In one aspect of the present disclosure, there is provided a use of gemcitabine in the manufacture of a medicament for the treatment of bladder cancer in a patient, wherein the medicament is to be locally administered into the bladder of the patient to achieve a sustained concentration of the gemcitabine in the urine in the bladder sufficient to produce a therapeutic concentration of the gemcitabine in the bladder tissues, wherein the locally administering into the patient's bladder at a mean average amount of from 1 mg/day to 300 mg/day of the gemcitabine (FBE) continuously over a period of from 1 day to 30 days, wherein the gemcitabine is to be delivered into the bladder from:

an intravesical drug delivery device which releases the gemcitabine into the urine in the bladder over the period,

a coating substance applied to the bladder, which coating substance releases the gemcitabine into the urine in the bladder over the period, or

a liquid form of the gemcitabine pumped into the bladder through a urethral or suprapubic catheter which is deployed into the bladder.

In embodiments, the local administer into the patient's bladder is at a mean average amount of from 1 mg/day to 200 mg/day of the gemcitabine (FBE), from 5 mg/day to 100 mg/day of

In a further aspect of the present disclosure, there is provided a drug delivery device comprising:

a housing configured for intravesical insertion, the housing being elastically deformable between a retention shape configured to retain the device in a patient's bladder and a deployment shape for passage of the device through the patient's urethra; and

a dosage form comprising gemcitabine,

wherein the housing holds the dosage form and is configured to release the gemcitabine into the bladder in an amount therapeutically effective for the treatment of bladder cancer,

wherein the housing is configured to release the gemcitabine by diffusion or osmotic pressure, without a predefined release aperture, and

wherein the device is configured to release gemcitabine into the bladder at a mean average amount of from 25 mg/day to 300 mg/day of the gemcitabine.

The present disclosure also providesmethods of treating bladder cancer are provide by locally administering the gemcitabine into the bladder of a patient to achieve a sustained concentration of the gemcitabine in the urine in the bladder sufficient to produce a therapeutic concentration of the gemcitabine in the bladder tissues. In embodiments, the

local administration into the patient's bladder is at a mean average amount of from 1 mg/day to about 300 mg/day of the gemcitabine (FBE). In one embodiment, the method further includes administering at least a second therapeutic agent to the patient. The second therapeutic agent may be administered intravesically. In another embodiment, the method further includes administering urea or another solubility altering agent into the bladder in an amount effective to enhance or otherwise alter solubilization of the gemcitabine. In embodiments, the second therapeutic agent and/or the solubility altering agent is released from an intravesical device which releases the gemcitabine.

Brief Description of the Drawings

FIGS. 1A-1B illustrate one embodiment of an intravesical drug delivery device that may be used for administering gemcitabine as described herein.

FIGS. 2A-2B illustrate another embodiment of an intravesical drug delivery device that may be used for administering gemcitabine as described herein.

FIGS. 3A-3C illustrate still another embodiment of an intravesical drug delivery device that may be used for administering gemcitabine as described herein.

FIGS. 4A-4B illustrate a method of inserting an intravesical drug delivery device into the bladder of a patient for local administration of gemcitabine as described herein.

FIG. 5A illustrates a material applied to the inner surface of the bladder wall for local administration of gemcitabine as described herein.

FIG. 5B illustrates a method of applying a coating material onto to the inner surface of the bladder wall for local administration of gemcitabine as described herein.

FIG. 6 illustrates a method of applying a liquid drug or drug formulation into the bladder.

FIG. 7 illustrates the concentration of gemcitabine in the prostate after bladder perfusion and intravenous administration.

FIG. 8 illustrates the plasma levels of gemcitabine after bladder perfusion and intravenous administration.

FIG. 9 illustrates ^{14}C gemcitabine concentration in the bladder after bladder perfusion and intravenous administration.

FIGS. 10A-C illustrate one embodiment of an intravesical drug delivery device for releasing gemcitabine via permeation disks. **FIG. 10A** is a plan view of the device. **FIG. 10B** is a cross-sectional view of one of the four drug reservoir modules of the device shown in **FIG. 10A**, showing the drug tablets and permeation disks of each module. **FIG. 10C** is a

We claim:

1. Use of gemcitabine in the manufacture of a medicament for the treatment of bladder cancer in a patient, wherein the medicament is to be locally administered into the bladder of the patient to achieve a sustained concentration of the gemcitabine in the urine in the bladder sufficient to produce a therapeutic concentration of the gemcitabine in the bladder tissues, wherein the locally administering into the patient's bladder is at a mean average amount of from 1 mg/day to 300 mg/day of the gemcitabine (FBE) continuously over a period of from 1 day to 30 days, wherein the gemcitabine is to be delivered into the bladder from:

an intravesical drug delivery device which releases the gemcitabine into the urine in the bladder over the period,

a coating substance applied to the bladder, which coating substance releases the gemcitabine into the urine in the bladder over the period, or

a liquid form of the gemcitabine pumped into the bladder through a urethral or suprapubic catheter which is deployed into the bladder.

2. The use of claim 1, wherein the locally administering into the patient's bladder is at a mean average amount of from 1 mg/day to 200 mg/day of the gemcitabine (FBE).

3. The use of claim 1, wherein the locally administering into the patient's bladder is at a mean average amount of from 5 mg/day to 100 mg/day of the gemcitabine (FBE).

4. The use of claim 1, wherein the locally administering into the patient's bladder is at a mean average amount of from 10 mg/day to 50 mg/day of the gemcitabine (FBE).

5. The use of claim 1, wherein the locally administering into the patient's bladder is at a mean average amount of from 15 mg/day to 25 mg/day of the gemcitabine (FBE).

6. The use of claim 1, wherein the locally administering into the patient's bladder is at a mean average amount of 20 mg/day of the gemcitabine (FBE).

7. The use of any one of claims 1 to 6, wherein the locally administering into the patient's bladder is continuous over a period from 1 day to 14 days.

8. The use of any one of claims 1 to 6, wherein the locally administering into the patient's bladder is continuous over a period from 1 day to 7 days.

9. The use of any one of claims 1 to 6, wherein the gemcitabine is to be delivered into the bladder from an intravesical drug delivery device which continuously releases the gemcitabine into the urine in the bladder over a sustained period.

10. The use of claim 9, wherein the intravesical drug delivery device continuously releases the gemcitabine into the urine in the bladder over a period of 1 day to 14 days.

11. The use of claim 10, wherein the intravesical drug delivery device comprises a housing which contains and controllably releases the gemcitabine and is elastically deformable between a retention shape configured to retain the device in a patient's bladder and a deployment shape for passage of the device through the patient's urethra.

12. The use of claim 11, wherein the gemcitabine contained in the housing is in a non-liquid form.

13. The use of claim 12, wherein the non-liquid form is selected from the group consisting of tablets, granules, semisolids, capsules, and combinations thereof.

14. The use of claim any one of claims 1 to 6, wherein the gemcitabine is to be delivered into the bladder from a coating substance applied to the bladder, which coating substance releases the gemcitabine into the urine in the bladder over a sustained period.

15. The use of claim 14, wherein the coating substance comprises a mucoadhesive formulation.

16. The use of claim 15, wherein the locally administering into the patient's bladder is continuous over a period from 1 day to 14 days.

17. The use of claim 16, wherein the locally administering into the patient's bladder is continuous over a period from 1 day to 7 days.

18. The use of any one of claims 1 to 6, wherein the locally administering comprises pumping a liquid form of the gemcitabine into the bladder through a urethral or suprapubic catheter which is deployed into the bladder.

19. The use of claim 18, wherein the locally administering into the patient's bladder is continuous or intermittent over a period from 1 day to 7 days.

20. A drug delivery device comprising a medicament according to any one of claims 1 to 19, configured to release the gemcitabine when the drug delivery device is inserted into the bladder.

21. A drug delivery device comprising:

a housing configured for intravesical insertion, the housing being elastically deformable between a retention shape configured to retain the device in a patient's bladder and a deployment shape for passage of the device through the patient's urethra; and

a dosage form comprising gemcitabine,

wherein the housing holds the dosage form and is configured to release the gemcitabine into the bladder in an amount therapeutically effective for the treatment of bladder cancer,

wherein the housing is configured to release the gemcitabine by diffusion or osmotic pressure, without a predefined release aperture, and

wherein the device is configured to release gemcitabine into the bladder at a mean average amount of from 25 mg/day to 300 mg/day of the gemcitabine.

22. The device of claim 21, wherein the housing releases the gemcitabine by diffusion through a drug permeable polymeric wall.