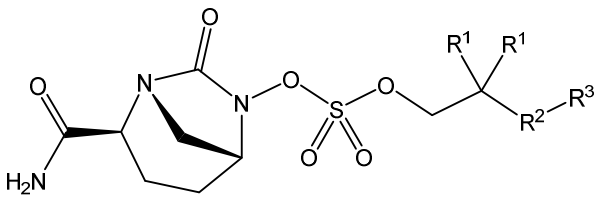
CLAIMS

1. A pharmaceutical composition comprising:

a β-lactam antibiotic or a pharmaceutically acceptable salt thereof; and

an avibactam derivative of Formula (1):



(1)

or a pharmaceutically acceptable salt thereof, wherein,

each R^1 is independently selected from C_{1-6} alkyl, or each R^1 and the geminal carbon atom to which they are bonded forms a C_{3-6} cycloalkyl ring, a C_{3-6} heterocycloalkyl ring, a substituted C_{3-6} cycloalkyl ring, or a substituted C_{3-6} heterocycloalkyl ring;

R^2 is selected from a single bond, C_{1-6} alkanediyl, C_{1-6} heteroalkanediyl, C_{5-6} cycloalkanediyl, C_{5-6} heterocycloalkanediyl, C_6 arenediyl, C_{5-6} heteroarenediyl, substituted C_{1-6} alkanediyl, substituted C_{1-6} heteroalkanediyl, substituted C_{5-6} cycloalkanediyl, substituted C_{5-6} heterocycloalkanediyl, substituted C_6 arenediyl, and substituted C_{5-6} heteroarenediyl;

R^3 is selected from C_{1-6} alkyl, –O–C(O)–R^4, –S–C(O)–R^4, –NH–C(O)–R^4, –O–C(O)–O–R^4, –S–C(O)–O–R^4, –NH–C(O)–O–R^4, –C(O)–O–R^4, –C(O)–S–R^4, –C(O)–NH–R^4, –O–C(O)–O–R^4, –O–C(O)–S–R^4, –O–C(O)–NH–R^4, –S–S–R^4, –S–R^4, –NH–R^4, –CH(–NH_2)(–R^4), C_{5-6} heterocycloalkyl, C_{5-6} heteroaryl, substituted C_{5-6} cycloalkyl, substituted C_{5-6} heterocycloalkyl, substituted C_{5-6} aryl, substituted C_{5-6} heteroaryl, and –CH=C(R^4)$_2$, wherein,

R^4 is selected from hydrogen, C_{1-8} alkyl, C_{1-8} heteroalkyl, C_{5-8} cycloalkyl, C_{5-8} heterocycloalkyl, C_{5-10} cycloalkylalkyl, C_{5-10} heterocycloalkylalkyl, C_{6-8} aryl, C_{5-8} heteroaryl, C_{7-10} arylalkyl, C_{5-10} heteroarylalkyl, substituted C_{1-8} alkyl, substituted C_{1-8} heteroalkyl, substituted C_{5-8} cycloalkyl, substituted C_{5-8} heterocycloalkyl, substituted C_{5-10} cycloalkylalkyl, substituted C_{5-10} heterocycloalkylalkyl, substituted C_{6-8} aryl, substituted C_{5-8} heteroaryl, substituted C_{7-10} arylalkyl, and substituted C_{5-10} heteroarylalkyl;

R^5 is selected from hydrogen, C_{1-6} alkyl, C_{5-8} cycloalkyl, C_{6-12} cycloalkylalkyl, C_{2-6} heteroalkyl, C_{5-8} heterocycloalkyl, C_{6-12} heterocycloalkylalkyl, substituted C_{1-6} alkyl, substituted C_{5-8} cycloalkyl, substituted C_{6-12} cycloalkylalkyl, substituted C_{2-6} heteroalkyl, substituted C_{5-8} heterocycloalkyl, and substituted C_{6-12} heterocycloalkylalkyl; and

R^6 is selected from hydrogen, C_{1-6} alkyl, C_{5-8} cycloalkyl, C_{6-12} cycloalkylalkyl, C_{2-6} heteroalkyl, C_{5-8} heterocycloalkyl, C_{6-12} heterocycloalkylalkyl, substituted C_{1-6} alkyl,

substituted C_{5-8} cycloalkyl, substituted C_{6-12} cycloalkylalkyl, substituted C_{2-6} heteroalkyl, substituted C_{5-8} heterocycloalkyl, and substituted C_{6-12} heterocycloalkylalkyl,

wherein the pharmaceutical composition comprises:

from 200 mg to 1,400 mg of the β-lactam antibiotic; and

from 200 mg to 1,400 mg of the avibactam derivative,

wherein the β-lactam antibiotic comprises ceftibuten or a pharmaceutically acceptable salt thereof, and

wherein the avibactam derivative is ethyl 3-(((((1*R*,2*S*,5*R*)-2-carbamoyl-7-oxo-1,6-diazabicyclo[3.2.1]octan-6-yl)oxy)sulfonyl)oxy)-2,2-dimethylpropanoate (3), or a pharmaceutically acceptable salt thereof.

2. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition comprises:

from 200 mg to 500 mg of ceftibuten or a pharmaceutically acceptable salt thereof; and

from 300 mg to 1,400 mg of the avibactam derivative or a pharmaceutically acceptable salt thereof.

3. The pharmaceutical composition of claim 1, wherein, following oral administration to a patient the composition provides a β-lactam antibiotic plasma concentration greater than 40% *f*T>MIC for a bacterial strain.

4. The pharmaceutical composition of claim 1, wherein, following oral administration to a patient, the composition provides an avibactam plasma concentration greater than 40% *f*T>C_t.

5. The pharmaceutical composition of claim 1, wherein, following oral administration to a patient, the composition provides an avibactam plasma concentration characterized by a *f*AUC:MIC ratio from 10 to 40.

6. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition comprises an oral formulation.