

CLAIMS

~~What is claimed is:~~

1. A panel for pre-operatively assessing a subject's risk of having ovarian cancer, the panel comprising and or consisting of markers:

i) _____ Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β 2-Microglobulin (β 2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), and follicle stimulating hormone (FSH), and one or more markers selected from the group consisting of Breast Cancer 1 (BRCA1), Breast Cancer 2 (BRCA2), Ataxia-Telangiesctasia mutated (ATM), BRCA1 Associated Ring Domain 1 (BARD1), BRCA1 Interacting Protein C-terminal Helicase 1 (BRIP1), Cadherin-1 (CDH1), Checkpoint Kinase 2 (CHEK2), Epithelial cell adhesion molecule (EPCAM), MutL homolog 1 (MLH1), MutS Homolog 2 (MSH2), MutS Homolog 6 (MSH6), Nibrin (NBN), partner and localizer of BRCA2 (PALB2), Phosphatase and tensin homolog (PTEN), RAD51 paralog D (RAD51D), Serine/Threonine Kinase 11 (STK11), Tumor protein p53 (TP53), Kirsten rat sarcoma viral oncogene homolog (KRAS), BRCA1 A complex subunit abraxas 1 (ABRAXAS1 or FAM175A), RAC-alpha serine/threonine-protein kinase (AKT1 or Protein Kinase B), Adenomatous polyposis coli (APC), axis inhibition protein 2 (AXIN2), Bone Morphogenetic Protein Receptor Type 1A (BMPR1A), proto-oncogene B-Raf (BRAF), Cell Division Cycle 25C (CDC25), Cyclin Dependent Kinase Inhibitor 2A (CDKN2A), Cyclin-dependent kinase 4 (CDK4), Catenin beta-1 (CTNNB1), helicase with RNase motif (DICER1), Erb-B2 Receptor Tyrosine Kinase 2 (ERBB2), Excision Repair Cross-Complementation Group 6 (ERCC6), Fanconi anemia complementation group M (FANCM), Fanconi anemia complementation group C (FANCC), Meiotic Recombination 11 (MRE11), mutY DNA glycosylase (MUTYH), Neurofibromin 1 (NF1), Endonuclease III-like protein 1 (NTHL1), Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha (PIK3CA), Postmeiotic segregation Increased 2 (PMS2), Protein phosphatase 2 regulatory subunit A alpha (PP2R1A), Protein Kinase DNA-Activated Catalytic Subunit (PRKDC), DNA Polymerase Delta 1 Catalytic Subunit (POLD1), RAD50 homolog (RAD50), RAD51 Paralog C (RAD51C), Ring Finger Protein 43 (RNF43), Succinate Dehydrogenase Complex Iron Sulfur Subunit B (SDHB), Succinate Dehydrogenase Complex Subunit D (SDHD), SWI/SNF Related Matrix Associated Actin Dependent Regulator Of Chromatin Subfamily A Member 4 (SMARCA4), X-ray repair complementing defective repair in Chinese hamster cells 2 (XRCC2), Werner syndrome ATP-dependent helicase (WRN or RECQL), Cell Division Cycle 73 (CDC73), Polypeptide N-Acetylgalactosaminyltransferase 12 (GALNT12), Gremlin 1 (GREM1), Homeobox B13 (HOXB13), MutS Homolog 3 (MSH3), DNA Polymerase Epsilon Catalytic Subunit (POLE),

RAD51 Recombinase (RAD51), RAD50 Interactor 1 (RINT1), 40S ribosomal protein S20 (RSP20), SLX4 Structure-Specific Endonuclease Subunit (SLX4), SMAD Family Member 4 (SMAD4), Dual specificity protein kinase TTK (TTK), Ras association domain family 1 isoform A (RASSF1A), Runt-related transcription factor 3 (RUNX3), Tissue factor pathway inhibitor 2 (TFPI2), Secreted frizzled-related protein 5 (SFRP5), Opioid-binding protein/cell adhesion molecule (OPCML), O⁶-alkylguanine DNA alkyltransferase (MGMT), Cadherin 13 (CDH13), sulfatase 1 (SULF1), Homeobox A9 (HOXA9), Homeobox A11 (HOXA11), Claudin 4 (CLDN4), T-cell differentiation protein (MAL), Brother of Regulator of Imprinted Sites (BORIS), ATP-binding cassette super-family G member 2 (ABCG2), Tubulin Beta 3 Class III (TUBB3), Methylation controlled DNAJ (MCJ), synucelin-γ (SNGG), alternative reading frame tumor suppressor (P14ARF), cyclin-dependent kinase inhibitor 2A (CDKN2A or P16INK4A), Cyclin-dependent kinase 4 inhibitor B (CDKN2B or P15), Death-associated protein kinase 1 (DAPK), Calcium channel voltage-dependent T type alpha 1G subunit (CACNA1G or MINT31), Retinoblastoma-interacting zinc-finger protein 1 (RIZ1), and target of methylation-induced silencing 1 (TMS1);

2. ~~_____ A panel for pre-operatively assessing a subject's risk of having ovarian cancer, the panel comprising or consisting of markers~~ ii) _____ Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β2-Microglobulin (β2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), and one or more markers selected from the group consisting of Breast Cancer 1 (BRCA1), Breast Cancer 2 (BRCA2), Ataxia-Telangiectasia mutated (ATM), BRCA1 Associated Ring Domain 1 (BARD1), BRCA1 Interacting Protein C-terminal Helicase 1 (BRIP1), Cadherin-1 (CDH1), Checkpoint Kinase 2 (CHEK2), Epithelial cell adhesion molecule (EPCAM), MutL homolog 1 (MLH1), MutS Homolog 2 (MSH2), MutS Homolog 6 (MSH6), Nibrin (NBN), partner and localizer of BRCA2 (PALB2), Phosphatase and tensin homolog (PTEN), RAD51 paralog D (RAD51D), Serine/Threonine Kinase 11 (STK11), Tumor protein p53 (TP53), Kirsten rat sarcoma viral oncogene homolog (KRAS), BRCA1 A complex subunit abraxas 1 (ABRAXAS1 or FAM175A), RAC-alpha serine/threonine-protein kinase (AKT1 or Protein Kinase B), Adenomatous polyposis coli (APC), axis inhibition protein 2 (AXIN2), Bone Morphogenetic Protein Receptor Type 1A (BMPRI1A), proto-oncogene B-Raf (BRAF), Cell Division Cycle 25C (CDC25), Cyclin Dependent Kinase Inhibitor 2A (CDKN2A), Cyclin-dependent kinase 4 (CDK4), Catenin beta-1 (CTNNB1), helicase with RNase motif (DICER1), Erb-B2 Receptor Tyrosine Kinase 2 (ERBB2), Excision Repair Cross-Complementation Group 6 (ERCC6), Fanconi anemia complementation group M (FANCM), Fanconi anemia complementation group C (FANCC), Meiotic Recombination 11 (MRE11), mutY DNA glycosylase (MUTYH),

Neurofibromin 1 (NF1), Endonuclease III-like protein 1 (NTHL1), Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha (PIK3CA), Postmeiotic segregation Increased 2 (PMS2), Protein phosphatase 2 regulatory subunit A alpha (PP2R1A), Protein Kinase DNA-Activated Catalytic Subunit (PRKDC), DNA Polymerase Delta 1 Catalytic Subunit (POLD1), RAD50 homolog (RAD50), RAD51 Paralog C (RAD51C), Ring Finger Protein 43 (RNF43), Succinate Dehydrogenase Complex Iron Sulfur Subunit B (SDHB), Succinate Dehydrogenase Complex Subunit D (SDHD), SWI/SNF Related Matrix Associated Actin Dependent Regulator Of Chromatin Subfamily A Member 4 (SMARCA4), X-ray repair complementing defective repair in Chinese hamster cells 2 (XRCC2), Werner syndrome ATP-dependent helicase (WRN or RECQL), Cell Division Cycle 73 (CDC73), Polypeptide N-Acetylgalactosaminyltransferase 12 (GALNT12), Gremlin 1 (GREM1), Homeobox B13 (HOXB13), MutS Homolog 3 (MSH3), DNA Polymerase Epsilon Catalytic Subunit (POLE), RAD51 Recombinase (RAD51), RAD50 Interactor 1 (RINT1), 40S ribosomal protein S20 (RSP20), SLX4 Structure-Specific Endonuclease Subunit (SLX4), SMAD Family Member 4 (SMAD4), Dual specificity protein kinase TTK (TTK), Ras association domain family 1 isoform A (RASSF1A), Runt-related transcription factor 3 (RUNX3), Tissue factor pathway inhibitor 2 (TFPI2), Secreted frizzled-related protein 5 (SFRP5), Opioid-binding protein/cell adhesion molecule (OPCML), O⁶-alkylguanine DNA alkyltransferase (MGMT), Cadherin 13 (CDH13), sulfatase 1 (SULF1), Homeobox A9 (HOXA9), Homeobox A11 (HOXAD11), Claudin 4 (CLDN4), T-cell differentiation protein (MAL), Brother of Regulator of Imprinted Sites (BORIS), ATP-binding cassette super-family G member 2 (ABCG2), Tubulin Beta 3 Class III (TUBB3), Methylation controlled DNAJ (MCJ), synucelin-γ (SNGG), alternative reading frame tumor suppressor (P14ARF), cyclin-dependent kinase inhibitor 2A (CDKN2A or P16INK4A), Cyclin-dependent kinase 4 inhibitor B (CDKN2B or P15), Death-associated protein kinase 1 (DAPK), Calcium channel voltage-dependent T type alpha 1G subunit (CACNA1G or MINT31), Retinoblastoma-interacting zinc-finger protein 1 (RIZ1), and target of methylation-induced silencing 1 (TMS1);

or

3. ~~A panel for pre-operatively assessing a subject's risk of having ovarian cancer, the panel comprising or consisting of markers~~ iii) Apolipoprotein A1 (ApoA1), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), follicle stimulating hormone (FSH), and one or more markers selected from the group consisting of Breast Cancer 1 (BRCA1), Breast Cancer 2 (BRCA2), Ataxia-Telangiectasia mutated (ATM), BRCA1 Associated Ring Domain 1 (BARD1), BRCA1 Interacting Protein C-terminal Helicase 1 (BRIP1), Cadherin-1 (CDH1), Checkpoint Kinase 2 (CHEK2), Epithelial cell adhesion molecule

(EPCAM), MutL homolog 1 (MLH1), MutS Homolog 2 (MSH2), MutS Homolog 6 (MSH6), Nibrin (NBN), partner and localizer of BRCA2 (PALB2), Phosphatase and tensin homolog (PTEN), RAD51 paralog D (RAD51D), Serine/Threonine Kinase 11 (STK11), Tumor protein p53 (TP53), Kirsten rat sarcoma viral oncogene homolog (KRAS), BRCA1 A complex subunit abraxas 1 (ABRAXAS1 or FAM175A), RAC-alpha serine/threonine-protein kinase (AKT1 or Protein Kinase B), Adenomatous polyposis coli (APC), axis inhibition protein 2 (AXIN2), Bone Morphogenetic Protein Receptor Type 1A (BMPRI1A), proto-oncogene B-Raf (BRAF), Cell Division Cycle 25C (CDC25), Cyclin Dependent Kinase Inhibitor 2A (CDKN2A), Cyclin-dependent kinase 4 (CDK4), Catenin beta-1 (CTNNB1), helicase with RNase motif (DICER1), Erb-B2 Receptor Tyrosine Kinase 2 (ERBB2), Excision Repair Cross-Complementation Group 6 (ERCC6), Fanconi anemia complementation group M (FANCM), Fanconi anemia complementation group C (FANCC), Meiotic Recombination 11 (MRE11), mutY DNA glycosylase (MUTYH), Neurofibromin 1 (NF1), Endonuclease III-like protein 1 (NTHL1), Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha (PIK3CA), Postmeiotic segregation Increased 2 (PMS2), Protein phosphatase 2 regulatory subunit A alpha (PP2R1A), Protein Kinase DNA-Activated Catalytic Subunit (PRKDC), DNA Polymerase Delta 1 Catalytic Subunit (POLD1), RAD50 homolog (RAD50), RAD51 Paralog C (RAD51C), Ring Finger Protein 43 (RNF43), Succinate Dehydrogenase Complex Iron Sulfur Subunit B (SDHB), Succinate Dehydrogenase Complex Subunit D (SDHD), SWI/SNF Related Matrix Associated Actin Dependent Regulator Of Chromatin Subfamily A Member 4 (SMARCA4), X-ray repair complementing defective repair in Chinese hamster cells 2 (XRCC2), Werner syndrome ATP-dependent helicase (WRN or RECQL), Cell Division Cycle 73 (CDC73), Polypeptide N-Acetylgalactosaminyltransferase 12 (GALNT12), Gremlin 1 (GREM1), Homeobox B13 (HOXB13), MutS Homolog 3 (MSH3), DNA Polymerase Epsilon Catalytic Subunit (POLE), RAD51 Recombinase (RAD51), RAD50 Interactor 1 (RINT1), 40S ribosomal protein S20 (RSP20), SLX4 Structure-Specific Endonuclease Subunit (SLX4), SMAD Family Member 4 (SMAD4), Dual specificity protein kinase TTK (TTK), Ras association domain family 1 isoform A (RASSF1A), Runt-related transcription factor 3 (RUNX3), Tissue factor pathway inhibitor 2 (TFPI2), Secreted frizzled-related protein 5 (SFRP5), Opioid-binding protein/cell adhesion molecule (OPCML), O⁶-alkylguanine DNA alkyltransferase (MGMT), Cadherin 13 (CDH13), sulfatase 1 (SULF1), Homeobox A9 (HOXA9), Homeobox A11 (HOXA11), Claudin 4 (CLDN4), T-cell differentiation protein (MAL), Brother of Regulator of Imprinted Sites (BORIS), ATP-binding cassette super-family G member 2 (ABCG2), Tubulin Beta 3 Class III (TUBB3), Methylation controlled DNAJ (MCJ), synucelin-γ (SNGG), alternative reading frame tumor suppressor (P14ARF), cyclin-dependent kinase inhibitor 2A (CDKN2A or P16INK4A),

Cyclin-dependent kinase 4 inhibitor B (CDKN2B or P15), Death-associated protein kinase 1 (DAPK), Calcium channel voltage-dependent T type alpha 1G subunit (CACNA1G or MINT31), Retinoblastoma-interacting zinc-finger protein 1 (RIZ1), and target of methylation-induced silencing 1 (TMS1).

42. A panel for pre-operatively assessing a subject's risk of having ovarian cancer, the panel comprising or consisting of markers:

i) _____ Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β 2-Microglobulin (β 2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), and Breast Cancer 1 (BRCA1);

5. ~~A panel for pre-operatively assessing a subject's risk of having ovarian cancer, the panel comprising or consisting of markers~~ ii) _____ Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β 2-Microglobulin (β 2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), and Breast Cancer 2 (BRCA2);

6. ~~A panel for pre-operatively assessing a subject's risk of having ovarian cancer, the panel comprising or consisting of markers~~ iii) _____ Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β 2-Microglobulin (β 2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), Breast Cancer 1 (BRCA1) and Breast Cancer 2 (BRCA2);

7. ~~A panel for pre-operatively assessing a subject's risk of having ovarian cancer, the panel comprising or consisting of markers~~ iv) _____ Apolipoprotein A1 (ApoA1), Transferrin (Tfr), Cancer Antigen 125 (CA125), HE4, follicle stimulating hormone (FSH), and Breast Cancer 1 (BRCA1);

8. ~~A panel for pre-operatively assessing a subject's risk of having ovarian cancer, the panel comprising or consisting of markers~~ v) _____ Apolipoprotein A1 (ApoA1), Transferrin (Tfr), Cancer Antigen 125 (CA125), HE4, follicle stimulating hormone (FSH), and Breast Cancer 2 (BRCA2);

9. ~~A panel for pre-operatively assessing a subject's risk of having ovarian cancer, the panel comprising or consisting of markers~~ vi) _____ Apolipoprotein A1 (ApoA1), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), follicle stimulating hormone (FSH), Breast Cancer 1 (BRCA1) and Breast Cancer 2 (BRCA2);

~~10. — A panel for pre-operatively assessing a subject's risk of having ovarian cancer, the panel comprising or consisting of markers vii)~~ Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β 2-Microglobulin (β 2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), follicle stimulating hormone (FSH), and Breast Cancer 1 (BRCA1);₂

~~11. — A panel for pre-operatively assessing a subject's risk of having ovarian cancer, the panel comprising or consisting of markers viii)~~ Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β 2-Microglobulin (β 2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), follicle stimulating hormone (FSH), and Breast Cancer 2 (BRCA2);₂
or

~~12. — A panel for pre-operatively assessing a subject's risk of having ovarian cancer, the panel comprising or consisting of markers ix)~~ Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β 2-Microglobulin (β 2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), follicle stimulating hormone (FSH), Breast Cancer 1 (BRCA1), and Breast Cancer 2 (BRCA2);₂

~~13. — The panel of any one of claims 4-12, and preferably~~ further comprising ~~of~~ one or more markers selected from the group consisting of Ataxia-Telangiesctasia mutated (ATM), BRCA1 Associated Ring Domain 1 (BARD1), BRCA1 Interacting Protein C-terminal Helicase 1 (BRIP1), Cadherin-1 (CDH1), Checkpoint Kinase 2 (CHEK2), Epithelial cell adhesion molecule (EPCAM), MutL homolog 1 (MLH1), MutS Homolog 2 (MSH2), MutS Homolog 6 (MSH6), Nibrin (NBN), partner and localizer of BRCA2 (PALB2), Phosphatase and tensin homolog (PTEN), RAD51 paralog D (RAD51D), Serine/Threonine Kinase 11 (STK11), Tumor protein p53 (TP53), Kirsten rat sarcoma viral oncogene homolog (KRAS), BRCA1 A complex subunit abraxas 1 (ABRAXAS1 or FAM175A), RAC-alpha serine/threonine-protein kinase (AKT1 or Protein Kinase B), Adenomatous polyposis coli (APC), axis inhibition protein 2 (AXIN2), Bone Morphogenetic Protein Receptor Type 1A (BMPRI1A), proto-oncogene B-Raf (BRAF), Cell Division Cycle 25C (CDC25), Cyclin Dependent Kinase Inhibitor 2A (CDKN2A), Cyclin-dependent kinase 4 (CDK4), Catenin beta-1 (CTNNB1), helicase with RNase motif (DICER1), Erb-B2 Receptor Tyrosine Kinase 2 (ERBB2), Excision Repair Cross-Complementation Group 6 (ERCC6), Fanconi anemia complementation group M (FANCM), Fanconi anemia complementation group C (FANCC), Meiotic Recombination 11 (MRE11), mutY DNA glycosylase (MUTYH), Neurofibromin 1 (NF1), Endonuclease III-like protein 1 (NTHL1), Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha (PIK3CA), Postmeiotic

segregation Increased 2 (PMS2), Protein phosphatase 2 regulatory subunit A alpha (PP2R1A), Protein Kinase DNA-Activated Catalytic Subunit (PRKDC), DNA Polymerase Delta 1 Catalytic Subunit (POLD1), RAD50 homolog (RAD50), RAD51 Paralog C (RAD51C), Ring Finger Protein 43 (RNF43), Succinate Dehydrogenase Complex Iron Sulfur Subunit B (SDHB), Succinate Dehydrogenase Complex Subunit D (SDHD), SWI/SNF Related Matrix Associated Actin Dependent Regulator Of Chromatin Subfamily A Member 4 (SMARCA4), X-ray repair complementing defective repair in Chinese hamster cells 2 (XRCC2), Werner syndrome ATP-dependent helicase (WRN or RECQL), Cell Division Cycle 73 (CDC73), Polypeptide N-Acetylgalactosaminyltransferase 12 (GALNT12), Gremlin 1 (GREM1), Homeobox B13 (HOXB13), MutS Homolog 3 (MSH3), DNA Polymerase Epsilon Catalytic Subunit (POLE), RAD51 Recombinase (RAD51), RAD50 Interactor 1 (RINT1), 40S ribosomal protein S20 (RSP20), SLX4 Structure-Specific Endonuclease Subunit (SLX4), SMAD Family Member 4 (SMAD4), Dual specificity protein kinase TTK (TTK), Ras association domain family 1 isoform A (RASSF1A), Runt-related transcription factor 3 (RUNX3), Tissue factor pathway inhibitor 2 (TFPI2), Secreted frizzled-related protein 5 (SFRP5), Opioid-binding protein/cell adhesion molecule (OPCML), O⁶-alkylguanine DNA alkyltransferase (MGMT), Cadherin 13 (CDH13), sulfatase 1 (SULF1), Homeobox A9 (HOXA9), Homeobox A11 (HOXA11), Claudin 4 (CLDN4), T-cell differentiation protein (MAL), Brother of Regulator of Imprinted Sites (BORIS), ATP-binding cassette super-family G member 2 (ABCG2), Tubulin Beta 3 Class III (TUBB3), Methylation controlled DNAJ (MCJ), synucelin-γ (SNGG), alternative reading frame tumor suppressor (P14ARF), cyclin-dependent kinase inhibitor 2A (CDKN2A or P16INK4A), Cyclin-dependent kinase 4 inhibitor B (CDKN2B or P15), Death-associated protein kinase 1 (DAPK), Calcium channel voltage-dependent T type alpha 1G subunit (CACNA1G or MINT31), Retinoblastoma-interacting zinc-finger protein 1 (RIZ1), and target of methylation-induced silencing 1 (TMS1).

143. The panel of ~~any one of claim 1-13~~claim 1 or 2, wherein each of the markers are bound to a separate capture reagent.

154. The panel of ~~claim 14~~3, wherein the capture reagents are attached to a solid support.

16. ~~The panel of claim 15~~, preferably wherein the solid support is a plate, chip, beads, microfluidic platform, membrane, planar microarray, or suspension array

~~175.~~ The panel of ~~any one of claims 14-16~~claim 3 or 4, wherein the capture reagent is an antibody, aptamer, Affibody, hybridization probe and/or fragments thereof.

~~186.~~ The panel of any one of claims ~~14-17~~3, 4 or 5, wherein each capture reagent specifically binds to one of the markers.

~~197.~~ The panel of any one of claims ~~1-18~~1, 2, 3, 4, 5 or 6 for use in a method for pre-operatively assessing a subject's risk of having ovarian cancer.

~~208.~~ A method for pre-operatively assessing a subject's risk of having ovarian cancer, the method comprising characterizing markers in a biological sample from the subject using the panel of any one of claims 1, 2, 3, 4, 5, or 6~~1-18~~.

~~219.~~ A method for pre-operatively assessing a subject as having a high or a low risk of ovarian cancer, the method comprising,

(a) characterizing markers comprising or consisting of Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β 2-Microglobulin (β 2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), and follicle stimulating hormone (FSH) in a biological sample derived from the subject to determine a first score, wherein the first score identifies the subject as having a high, intermediate or low cancer risk; and

(b) characterizing markers comprising or consisting of CA125, β 2M, Tfr, TT and ApoA1; or FSH, CA125, HE4, Tfr, and ApoA1, in the biological sample derived from the subject identified by the first score as having an intermediate cancer risk to determine a second score, wherein the second score identifies the subject as having a low or high cancer risk.

~~22. — A method for pre-operatively assessing a subject as having a high or low risk of ovarian cancer, the method comprising,~~

~~(a) characterizing markers comprising or consisting of Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β 2-Microglobulin (β 2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), and follicle stimulating hormone (FSH) in a biological sample derived from the subject to determine a first score, wherein the first score identifies the subject as having a high, intermediate or low cancer risk; and~~

~~(b) characterizing markers comprising or consisting of FSH, CA125, HE4, Tfr, and ApoA1 in the biological sample derived from the subject identified by the first score as having~~

an intermediate cancer risk to determine a second score, wherein the second score identifies the subject as having a low or high cancer risk.

2310. A method for pre-operatively assessing a subject as having a high or low risk of ovarian cancer, the method comprising,

(a) characterizing markers comprising or consisting of Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β 2-Microglobulin (β 2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), and follicle stimulating hormone (FSH) in a biological sample derived from the subject to determine first score, wherein the first score identifies the subject as having a high, intermediate or low cancer risk;

(b) characterizing markers comprising or consisting of CA125, β 2M, Tfr, TT and ApoA1 in the biological sample derived from the subject identified by the first score as having an intermediate cancer risk to determine a second score, which identifies the subject as low, intermediate, or high risk; and

(c) characterizing markers comprising or consisting of FSH, CA125, HE4, Tfr, and ApoA1 in the biological sample derived from the subject identified by the second score as having an intermediate or high cancer risk to determine a third score, wherein the third score identifies the subject as having a low or high cancer risk.

2411. A method for pre-operatively assessing an asymptomatic subject, the method comprising,

(a) characterizing markers comprising or consisting of Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β 2-Microglobulin (β 2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), and follicle stimulating hormone (FSH) in a biological sample derived from the subject to determine first score, wherein the first score identifies the subject as having a high, intermediate or low cancer risk; and

(b) characterizing one or more markers selected from the group consisting of Breast Cancer 1 (BRCA1), Breast Cancer 2 (BRCA2), Ataxia-Telangiectasia mutated (ATM), BRCA1 Associated Ring Domain 1 (BARD1), BRCA1 Interacting Protein C-terminal Helicase 1 (BRIP1), Cadherin-1 (CDH1), Checkpoint Kinase 2 (CHEK2), Epithelial cell adhesion molecule (EPCAM), MutL homolog 1 (MLH1), MutS Homolog 2 (MSH2), MutS Homolog 6 (MSH6), Nibrin (NBN), partner and localizer of BRCA2 (PALB2), Phosphatase and tensin homolog (PTEN), RAD51 paralog D (RAD51D), Serine/Threonine Kinase 11 (STK11), Tumor protein p53 (TP53), Kirsten rat sarcoma viral oncogene homolog (KRAS), BRCA1 A complex subunit abraxas 1 (ABRAXAS1 or FAM175A), RAC-alpha serine/threonine-protein kinase (AKT1 or Protein Kinase B), Adenomatous polyposis coli (APC), axis inhibition protein 2 (AXIN2), Bone

Morphogenetic Protein Receptor Type 1A (BMPRI1A), proto-oncogene B-Raf (BRAF), Cell Division Cycle 25C (CDC25), Cyclin Dependent Kinase Inhibitor 2A (CDKN2A), Cyclin-dependent kinase 4 (CDK4), Catenin beta-1 (CTNNB1), helicase with RNase motif (DICER1), Erb-B2 Receptor Tyrosine Kinase 2 (ERBB2), Excision Repair Cross-Complementation Group 6 (ERCC6), Fanconi anemia complementation group M (FANCM), Fanconi anemia complementation group C (FANCC), Meiotic Recombination 11 (MRE11), mutY DNA glycosylase (MUTYH), Neurofibromin 1 (NF1), Endonuclease III-like protein 1 (NTHL1), Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha (PIK3CA), Postmeiotic segregation Increased 2 (PMS2), Protein phosphatase 2 regulatory subunit A alpha (PP2R1A), Protein Kinase DNA-Activated Catalytic Subunit (PRKDC), DNA Polymerase Delta 1 Catalytic Subunit (POLD1), RAD50 homolog (RAD50), RAD51 Paralog C (RAD51C), Ring Finger Protein 43 (RNF43), Succinate Dehydrogenase Complex Iron Sulfur Subunit B (SDHB), Succinate Dehydrogenase Complex Subunit D (SDHD), SWI/SNF Related Matrix Associated Actin Dependent Regulator Of Chromatin Subfamily A Member 4 (SMARCA4), X-ray repair complementing defective repair in Chinese hamster cells 2 (XRCC2), Werner syndrome ATP-dependent helicase (WRN or RECQL), Cell Division Cycle 73 (CDC73), Polypeptide N-Acetylgalactosaminyltransferase 12 (GALNT12), Gremlin 1 (GREM1), Homeobox B13 (HOXB13), MutS Homolog 3 (MSH3), DNA Polymerase Epsilon Catalytic Subunit (POLE), RAD51 Recombinase (RAD51), RAD50 Interactor 1 (RINT1), 40S ribosomal protein S20 (RSP20), SLX4 Structure-Specific Endonuclease Subunit (SLX4), SMAD Family Member 4 (SMAD4), Dual specificity protein kinase TTK (TTK), Ras association domain family 1 isoform A (RASSF1A), Runt-related transcription factor 3 (RUNX3), Tissue factor pathway inhibitor 2 (TFPI2), Secreted frizzled-related protein 5 (SFRP5), Opioid-binding protein/cell adhesion molecule (OPCML), O⁶-alkylguanine DNA alkyltransferase (MGMT), Cadherin 13 (CDH13), sulfatase 1 (SULF1), Homeobox A9 (HOXA9), Homeobox A11 (HOXA11), Claudin 4 (CLDN4), T-cell differentiation protein (MAL), Brother of Regulator of Imprinted Sites (BORIS), ATP-binding cassette super-family G member 2 (ABCG2), Tubulin Beta 3 Class III (TUBB3), Methylation controlled DNAJ (MCJ), synucelin-γ (SNGG), alternative reading frame tumor suppressor (P14ARF), cyclin-dependent kinase inhibitor 2A (CDKN2A or P16INK4A), Cyclin-dependent kinase 4 inhibitor B (CDKN2B or P15), Death-associated protein kinase 1 (DAPK), Calcium channel voltage-dependent T type alpha 1G subunit (CACNA1G or MINT31), Retinoblastoma-interacting zinc-finger protein 1 (RIZ1), and target of methylation-induced silencing 1 (TMS1) in the biological sample derived from the subject identified by the first score as having a high, intermediate or low cancer risk, wherein the presence of one or more mutations in one or more markers or the presence of an aberrant methylation in one or more markers

identifies the subject as having a higher [increased] cancer risk relative to a subject that does not have a mutation or an aberrant methylation in the one or more markers.

25. —The method of any one of claims 19-23, further comprising characterizing one or more markers selected from the group consisting of Breast Cancer 1 (BRCA1), Breast Cancer 2 (BRCA2), Ataxia-Telangiectasia mutated (ATM), BRCA1 Associated Ring Domain 1 (BARD1), BRCA1 Interacting Protein C terminal Helicase 1 (BRIP1), Cadherin 1 (CDH1), Checkpoint Kinase 2 (CHEK2), Epithelial cell adhesion molecule (EPCAM), MutL homolog 1 (MLH1), MutS Homolog 2 (MSH2), MutS Homolog 6 (MSH6), Nibrin (NBN), partner and localizer of BRCA2 (PALB2), Phosphatase and tensin homolog (PTEN), RAD51 paralog D (RAD51D), Serine/Threonine Kinase 11 (STK11), Tumor protein p53 (TP53), Kirsten rat sarcoma viral oncogene homolog (KRAS), BRCA1 A complex subunit abraxas 1 (ABRAXAS1 or FAM175A), RAC-alpha serine/threonine-protein kinase (AKT1 or Protein Kinase B), Adenomatous polyposis coli (APC), axis inhibition protein 2 (AXIN2), Bone Morphogenetic Protein Receptor Type 1A (BMPRI1A), proto-oncogene B-Raf (BRAF), Cell Division Cycle 25C (CDC25), Cyclin Dependent Kinase Inhibitor 2A (CDKN2A), Cyclin-dependent kinase 4 (CDK4), Catenin beta 1 (CTNNB1), helicase with RNase motif (DICER1), Erb-B2 Receptor Tyrosine Kinase 2 (ERBB2), Excision Repair Cross-Complementation Group 6 (ERCC6), Fanconi anemia complementation group M (FANCM), Fanconi anemia complementation group C (FANCC), Meiotic Recombination 11 (MRE11), mutY DNA-glycosylase (MUTYH), Neurofibromin 1 (NF1), Endonuclease III-like protein 1 (NTHL1), Phosphatidylinositol 4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha (PIK3CA), Postmeiotic segregation Increased 2 (PMS2), Protein phosphatase 2 regulatory subunit A alpha (PP2R1A), Protein Kinase DNA-Activated Catalytic Subunit (PRKDC), DNA Polymerase Delta 1 Catalytic Subunit (POLD1), RAD50 homolog (RAD50), RAD51 Paralog C (RAD51C), Ring Finger Protein 43 (RNF43), Succinate Dehydrogenase Complex Iron Sulfur Subunit B (SDHB), Succinate Dehydrogenase Complex Subunit D (SDHD), SWI/SNF Related Matrix Associated Actin Dependent Regulator Of Chromatin Subfamily A Member 4 (SMARCA4), X-ray repair complementing defective repair in Chinese hamster cells 2 (XRCC2), Werner syndrome ATP-dependent helicase (WRN or RECQL), Cell Division Cycle 73 (CDC73), Polypeptide N-Acetylgalactosaminyltransferase 12 (GALNT12), Gremlin 1 (GREM1), Homeobox B13 (HOXB13), MutS Homolog 3 (MSH3), DNA Polymerase Epsilon Catalytic Subunit (POLE), RAD51 Recombinase (RAD51), RAD50 Interactor 1 (RINT1), 40S ribosomal protein S20 (RSP20), SLX4 Structure-Specific Endonuclease Subunit (SLX4), SMAD Family Member 4 (SMAD4), and Dual specificity protein kinase TTK (TTK), Ras-association domain family 1 isoform A (RASSF1A), Runt-

~~related transcription factor 3 (RUNX3), Tissue factor pathway inhibitor 2 (TFPI2), Secreted frizzled-related protein 5 (SFRP5), Opioid-binding protein/cell adhesion molecule (OPCML), O⁶-alkylguanine DNA alkyltransferase (MGMT), Cadherin 13 (CDH13), sulfatase 1 (SULF1), Homeobox A9 (HOXA9), Homeobox A11 (HOXA11), Claudin 4 (CLDN4), T-cell differentiation protein (MAL), Brother of Regulator of Imprinted Sites (BORIS), ATP-binding cassette super-family G member 2 (ABCG2), Tubulin Beta 3 Class III (TUBB3), Methylation controlled DNAJ (MCJ), synucelin-γ (SNGG), alternative reading frame tumor suppressor (P14ARF), cyclin-dependent kinase inhibitor 2A (CDKN2A or P16INK4A), Cyclin-dependent kinase 4 inhibitor B (CDKN2B or P15), Death-associated protein kinase 1 (DAPK), Calcium channel voltage-dependent T type alpha 1G subunit (CACNA1G or MINT31), Retinoblastoma-interacting zinc-finger protein 1 (RIZ1), and target of methylation-induced silencing 1 (TMS1) in the biological sample derived from the subject identified by the first score as having a high, intermediate or low cancer risk, wherein the presence of one or more mutations in one or more markers or the presence of an aberrant methylation in one or more markers identifies the subject as having a higher [increased] cancer risk relative to a subject that does not have one or more mutations or an aberrant methylation in the one or more markers~~

2612. A method for pre-operatively monitoring a subject with one or more mutations or an aberrant methylation in one or more germline and/or somatic markers, the method comprising:

- (a) characterizing markers comprising or consisting of Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β2-Microglobulin (β2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), and follicle stimulating hormone (FSH) in a first biological sample derived from the subject to determine a first score at a first time point, wherein the first score identifies the subject as having a high, intermediate or low ovarian cancer risk; and
- (b) repeating step (a) in one or more biological samples from the subject identified as having an intermediate or low ovarian cancer risk at one or more time points, thereby monitoring the subject.

~~27. — A method for pre-operatively monitoring a subject with one or more mutations or an aberrant methylation in one or more germline and/or somatic markers, the method comprising:~~

- ~~(a) characterizing markers comprising or consisting of Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β2-Microglobulin (β2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), and follicle stimulating hormone (FSH) in a first biological sample derived from the subject to determine a first score at a first time point, wherein the first score identifies the subject as having a high, intermediate or low ovarian cancer risk;~~

~~(b) characterizing markers comprising or consisting of CA125, β 2M, Tfr, TT and ApoA1 in the biological sample derived from the subject identified by the first score as having a low or intermediate cancer risk to determine a second score at the first time point, wherein the second score identifies the subject as having a low or high cancer risk; and~~

~~(c) repeating steps (a) and (b) in one or more biological samples from the subject identified as having low ovarian cancer risk in step (b) at one or more time points, thereby monitoring the subject.~~

28. — A method for pre-operatively monitoring a subject with one or more mutations or an aberrant methylation in one or more germline and/or somatic markers, the method comprising:

~~(a) characterizing markers comprising or consisting of Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β 2-Microglobulin (β 2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), and follicle stimulating hormone (FSH) in a first biological sample derived from the subject to determine a first score at a first time point, wherein the first score identifies the subject as having a high, intermediate or low ovarian cancer risk;~~

~~(b) characterizing markers comprising or consisting of FSH, CA125, HE4, Tfr, and ApoA1 in the biological sample derived from the subject identified by the first score as having a low or intermediate cancer risk to determine a second score at the first time point, wherein the second score identifies the subject as having a low or high cancer risk; and~~

~~(c) repeating steps (a) and (b) in one or more biological samples from the subject identified as having low ovarian cancer risk in step (b) at one or more time points, thereby monitoring the subject.~~

29. — A method for pre-operatively monitoring a subject with one or more mutations or an aberrant methylation in one or more germline and/or somatic markers identified as having a low or intermediate ovarian cancer risk, the method comprising:

~~(a) characterizing markers comprising or consisting of Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β 2-Microglobulin (β 2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), and follicle stimulating hormone (FSH) in a first biological sample derived from the subject to determine a first score at a first time point, wherein the first score identifies the subject as having a high, intermediate or low ovarian cancer risk;~~

~~(b) characterizing markers comprising or consisting of CA125, β 2M, Tfr, TT and ApoA1 in the biological sample derived from the subject identified by the first score as having a low, intermediate cancer risk to determine a second score at the first time point, wherein the second score identifies the subject as having a low, intermediate or high cancer risk;~~

~~(c) characterizing markers comprising or consisting of FSH, CA125, HE4, Tfr, and ApoA1 in the biological sample derived from the subject identified by the second score as having an intermediate or high cancer risk to determine a third score at the first time point, wherein the third score identifies the subject as having a low or high cancer risk; and~~

~~(d) repeating steps (a)–(c) in one or more biological samples from the subject identified as having a low or intermediate risk in step (b) or a low ovarian cancer risk in step (c) at one or more time points, thereby monitoring the subject.~~

30. —~~The method of any one of claims 26–29, wherein the one or more germline and/or somatic markers are selected from the group consisting of Breast Cancer 1 (BRCA1), Breast Cancer 2 (BRCA2), Ataxia-Telangiesctasia mutated (ATM), BRCA1 Associated Ring Domain 1 (BARD1), BRCA1 Interacting Protein C terminal Helicase 1 (BRIP1), Cadherin 1 (CDH1), Checkpoint Kinase 2 (CHEK2), Epithelial cell adhesion molecule (EPCAM), MutL homolog 1 (MLH1), MutS Homolog 2 (MSH2), MutS Homolog 6 (MSH6), Nibrin (NBN), partner and localizer of BRCA2 (PALB2), Phosphatase and tensin homolog (PTEN), RAD51 paralog D (RAD51D), Serine/Threonine Kinase 11 (STK11), Tumor protein p53 (TP53), Kirsten rat sarcoma viral oncogene homolog (KRAS), BRCA1 A complex subunit abraxas 1 (ABRAXAS1 or FAM175A), RAC-alpha serine/threonine-protein kinase (AKT1 or Protein Kinase B), Adenomatous polyposis coli (APC), axis inhibition protein 2 (AXIN2), Bone Morphogenetic Protein Receptor Type 1A (BMPRI1A), proto-oncogene B-Raf (BRAF), Cell Division Cycle 25C (CDC25), Cyclin Dependent Kinase Inhibitor 2A (CDKN2A), Cyclin-dependent kinase 4 (CDK4), Catenin beta 1 (CTNNB1), helicase with RNase motif (DICER1), Erb-B2 Receptor Tyrosine Kinase 2 (ERBB2), Excision Repair Cross-Complementation Group 6 (ERCC6), Fanconi anemia complementation group M (FANCM), Fanconi anemia complementation group C (FANCC), Meiotic Recombination 11 (MRE11), mutY DNA glycosylase (MUTYH), Neurofibromin 1 (NF1), Endonuclease III-like protein 1 (NTHL1), Phosphatidylinositol 4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha (PIK3CA), Postmeiotic segregation Increased 2 (PMS2), Protein phosphatase 2 regulatory subunit A alpha (PP2R1A), Protein Kinase DNA-Activated Catalytic Subunit (PRKDC), DNA Polymerase Delta 1 Catalytic Subunit (POLD1), RAD50 homolog (RAD50), RAD51 Paralog C (RAD51C), Ring Finger Protein 43 (RNF43), Succinate Dehydrogenase Complex Iron Sulfur Subunit B (SDHB), Succinate Dehydrogenase Complex Subunit D (SDHD), SWI/SNF Related Matrix Associated Actin Dependent Regulator Of Chromatin Subfamily A Member 4 (SMARCA4), X-ray repair complementing defective repair in Chinese hamster cells 2 (XRCC2), Werner syndrome ATP-dependent helicase (WRN or RECQL), Cell Division Cycle 73 (CDC73), Polypeptide N-Acetylgalactosaminyltransferase 12~~

(GALNT12), Gremlin 1 (GREM1), Homeobox B13 (HOXB13), MutS Homolog 3 (MSH3), DNA Polymerase Epsilon Catalytic Subunit (POLE), RAD51 Recombinase (RAD51), RAD50 Interactor 1 (RINT1), 40S ribosomal protein S20 (RSP20), SLX4 Structure Specific Endonuclease Subunit (SLX4), SMAD Family Member 4 (SMAD4), and Dual specificity protein kinase TTK (TTK), Ras association domain family 1 isoform A (RASSF1A), Runt-related transcription factor 3 (RUNX3), Tissue factor pathway inhibitor 2 (TFPI2), Secreted frizzled-related protein 5 (SFRP5), Opioid-binding protein/cell adhesion molecule (OPCML), O⁶-alkylguanine DNA alkyltransferase (MGMT), Cadherin 13 (CDH13), sulfatase 1 (SULF1), Homeobox A9 (HOXA9), Homeobox A11 (HOXA11), Claudin 4 (CLDN4), T-cell differentiation protein (MAL), Brother of Regulator of Imprinted Sites (BORIS), ATP-binding cassette super-family G member 2 (ABCG2), Tubulin Beta 3 Class III (TUBB3), Methylation controlled DNAJ (MCJ), synucelin-γ (SNGG), alternative reading frame tumor suppressor (P14ARF), cyclin-dependent kinase inhibitor 2A (CDKN2A or P16INK4A), Cyclin-dependent kinase 4 inhibitor B (CDKN2B or P15), Death-associated protein kinase 1 (DAPK), Calcium channel voltage-dependent T-type alpha 1G subunit (CACNA1G or MINT31), Retinoblastoma-interacting zinc-finger protein 1 (RIZ1), and target of methylation-induced silencing 1 (TMS1).

31. — A method for pre-operatively monitoring a subject with an adnexal mass, the method comprising,

(a) characterizing markers comprising or consisting of Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β2 Microglobulin (β2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), and follicle stimulating hormone (FSH) in a biological sample derived from the subject to determine a first score at a first time point, wherein the first score identifies the subject as having a high, intermediate or low ovarian cancer risk;

(b) characterizing markers comprising or consisting of CA125, β2M, Transferrin, Transthyretin and ApoA1 in the biological sample derived from the subject identified by the first score as having an intermediate cancer risk to determine a second score at the first time point, wherein the second score identifies the subject as having a low or high cancer risk; and

(c) repeating steps (a) and (b) in one or more biological samples from the subject identified as having low risk of ovarian cancer risk in step (b) at one or more time points, thereby monitoring the subject.

32. — A method for pre-operatively monitoring a subject with an adnexal mass, the method comprising,

~~(a) characterizing markers comprising or consisting of Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β 2-Microglobulin (β 2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), and follicle stimulating hormone (FSH) in a biological sample derived from the subject to determine a first score at a first time point, wherein the first score identifies the subject as having a high, intermediate or low ovarian cancer risk;~~

~~(b) characterizing markers comprising or consisting of FSH, CA125, HE4, Tfr, and ApoA1 in the biological sample derived from the subject identified by the first score as having an intermediate cancer risk to determine a second score at the first time point, wherein the second score identifies the subject as having a low or high ovarian cancer risk; and~~

~~(c) repeating steps (a) and (b) in one or more biological samples from the subject identified as having low risk of ovarian cancer risk in step (b) at one or more time points, thereby monitoring the subject.~~

33. — A method for monitoring a subject with an adnexal mass, the method comprising,

~~(a) characterizing markers comprising or consisting of Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β 2-Microglobulin (β 2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), Human epididymis protein 4 (HE4), and follicle stimulating hormone (FSH) in a first biological sample derived from the subject to determine a first score at a first time point, wherein the first score identifies the subject as having a high, intermediate or low risk of ovarian cancer;~~

~~(b) characterizing markers comprising or consisting of CA125, β 2M, Tfr, TT and ApoA1 in the biological sample derived from the subject identified by the first score as having a low or intermediate cancer risk to determine a second score at the first time point, wherein the second score identifies the subject as having a low, intermediate, or high ovarian cancer risk;~~

~~(c) characterizing markers comprising or consisting of FSH, CA125, HE4, Tfr, and ApoA1 in the biological sample derived from the subject identified by the first score as having an intermediate or high cancer risk to determine a third score at the first time point, wherein the third score identifies the subject as having a low or high cancer risk; and~~

~~(d) repeating steps (a)–(c) in one or more biological samples from the subject identified as having a low or intermediate risk in step (b) or a low risk of ovarian cancer risk in step (c) at one or more time points, thereby monitoring the subject.~~

3413. The method of ~~any one of claims 24–30~~claim 11 or 12, wherein the one or more germline markers are BRCA1 and/or BRCA2.

35. — The method of claim 34, preferably wherein the one or more mutations in BRCA1 comprises c. 68_69del and/or c.5266dup, and/or the one or more mutations in BRCA2 comprises c.5946del.

3614. The method of any one of claims ~~19-35~~7-9, 10, 11, 12, or 13, wherein the one or more markers are characterized by detecting cell-free tumor DNA (cftDNA).

~~37. — The method of any one of claims 21-36, wherein the first score ranges from 0 to 20, and wherein a first score less than or equal to 5 identifies the subject as having a low cancer risk, a first score greater than 5 and less than 10 in a pre-menopausal subject or a first score greater than 5 and less than 14 in a post-menopausal subject identifies the subject as having an intermediate cancer risk, and a first score greater than or equal to 10 in a pre-menopausal subject or a first score greater than or equal to 14 in a post-menopausal subject identifies the subject as having a high cancer risk.~~

~~38. — The method of any one of claims 21-22, 25, 27-28, 30-32, or 34-37, wherein the second score ranges from 0 to 20, and wherein a second score less than 5 identifies the subject as having a low cancer risk and a first score of 5 or greater identifies the subject as having a high cancer risk.~~

~~39. — The method of any one of claims 23, 29, 30 or 33-38, wherein the second score ranges from 0 to 20, and wherein a second score less than or equal to 5 in a pre-menopausal subject or a second score less than 4.4 in a post-menopausal subject identifies the subject as having a low cancer risk, a second score greater than 5 and less than 7 in a pre-menopausal subject or a second score greater than 4.4 and less than 6 in a post-menopausal subject identifies the subject as having an intermediate cancer risk, and a second score greater than or equal to 7 in a pre-menopausal subject or a second score greater than or equal to 6 in a post-menopausal subject identifies the subject as having a high cancer risk; and~~

~~wherein the third score ranges from 0 to 20, and wherein a third score less than or equal to 5 identifies the subject as having a low cancer risk and a third score greater than 5 identifies the subject as having a high cancer risk.~~

~~40. — The method of any of claims 19-39, wherein each of the markers are bound to a separate capture reagent.~~

~~41. The method of claim 40, wherein the capture reagents are attached to a solid support.~~

~~42. The method of claim 41, wherein the solid support is a plate, chip, beads, microfluidic platform, membrane, planar microarray, or suspension array~~

~~43. The method of any one of claims 40-42, wherein the capture reagent is an antibody, aptamer, Affibody, hybridization probe and/or fragments thereof.~~

~~44. The method of any one of claims 40-43, wherein each capture reagent specifically binds to one of the markers.~~

~~45~~15. The method of any of claims 7-9, 10, 11, 12, 13, or 14~~19-44~~, wherein the markers are characterized by immunoassay, sequencing and/or nucleic acid microarray.

~~46. The method of claim 45, wherein the sequencing is next-generation sequencing (NGS) or Sanger sequencing.~~

~~47. The method of claim 45, wherein the immunoassay comprises affinity capture assay, immunometric assay, heterogeneous chemiluminescence immunometric assay, homogeneous chemiluminescence immunometric assay, ELISA, western blotting, radioimmunoassay, magnetic immunoassay, real-time immunoquantitative PCR (iqPCR) and SERS label free assay.~~

~~48~~16. The method of any one of claims 7-9, 10, 11, 12, 13, 14, or 15~~19-47~~, wherein the method further characterizes one or more clinical biomarkers of ovarian cancer risk in the subject, wherein the one or more clinical biomarkers are selected from group consisting of age, pre-menopausal status, post-menopausal status, ethnicity, pathology, adnexal mass diagnosis, family history, physical examination, imaging results, and/or history of smoking, wherein the one or more clinical biomarkers further identifies the subject as having a low or high cancer risk.

~~49~~17. A method for classifying a subject's risk of having ovarian cancer, the method comprising:

receiving, by at least one processor, a first panel signal representing a marker spectrum peak detected for each marker of a panel comprising or consisting of markers Transthyretin/prealbumin (TT), Apolipoprotein A1 (ApoA1), β 2-Microglobulin (β 2M), Transferrin (Tfr), Cancer Antigen 125 (CA125), HE4, and follicle stimulating hormone (FSH)

and one or more markers selected from the group consisting of Breast Cancer 1 (BRCA1), Breast Cancer 2 (BRCA2), ATM, BARD1, BRIP1, CDH1, CHEK2, EPCAM, MLH1, MSH2, MSH6, NBN, PALB2, PTEN, RAD51D, STK11, TP53, KRAS, ABRAXAS1, AKT1, APC, AXIN2, BMPR1A, BRAF, CDC25, CDKN2A, CDK4, CTNNB1, DICER1, ERBB2, ERCC6, FANCM, FANCC, MRE11, MUTYH, NF1, NTHL1, PIK3CA, PMS2, PP2R1A, PRKDC, POLD1, RAD50, RAD51C, RNF43, SDHB, SDHD, SMARCA4, XRCC2, WRN, CDC73, GALNT12, GREM1, HOXB13, MSH3, POLE, RAD51, RINT1, RSP20, SLX4, SMAD4, TTK, RASSF1A, RUNX3, TFPI2, SFRP5, OPCML, MGMT, CDH13, SULF1, HOXA9, HOXAD11, CLDN4, MAL, BORIS, ABCG2, TUBB3, MCJ, SNGG, P14ARF, P16INK4A, DAPK, P15, MINT31, RIZ1, and TMS1;

utilizing, by the at least one processor, a first stage cancer risk classifier to predict a cancer risk classification score representative of a predicted risk of developing ovarian cancer, the cancer risk classification score being based on learned risk classification parameters and the first panel signal;

determining, by the at least one processor, a cancer risk level associated with the cancer risk classification score, the cancer risk level selected from one of at least the selection comprising low risk, intermediate risk and high risk; and

generating, by the at least one processor, a cancer risk level prediction at a computing device associated with a care provider indicative of the cancer risk level of the subject.

50. — The method of claim 49, further comprising:

~~determining, by the at least one processor, the cancer risk level as intermediate risk;~~

~~utilizing, by the at least one processor, a second stage cancer risk classifier to predict an enhanced cancer risk classification score based on second stage learned risk classification parameters and second panel signal comprising a subset of the first panel signal; and~~

~~determining, by the at least one processor, an enhanced cancer risk level associated with the enhanced cancer risk classification score, the enhanced cancer risk level selected from one of at least the selection comprising low risk and high risk.~~

51. — The method of claim 50, wherein the second panel signal represents the marker spectrum peak of markers comprising or consisting of CA125, β 2M, Transferrin, Transthyretin and ApoA1.

52. — The method of claim 50, wherein the second panel signal represents the marker spectrum peak of markers comprising or consisting of FSH, CA125, HE4, Transferrin, ApoA1.

53. — The method of claim 49, further comprising:
determining, by the at least one processor, the cancer risk level as intermediate risk;
utilizing, by the at least one processor, a second stage cancer risk classifier to predict an enhanced cancer risk classification score based on second stage learned risk classification parameters and second panel signals comprising a different subset of the first panel signal;
utilizing, by the at least one processor, a third stage cancer risk classifier to predict an enhanced cancer risk classification score based on second stage learned risk classification parameters and third panel signals comprising a different subset of the first panel signal; and
determining, by the at least one processor, an enhanced cancer risk level associated with the enhanced cancer risk classification score, the enhanced cancer risk level selected from one of at least the selection comprising low risk and high risk.

54. — The method of claim 53, wherein the second panel signal represents the marker spectrum peak of markers comprising or consisting of CA125, β 2M, Transferrin, Transthyretin and ApoA1 and the third panel signal represents the marker spectrum peak of markers comprising or consisting of FSH, CA125, HE4, Transferrin, ApoA1.

55. — The method of any one of claims 49–54, further comprising:
determining, by the at least one processor, the low risk of the cancer risk level where the cancer risk classification score is between 0.0 and 5.0;
determining, by the at least one processor, the intermediate risk of the cancer risk level where the cancer risk classification score is between 5.1 and 9.9; and
determining, by the at least one processor, the high risk of the cancer risk level where the cancer risk classification score is between 10.0 and 20.0.

56. — The method of any one of claims 49–54, wherein the first stage cancer risk classifier comprises:
a pre-menopausal first stage cancer risk prediction model having learned pre-menopausal risk classification parameters of the learned risk classification parameters; and
a post-menopausal first stage cancer risk prediction model having learned post-menopausal risk classification parameters of the learned risk classification parameters.

57. — The method of claim 56, further comprising:
determining, by the at least one processor, the low risk of the cancer risk level where the cancer risk classification score is between 0.0 and 5.0;

determining, by the at least one processor, the intermediate risk of the cancer risk level where the cancer risk classification score is between 5.1 and 13.9 for a post-menopausal subject; and

determining, by the at least one processor, the low risk of the cancer risk level where the cancer risk classification score is between 14.0 and 20.0 for a post-menopausal subject.

58. — The method of claim 56, further comprising:

determining, by the at least one processor, the low risk of the cancer risk level where the cancer risk classification score is between 0.0 and 5.0;

determining, by the at least one processor, the intermediate risk of the cancer risk level where the cancer risk classification score is between 5.1 and 9.9 for a pre-menopausal subject; and

determining, by the at least one processor, the high risk of the cancer risk level where the cancer risk classification score is between 10.0 and 20.0 for a pre-menopausal subject.

59. — The method of any one of claims 49–58, further comprising generating, by the at least one processor, a recommendation on a display of the computing device recommending surgical intervention where the cancer risk level is the high risk.

60. — The method of any one of claims 49–58, further comprising generating, by the at least one processor, a recommendation on a display of the computing device recommending no surgical intervention where the cancer risk level is the low risk.

61. — The method of any one of claims 49–60, further comprising:

receiving, by the at least one processor, a modification to the cancer risk level prediction from the computing device; and

retraining, by the at least one processor, the learned risk classification parameters based on a difference between the modification and the cancer risk level.

62. — The method of any one of claims 49–61, wherein the first panel signal is received from a mass spectrometer or a biochip or both in communication with the at least one processor.

63. — The method of any one of claims 49–62, wherein the first stage cancer risk classifier comprises a classification tree or an artificial neural network.

64. — ~~The method of any one of claims 49–63, where the first stage cancer risk classifier comprises a supervised classification model.~~

65. — ~~The method of any one of claims 49–63, where the first stage cancer risk classifier comprises an unsupervised classification model.~~

66. — ~~The method of any one of claims 19–65, wherein the subject is diagnosed with an asymptomatic adnexal mass.~~

67. — ~~The method of any one of claims 19–65, wherein the subject is diagnosed with a symptomatic adnexal mass.~~

68. — ~~The method of any one of claims 19–56 or 58–67, wherein the subject is pre-menopausal.~~

69. — ~~The method of any one of claims 19–57 or 59–67, wherein the subject is post-menopausal.~~

70. — ~~The method of any one of claims 20–48 or 67–69, wherein the biological sample is serum.~~

~~71~~18. A system comprising the at least one processor configured to execute instructions causing the at least one processor to perform the method of ~~any one of claims 49–70~~claim 17.

72. — ~~The system of claim 71, wherein the at least one processor is in communication with a memory having the instructions stored thereon.~~

73. — ~~The system of claim 71 or 72, wherein the at least one processor is further configured to execute the instructions to perform steps to generate recommendation on a display of the computing device recommending surgical intervention where the cancer risk level is the high risk.~~

74. — ~~The system of any one of claims 71–73, wherein the at least one processor is further configured to execute the instructions to perform steps to generate a recommendation on a display of the computing device recommending no surgical intervention where the cancer risk level is the low risk.~~

~~75. — The system of any one of claims 71–74, wherein the at least one processor is further configured to execute the instructions to perform steps to:~~

~~receive a modification to the cancer risk level prediction from the computing device; and
retrain the learned risk classification parameters based on a difference between the
modification and the cancer risk level.~~

~~76. — The system of any one of claims 71–75, further comprising a mass spectrometer in
communication with the at least one processor.~~

~~77~~19. A non-transitory computer readable medium storing thereon software, the software
comprising program instructions configured to cause the at least one processor to perform the
method of ~~any one of claims 49–70~~claim 17.

~~78. — The non-transitory computer readable medium of claim 77, wherein the method further
comprises the step of generating a recommendation on a display of the computing device
recommending surgical intervention where the cancer risk level is the high risk.~~

~~79. — The non-transitory computer readable medium of claim 77 or 78, wherein the method
further comprises the step of generating a recommendation on a display of the computing device
recommending no surgical intervention where the cancer risk level is the low risk.~~

~~80. — The non-transitory computer readable medium of any one of claims 77–79, wherein the
method comprises the steps of:~~

~~receiving a modification to the cancer risk level prediction from the computing device;
and~~

~~retraining the learned risk classification parameters based on a difference between the
modification and the cancer risk level.~~

~~81. — The non-transitory computer readable medium of any one of claims 77–80, wherein the
first stage cancer risk classifier comprises a classification tree or an artificial neural network.~~

~~82. — The non-transitory computer readable medium of any one of claims 77–81, where the first
stage cancer risk classifier comprises a supervised classification model.~~

~~83. The non-transitory computer readable medium of any one of claims 77-81, where the first stage cancer risk classifier comprises an unsupervised classification model.~~

8420. A kit comprising:

- (a) the panel of markers of any one of claims 1, 2, 3, 4, 5, or 61-18; and
- (b) instructions for using the panel for pre-operatively assessing a subject's risk of having ovarian cancer.