Because of the drug resistance, many cancers prove or become refractory to standard chemotherapeutic treatment protocols.

Other diseases or conditions associated with, or characterized by, undesired angiogenesis are also difficult to treat. However, some compounds such as protamine, hepain and steroids have been proposed to be useful in the treatment of certain specific diseases. Taylor *et al.*, *Nature* 297:307 (1982); Folkman *et al.*, *Science* 221:719 (1983); and U.S. Pat. Nos. 5,001,116 and 4,994,443.

Still, there is a significant need for effective methods of treating, preventing and managing cancer and other diseases and conditions, including for diseases that are refractory to standard treatments, such as surgery, radiation therapy, chemotherapy and hormonal therapy, while reducing or avoiding the toxicities and/or side effects associated with the conventional therapies.

3. SUMMARY ~~OF THE INVENTION~~

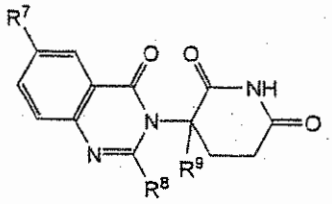
Provided herein are quinazolinone compounds, and pharmaceutically acceptable salts, solvates (*e.g.*, hydrates), prodrugs, clathrates, or stereoisomers thereof.

Also provided are methods of treating and managing various diseases or disorders. The methods comprise administering to a patient in need of such treatment or management, or having such a disease or disorder, a therapeutically effective amount of a compound provided herein, or a pharmaceutically acceptable salt, solvate, prodrug, clathrate, or stereoisomer thereof.

Also provided herein are methods of preventing various diseases and disorders, which comprise administering to a patient in need of such prevention, or at a risk of such a disease or disorder, a prophylactically effective amount of a compound provided herein, or a pharmaceutically acceptable salt, solvate, prodrug, clathrate, or stereoisomer thereof.

Also provided herein are pharmaceutical compositions, single unit dosage forms, dosing regimens and kits which comprise a compound provided herein, or a pharmaceutically acceptable salt, solvate, prodrug, clathrate, or stereoisomer thereof.

In one aspect, there is provided a compound having a structure of formula (II):



(II),

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^7 is : $-(CH_2)_nNHR^d$, wherein R^d is:

$-(CH_2)_n$-(6 to 10 membered aryl);

$-C(O)-(CH_2)_n$-(6 to 10 membered aryl) or $-C(O)-(CH_2)_n$-(6 to 10 membered heteroaryl), wherein the aryl or heteroaryl is optionally substituted with one or more of: halo; $-SCF_3$; (C_1-C_6)alkyl, itself optionally substituted with one or more halo; or (C_1-C_6)alkoxy, itself optionally substituted with one

or more halo;

$-C(O)-(CH_2)_n-(C_3-C_{10}$-cycloalkyl);

$-C(O)-(CH_2)_n-NR^eR^f$, wherein R^e and R^f are each independently:

hydrogen;

6 to 10 membered aryl, optionally substituted with one or more of: halo;

(C_1-C_6)alkyl, itself optionally substituted with one or more halo; or

(C_1-C_6)alkoxy, itself optionally substituted with one or more halo; or

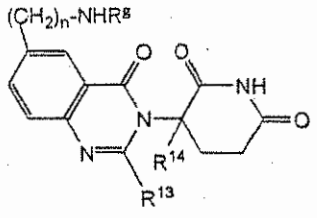
$-C(O)-(CH_2)_n-O-(CH_2)_n-$(6 to 10 membered aryl);

R^8 is: hydrogen; $-(CH_2)_nOH$; phenyl; $-O-(C_1-C_6)$alkyl; or (C_1-C_6)alkyl, optionally substituted with one or more halo;

R^9 is: hydrogen; or (C_1-C_6)alkyl, optionally substituted with one or more halo; and

n is 0, 1, or 2.

In another aspect, there is provided a compound having a structure of formula (IV):



(IV),

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^8 is:

$-(CH_2)_n-$(6 to 10 membered aryl);

$-C(O)-(CH_2)_n-$(6 to 10 membered aryl) or $-C(O)-(CH_2)_n-$(6 to 10 membered heteroaryl), wherein the aryl or heteroaryl is optionally substituted with one or more of: halo; $-SCF_3$; (C_1-C_6)alkyl, itself optionally substituted with one or more halo; or (C_1-C_6)alkoxy, itself optionally substituted with one or more halo;

$-C(O)-(CH_2)_n-(C_3-C_{10}$-cycloalkyl);

$-C(O)-(CH_2)_n-NR^hR^i$, wherein R^h and R^i are each independently:

hydrogen;

6 to 10 membered aryl, optionally substituted with one or more of: halo;

(C_1-C_6)alkyl, itself optionally substituted with one or more halo; or

(C_1-C_6)alkoxy, itself optionally substituted with one or more halo; or

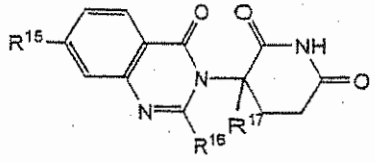
$-C(O)-(CH_2)_n-O-(CH_2)_n-$(6 to 10 membered aryl);

R^{13} is: hydrogen; $-(CH_2)_nOH$; phenyl; $-O-(C_1-C_6)$alkyl; or (C_1-C_6)alkyl, optionally substituted with one or more halo;

R^{14} is: hydrogen; or (C_1-C_6)alkyl, optionally substituted with one or more halo; and

n is 0, 1, or 2.

In another aspect, there is provided a compound having a structure of formula (V):



(V),

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{15} is : $-(CH_2)_nNHR^j$, wherein R^j is:

$-(CH_2)_n$-(6 to 10 membered aryl);

$-C(O)-(CH_2)_n$-(6 to 10 membered aryl) or $-C(O)-(CH_2)_n$-(6 to 10 membered heteroaryl), wherein the aryl or heteroaryl is optionally substituted with one or more of: halo; $-SCF_3$; (C_1-C_6)alkyl, itself optionally substituted with one or more halo; or (C_1-C_6)alkoxy, itself optionally substituted with one or more halo;

$-C(O)-(CH_2)_n-(C_3-C_{10}$-cycloalkyl);

$-C(O)-(CH_2)_n-NR^kR^l$, wherein R^k and R^l are each independently:

hydrogen;

6 to 10 membered aryl, optionally substituted with one or more of: halo; (C_1-C_6)alkyl, itself optionally substituted with one or more halo; or (C_1-C_6)alkoxy, itself optionally substituted with one or more halo; or

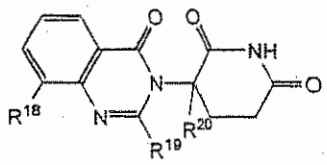
$-C(O)-(CH_2)_n-O-(CH_2)_n$-(6 to 10 membered aryl);

R^{16} is: hydrogen; $-(CH_2)_nOH$; phenyl; $-O-(C_1-C_6)$alkyl; or (C_1-C_6)alkyl, optionally substituted with one or more halo;

R^{17} is: hydrogen; or (C_1-C_6)alkyl, optionally substituted with one or more halo; and

n is 0, 1, or 2.

In another aspect, there is provided a compound having a structure of formula (VI):



(VI),

or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{18} is : $-(CH_2)_nNHR^m$, wherein R^m is:

$-(CH_2)_n$-(6 to 10 membered aryl);

$-C(O)-(CH_2)_n$-(6 to 10 membered aryl) or $-C(O)-(CH_2)_n$-(6 to 10 membered heteroaryl), wherein the aryl or heteroaryl is optionally substituted with

one or more of: halo; $-SCF_3$; (C_1-C_6)alkyl, itself optionally substituted with one or more halo; or (C_1-C_6)alkoxy, itself optionally substituted with one or more halo;

$-C(O)-(CH_2)_n-(C_3-C_{10}$-cycloalkyl);

$-C(O)-(CH_2)_n-NR^nR^o$, wherein R^n and R^o are each independently:

hydrogen;

6 to 10 membered aryl, optionally substituted with one or more of: halo; (C_1-C_6)alkyl, itself optionally substituted with one or more halo; or (C_1-C_6)alkoxy, itself optionally substituted with one or more halo; or

$-C(O)-(CH_2)_n-O-(CH_2)_n-$(6 to 10 membered aryl);

R^{19} is: hydrogen; $-(CH_2)_nOH$; phenyl; $-O-(C_1-C_6)$alkyl; or (C_1-C_6)alkyl, optionally substituted with one or more halo;

R^{20} is: hydrogen; or (C_1-C_6)alkyl, optionally substituted with one or more halo; and

n is 0, 1, or 2.

In another aspect, there is provided a pharmaceutical composition comprising a compound as defined above, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

In another aspect, there is provided the use of a compound as defined above, or a pharmaceutically acceptable salt,

solvate, or stereoisomer thereof, in the manufacture of a medicament for treating, managing or preventing a disease or disorder wherein the disease or disorder is cancer; endometriosis; heart failure; periodontis; gingivitis; pain; atrophic macular degeneration; exudative macular degeneration; age-related maculopathy (ARM); choroidal neovascularisation (CNVM); retinal pigment epithelium detachment (PED); atrophy of retinal pigment epithelium (RPE); mesothelioma; asbestosis; malignant pleural effusion; benign exudative effusion; pleural plaques; pleural calcification; diffuse pleural thickening; rounded atelectasis; fibrotic masses; lung cancer; atherosclerosis; restenosis after vascular intervention; dysfunctional sleep; snoring; sleep apnea; insomnia; narcolepsy; restless leg syndrome; sleep terrors; sleep walking; sleep eating; hemoglobinopathy; sickle cell anemia; endotoxemia or toxic shock syndrome; adult respiratory distress syndrome; arthritis; hypercalcemia; Graft versus Host Reaction; cerebral malaria; inflammation; tumor growth; chronic pulmonary inflammatory diseases; reperfusion injury; myocardial infarction; stroke; circulatory shock; Crohn's disease; HIV infection and AIDS; rheumatoid arthritis; rheumatoid spondylitis; osteoarthritis; psoriatic arthritis; septic shock; wasting; ulcerative colitis; multiple sclerosis; systemic lupus; erythromatosis; ENL in leprosy; sepsis; hemodynamic shock and sepsis syndrome; post ischemic reperfusion injury; malaria; meningitis, psoriasis; congestive heart failure; fibrotic disease; cachexia; graft rejection; asthma; hyperoxic alveolar injury; viral conjunctivitis; or atopic dermatitis.

4. DETAILED DESCRIPTION OF THE INVENTION

In one embodiment, provided are quinazolinone compounds, and pharmaceutically acceptable salts, solvates, prodrugs, clathrate, and stereoisomers thereof.

In another embodiment, provided are methods of treating, managing, and preventing various diseases and disorders, which comprises administering to a patient a therapeutically or prophylactically effective amount of a compound provided herein, or a pharmaceutically acceptable salt, solvate, prodrug, clathrate, or stereoisomer thereof. Examples of diseases and disorders are described herein.

In other embodiments, a compound provided herein, or a pharmaceutically acceptable salt, solvate, prodrug, clathrate, or stereoisomer thereof, is administered in combination with another drug ("second active agent") or treatment. Second active agents include small molecules and large molecules (*e.g.*, proteins and antibodies), examples of which are provided