Cellworks
PERSONALIZED THERAPY. TRANSPARENT DESIGN.

SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Atezolizumab				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
CDKN2A	DEL	S	**ATEZOLIZUMAB** ⊣ **CD274** → **PD-1** ⊣ **CTL_Activation** CDKN2A → CHEK2 → BRCA1/2 → DNA REPAIR (HR) ⊣ APM_Machinery → CTL_Activation → GZMB → CASP3 → APOPTOSIS	28492290 30291219
TP53	SOF	S	**ATEZOLIZUMAB** ⊣ **CD274** → **PD-1** ⊣ **CTL_Activation** Mut_TP53 ⊣ TP53 → MIR34A ⊣ CD274 → PD-1 ⊣ CTL_Activation → GZMB → CASP3 → APOPTOSIS	31857991 30456447 29863979

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SINGULA™
PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Bevacizumab				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
TP53	SOF	S	**BEVACIZUMAB** ⊣ **para_VEGFA** Mut_TP53 ⊣ TP53 ⊣ HIF1A → VEGFA → para_VEGFA → KDR → SRC → PIK3CA → AKT ⊣ GSK3B ⊣ MYC → FOXM1 → CANCER PROGRESSION	32722340 25672981 28784180 15961063 14656735

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Brigatinib				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
NRAS	GOF	R	**BRIGATINIB** ⊣ **ALK** → **IRS1** NRAS → RAF1 → MAP2K1/2 → MAPK1//3 ⊣ IRS1	27432227 27049722 29336091
KRAS	SOF	R	**BRIGATINIB** ⊣ **ALK** → **IRS1** KRAS → RAF1 → MAP2K1/2 → MAPK1/3 ⊣ IRS1	27432227 27049722 29336091

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Cabozantinib				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
KRAS	SOF	R	**CABOZANTINIB** ⊣ **MET** KRAS → RAF1 → MAP2K1/2 → MAPK1/3 → ADAM17 ⊣ MET	26536165 28500237 21926191
NRAS	GOF	R	**CABOZANTINIB** ⊣ **MET** NRAS → RAF1 → MAP2K1/2 → MAPK1/3 → ADAM17 ⊣ MET	26536165 28500237 21926191

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Carboplatin				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
BRCA1	LOF	S	**CARBOPLATIN** → **ICL** → **DSB** → **DNA DAMAGE** BRCA1 → DNA REPAIR (HR) ⊣ DNA DAMAGE	26957554 30272304 25847936 10843985
KMT2D	LOF	R	**CARBOPLATIN** → **AP** → **FUTILE DNA REPAIR (MMR)** → **DNA DAMAGE** KMT2D → H3K4 METHYLATION → MLH1 → MMR	27997699 27688757 19286655
NFE2L2	GOF	R	**CARBOPLATIN** → **ICL** → **DSB** → **DNA DAMAGE** NFE2L2 → GSTP1 ⊣ CARBOPLATIN	3512077 16696564 25010864

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Cemiplimab				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
CDKN2A	DEL	S	**CEMIPLIMAB** ⊣ **CD274** → **PD-1** ⊣ **CTL_Activation** CDKN2A → CHEK2 → BRCA1/2 → DNA REPAIR (HR) ⊣ APM_Machinery → CTL_Activation → GZMB → CASP3 → APOPTOSIS	29863979 30291219
TP53	SOF	S	**CEMIPLIMAB** ⊣ **CD274** → **PD-1** ⊣ **CTL_Activation** Mut_TP53 ⊣ TP53 → MIR34A ⊣ CD274 → PD-1 ⊣ CTL_Activation → GZMB → CASP3 → APOPTOSIS	30456447 31857991 29863979

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PERSONALIZED THERAPY. TRANSPARENT DESIGN.

SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Ceritinib				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
KRAS	SOF	R	**CERITINIB** ⊣ **ALK** → **IRS1** KRAS → RAF1 → MAP2K1/2 → MAPK1/3 ⊣ IRS1	15713122 9395471 27899961 23742252
NRAS	GOF	R	**CERITINIB** ⊣ **ALK** → **IRS1** NRAS → RAF1 → MAP2K1/2 → MAPK1/3 ⊣ IRS1	15713122 9395471 27899961 23742252

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Cetuximab				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
NRAS	GOF	R	**CETUXIMAB** ⊣ **EGFR** NRAS → RAF1 → MAP2K1/2 → MAPK1/3 ⊣ EGFR	26989027

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Cisplatin				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
BRCA1	LOF	S	**CISPLATIN** → **ICL** → **DSB** → **DNA DAMAGE** BRCA1 → DNA REPAIR (HR) ⊣ DNA DAMAGE	23229133 25847936 10843985 26957554
NFE2L2	GOF	R	**CISPLATIN** → **ICL** → **DSB** → **DNA DAMAGE** NFE2L2 → GSTP1 ⊣ CISPLATIN	20598602 23229133 20538911

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Crizotinib				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
NRAS	GOF	R	**CRIZOTINIB** ⊣ **MET** **CRIZOTINIB** ⊣ **ALK** → **IRS1** NRAS → RAF1 → MAP2K1/2 → MAPK1/3 → ADAM17 ⊣ MET NRAS → RAF1 → MAP2K1/2 → MAPK1/3 ⊣ IRS1	29042798 24931611 15713122 22235099 26045026
KRAS	SOF	R	**CRIZOTINIB** ⊣ **MET** **CRIZOTINIB** ⊣ **ALK** → **IRS1** KRAS → RAF1 → MAP2K1/2 → MAPK1/3 → ADAM17 ⊣ MET KRAS → RAF1 → MAP2K1/2 → MAPK1/3 ⊣ IRS1	29042798 24931611 15713122 22235099 26045026

Cellworks
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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Dabrafenib				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
KRAS	SOF	R	**DABRAFENIB** ⊣ **BRAF** ⊣ **RAF1** KRAS → RAF1 → MAP2K1/2 → MAPK1/3 → FOXM1 → CANCER PROGRESSION	24265153 27124486
NRAS	GOF	R	**DABRAFENIB** ⊣ **BRAF** ⊣ **RAF1** NRAS → RAF1 → MAP2K1/2 → MAPK1/3 → FOXM1 → CANCER PROGRESSION	24265153 27124486

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Dacomitinib				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
KRAS	SOF	R	**DACOMITINIB** ⊣ **EGFR** KRAS → RAF1 → MAP2K1/2 → MAPK1/3 ⊣ EGFR	31050691 25439692 29156674
NRAS	GOF	R	**DACOMITINIB** ⊣ **EGFR** NRAS → RAF1 → MAP2K1/2 → MAPK1/3 ⊣ EGFR	31050691 25439692 29156674

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Docetaxel				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
KRAS	SOF	R	**DOCETAXEL → SPINDLE POISON ⊣** **ANAPC1_CDC26_CDC20 ⊣ CCNB1_CDK1 →** **MITOTIC_CATASTROPHE ⊣ MITOTIC_SLIPPAGE ⊣** **APOPTOSIS** KRAS → RAF1 → MAP2K1/2 → MAPK1/3 → CHUK_IKBKB → NFKB1 → BIRC5 → MITOTIC_SLIPPAGE ⊣ APOPTOSIS	31096466 20498641 26035434 27177222 24168763 10962577 27484466 15729715

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Durvalumab				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
CDKN2A	DEL	S	**DURVALUMAB** ⊣ **CD274** → **PD-1** ⊣ **CTL_Activation** CDKN2A → CHEK2 → BRCA1/2 → DNA REPAIR (HR) ⊣ APM_Machinery → CTL_Activation → GZMB → CASP3 → APOPTOSIS	29416316 30291219
TP53	SOF	S	**DURVALUMAB** ⊣ **CD274** → **PD-1** ⊣ **CTL_Activation** Mut_TP53 ⊣ TP53 → MIR34A ⊣ CD274 → PD-1 ⊣ CTL_Activation → GZMB → CASP3 → APOPTOSIS	31857991 30456447 29863979

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Entrectinib				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
KRAS	SOF	R	**ENTRECTINIB** ⊣ **NTRK1** → **GRB2** → **SOS1** → **RAS** → **RAF1** KRAS → RAF1 → MAP2K1/2 → MAPK1/3 → STAT3 → CANCER PROGRESSION (Alternative activation of ERK signaling)	21840963 32306207

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Erlotinib				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
NRAS	GOF	R	**ERLOTINIB** ⊣ **EGFR** NRAS → RAF1 → MAP2K1/2 → MAPK1/3 ⊣ EGFR	27480147 28090522 28149890 25705018 20921461
KRAS	SOF	R	**ERLOTINIB** ⊣ **EGFR** KRAS → RAF1 → MAP2K1/2 → MAPK1/3 ⊣ EGFR	27480147 28090522 28149890 25705018 20921461

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Etoposide				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
TP53	SOF	R	**ETOPOSIDE → TOP2CC → DSB → DNA DAMAGE** Mut_TP53 → TDP2 ⊣ TOP2CC → DSB → DNA DAMAGE	24766193 22508727
BRCA1	LOF	S	**ETOPOSIDE → TOP2CC → DSB → DNA DAMAGE** BRCA1 → DNA REPAIR (HR) ⊣ DNA DAMAGE	26880199 24130054 24244429 20824055 9665145

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Gefitinib				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
NRAS	GOF	R	**GEFITINIB** ⊣ **EGFR** NRAS → RAF1 → MAP2K1/2 → MAPK1/3 ⊣ EGFR	25202123 11524555 22549160
KRAS	SOF	R	**GEFITINIB** ⊣ **EGFR** KRAS → RAF1 → MAP2K1/2 → MAPK1/3 ⊣ EGFR	11585753 15696205 19943202 11896055

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Gemcitabine				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
KMT2D	LOF	S	**GEMCITABINE** → **dFdCTP** → **DNA DAMAGE** KMT2D → H3K4 METHYLATION → MLH1 → DNA REPAIR (MMR) ⊣ DNA DAMAGE	10340887 23361057 26366712 27280393
TP53	SOF	S	**GEMCITABINE** → **dFdCDP** ⊣ **RRM1/2** → **dCTP** ⊣ **REPLICATION STRESS** Mut_TP53 ⊣ TP53 → POLH ⊣ REPLICATION STRESS → APOPTOSIS	19598259 25564970 10340887 18765824

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Ipilimumab				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
CDKN2A	DEL	S	**IPILIMUMAB** ⊣ **CTLA4** ⊣ **CTL_Activation** CDKN2A → CHEK2 → BRCA1/2 → DNA REPAIR (HR) ⊣ APM_Machinery → CTL_Activation → GZMB → CASP3 → APOPTOSIS	23047236 30291219

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PERSONALIZED THERAPY. TRANSPARENT DESIGN.

SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Larotrectinib				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
KRAS	SOF	R	**LAROTRECTINIB** ⊣ **NTRK1** → **GRB2** → **SOS1** → **RAS** → **RAF1** KRAS → RAF1 → MAP2K1/2 → MAPK1/3 → STAT3 → CANCER PROGRESSION (Alternative activation of ERK signaling)	21840963 28578312

Cellworks
PERSONALIZED THERAPY. TRANSPARENT DESIGN.

SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Lorlatinib				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
KRAS	SOF	R	**LORLATINIB** ⊣ **ALK** → **IRS1** KRAS → RAF1 → MAP2K1/2 → MAPK1/3 ⊣ IRS1	27899961 15713122 24819116 9395471
NRAS	GOF	R	**LORLATINIB** ⊣ **ALK** → **IRS1** NRAS → RAF1 → MAP2K1/2 → MAPK1/3 ⊣ IRS1	27899961 15713122 24819116 9395471

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Nivolumab				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
CDKN2A	DEL	S	**NIVOLUMAB** ⊣ **CD274** → **PD-1** ⊣ **CTL_Activation** CDKN2A → CHEK2 → BRCA1/2 → DNA REPAIR (HR) ⊣ APM_Machinery → CTL_Activation → GZMB → CASP3 → APOPTOSIS	30291219 24872026
TP53	SOF	S	**NIVOLUMAB** ⊣ **CD274** → **PD-1** ⊣ **CTL_Activation** Mut_TP53 ⊣ TP53 → MIR34A ⊣ CD274 → PD-1 ⊣ CTL_Activation → GZMB → CASP3 → APOPTOSIS	31857991 30456447 29863979
BRCA1	LOF	S	**NIVOLUMAB** ⊣ **CD274** → **PD-1** ⊣ **CTL_Activation** BRCA1 → DNA REPAIR (HR) ⊣ APM_Machinery → CTL_Activation → GZMB → CASP3 → APOPTOSIS	29998185 30004857

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Osimertinib				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
KRAS	SOF	R	**OSIMERTINIB** ⊣ **EGFR** KRAS → RAF1 → MAP2K1/2 → MAPK1/3 ⊣ EGFR	24893891 27252416
NRAS	GOF	R	**OSIMERTINIB** ⊣ **EGFR** NRAS → RAF1 → MAP2K1/2 → MAPK1/3 ⊣ EGFR	24893891 27252416
TP53	SOF	R	**OSIMERTINIB** ⊣ **EGFR** Mut_TP53 ⊣ TP53 ⊣ PIK3CA → PDPK1 → AKT → PIKFYVE ⊣ EGFR	32272775 27448564 28241017 25939061

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Paclitaxel				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
NFE2L2	GOF	R	**PACLITAXEL** → **SPINDLE POISON** ⊣ **ANAPC1_CDC26_CDC20** ⊣ **CCNB1_CDK1** → **MITOTIC_CATASTROPHE** ⊣ **MITOTIC_SLIPPAGE** ⊣ **APOPTOSIS** NFE2L2 → NFE2L2_MAFK → ABCC1/2 ⊣ PACLITAXEL	10861441 20124447 19638449 23727018
KRAS	SOF	R	**PACLITAXEL** → **SPINDLE POISON** ⊣ **ANAPC1_CDC26_CDC20** ⊣ **CCNB1_CDK1** → **MITOTIC_CATASTROPHE** ⊣ **MITOTIC_SLIPPAGE** ⊣ **APOPTOSIS** KRAS → RAF1 → MAP2K1/2 → MAPK1/3 → CHUK_IKBKB → NFKB1 → BIRC5 → MITOTIC_SLIPPAGE ⊣ APOPTOSIS	31096466 20498641 26035434 27177222 24168763 10962577 27484466 15729715

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SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Pembrolizumab				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
CDKN2A	DEL	S	**PEMBROLIZUMAB** ⊣ **CD274** → **PD-1** ⊣ **CTL_Activation** CDKN2A → CHEK2 → BRCA1/2 → DNA REPAIR (HR) ⊣ APM_Machinery → CTL_Activation → GZMB → CASP3 → APOPTOSIS	26225694 25685857
BRCA1	LOF	S	**PEMBROLIZUMAB** ⊣ **CD274** → **PD-1** ⊣ **CTL_Activation** BRCA1 → DNA REPAIR (HR) ⊣ APM_Machinery → CTL_Activation → GZMB → CASP3 → APOPTOSIS	30004857 29998185
TP53	SOF	S	**PEMBROLIZUMAB** ⊣ **CD274** → **PD-1** ⊣ **CTL_Activation** Mut_TP53 ⊣ TP53 → MIR34A ⊣ CD274 → PD-1 ⊣ CTL_Activation → GZMB → CASP3 → APOPTOSIS	31857991 30456447 29863979

Cellworks
PERSONALIZED THERAPY. TRANSPARENT DESIGN.

SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Radiation				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
SETD2	LOF	S	**RADIATION** → **DSB** → **DNA DAMAGE** SETD2 → H3K36 METHYLATION → BRCA1 → DNA REPAIR (HR) ⊣ DNA DAMAGE	24931610 25988165 12947386 17629934 24003211
BRCA1	LOF	S	**RADIATION** → **DSB** → **DNA DAMAGE** BRCA1 → DNA REPAIR (HR) ⊣ DNA DAMAGE	23849504 15546503 25210685
CDKN2A	DEL	R	**RADIATION** → **DSB** → **DNA DAMAGE** CDKN2A ⊣ CDK4_CCND1 → FOXM1 → BRCA2 → DNA REPAIR (HR) ⊣ DNA DAMAGE	22094256 25287128
KRAS	SOF	R	**RADIATION** → **DSB** → **DNA DAMAGE** KRAS → PIK3CA → PDPK1 → AKT → PRKDC_XRCC6_XRCC5 → DNA REPAIR (NHEJ) ⊣ DNA DAMAGE	14530152 21779497 18644989 12947393
NFE2L2	GOF	R	**RADIATION** → **DSB** → **DNA DAMAGE** NFE2L2 → GSS → GSH ⊣ ROS → DNA DAMAGE	24180216 27663899 29018201
NRAS	GOF	R	**RADIATION** → **DSB** → **DNA DAMAGE** NRAS → PIK3CA → PDPK1 → AKT → PRKDC → DNA REPAIR (NHEJ) ⊣ DNA DAMAGE	12947393 14530152

Cellworks
PERSONALIZED THERAPY. TRANSPARENT DESIGN.

SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Trametinib				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
KRAS	SOF	S	**TRAMETINIB** ⊣ **MAP2K1/2** KRAS → RAF1 → MAP2K1/2 → MAPK1/3 → FOXM1 → CANCER PROGRESSION	21523318 10969079 25199829 21858223 25722381
NRAS	GOF	S	**TRAMETINIB** ⊣ **MAP2K1/2** NRAS → RAF1 → MAP2K1/2 → MAPK1/3 → MYC → FOXM1 → AURKB → CANCER PROGRESSION	26347206 12835716 11773061 21858223 22507781

Cellworks
PERSONALIZED THERAPY. TRANSPARENT DESIGN.

SINGULA™ PRECISION MEDICINE

Clinical ID: ABC123 **Cellworks ID:** 123456 **Ref Physician:** Dr. Smith

Biopsy Sequence: 1 **Gender/Age:** Male / 65 **Date of Report:** Jan 01, 2021

Indication: Non-Small Cell Lung Cancer (NSCLC) - NOS

Vemurafenib				
Gene	Status	Type	Gene Status Drug Action Pathway(s)	Supporting PMID(s)
KRAS	SOF	R	**VEMURAFENIB** ⊣ **BRAF** ⊣ **RAF1** KRAS → RAF1 → MAP2K1/2 → MAPK1/3 → FOXM1 → CANCER PROGRESSION	24265153 24508103 27124486
NRAS	GOF	R	**VEMURAFENIB** ⊣ **BRAF** ⊣ **RAF1** NRAS → RAF1 → MAP2K1/2 → MAPK1/3 → FOXM1 → CANCER PROGRESSION	24265153 24508103 27124486

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6. Genomic Aberration to Key Biomarker Pathway(s)

This section provides a snapshot of paths connecting the most significant gene aberrations with patient biomarkers and references to published research supporting these pathways.

RED: Gain of Function/Switch of Function Mutation(s) or Amplified Gene(s) BLUE: Loss of Function Mutation(s) or Deleted Gene(s)

TRANSCRIPTION FACTORS:

Key Biomarker(s)	Molecular Pathway Rationale for Biomarker(s)	Reference PMID(s)
FOXM1	BRCA1 → CDKN1A ⊣ CCNA2_CDK2 → FOXM1	
	NRAS → ARAF → BRAF ⊣ BAD ⊣ BCL2 ⊣ BRCA1 → CDKN1A ⊣ CCNB1_CDK1 → FOXM1	15694340 15990872 17322918 19667065 21444675 27034005
	SETD2 → CDKN1A ⊣ CCNA2_CDK2 → FOXM1	18585004
	KRAS → RALGDS → RALA → CCNB1_CDK1 → FOXM1	11322487 15208305

** Assayable key kinase biomarkers identified for this patient.

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7. Singula™ Assessment sections

1. Drug Response Prediction

This section illustrates predicted response to Standard Care therapy or any specific therapy of interest for an indication. The response is indicated as an easily interpretable, 'Responder' or 'Non-Responder'.

2. Patient Disease Characteristics: Key Biomarker(s)

Using biosimulation modeling, Cellworks determines key biomarkers in the patient's genomic profile. They are points of convergence of the pathways impacted by the mutations in the patient's profile. These key biomarkers are tumor promoter/suppressor genes that the drug needs to impact in order for the patient to repsond to treatment.

3. Biomarker Impact

This table shows the impact that the therapies of interest have on the 'Key Biomarkers' identified for the patient profile. The check symbol ('✓') implies that the therapy is predicted to be successful in impacting the biomarker. Not all therapies impact key biomarkers equally. Please see the therapy rationale in Section 5 for a more thorough explanation.

4. Summary of Patient Genomic Profile

This section provides an aggregated overview of the patient genomics used for therapy assessment. It shows the type of input received from the next generation sequencing data (NGS) with the number of genetic mutations, copy number variations (CNVs) and any epigenetic data that is reported.

4.1 Detailed Information of Genomic Aberration(s) Modeled

This section lists all the mutations, CNVs and epigenetic data which are modelled via the Cellworks biosimulation for the patient. This information forms the patient-specific input on which a Cellworks assessment is based.

5. Therapy Rationales

A therapy rationale illustrates the role of key mutations in causing sensitivity or resistance to drugs. A drug will have a therapy rationale for every mutation that contributes significantly to its sensitivity or resistance.

The first illustration in the rationale defines the mechanism of action of the drug.

The second illustration articulates the signalling or metabolic pathway by which the mutation of interest contributes to drug sensitivity or resistance including the point of intersection (if any) with the drug's mechanism of action.

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The description is accompanied by relevant PMIDs that were used to determine the interaction.

6. Genomic Aberration to Key Biomarker Pathway(s)

This section illustrates moelecular biochemical pathways from a genomic aberration in the patient profile to critical biomarkers identified by Cellworks biosimulation. The description is accompanied by relevant PMIDs that were used to determine the interaction

Regarding Toxicity

The current assessment assumes that the drugs are faithfully delivered to the site of action. Cellworks considers all molecular interactions once delivered to the site of action (Pharmacodynamics of the drug compound). Cellworks does not account for absorption, distribution, metabolism & excretion (ADME) properties of the drug that determine how the drug is delivered to the site of action. Any toxicity in the delivery process, or pharmacokinetics, is not considered.

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8. Terms of Usage

Cellworks Therapeutic Solutions

The Cellworks proprietary workflow solution used to generate this test report from patient's medical records (Test Report), has not been approved by any regulatory or medical authority. Cellworks generated information is adjunctive information to physicians and molecular tumor boards. CELLWORKS DOES NOT ASSURE OR GUARANTEE THE SUCCESS OF ANY THERAPEUTIC OPTION IDENTIFIED IN THIS TEST REPORT. Cellworks reports have not been validated or specifically developed for pregnant women or nursing mothers. The therapeutic options provided in the Test Report are not ranked in order of efficacy, safety or cost-effectiveness and are sorted based on our model's analysis of the input data. All individual drugs included in therapy options identified in the Test Report have been cleared and approved by the United States Food and Drug Administration (FDA) for other indications. At the specific request of the patient or treating physician, the Test Report may identify drugs or therapy options that are also in an advanced stage of clinical trials and yet to be approved. This will provide adjunctive information to the physicians for selecting a clinical trial for the patient.

Therapeutic agents associated with potential benefit or lack of benefit, as indicated in the Test Report are based on biomarker results provided in the report and on published evidence with PMID references. This evidence in some cases may have been obtained from studies performed in the cancer type present in the tested patient's sample.

No Guarantee of Clinical Benefit

The finding of a biomarker expression does not necessarily indicate pharmacologic effectiveness or lack thereof. The agents identified may or may not be suitable for use with a particular patient and the Test Report does not guarantee or suggest that any particular agent will be effective with the treatment of any particular condition. The user of this Test Report remains responsible for the conduct of patient care and for evaluating the clinical relevance of information provided by the prediction software.

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