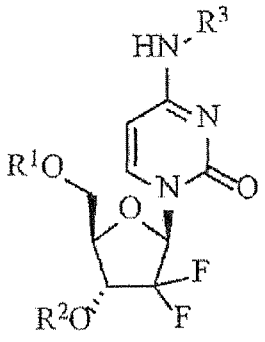
~~REPLACEMENT SHEET~~

BRIEF SUMMARY ~~OF THE INVENTION~~

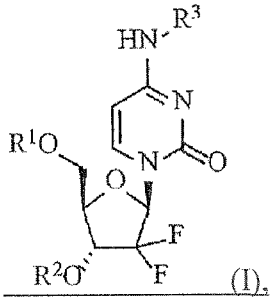
~~In one aspect, t~~The ~~invention~~ disclosure provides compounds according to formula I:



(I),

and pharmaceutically acceptable salts thereof. For compounds of formula I, R^1 and R^2 are independently selected from H, –C(=O)-$(CH_2)_2$-aryl, and –C(=O) - $(CH_2)_n$-C(=O) -NH-aryl, and at least one of R^1 and R^2 is other than H. The subscript n is from 2 to 6. R^3 is selected from H and –C(=O)-O-R^4; and R^4 is selected from alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, heteroalkyl and substituted heteroalkyl.

In one aspect, there is provided a compound according to formula I:



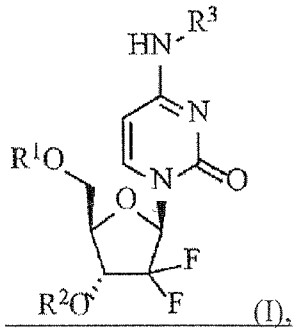
(I),

or a pharmaceutically acceptable salt thereof; wherein R^1 and R^2 are independently selected from the group consisting of H, -C(=O)-$(CH_2)_2$-Ar and –C(=O)-$(CH_2)_n$-C(=O)-NH-Ar, and at least one of R^1 and R^2 is other than H, and Ar is aryl or heteroaryl; R^3 is selected from the group consisting of H and –C(=O)-O-R^4; R^4 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, cycloheteroalkyl,

substituted cycloheteroalkyl, heteroalkyl and substituted heteroalkyl; and the subscript n is an integer of from 2 to 6.

~~In a second aspect, t~~The ~~invention~~ disclosure also provides pharmaceutical compositions containing a pharmaceutically acceptable carrier and one or more compounds according to formula I as described above, prodrugs thereof, or pharmaceutically acceptable salts of the compounds and prodrugs.

In another aspect, there is provided a pharmaceutical composition comprising a compound of formula I:



(I),

or a pharmaceutically acceptable salt of thereof; wherein R^1 and R^2 are independently selected from the group consisting of H, -C(=O)-$(CH_2)_2$-Ar and –C(=O)-$(CH_2)_n$-C(=O)-NH-Ar, and at least one of R^1 and R^2 is other than H, and Ar is aryl or heteroaryl; R^3 is selected from the group consisting of H and –C(=O)-O-R^4; R^4 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, heteroalkyl and substituted heteroalkyl; and the subscript n is 2-6; and a pharmaceutically acceptable carrier.

~~In a third aspect, t~~The ~~invention~~ disclosure also provides methods for inhibiting the growth of cancer cells. The methods include contacting the cells with an effective amount of a compound of the ~~invention~~disclosure.

In another aspect, there is provided a compound as defined herein for use in inhibiting the growth of cancer cells.

~~In a fourth aspect, t~~The ~~invention~~ disclosure also provides methods for treating cancer. The methods include administering to the subject an effective amount of a pharmaceutical composition of the ~~invention~~disclosure.

In another aspect, there is provided a pharmaceutical composition as defined herein for use in the treatment of cancer.

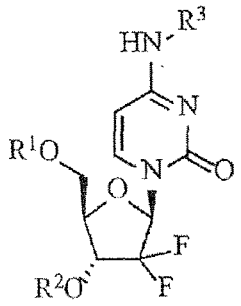
In another aspect, there is provided use of a compound as defined herein in the manufacture of a medicament for the treatment of cancer.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows a synthetic route for the preparation of 5′*O*-derivatized gemcitabine prodrugs.

WHAT IS CLAIMED IS:

1. A compound according to formula I:



(I),

or a pharmaceutically acceptable salt thereof; wherein

R^1 and R^2 are independently selected from the group consisting of H, -C(=O)-$(CH_2)_2$-Ar and –C(=O)-$(CH_2)_n$-C(=O)-NH-Ar, and at least one of R^1 and R^2 is other than H, and Ar is aryl or heteroaryl;

R^3 is selected from the group consisting of H and –C(=O)-O-R^4;

R^4 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, heteroalkyl and substituted heteroalkyl; and

the subscript n is an integer of from 2 to 6.

2. A compound according to claim **1**, wherein

R^1 and R^2 are independently selected from the group consisting of H, -C(=O)-$(CH_2)_2$-Ar and –C(=O)-$(CH_2)_n$-C(=O)-NH-phenyl, and at least one of R^1 and R^2 is other than H, and Ar is phenyl or 3-pyridyl; and

the subscript n is 2, 4 or 6.

3. A compound according to claim **2**, wherein R^2 and R^3 are H.

4. A compound according to claim **2**, wherein R^2 is H and R^1 and R^3 are other than H.

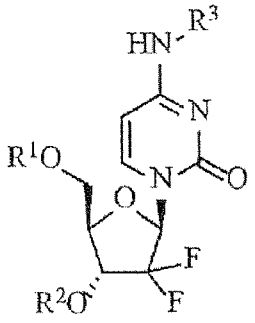
5. A compound according to claim **2**, wherein R^1 is H and R^2 and R^3 are other than H.

6. A compound according to claim **4** or claim **5**, wherein R^4 is selected from the group consisting of alkyl and substituted alkyl.

7. A compound according to claim **6**, wherein R^4 is C_1-C_8 alkyl.

8. A compound according to claim **4** or claim **5**, wherein R^4 is C_3-C_8 heteroalkyl.

9. A pharmaceutical composition comprising a compound of formula I:



(I),

or a pharmaceutically acceptable salt of thereof; wherein

R^1 and R^2 are independently selected from the group consisting of H, -C(=O)-$(CH_2)_2$-Ar and –C(=O)-$(CH_2)_n$-C(=O)-NH-Ar, and at least one of R^1 and R^2 is other than H, and Ar is aryl or heteroaryl;

R^3 is selected from the group consisting of H and –C(=O)-O-R^4;

R^4 is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, heteroalkyl and substituted heteroalkyl; and

the subscript n is 2-6; and

a pharmaceutically acceptable carrier.

10. A pharmaceutical composition according to claim **9**, wherein

R^1 and R^2 are independently selected from the group consisting of H, -C(=O)-$(CH_2)_2$-Ar or–C(=O)-$(CH_2)_n$-C(=O)-NH-phenyl, and at least one of R^1 and R^2 is other than H, and Ar is phenyl or 3-pyridyl; and

the subscript n is 2, 4 or 6.

11. A pharmaceutical composition according to claim **10**, wherein R^2 and R^3 are H.

12. A pharmaceutical composition according to claim **10**, wherein R^2 is H and R^1 and R^3 are other than H.

13. A pharmaceutical composition according to claim **10**, wherein R^1 is H and R^2 and R^3 are other than H.

14. A pharmaceutical composition according to claim **12** or claim **13**, wherein R^4 is selected from the group consisting of alkyl and substituted alkyl.

15. A pharmaceutical composition according to claim **14**, wherein R^4 is C_1-C_8 alkyl.

16. A pharmaceutical composition according to claim **12** or claim **13**, wherein R^4 is C_3-C_8 heteroalkyl.

17. A ~~method for inhibiting the growth of cancer cells, the method comprising contacting the cells with an effective amount of a~~ compound according to any of claims **1-8** for use in inhibiting the growth of cancer cells.

18. A compound ~~method~~ according to claim **17**, further comprising ~~contacting the cells with~~ use of an anti-cancer agent.

19. A compound ~~method~~ according to claim **18**, wherein the anti-cancer agent is selected from the group consisting of a conventional chemotherapeutic agent, a targeted therapeutic agent, a radiotherapeutic agent, and a mixture thereof.

20. A compound ~~method~~ according to claim **18**, wherein the anti-cancer agent is selected from the group consisting of cisplatin, oxaliplatin, carboplatin, erlotinib, gefitinib, lapatinib, cetuximab, zalutumumab, minotuzumab, and matuzumab.

21. A compound ~~method~~ according to claim **17**, wherein the cancer cells are selected from the group consisting of pancreatic cancer cells, non-small cell lung cancer cells, breast cancer cells, ovarian cancer cells, and bladder cancer cells.

22. A ~~method for treating cancer, the method comprising administering to the subject an effective amount of a~~ pharmaceutical composition according to any of claims **9-16** for use in the treatment of cancer.

23. A pharmaceutical composition ~~method~~ according to claim **22**, further comprising ~~administering to the subject~~ an anti-cancer agent.

24. A pharmaceutical composition ~~method~~ according to claim **23**, wherein the anti-cancer agent is selected from the group consisting of a conventional chemotherapeutic agent, a targeted therapeutic agent, a radiotherapeutic agent and a mixture thereof.

25. A pharmaceutical composition ~~method~~ according to claim **23**, wherein the anti-cancer agent is selected from the group consisting of cisplatin, oxaliplatin, carboplatin, erlotinib, gefitinib, lapatinib, cetuximab, zalutumumab, minotuzumab, and matuzumab.

26. A pharmaceutical composition ~~method~~ according to claim **22**, wherein the pharmaceutical composition is to be administered ~~administering the composition is conducted~~ orally.

27. A pharmaceutical composition ~~method~~ according to claim **22**, wherein the pharmaceutical composition is to be administered ~~administering the composition is conducted~~ parenterally.

28. A pharmaceutical composition ~~method~~ according to claim **22**, wherein the cancer is selected from the group consisting of pancreatic cancer, non-small cell lung cancer, breast cancer, ovarian cancer, and bladder cancer.

29. Use of a compound according to any of claims **1-8** in the manufacture of a medicament for the treatment of cancer.