

CLAIMS

What is claimed is:

1. Use of an antimetabolite in the manufacture of a medicament for treating a urothelial carcinoma of the lower tract in an individual, wherein the antimetabolite is to be delivered locally to the bladder, wherein the urothelial carcinoma of the lower tract is muscle invasive bladder cancer.
2. The use of claim 1, wherein the individual is unfit for radical cystectomy.
3. The use of claim 1 or 2, wherein the individual cannot tolerate systemic chemotherapy and/or chemotherapy with an agent other than the antimetabolite.
4. The use of any one of claims 1-3, wherein the individual does not receive a radical cystectomy.
5. Use of an antimetabolite in the manufacture of a medicament for treating a urothelial carcinoma of the lower tract in an individual, wherein the antimetabolite is to be delivered locally to the bladder, wherein the urothelial carcinoma of the lower tract is non-muscle invasive bladder cancer.
6. Use of a combination of an antimetabolite with a second agent in the manufacture of a medicament for treating a urothelial carcinoma of the lower tract in an individual, wherein the antimetabolite is to be delivered locally to the bladder.
7. The use of any of claims 1-6, wherein the antimetabolite is a nucleoside analog.
8. The use of any one of claims 1-7, wherein the antimetabolite is gemcitabine.

9. The use of claim 8, wherein the gemcitabine is to be delivered continuously to the bladder of the individual for 24 hours to 6 weeks.
10. Use of an antimetabolite in the manufacture of a medicament for bladder preservation in an individual, wherein the antimetabolite is gemcitabine, wherein gemcitabine is to be delivered continuously to the bladder of the individual for 24 hours to 6 weeks, wherein the individual has a urothelial carcinoma of the lower tract.
11. The use of any one of claims 8-10, wherein the gemcitabine is to be delivered continuously to the bladder of the individual for a period of 24 hours to three weeks.
12. The use of any one of claims 8-11, wherein the gemcitabine is to be delivered continuously to the bladder of the individual for 7 days.
13. The use of any one of claims 8-11, wherein the gemcitabine is to be delivered continuously to the bladder of the individual for 3 weeks.
14. The use of any one of claims 8-13, wherein the use comprises a first gemcitabine delivery period and a second gemcitabine delivery period.
15. The use of claim 14, wherein the first and second gemcitabine delivery periods are each 7 days.
16. The use of claim 14, wherein the first and second gemcitabine delivery periods are each 3 weeks.
17. The use of any one of claims 14-16, wherein the first and second gemcitabine delivery periods are separated by a rest period of 14 days.

18. The use of any of claims 1-17, wherein the antimetabolite is to be delivered in a first phase of the delivery at a first release rate followed by a second phase of the delivery having a second release rate.
19. The use of any of claims 1-18, wherein the antimetabolite is to be delivered at a dose of from about 1 mg/day to about 300 mg/day.
20. The use of any of claims 1-19, wherein the concentration of antimetabolite in the urine is from about 0.1 $\mu\text{g/mL}$ to about 200 $\mu\text{g/mL}$ during the delivery period.
21. The use of claim 20, wherein the concentration of antimetabolite in the urine is from about 1 $\mu\text{g/mL}$ to about 10 $\mu\text{g/mL}$ during the delivery period.
22. The use of claim 20, wherein the concentration of antimetabolite in the urine is about 10 $\mu\text{g/mL}$ during the delivery period.
23. The use of any of claims 1-22, comprising
- a) a first antimetabolite delivery period, wherein the concentration of antimetabolite in the urine of the individual is at least about 0.1 $\mu\text{g/mL}$;
 - b) a rest period; and
 - c) a second antimetabolite delivery period, wherein the concentration of antimetabolite in the urine of the individual is greater than about 0.1 $\mu\text{g/mL}$.
24. The use of any one of claims 1-5 and 7-23, wherein an effective amount of a second agent is to be administered to the individual.
25. The use of claim 6 or 24, wherein the second agent is to be delivered systemically.

26. The use of claim 6 or 24, wherein the second agent or second chemotherapeutic agent is to be delivered locally.
27. The use any one of claims 24-26, wherein the second agent is an immunomodulating agent.
28. The use of claim 27, wherein the immunomodulating agent is an immune checkpoint inhibitor.
29. The use of claim 28, wherein the immune checkpoint inhibitor is an inhibitor of an immune checkpoint protein selected from the group consisting of PD-L1, CTLA4, PD-L2, PD-1, B7-H3, B7-H4, HVEM, B- and T-lymphocyte attenuator (BTLA), Killer inhibitory receptor (KIR), GAL9, TIM3, A2AR, LAG-3, phosphatidylserine, CD27, TNF- α , CD33, Siglec-5, Siglec-7, Siglec-9, and Siglec-11.
30. The use of any of claims 1-29, wherein the individual does not receive radiation therapy.
31. The use of any one of claims 1-29, wherein the use further comprises radiation therapy.
32. The use of any of claims 1-31, wherein the antimetabolite is to be delivered in a neoadjuvant setting.
33. The use of any of claims 1-31, wherein the antimetabolite is to be delivered in an adjuvant setting.
34. The use of any of claims 1-33, wherein the antimetabolite is to be delivered into the bladder by an intravesicular device.
35. The use of claim 34, wherein the intravesicular device contains 100 mg to 500 mg of gemcitabine.

36. The use of claim 35, wherein the intravesicular device contains 225 mg of gemcitabine.
37. The use of any of claims 6-36, wherein the urothelial carcinoma of the lower tract is bladder cancer.
38. The use of claim 37, wherein the bladder cancer is muscle invasive bladder cancer.
39. The use of claim 37, wherein the bladder cancer is non-muscle invasive bladder cancer.
40. The use of any one of claims 1-39, wherein the individual is human.
41. The use of any one of claims 1-40, wherein the individual is unsuitable for systemic chemotherapy.
42. The use of any one of claims 1-41, wherein the individual has a compromised immune system.