Table S5. List of anthelmintic agents that are currently being investigated in clinical trials for their effectiveness against different cancer types when alone and/or in combination with chemotherapeutic agents as well as anthelmintics that are potential new anti-cancer drugs shown to inhibit malignant cells *in vivo*/*in vitro*. The summarized data is obtained from clinicaltrials.gov, the National Institute of Health (NIH), the Drugbank, and the ReDo databank. PubMed and Google Scholar have been used to gain detailed information about the mechanism(s) of action of the potential repurposed drugs *in vitro* and *in vivo*. The keywords used for the search are "anti-cancer" and "repurposed".

Drug	**Original application / target**	**New application (anti-cancer) / Proposed Target/Mechanism of action**	**Stage of development**
Mebendazole	**Anthelmintic** Binds to tubulin – inhibition of tubulin formation [1]	**Meningioma:** **-**As single treatment: Inhibits colony formation, activates caspase-3, reduces angiogenesis [2] -In combination: Enhances radiation' effect (radiosensitizer) [2] **Lung cancer:** **-**As single treatment: Stimulates CD14+ myeloid cells → enhances T-cell activation → enhances tumor cell killing/induces apoptosis [3] **Medulla blastoma:** **-**As single treatment: Suppresses primary cilium formation (tubulin based organelle, signaling hub for the Hedgehog pathway) → inhibits Hedgehog pathway → inhibits cell growth [4] Stimulates immune system → increases TNFα and IFN-γ [3]	**Clinical trials Phase III:** -Cancer overall survival (NCT02201381) -Neoplasms (NCT02366884) *In combination* -Colorectal cancer – Mebendazole with FOLFOX (NCT03925662) **Clinical trials Phase II:** -Cancer of unknown origin (NCT03628079) **Clinical trials Phase I:** -Recurrent pediatric brain cancers (NCT02644291) -Cancer of the gastrointestinal tract (NCT03628079) -High grade glioma (NCT01729260) -Pilomyxoid Astrocytoma (NCT01837862) ***In vivo:*** -Female athymic mice with meningioma cells KT21MG1 cells [2] ***In vitro:*** -Meningioma cells KT21MG1, IOMM LEE, AC-1, SF4068, SF6717, SF1335, SF1335 + YAP [2] -Medulla blastoma cells 293T and hTERT-RPE1 [4]

Niclosanide	**Anthelmintic** Inhibition glucose uptake by worms [5]	**Renal cancer:** **-**As single treatment: Inhibits C-MYC and E2F1 expression, enhances PTEN expression, inhibits cell proliferation, migration and progression, and induces apoptosis [6] -In combination: Synergizes Sorafenib's effect [6] **Adeno cortical carcinoma:** **-**As single treatment: Inhibits tumor growth and proliferation, induces cell cycle arrest and apoptosis; decreases cellular migration, downregulates the level of β-catenin [7] **Glioblastoma:** **-**As single treatment: Induces cell arrest and decreases cell viability, by inhibiting tubulin formation [8] **Lung cancer:** -In combination: Enhances radiation' effect (radiosensitizer) [9]	**Clinical trial phase II:** -Prostate cancer (NCT02807805) -Familial Adenomatous Polyposis (NCT04296851) **Clinical trial phase I:** -Prostate cancer (NCT03123978) -Enzalutamine with Niclosamide, prostate cancer (NCT02532114) ***In vivo:*** -Nude mice with renal cancer cells Caki-1 [6] -Adeno cortical carcinoma cells NCI-H295R in Nu^+/Nu^+ mice [7] -Female C57BL/6 mice with glioblastoma cells GL-261 [8] ***In vitro:*** -Renal cancer cells A498 and Caki-1 [6] -Adeno cortical carcinoma cells NCI-H295R and SW-13 [7] -Glioblastoma cells GL-261 [8] -Lung cancer cells H1299 [9]
Ivermectin	**Anthelmintic** Modulator of the γ-aminobutyric acid (GABA) receptor activity or glutamate-gated chloride ion channels (Glu-Cl) [10–12]	**Ovarian cancer:** **-**As single treatment: Induces DNA damage – double-strand breaks, breaks down mitochondrial membrane, upregulates BAX/BCL-2, releases free cytochrome C in cytosol, inhibits cell viability, induces apoptosis via caspase-9/3 activation [11] **Liver cancer:** **-**As single treatment: Induces morphological changes – DNA fragmentation and chromatin condensation, produces ROS, decreases mitochondrial membrane potential, upregulates BAX/BCL-2, induces apoptosis via caspase-9/3 activation [12]	**Clinical Phase II:** -Neoplasms (NCT02366884) **In vivo:** -MDAY-D2 murine leukemia cells in mice [13] -Glioblastoma cancer xenograft in SCID mice [14] -Female NOD/SCID and Balb/c mice with breast cancer cells MDA-MB-231 [15]

Ivermectin *(Continued)*		**Leukemia:** **-**As single treatment: Increases intracellular chloride ion concentration – plasma membrane hyperpolarization, enhances ROS level, and induces cell death [13] **Glioma, Melanoma, and Bronchio-alveolar carcinoma :** **-**As single treatment: Blocks WNT-TCF signaling, inhibits cell proliferation, induces apoptosis; *in vivo* only active against TCF dependent cancer types [16] **Glioblastoma:** **-**As single treatment: Inhibits angiogenesis, induces mitochondrial stress and enhances ROS levels, deactivates Akt/mTOR signaling pathway [14] **Breast cancer:** **-**As single treatment: Inhibits cell growth, downregulates self-renewal transcription factors such as homeobox protein nanog (nanog), octamer-binding protein 4 (oct-4) and SRY-box 2 (sox-2) [17] Activates cytostatic autophagy, decreases P21-activated kinase 1 (PAK1) expression → blocks Akt/mTOR signaling pathway [15]	***In vitro:*** -Ovarian cancer cells HeLa [11] -Liver cancer cells HepG2 [12] -Leukemia cells OCI-AML2, HL60, U937, KG1a, MDAY-D2 [13] -Human colon cancer cells CC14, CC36, Ls174T, HT-29, and DLD-1 -Bronchio-alveolar carcinoma H358, 293T cells, GBM primary cells, U251 glioma, and SKMel2 melanoma cells [16] -Glioblastoma cells A172 and U138-MG [14] -Breast cancer cells MDA-MB-231 [17], MDA-MB-435, HS578T, 4T1, and HEK 293T [15]
Praziquantel	**Anthelmintic** Induction of spastic paralysis of the worm musculature - related to the Ca^{2+} level [18, 19]	**Colon cancer, breast cancer, lung cancer, cervical cancer:** -In combination: Synergizes Paclitaxel's effects – inhibition of cell growth [20]	**Clinical trial Phase II:** -Neoplasms – single treatment (NCT02366884) ***In vivo:*** -DLD-1 cells in athymic nude mice [20] ***In vitro:*** -Colon cancer cells DLD-1, breast cancer cells ZR-7530, lung cancer cells SPC-A-1 and Ltep-a-2, cervical cancer cells HeLa and breast cancer cells Bcap37 [20]

Nitazoxamide	**Anthelmintic** Inhibition of pyruvate-ferredoxin oxidoreductase - down-regulates anaerobic metabolism [21, 22]	**Colon cancer:** **-**As single treatment: Interacts with glutathione-S-transferase P1 (GSTP1), inhibits cell growth, and induces nuclear condensation/DNA fragmentation/apoptosis [23] Activates the AMPK pathway and downregulates the c-Myc, mTOR, and Wnt signaling [24] **Glioblastoma:** **-**As single treatment: Affects autophagy regulation by blockage of late-stage lysosome acidification, suppresses cell growth and induces cell cycle arrest via upregulation of inhibitor growth protein 1 (ING1) expression [25] **Breast cancer:** **-**As single treatment: Inhibits c-Myc, suppresses tumor growth, and induces apoptosis [26]	**Clinical trial Phase II:** -Neoplasms (NCT02366884) ***In vivo:*** -Glioblastoma cells LN229 in ALB/C nude mice[25] -Female NMRI nu/nu mice with colon cancer cells HCT-116 cells [24] ***In vitro:*** -Colon cancer cells Caco-2 [23], HCT-116 and HT29 [24] -Glioblastoma cells LN229, A172, U87, and HUVEC [25] -Breast cancer cells SKBR3 [26]
Albendazole	**Anthelmintic** Inhibition of tubulin formation [1]	**Ovarian cancer:** **-**As single treatment: Inhibits cell proliferation and colony formation [27] Disrupts tubulin formation, inhibits tumor growth and angiogenesis [28] As BSA-Albendazol nano-particles: Inhibits vascular endothelial growth factor [29]	**Clinical trial Phase II:** -Neoplasms (NCT02366884) ***In vivo:*** -Female athymic nude mice with ovarian cancer cells OVCAR3 [29] ***In vitro:*** -Ovarian cancer cells 1A9, OVCAR-3 and SKOV-3 [27], OVCAR3 and SKOV3 [29], 1A9PTX22 [28]

Levamisole	**Anthelmintic** Agonist of nicotinic acetylcholine receptors [30–32]	**Myeloma:** **-**As single treatment: Inhibits CD138 expression (transmembrane heparin sulfate glycoprotein, standard marker to identify tumor cells), increases IL-6 secretion [33] **Lung cancer:** **-**As single treatment: Inhibits cJNK phosphorylation, induces cell cycle arrest and tumor necrosis factor-related apoptosis [34]	**Clinical trials phase III:** -Colon cancer – Levamisol hydrochloride in combination with 5-fluorouracil and leucovorin calcium (NCT00002593, NCT00425152, NCT00002551) -Colon cancer – Levamisol in combination with 5-flurouracil and interleukin (NCT00309530, NCT00003063) -Intrahepatic Cholangiocarcinoma (NCT03940378) **Clinical trials phase II:** -Neoplasms (NCT02366884) ***In vivo:*** -Lung cancer cells H460 in female BALB/c nude mice [34] ***In vitro***: -Myeloma cells and U266 B1 [33] -Lung cancer cells HCC827, H1975, H157, H460, and A549 [34]
Pyrvinium	**Anthelmintic** Inhibition of glucose uptake [35]	**Breast cancer:** **-**As single treatment: Inhibits cell proliferation → inhibits Wnt pathway, suppresses EMT marker expression, and inhibits tumor cell self-renewal [36] **Colon cancer:** **-**As single treatment: Inhibits cell viability, downregulates Wnt signaling mRNA transcription and protein expression, induces p21 [37] -In combination: Enhances 5-fluorouracil' effect [37] **Various cancer cells:** **-**As single treatment: Inhibits autophagy [38]	***In vivo:*** -Breast cancer cells MDA-MB-231 in NOD/SCID mice [36] -Healthy female mice with breast cancer cells 4T1 [38] -Nude mice with colon cancer cells HCT-116 [37]

Pyrvinium *(continued)*		**Cancer stem-like cells:** **-**As single treatment: Inhibits lipid anabolism, impairs anabolic flux from glucose to cholesterol and fatty acids [39] **Breast, DCIS, ovarian, prostate, lung, pancreatic, melanoma, and glioblastoma:** -As single treatment: Disrupts mitochondrial biogenesis [40] Intercalates into DNA [41]	***In vitro:*** -Breast cancer cells MCF-7, T47D, MDA-MB-231, MDA-MB-468, Her-2, MCF10.DCIS, and SkBr-3 [36] -Colon cancer cells HCT-25, HCT-116, LS174T, HT29, SW620, T84 [37] -Cervical cancer cells HeLa, HeLa-GFP-LC3 [38] -Kidney cancer cells HEK293[38] -Ovarian cancer SKOV3, Tov21G, ES2 [40] -Prostate cancer cells P3C [40] -Pancreas cancer cells Ma PaCa2 [36], PANC1 [38] -Lung caner cells A549 [36]-Melanoma cells A379 [36] -Glioma cells U-87 MG [36] [40]

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