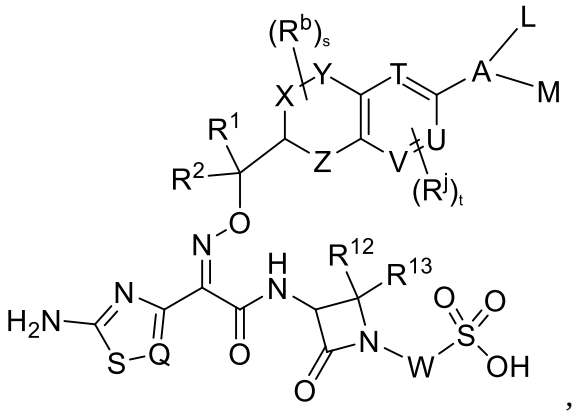
wherein C_1-C_3 alkyl unsubstituted or substituted with one to three R^b;

each n is independently 0, 1, 2, 3, 4, 5 or 6;
each m is independently 0, 1 or 2;
each p is independently 1 or 2;
each q is independently 0, 1, 2, 3, 4, 5 or 6;
each s is independently 0, 1, 2 or 3;
each t is independently 0, 1, 2 or 3;
each u is independently 0, 1, 2, 3, 4, 5 or 6; and
each v is independently 0, 1, or 2.

In one aspect, the present disclosure relates to a compound of Formula I



(I)

or a pharmaceutically acceptable salt thereof, wherein:

T, U and V are each CH;

W is O;

Q is CR^3;

X is CH_2;

Y is O or CH_2;

Z is O or CH_2;

A is
–C(=NH)-NH,

AryC, or
HetC,
wherein A is unsubstituted or substituted with one to four R^i;

AryC is a 5- to 6-membered monocyclic aromatic ring with 0, 1, 2, or 3 ring atoms independently selected from N, N as a quaternary salt, O and S, unsubstituted or substituted with one to four R^i, wherein AryC is optionally fused to a 4- to 7- membered heterocycloalkyl ring containing one to two heteroatoms selected from O, S and $–NR^g$;

HetC is a 4- to 7-membered saturated or monounsaturated monocyclic ring with 1, 2, or 3 heteroatom ring atoms independently selected from N, N as a quaternary salt, O and S, unsubstituted or substituted with one to four R^i;

L is
absent,
R^4,
$-NHR^4$,
$-N(R^4)2$,
$- R^4$,
$-(CH_2)_nR^4$,
$-C(O)R^4$,
$-C(NH)R^4$, or
$-S(O)_mR^4$,
wherein L is unsubstituted or substituted with 1-4 substituents selected from R^e;

M is
R^5,
$-NHR^5$,
$-N(R^5)_2$,
$-OR^5$,
$-(CH_2)_uR^5$,
$-C(O)R^5$,
$-C(NH)R^5$, or
$-S(O)_vR^5$,
wherein M is unsubstituted or substituted with 1 - 4 substituents selected from R^6;

R^1 and R^2 are independently selected from:
hydrogen,

-C_1-C_8 alkyl, and
-C(O)OR^e,
wherein -C_1-C_8 alkyl is unsubstituted or substituted with one to three R^a,

provided that if R^1 is -C(O)OR^e, then R^2 is not -C(O)OR^e;

R^3 is hydrogen;

each occurrence of R^4 is independently:
hydrogen,
-C_1-C_{10} alkyl,
-C_2-C_8 alkenyl,
-$(CH_2)_n$$OR^e$,
-$S(O)_m$$R^e$,
-$S(O)_m$$NR^cR^d$,
-$(CH_2)_n$$NR^cR^d$,
-OC(O)R^e,
-C(O)OR^e,
-CN,
-C(O)NR^cR^d,
-NR^cC(O)R^e,
-NR^cC(O)OR^e,
-NR^cC(O)NR^cR^d,
-$NR^c$$S(O)_m$$R^e$,
=NR^{11},
-C_3-C_7 cycloalkyl,
-O-C_3-C_6cycloalkyl,
-C_1-C_{10}alkylene-C_3-C_6cycloalkyl,
-O-C_1-C_{10}alkylene-C_3-C_6cycloalkyl,
HetB,
-O-HetB,
-C_1-C_{10}alkylene-HetB,
-O-C_1-C_{10}alkylene-HetB,
AryB,
-O-AryB,
-C_1-C_{10}alkylene-AryB, or
-O-C_1-C_{10}alkylene-AryB,
wherein R^4 is unsubstituted or substituted with one to four R^6;

AryB is a 5- to 6-membered monocyclic aromatic ring with 0, 1, 2, or 3 ring atoms independently selected from N, O and S, unsubstituted or substituted with one to four R^c;

HetB is a 4- to 7-membered saturated or monounsaturated monocyclic ring with 1, 2, or 3 heteroatom ring atoms independently selected from N, N as a quaternary salt, O and S, unsubstituted or substituted with one to three R^a;

R^5 is
hydrogen,
C_1-C_{10} alkyl,
-C_2-C_8 alkenyl,
-$(CH_2)_uOR^e$,
-$S(O)_vR^e$,
-$S(O)_vNR^cR^d$,
-$(CH_2)_uNR^cR^d$,
-$OC(O)R^e$,
-$C(O)OR^e$,
-CN,
-$C(O)NR^cR^d$,
-$NR^cC(O)R^e$,
-$NR^cC(O)OR^e$,
-$NR^cC(O)NR^cR^d$,
-$NR^cS(O)_vR^e$,
$=NR^{11}$,
-C_3-C_7 cycloalkyl,
-O-C_3-C_6cycloalkyl,
-C_1-C_{10}alkylene-C_3-C_6cycloalkyl,
-O-C_1-C_{10} alkylene-C_3-C_6cycloalkyl,
HetB,
-O-HetB,
-C1-C10alkylene-HetB,
-O-C1-C10 alkylene-HetB,
AryB,
-O-AryB,
-C_1-C_{10}alkylene-AryB, or
-O-C_1-C_{10}alkylene-AryB,
wherein R^5 is unsubstituted or substituted with one to four R^6;

each occurrence of R^6 is independently:
halogen,
-C_1-C_6alkyl,
-OR^e,
-$S(O)_vR^e$,
-$S(O)_vNR^cR^d$,
-$C(O)R^e$,
-$OC(O)R^e$,
-$C(O)OR^e$,
-CN,
-$C(O)NR^cR^d$,
-$C(NH)NR^cR^d$,
-$(CH_2)_uNR^cR^d$,
-$(CH_2)_uNR^cR^d$,
-$N(R^c)(C(O)R^e)$,
-$N(R^c)(C(O)OR^e)$,
-$N(R^c)(C(O)NR^cR^d)$,
-$N(R^c)(S(O)_vR^e)$, or
HetB;

R^9 is
hydrogen,
C_1-C_4 alkyl, or
C_3-C_7 cycloalkyl;

R^{10} is
hydrogen,
C_1-C_4 alkyl, or
C_3-C_7 cycloalkyl;

R^{11} is
hydrogen,
C_1-C_4 alkyl, or
C_3-C_7 cycloalkyl;

R^{12} and R^{13} are independently C_1-C_3 alkyl, wherein C_1-C_3 alkyl is unsubstituted or substituted with one to seven fluorines,

or alternatively R^{12} and R^{13} together with the carbon to which they are attached form a monocyclic C_4-C_6 cycloalkyl unsubstituted or substituted with one to three substituents independently selected from -F, -OH and -OC_1-C_3alkyl;

each occurrence of R^a is independently:
hydrogen,
halogen,
C_1-C_3alkyl,
-NR^cR^d, or
-OR^e;

each occurrence of R^b is independently:
hydrogen,
-C_1-C_6 alkyl,
-OC_1-C_6 alkyl,
OH,
$N(R^9)_2$, or
halogen,
wherein -C_1-C_3 alkyl is unsubstituted or substituted with one to three R^a;

R^c and R^d are independently selected from:
hydrogen,
-C_1-C_{10} alkyl, and
-C_2-C_{10} alkenyl,
wherein each R^c and R^d is unsubstituted or substituted with one to three R^f;

each occurrence of R^e is independently hydrogen, or -C_1-C_{10}alkyl, wherein each R^e is unsubstituted or substituted with one to three R^h;

each occurrence of R^f is independently:
halogen,
-C_1-C_{10} alkyl,
-OH,
-OC_1-C_4 alkyl,
-$S(O)_mC_1$-C_4 alkyl,
-CN,
-CF_3,
-$OCHF_2$,

-OCF_3, or
NH_2,
wherein -C_1-C_{10} alkyl is unsubstituted or substituted with one to three substituents independently selected from –OH, halogen, cyano, and -$S(O)_2CH_3$;

each occurrence of R^g is independently:
hydrogen,
-$C(O)R^e$, or
-C_1-C_{10} alkyl,
wherein -C_1-C_{10}alkyl is unsubstituted or substituted with one to five fluorines;

each occurrence of R^h is independently:
halogen,
-C_1-C_{10}alkyl,
-OH,
-OC_1-C_4 alkyl,
-$S(O)_mC_1$-C_4 alkyl,
-CN,
-CF_3,
-$OCHF_2$, or
-OCF_3,
wherein -C_1-C_{10} alkyl is unsubstituted or substituted with one to three substituents independently selected from: -OH, halogen, cyano, or–$S(O)_2CH_3$;

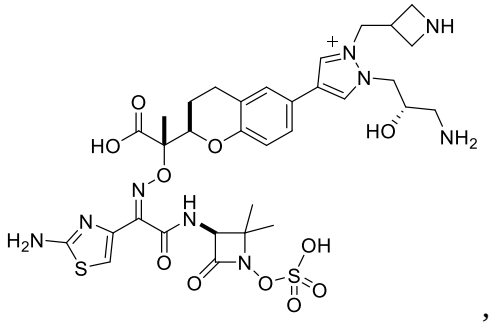
each occurrence of R^i is independently:
-C_1-C_8 alkyl,
-C_2-C_8 alkenyl,
-C_2-C_8 alkynyl,
halogen,
-OR^e,
-$S(O)_mR^e$,
-$S(O)_mNR^cR^d$,
-$C(O)R^e$,
-$OC(O)R^e$,
-$C(O)OR^e$,
-CN,
-$C(O)NR^cR^d$,
-NR^cR^d,

$-(CH_2)_nNR^cR^d$,
$-NR^cC(O)R^e$,
$-NR^cC(O)OR^e$,
$-NR^cC(O)NR^cR^d$,
$-NR^cS(O)_mR^e$,
=NH,
$-CF_3$,
$-OCF_3$, or
$-OCHF_2$;

each occurrence of R^j is independently:
hydrogen,
C_1-C_3 alkyl,
OR^{10},
$=NR^{10}$,
$N(R^{10})_2$, or
halogen,
wherein C_1-C_3 alkyl unsubstituted or substituted with one to three R^b;

each n is independently 0, 1, 2, 3, 4, 5 or 6;
each m is independently 0, 1 or 2;
each s is independently 0, 1, 2 or 3;
each t is independently 0, 1, 2 or 3;
each u is independently 0, 1, 2, 3, 4, 5 or 6; and
each v is independently 0, 1, or 2.

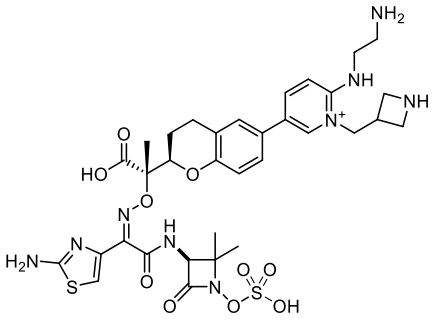
In another aspect, there is provided a compound which is:



,

or a pharmaceutically acceptable salt thereof.

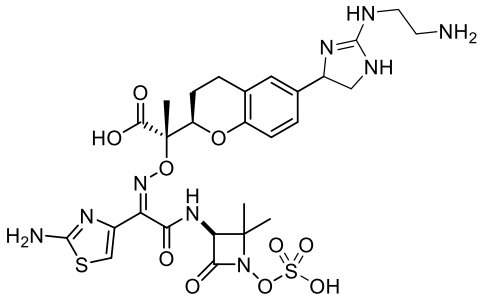
In another aspect, there is provided a compound which is:



,

or a pharmaceutically acceptable salt thereof.

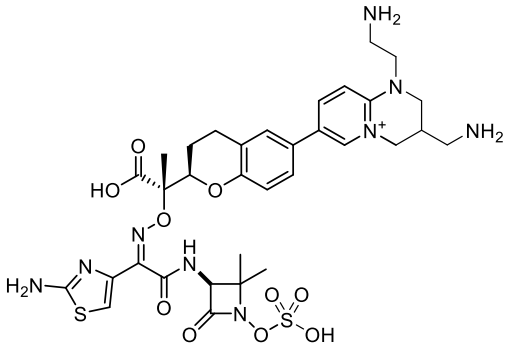
In yet another aspect, there is provided a compound which is:



,

or a pharmaceutically acceptable salt thereof.

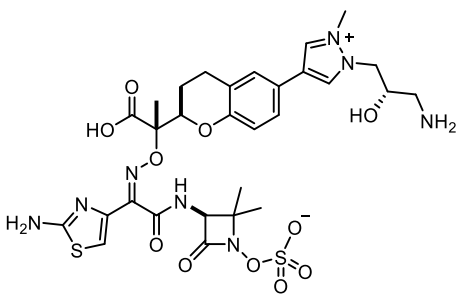
In another aspect, there is provided a compound which is:



,

or a pharmaceutically acceptable salt thereof.

In yet another aspect, there is provided a compound which is:



,

or a pharmaceutically acceptable salt thereof.

The present disclosure also relates to a pharmaceutical composition for treating a bacterial infection in a subject, including infection with multidrug resistant Gram-negative bacterial strains, comprising a monobactam compound of the disclosure and a pharmaceutically acceptable carrier, diluent or excipient.

In another aspect, there is provided a pharmaceutical composition comprising a therapeutically effective amount of a compound as defined herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

The Compounds of Formula (I), also referred to herein as the "monobactam compounds", and pharmaceutically acceptable salts thereof can be useful, for example, for inhibiting the growth of Gram-negative bacterial strains, including but not limited to, Pseudomonas, Klebsiella and Acinetobacter strains, including Pseudomonas aeruginosa, Klebsiella pneumoniae and Acinetobacter baumannii, and/or for treating or preventing the clinical maifestations thereof in a patient.

The present disclosure is also directed to methods of treating Gram-negative bacterial infections in a subject in need of treatment thereof, comprising administering to the subject an effective amount of a monobactam compound of the disclosure. In specific examples of the disclosure, the method includes administration of a beta lactamase inhibitor compound.

In another aspect, there is provided a compound as defined herein, or a pharmaceutically acceptable salt thereof, optionally in combination with a beta-lactamase inhibitor compound or a pharmaceutical composition as defined herein for use in treating a bacterial infection.

In another aspect, there is provided use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, optionally in combination with a beta-lactamase inhibitor compound or a pharmaceutical composition as defined herein in the manufacture of a medicament for treating a bacterial infection.

In another aspect, there is provided use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a bacterial infection, in combination with a beta-lactamase inhibitor compound for treating a bacterial infection, or in combination with a beta-lactamase inhibitor compound in the manufacture of a medicament for treating a bacterial infection.

Embodiments, sub-embodiments, examples and features of the present disclosure are either further described in or will be apparent from the ensuing description, examples and appended claims.