CLAIMS:

1. Use of at least one epigenetic drug in the manufacture of a medicament for the treatment of pancreatic ductal adenocarcinoma (PDAC) in a subject identified as epigenetic drug treatment-sensitive, wherein the subject is identified as epigenetic drug treatment-sensitive by an in vitro assay performed on a tumor sample obtained from the subject, the assay comprising:

enriching the tumor sample for Epithelial Cell Adhesion Molecule (EpCAM) positive (EpCAM+) tumor cells to generate an EpCAM+ tumor sample;

contacting the EpCAM+ tumor sample with a transposase complex to produce a population of tagged Accessible Chromatin Regions (ACRs);

contacting the tagged ACRs with a solid support comprising

(i) a first plurality of oligonucleotide probes complementary to a first set of ACRs selected from ARHGEF10, CLDN23, C12orf36, and SPATA4,

(ii) (ii) a second plurality of oligonucleotide probes complementary to a second set of ACRs selected from MAP2K2, PPAP2B, CNBP, FIG4, TTC19, PAPL, RN7SL300P, and ITGAV, and

(iii) (iii) a third plurality of oligonucleotide probes complementary to a third set of ACRs selected from GTF3C6, LINC01703, C1orf131, and XRCC2; detecting a first median hybridization intensity value from (i), a second median hybridization intensity value from (ii), and a third median hybridization intensity value from (iii);

calculating a prognostic score by determining a first normalized differential value of the first median hybridization intensity value and a second normalized differential value of the second median hybridization intensity value and comparing the first normalized differential value to the second normalized differential value; and

identifying the subject as epigenetic drug treatment-sensitive when the prognostic score is less than 0.6,

wherein the at least one epigenetic drug is a histone deacetylase (HDAC) inhibitor selected from (1*S*,4*S*,7*Z*,10*S*,16*E*,21*R*)-7-ethylidene-4,21-di(propan-2-yl)-2-oxa-12,13-dithia-5,8,20,23-tetrazabicyclo[8.7.6]tricos-16-ene-3,6,9,19,22-pentone, N'-hydroxy-N-phenyloctanediamide, (E)-N-hydroxy-3-[3-(phenylsulfamoyl)phenyl]prop-2-enamide, (E)-N-

hydroxy-3-[4-[[2-(2-methyl-1H-indol-3-yl)ethylamino]methyl]phenyl]prop-2-enamide, pyridin-3-ylmethyl N-[[4-[(2-aminophenyl)carbamoyl]phenyl]methyl]carbamate, N-(2-aminophenyl)-4-[[(4-pyridin-3-ylpyrimidin-2-yl)amino]methyl]benzamide, 7-[4-(3-ethynylanilino)-7-methoxyquinazolin-6-yl]oxy-N-hydroxyheptanamide, cyclopentyl (2S)-2-[[4-[[8-(hydroxyamino)-8-oxooctanoyl]amino]phenyl]methylamino]-2-phenylacetate, 3-[(dimethylamino)methyl]-N-[2-[4-(hydroxycarbamoyl)phenoxy]ethyl]-1-benzofuran-2-carboxamide, N-hydroxy-2-[4-[[(1-methylindol-3-yl)methylamino]methyl]piperidin-1-yl]pyrimidine-5-carboxamide, and [6-(diethylaminomethyl)naphthalen-2-yl]methyl N-[4-(hydroxycarbamoyl)phenyl]carbamate; or

wherein the at least one epigenetic drug is a DNA methyltransferase (DNMT) inhibitor selected from 4-amino-1-[(2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-1,3,5-triazin-2-one, 4-amino-1-[(2*R*,4*S*,5*R*)-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-1,3,5-triazin-2-on, and [(2R,3S,5R)-5-(2-amino-6-oxo-1H-purin-9-yl)-3-hydroxyoxolan-2-yl]methyl [(2R,3S,5R)-5-(4-amino-2-oxo-1,3,5-triazin-1-yl)-2-(hydroxymethyl)oxolan-3-yl] hydrogen phosphate; or

wherein the at least one epigenetic drug is a bromodomain and extra-terminal motif (BET) inhibitor selected from tert-butyl 2-[(9S)-7-(4-chlorophenyl)-4,5,13-trimethyl-3-thia-1,8,11,12-tetrazatricyclo[8.3.0.02,6]trideca-2(6),4,7,10,12-pentaen-9-yl]acetate and 2-[7-(4-chlorophenyl)-4,5,13-trimethyl-3-thia-1,8,11,12-tetrazatricyclo[8.3.0.$0^{2,6}$]trideca-2(6),4,7,10,12-pentaen-9-yl]-*N*-(4-hydroxyphenyl)acetamide; or

wherein the at least one epigenetic drug is a Enhancer of Zeste Homolog 2 (EZH2) inhibitor selected from 1-isopropyl-6-(6-(4-isopropylpiperazin-1-yl)pyridin-3-yl)-N-((6-methyl-2-oxo-4-propyl-1,2-dihydropyridin-3-yl)methyl)-1H-indazole-4-carboxamide, 1-[(2*S*)-butan-2-yl]-*N*-[(4,6-dimethyl-2-oxo-1*H*-pyridin-3-yl)methyl]-3-methyl-6-(6-piperazin-1-yl-3-pyridinyl)indole-4-carboxamide, 1-cyclopentyl-N-[(4,6-dimethyl-2-oxo-1H-pyridin-3-yl)methyl]-6-[4-(morpholin-4-ylmethyl)phenyl]indazole-4-carboxamide, and N-[(4,6-dimethyl-2-oxo-1H-pyridin-3-yl)methyl]-3-[ethyl(oxan-4-yl)amino]-2-methyl-5-[4-(morpholin-4-ylmethyl)phenyl]benzamide; or

wherein the at least one epigenetic drug is (2R,3R,4S,5R)-2-(6-aminopurin-9-yl)-5-[[[3-[2-(6-tert-butyl-1H-benzimidazol-2-yl)ethyl]cyclobutyl]-propan-2-ylamino]methyl]oxolane-3,4-diol; or

wherein the at least one epigenetic drug is a PRMT inhibitor selected from (2S,4R)-1-[(2S)-2-[[2-[3-[2-[[2-[(9S)-7-(4-chlorophenyl)-4,5,13-trimethyl-3-thia-1,8,11,12-tetrazatricyclo[8.3.0.02,6]trideca-2(6),4,7,10,12-pentaen-9-yl]acetyl]amino]ethoxy]propoxy]acetyl]amino]-3,3-dimethylbutanoyl]-4-hydroxy-N-[(1S)-1-[4-(4-methyl-1,3-thiazol-5-yl)phenyl]ethyl]pyrrolidine-2-carboxamide, 2-[(9S)-7-(4-chlorophenyl)-4,5,13-trimethyl-3-thia-1,8,11,12-tetrazatricyclo[8.3.0.02,6]trideca-2(6),4,7,10,12-pentaen-9-yl]-N-[4-[2-[2-[2-[2-[[2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindol-4-yl]amino]ethoxy]ethoxy]ethoxy]ethoxy]phenyl]acetamide, and (2S,4R)-1-[(2S)-2-[[2-[2-[2-[[4-[(2S,4R)-1-acetyl-4-(4-chloroanilino)-2-methyl-3,4-dihydro-2H-quinolin-6-yl]benzoyl]amino]ethoxy]ethoxy]acetyl]amino]-3,3-dimethylbutanoyl]-4-hydroxy-N-[[4-(4-methyl-1,3-thiazol-5-yl)phenyl]methyl]pyrrolidine-2-carboxamide.

2. The use of claim 1, further comprising assaying the tumor sample for a HNF1b nuclear localization staining signal.

3. The use of claim 2, further comprising detecting a negative nuclear localization staining signal for HNF1b.

4. The use of claim 1, further comprising assaying the tumor sample for a nuclear localization staining signal for at least one of ZKSCAN1, EPAS1, RUNX2, ZNF410, MAFF, RREB1, NR3C2, SMAD1, RUNX1, ZNF32, ZSCAN4, HOXB1, POU3F1, ZBTB3, CLOCK, TCF15, and GCM1.

5. The use of claim 4, further comprising determining a positive nuclear localization staining signal for at least one of ZKSCAN1, EPAS1, RUNX2, ZNF410, MAFF, RREB1, NR3C2, SMAD1, RUNX1, ZNF32, ZSCAN4, HOXB1, POU3F1, ZBTB3, CLOCK, TCF15, and GCM1.

6. The use of claim 1, further comprising assaying the tumor sample for a nuclear localization staining signal for at least one of HNF1A, CTCF, CTCFL, DNMT1, E2F3, TET1, ONECUT1, ZFHX3, NRF1, HOMEZ, HMBOX1, GATA1, GATA2, MLL, ISL1, FOXD2,

GRHL1, IRF6, HOXB7, TCFL5, PRRX1, HNF4A, DLX2, ONECUT3, XBTB33, PBX3, OTP, ZFP161, ARID5A, SP3, E2F2, ATF2, CREB1, HNF4G, HOXC9, ZBTB7B, AC012531.1, E2F5, GMEB2, ZNF384, MYPOP, CGBP, and HINFP.

7. The use of claim 6, further comprising determining a negative nuclear localization staining signal for at least one of HNF1A, CTCF, CTCFL, DNMT1, E2F3, TET1, ONECUT1, ZFHX3, NRF1, HOMEZ, HMBOX1, GATA1, GATA2, MLL, ISL1, FOXD2, GRHL1, IRF6, HOXB7, TCFL5, PRRX1, HNF4A, DLX2, ONECUT3, XBTB33, PBX3, OTP, ZFP161, ARID5A, SP3, E2F2, ATF2, CREB1, HNF4G, HOXC9, ZBTB7B, AC012531.1, E2F5, GMEB2, ZNF384, MYPOP, CGBP, and HINFP.

8. The use of claim 1, wherein the tumor sample is a biopsied tissue sample, tissue section, cytological sample, or blood sample.

9. The use of claim 1, wherein the subject has or is suspected of having pancreatic cancer.

10. The use of claim 1, wherein the subject is treatment naïve.

11. Use of at least one chemotherapy drug in the manufacture of a medicament for the treatment of pancreatic ductal adenocarcinoma (PDAC) in a subject identified as chemotherapy-sensitive, wherein the subject is identified as chemotherapy-sensitive by an in vitro assay performed on a tumor sample obtained from the subject, the assay comprising:

(a) obtaining a tumor sample from a subject and enriching for Epithelial Cell Adhesion Molecule (EpCAM) positive (EpCAM+) tumor cells from the tumor sample to generate an EpCAM+ tumor sample;

(b) contacting the EpCAM+ tumor sample with a transposase complex to produce a population of tagged Accessible Chromatin Regions (ACRs);

(c)(i) contacting the tagged ACRs with a solid support comprising a first plurality of oligonucleotide probes bound thereto, the first plurality of oligonucleotide probes being complementary to a first set of ACRs selected from ARHGEF10, CLDN23, C12orf36, and SPATA4;

(c)(ii) contacting the tagged ACRs with a solid support comprising a second plurality of oligonucleotide probes bound thereto, the second plurality of oligonucleotide probes being complementary to a second set of ACRs selected from MAP2K2, PPAP2B, CNBP, FIG4, TTC19, PAPL, RN7SL300P, and ITGAV;

(c)(iii) contacting the tagged ACRs with a solid support comprising a third plurality of oligonucleotide probes bound thereto, the third plurality of oligonucleotide probes being complementary to a third set of ACRs selected from GTF3C6, LINC01703, C1orf131, and XRCC2;

(d) calculating a prognostic score, the prognostic score determined by:

i. detecting a first median hybridization intensity value from the contacting of (c)(i);

ii. detecting a second median hybridization intensity value from the contacting of (c)(ii);

iii. detecting a third median hybridization intensity value from the contacting of (c)(iii);

wherein the prognostic score is calculated by determining a first normalized differential value of (d)(i), determining a second normalized differential value of (d)(ii), and comparing the first normalized differential value to the second normalized differential value; and

(e) diagnosing the subject with a chemotherapy-sensitive PDAC tumor when the prognostic score is greater than 0.6; and

(f) administering at least one chemotherapy agent to the diagnosed subject of (e),

wherein the at least one chemotherapy agent is selected from gemcitabine, capecitabine, 5-fluorouracil, oxaliplatin, irinotecan, leucovorin, and nab-paclitaxel.

12. The use of claim 11, further comprising assaying the tumor sample for a HNF1b nuclear localization staining signal.

13. The use of claim 12, further comprising detecting a positive nuclear localization staining signal for HNF1b.

14. The use of claim 11, further comprising assaying the tumor sample for a nuclear localization staining signal for at least one of ZKSCAN1, EPAS1, RUNX2, ZNF410, MAFF, RREB1, NR3C2, SMAD1, RUNX1, ZNF32, ZSCAN4, HOXB1, POU3F1, ZBTB3, CLOCK, TCF15, and GCM1.

15. The use of claim 14, further comprising determining a negative nuclear localization staining signal for at least one of ZKSCAN1, EPAS1, RUNX2, ZNF410, MAFF, RREB1, NR3C2, SMAD1, RUNX1, ZNF32, ZSCAN4, HOXB1, POU3F1, ZBTB3, CLOCK, TCF15, and GCM1.

16. The use of claim 11, further comprising assaying the tumor sample for a nuclear localization staining signal for at least one of HNF1A, CTCF, CTCFL, DNMT1, E2F3, TET1, ONECUT1, ZFHX3, NRF1, HOMEZ, HMBOX1, GATA1, GATA2, MLL, ISL1, FOXD2, GRHL1, IRF6, HOXB7, TCFL5, PRRX1, HNF4A, DLX2, ONECUT3, XBTB33, PBX3, OTP, ZFP161, ARID5A, SP3, E2F2, ATF2, CREB1, HNF4G, HOXC9, ZBTB7B, AC012531.1, E2F5, GMEB2, ZNF384, MYPOP, CGBP, and HINFP.

17. The use of claim 16, further comprising determining a positive nuclear localization staining signal for at least one of HNF1A, CTCF, CTCFL, DNMT1, E2F3, TET1, ONECUT1, ZFHX3, NRF1, HOMEZ, HMBOX1, GATA1, GATA2, MLL, ISL1, FOXD2, GRHL1, IRF6, HOXB7, TCFL5, PRRX1, HNF4A, DLX2, ONECUT3, XBTB33, PBX3, OTP, ZFP161, ARID5A, SP3, E2F2, ATF2, CREB1, HNF4G, HOXC9, ZBTB7B, AC012531.1, E2F5, GMEB2, ZNF384, MYPOP, CGBP, and HINFP.

18. The use of claim 11, wherein the tumor sample is a biopsied tissue sample, tissue section, cytological sample, or blood sample.

19. The use of claim 11, wherein the subject has or is suspected of having pancreatic cancer.

20. The use of claim 11, wherein the subject is treatment naïve.