solution is 1.007 g/mL			
25.0 mM Citric Buffer			

[0256] The procedure for making the intravenous formulation is as follows:

1. Weigh dextrose 5% solution for injection, approximately 80% of the total batch weight, into a suitable container.
2. Add the required amount of citric acid and sodium citrate tribasic (dihydrate) to the solution and mix until dissolved. Record pH.
3. Heat up the solution to 35-43 °C.
4. With continuous heating at 35-43 °C, add radezolid HC1 salt corrected for purity and mix until dissolved.
5. Lower the solution temperature to 25 °C (±3).
6. Test for pH. The target pH is 3.5 (±0.1). Adjust with 1 Normal Sodium Hydroxide or Phosphoric acid as needed.
7. Q.S. to the final weight with dextrose 5% solution for injection.
8. Test for pH. Adjust if outside of 3.5 (±0.1). Record final pH and solution weight.
9. Filter solution (0.22 μm) and fill into vials.

Table 23. Intravenous Radezolid Hydrochloride Formulation with 2.778 mg/mL of free base in 10 mM Buffer

		Batch size, mL	1,000 gram batch
Ingredient	**Mg/mL**	**% (w/w)**	**Amt (g)/batch**
Radezolid Hydrochloride	3.009	0.30%	3.009
Anhydrous Citric Acid (MW = 192.12)	1.50	0.15%	1.500
Sodium citrate tribasic (dihydrate) (MW = 294.10)	0.65	0.06%	0.650
Dextrose Powder	50	4.97%	q.s.
1N Sodium hydroxide and/or phosphoric acid	q.s.	q.s.	q.s.
Total, mg	1007	100.00%	1007.000
Final pH = 3.5 ± 0.1			
Density of the solution is 1.007 g/mL			
10.0 mM Citric buffer			

[0257] The procedure for making the intravenous formulation is as follows:

1. Weigh Dextrose Powder for injection into a suitable container.
2. Add the required amount of citric acid and sodium citrate tribasic (dihydrate) to the solution and mix until dissolved. Record pH.
3. Heat up the solution to 35-43 °C.
4. With continuous heating at 35-43 °C, add radezolid HC1 salt corrected for purity and mix until dissolved.
5. Lower the solution temperature to 25 °C (±3)
6. Test for pH. The target pH is 3.5 (+0.1). Adjust with 1 Normal Sodium Hydroxide or Phosphoric acid as needed.
7. Q.S. to the final weight with dextrose 5% solution for injection.
8. Test for pH. Adjust if outside of 3.5 (±0.1). Record final pH and solution weight.
9. Filter solution (0.22 μm) and fill into vials.

EXAMPLE 8: Dissolution Testing in Simulated Gastrointestinal System

A. To develop an easy-to-use 2-step dissolution method simulating gastrointestinal systems.

[0258] The common ion effect was studied using dissolution and microscopic methods. The microscopic method was conducted with drug suspended in water, pH 1.2, pH 4 and pH 6.5 buffers with and without sodium chloride. The dissolution of the drug and its granulations were studied using three different 2-step dissolution methods which entail the following: Method #1: simple 2-step buffers at pH 4 from 0-30 minutes and at pH 6.5 from 30-90 minutes; Method #2: simple 2-step buffers with the presence of chloride ion in both steps; Method #3: simple buffer at pH 4 with presence of chloride ion from 0-30 minutes, and buffer with bile salts and surfactants at pH 6.5 from 30-90 minutes. The two steps represent fed stomach and intestinal conditions, respectively.

[0259] The microscopy indicated that the drug formed aggregates in the presence of chloride ion. Unexpectedly, the alternative non-chloride salt (neat drug) flocculated into larger aggregates. Thus dissolution methods addressing both common ion effects and gastrointestinal conditions were studied. The results indicated that the simple buffer in the presence of chloride ion was the most discriminating dissolution medium. For the same formulations, the dissolution rates were in the following order: 2-step simple buffer without sodium chloride > 2-step with bile-salts and surfactants > simple buffer with sodium chloride. Using the simple buffer system with sodium chloride enabled screen formulations to achieve the most super-saturation with a reduced common ion effect. The simple buffer system without chloride ion, on the other hand, did not provide enough power to discriminate the formulations of a drug with a low chloride K_{sp}.

[0260] 2-Step dissolution using simple buffer with sodium chloride present is an easy-to-use surrogate for the conventional 2-step dissolution system with bile-salts and surfactants. The dissolution in such medium enables the study of super-saturation and common ion effects for formulations of high dose hydrochloride salt drugs with sub-microgram water solubility.

B. Formulation Approaches to Achieve Super-Saturation

[0261] Investigate formulation approaches to overcome poor water solubility, common ion effect, and obtain super-saturation for a drug with sub-microgram solubility.

[0262] Drug compound was granulated with various mixtures of excipients. The drug substances and the granulations were studied using 2-step dissolution methods at pH 4 from 0 to 30 minutes and at pH 6.5 from 30 to 90 minutes in the presence and absence of sodium chloride.

[0263] The dissolution data, conducted in gastrointestinal representative system, indicated that the pH modifier with a relative lower solubility improved dissolution to a greater extent than a pH modifier with a higher solubility. The data also indicated that certain surfactants and polymers selected for the formulation further enhanced supersaturation and reduced the common ion effect from chloride. Usage of common water soluble excipients in the formulation facilitated the dissolution in addition to manufacturability. Even though the alternative non-chloride salt has significantly increased solubility at acidic medium, the dissolution of neat non-chloride salt is similar to that of chloride salt. The microscopy showed that the non-chloride salt formed aggregates in the presence of chloride ion. However, once formulated with selected excipients, the advantage of the non-chloride salt is shown in dissolution.

[0264] Dissolution and bioavailability of a basic drug with poor solubility can be enhanced by using selected pH modifying agents, surfactants, and polymers. The alternative salts, when formulated with the optimized excipients, can also increase dissolution. Selecting a dissolution method which addresses both gastrointestinal system and the common ion effect is critical to selecting formulations for maximum exposure.

C. Studies on 2-Step Dissolution Testing of a Drug in a Simulated Gastrointestinal System

[0265] To develop a simple 2-step dissolution method to screen formulations aimed to provide supersaturation.

[0266] To examine the effects of sodium chloride on dissolution of a hydrochloride salt of a water insoluble drug.

[0267] To discriminate formulations under fed GI pH conditions.

[0268] To study *in-vivo in-vitro* correlation of the dissolution system.

[0269] Traditional 2-step dissolution systems use bile salts and surfactant that is time consuming to use and sometimes not discriminating enough for formulation screening.

[0270] The goal is to develop a easy to use 2-step dissolution method, which simulates gastrointestinal pH values and the common ion effect without using bile salt and surfactant.

[0271] It is well known that hydrochloride salt of a water insoluble compound presents the common ion effect. Thus, sodium chloride was added in the dissolution buffer to simulate the common ion effect.

[0272] A hydrochloride salt of a water insoluble drug was selected as a model compound, which has the following biopharmaceutical properties:

pKa = 6.8 and 9.4;

log P = 0.7;

intrinsic solubility = 0.01 mg/ml at pH 6.8;

solubility of salt in water = 2.6, 0.2, and 0.06 mg/ml at pH 4, 5.4, and 6.5, respectively;

caco-2 permeability = 0.5 x 10^{-6} cm/s

monkey oral bioavailability = 15% at 20 mg/kg dose

positive food effect (4X).

Table 24. pH of Gastrointestinal System and that of the Dissolution Medium

	Stomach pH	**Intestine pH**
Fast	pH 1.7 Buffer Capacity: 7-18 mM/pH	pH 6.2 Buffer Capacity: 5.6 mM/pH
Fed	pH 4 (ave): 6.4 (im.) to 2.7 (3.5 hrs) Buffer Capacity: 14-28 mM/pH	pH 5.4 for 4 hrs Buffer Capacity: 18-30 mM/pH

[0273] Bulk drug powders were wet granulated with and without excipients. Granules were dried and sized through a #18 mesh screen.

[0274] Microscopic test was conducted with drug suspended in water, pH 1.2, 4, and 6.5 buffers with and without sodium chloride.

[0275] Four dissolution media were tested. Results of these tests are shown in line-graph formats in **FIGs. 5-9**. Bulk drug powders were wet granulated with and without excipients. Granules were dried and sized through a No. 18 mesh screen. Dissolution of the drug and its granulations were studied using four different 2-step dissolution methods listed in the table below. The two steps represent fed stomach and intestinal conditions respectively. Intestine pH (literature) indicates published conditions in Dressman, *Pharmaceutical Research*, 23(1):165-176 (2006). These four methods are listed below.

Table 25. The Four 2-Step Dissolution Methods Tested

#	**0-30 minutes**	**30-90 minutes**
1	pH 4 acetate buffer (100 mM)	pH 5.4 (add pH 6.4 phosphate buffer, 50 mM)
2	pH 4 acetate buffer (100 mM)	pH 6.5 (add pH 7.0 phosphate buffer, 50 mM)
3	pH 4 acetate buffer (100 mM) + 0.9% NaCl	pH 6.5 + 0.9% NaCl (add pH 7.0 phosphate buffer, 50 mM)
4	pH 4 acetate buffer (100 mM) + 0.9% NaCl	pH 6.5 + KCl + Taurocholate, and lecithin (add phosphate buffer, 50 mM with potassium chloride, taurocholate, and lecithin)

[0276] The results of the study are shown in **FIGs. 5-9**.

[0277] **FIG. 5** depicts the results of the 2-step dissolution test performed following Method 1. Dissolution of the radezolid formulation was tested in a buffer at pH 4.0 for 0-30 minutes and then after transferring to a buffer at pH 5.4 for 30-90 minutes. The two conditions did not distinguish the formulations (A-C, shown in the Table in **FIG. 5**) except for drug substance (not shown).

[0278] **FIG. 6** depicts the results of the 2-step dissolution test performed following Method 2. Dissolution of the radezolid formulation was tested in a buffer at pH 4.0 for 0-30 minutes and then after transferring to a buffer at pH 6.5 for 30-90 minutes. The percent dissolved from the formulations A and B (shown in the Table in **FIG. 6**) with acidifier reached 6-8 times higher than the control. But the dissolution did not address the common ion effect, and it did not distinguish acidified formulation with and without polymer dispersant.

[0279] **FIG. 7** depicts the results of the 2-step dissolution test performed following Method 3. Dissolution of the radezolid formulation was tested in a buffer at pH 4.0 for 0-30 minutes and then after transferring to a buffer at pH 6.5 for 30-90 minutes. Both buffers had 0.9% NaC1. The two-step dissolution with 0.9% NaCl was used to simulate common ion effect. Method 3 is more discriminating and slowed the release of formulation A by 50% due to common ion effect. The dissolution of formulation C (shown in the Table in **FIG. 7**) with Gelucire and crystallization retardant, on the other hand, increased significantly, but still less than formulation A (also shown in the Table in **FIG. 7**), which contains acidifier in addition to Gelucire and binder.

[0280] **FIG. 8** depicts the results of the 2-step dissolution test performed following Method 4. Dissolution of the radezolid formulation was tested in a buffer at pH 4 containing NaC1 for 0-

30 minutes, and then transferred to a buffer at pH 6.5 containing bile salt, surfactant and KC1 for 30-90 minutes. Method 4 resulted in similar rank order as was observed under Method 3.

[0281] The 2-Step dissolution using simple buffer with sodium chloride presents an easy-to-use surrogate for the conventional 2-step dissolution system with bile-salts and surfactants. The dissolution in such medium enables the study of super-saturation and common ion effects for formulations of high dose hydrochloride salt drugs with microgram water solubility. The exposure in dog of the model compound is in agreement with the result of dissolution. On the other hand: The simple buffer system without chloride ion did not discriminate the formulations of a drug with a low chloride K_{sp}. The dissolution with bile salt and surfactant did not provide enough discriminating to rank order the formulations.

[0282] The results of the study also indicated that: inclusion of the polymer and surfactant in the formulations effectively improves dissolution and degree of super-saturation of the model compound, a basic salt, in dual pH media; and inclusion of a pH modifier in addition to the polymer and surfactant improved dissolution, super-saturation, and *in vivo* exposure of the compound further.

In Vivo Dog Study

[0283] An in-vivo dog study was conducted with beagle dogs (weight = l 2 kg, n=3). The dogs were dosed orally at 150 mg under fasting conditions. Serial of plasma samples were collected, extracted, and analyzed by LC/MS/MS. C_{max} and AUC were estimated to evaluate the overall exposure from different formulations. Formulation A provided higher exposure than formulation C, which is in agreement with dissolution method C (described in Example 8). The Table in **FIG. 9** lists the C_{max}, T_{max}, $T_{1/2}$, and AUC values for Formulations A and C, indicating that Formulation A showed superior bioavailability to Formulation C with respect to C_{max}, $T_{1/2}$ and AUC, though Formulation C showed a better T_{max} than Formulation A.

EXAMPLE 9: Use of Radezolid for Treating Skin Infections

[0284] Treatment with a variety of topical radezolid formulations can be used as a method to treat, prevent, or reduce the risk of various conditions caused or mediated by various radezolid-sensitive microbial pathogens. Conditions include skin and soft tissue infections (*e.g.*, impetigo, rosacea, bacterial conjunctivitis, otitis externa, folliculitis, and local wound infections), acne, nosocomial or staph carrier nasal prophylaxis, and other bacterial infections such as bacterial

vaginosis. Radezolid-sensitive microbial pathogens include *Propionibacterium acnes*, *Gardnerella vaginalis*, and *Staphylococcus aureus* (including Methicillin-resistant *Staphylococcus aureus*).

Proposed Formulations

[0285] For uncomplicated skin and soft tissues infections, nasal colonization and acne, radezolid will be formulated as a topical semi-solid dosage form (*e.g.*, ointment, cream, lotion, solution, foam or gel) for topical cutaneous applications.

[0286] Radezolid will be formulated in ovules, soft-gel capsules, suppositories, creams, or foams for intravaginal application to treat bacterial vaginosis caused by Gardnerella vaginalis.

[0287] Typical compositions that can be used include from 0.1 to 1500 mg of radezolid.

Mode of Administration and Duration of Treatment (Anticipated Ranges Based on Possible Effectiveness)

[0288] For acne, topical application 1-2 times daily for 4 – 12 weeks is envisioned.

[0289] For uncomplicated skin and soft tissues infections caused by *S. aureus/MRSA* (*e.g.*, impetigo, rosacea, bacterial conjunctivitis, otitis externa, folliculitis, and local wound infections), topical application 1-2 times daily for days to 2 weeks is envisioned.

[0290] For nosocomial or staph carrier nasal prophylaxis including MRSA, topical application 1-2 times daily for 3-7 days is envisioned.

[0291] For bacterial vaginosis/vaginitis, intravaginal administration 1-2 times daily for 3-7 days is envisioned.

Endpoint of Treatment

[0292] For acne, the endpoint will be clearance or material reduction of inflammatory and/or non-inflammatory lesions.

[0293] For uncomplicated skin and soft tissues, the endpoint will be resolution of all clinical signs and symptoms of infection (*e.g.*, erythema, crusting, burning/stinging, pruritus etc.).

[0294] For nosocomial or staph carrier nasal prophylaxis including MRSA, the endpoint will be a negative culture.

[0295] For bacterial vaginosis/vaginitis, the endpoint will be resolution of all clinical signs and symptoms of infection (*e.g.*, reversal of AMSEL criteria, vaginal discharge, odor, burning/stinging, pH $\leq$ 4.5, and elimination of clue cell(s)).

[0296] The disclosed methods are sufficient to meet the proposed endpoints.

INCORPORATION BY REFERENCE

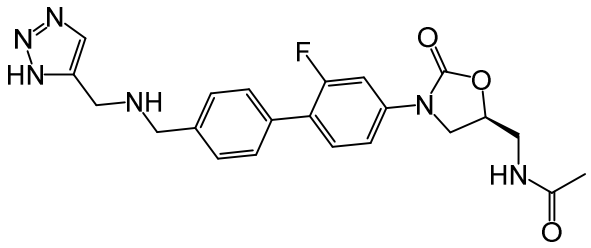
[0297] The entire disclosure of each of the patent documents, including certificates of correction, patent application documents, scientific articles, governmental reports, websites, and other references referred to herein is incorporated by reference in its entirety for all purposes.

EQUIVALENTS

[0298] The invention can be embodied in other specific forms without departing from the spirit or essential characteristics thereof. The foregoing embodiments are therefore to be considered in all respects illustrative rather than limiting on the invention described herein. Scope of the invention is thus indicated by the appended claims rather than by the foregoing description, and all changes that come within the meaning and range of equivalency of the claims are intended to be embraced therein.

CLAIMS

1. Use of a compound having the formula:



or a pharmaceutically acceptable tautomer or salt thereof, in the manufacture of a medicament for treating, preventing, or reducing the risk of a skin infection caused or mediated by *Propionibacterium acnes* or *Gardnerella vaginalis* in a patient.

2. The use according to claim 1, wherein the compound is a pharmaceutically acceptable salt selected from the group consisting of acetate, ascorbate, benzoate, citrate, esylate, ethanedisulfonate, fumarate, hydrochloride, lactate, maleate, mesylate, phosphate, pyroglutamate, salicylate, succinate, sulfate, tartrate, and tosylate.

3. The use according to any one of claims 1-2, wherein the skin infection is caused or mediated by *Propionibacterium acnes*.

4. The use according to any one of claims 1-2, wherein the skin infection is caused or mediated by *Gardnerella vaginalis*.

5. The use according to any one of claims 1-4, wherein the skin infection is selected from acne vulgaris, bacterial conjunctivitis, and bacterial vaginosis.

6. The use according to claim 5, wherein the skin infection is acne vulgaris.

7. The use according to claim 5, wherein the skin infection is bacterial vaginosis.

8. The use according to any one of claims 1-7, wherein the medicament is to be administered orally, parentally, or topically.

9. The use according to claim 8, wherein the medicament is to be administered topically.

10. The use according to any one of claims 1 through 9, wherein the patient is a mammal or domestic animal.

11. The use according to any one of claims 1 through 10, wherein the patient is a human.

12. The use according to any one of claims 1 through 11, wherein the compound is to be administered once daily or twice daily.

13. The use according to any one of claims 1 through 12, wherein the compound is to be administered once daily.

14. The use according to any one of claims 1 through 12, wherein the compound is to be administered twice daily.

15. The use according to any one of claims 1 through 14, wherein the medicament is a topical formulation further comprising one or more dermatologically acceptable carriers.