

Table S2: Immuno-Modulating SMDs that have Entered Clinical Trials Either as Single-Agent Studies or as Part of a Combination Therapy Exploration.

Trial Title	Disease Type(s)	Trial Phase(s)	Sponsor / Collaborator	Primary SMD(s)	Primary Immunotherapy Drug Target	Other Drugs	Trial Status	Start Date	Reference
1-Methyl-D-Tryptophan in Treating Patients With Metastatic or Refractory Solid Tumors That Cannot Be Removed By Surgery	Unspecified Adult Solid Tumor, Protocol Specific	I	National Cancer Institute (NCI)	Indoximod (1-MT)	IDO1 inhibitor		Completed	Oct-07	NCT00567931
IDO Inhibitor Study for Relapsed or Refractory Solid Tumors	Breast Cancer, Lung Cancer, Melanoma, Pancreatic Cancer, Solid Tumors	I	NewLink Genetics Corporation	Indoximod (1-MT)	IDO1 inhibitor		Terminated	Aug-08	NCT00739609
Vaccine Therapy and 1-MT in Treating Patients With Metastatic Breast Cancer	Male Breast Cancer, Recurrent Breast Cancer, Stage IV Breast Cancer, Unspecified Adult Solid Tumor, Protocol Specific	I/II	H. Lee Moffitt Cancer Center and Research Institute   NCI	Indoximod (1-MT)	IDO1 inhibitor	Biological: adenovirus-p53 transduced dendritic cell (DC) vaccine	Open, not recruiting	Dec-09	NCT01042535
1-Methyl-D-Tryptophan and Docetaxel in Treating Patients With Metastatic Solid Tumors	Unspecified Adult Solid Tumor, Protocol Specific	I	NCI	Indoximod (1-MT)	IDO1 inhibitor	Docetaxel	Completed	Sep-10	NCT01191216
Phase II Study of Sipuleucel-T and Indoximod for Patients With Refractory Metastatic Prostate Cancer	Metastatic Prostate Cancer	II	Masonic Cancer Center, University of Minnesota	Indoximod (1-MT)	IDO1 inhibitor	Sipuleucel-T	Open	Oct-12	NCT01560923
Study of Chemotherapy in Combination With IDO Inhibitor in Metastatic Breast Cancer	Metastatic Breast Cancer	II	NewLink Genetics Corporation	Indoximod (1-MT)	IDO1 inhibitor	Docetaxel	Open	Feb-13	NCT01792050

Study of IDO Inhibitor and Temozolomide for Adult Patients With Primary Malignant Brain Tumors	Glioblastoma Multiforme, Glioma, Gliosarcoma, Malignant Brain Tumor	I/II	NewLink Genetics Corporation	Indoximod (1-MT)	IDO1 inhibitor	Temozolomide	Open	Mar-14	NCT02052648
Study of IDO Inhibitor in Combination With Ipilimumab for Adult Patients With Metastatic Melanoma	Metastatic Melanoma, Stage III Melanoma, Stage IV Melanoma	I/II	NewLink Genetics Corporation	Indoximod (1-MT)	IDO1 inhibitor	Ipilimumab	Open	Jul-14	NCT02073123
Study of IDO Inhibitor in Combination With Gemcitabine and Nab-Paclitaxel in Patients With Metastatic Pancreatic Cancer	Metastatic Pancreatic Adenocarcinoma, Metastatic Pancreatic Cancer	I/II	NewLink Genetics Corporation	Indoximod (1-MT)	IDO1 inhibitor	Nab-Paclitaxel, Gemcitabine	Open	Aug-14	NCT02077881
Indoleamine-2,3-dioxygenase (IDO) Inhibition With INCB024360 and Intraperitoneal Delivery of Allogeneic Natural Killer Cells for Women With Recurrent Ovarian, Fallopian Tube, and Primary Peritoneal Cancer	Recurrent Ovarian, Fallopian Tube, and Primary Peritoneal Cancer	I	Incyte University of Minnesota Cancer Center	INCB-24360	IDO-1 inhibitor	CD3/CD19 natural killer cells, IL-2, Cyclophosphamide fludarabine (IV)	Open	Apr-14	NCT02118285
A Phase I/IIb Study of DEC205mAb-NY-ESO-1 Fusion Protein (CDX-1401) Given With Adjuvant Poly-ICLC in Combination With INCB024360 for Patients in Remission With Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Carcinoma Whose Tumors Express NY-ESO-1 or LAGE-1 Antigen	Ovarian, Fallopian Tube, or Primary Peritoneal Cancer in Remission	I/IIb	National Institutes of Health (NIH)/NCI Roswell Park Cancer Institute	INCB-24360	IDO-1 inhibitor	DEC-205/NY-ESO-1 Fusion Protein CDX-1401, poly-ICLC	Open	Aug-14	NCT02166905
Phase I/II study of the efficacy and safety of MEDI4736 in combination with INCB24360 in solid tumors	Head/Neck Lung, Non-Small Cell Melanoma Pancreas	I/II	AstraZeneca/MedImmune Incyte	INCB-24360	IDO-1 inhibitor	Durvalumab	Planned	Dec-14	Incyte & AstraZeneca/MedImmune press releases; NCT02318277
A Phase I, Open-Label, Dose-Escalation Study to Determine the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of INCB024360 in Patients With Advanced Malignancies	Advanced Malignancies	I/II	Incyte Corporation	INCB-24360	IDO-1 inhibitor		Completed	Jul-14	Newton, 2012 <sup>1</sup> ; NCT01195311

A Phase I/II Randomized, Blinded, Placebo Controlled Study of Ipilimumab in Combination With INCB024360 or Placebo in Subjects With Unresectable or Metastatic Melanoma	Metastatic Melanoma	I/II	Incyte Corporation	INCB-24360	IDO-1 inhibitor	ipilimumab	Open	Mar-12	Gibney <sup>2</sup> ; NCT01604889
A Randomized, Open-label, Phase II study of the IDO inhibitor INCB024360 versus Tamoxifen for subjects with biochemical-recurrent -only epithelial ovarian cancer, primary peritoneal carcinoma, or fallopian tube cancer following complete remission with first-line chemotherapy.	Biochemical-recurrent Only Epithelial Ovarian Cancer, Primary Peritoneal Carcinoma, Fallopian Tube Cancer	II	Incyte Corporation	INCB-24360	IDO-1 inhibitor	Tamoxifen	Closed	Aug-12	Incyte press releases; NCT01685255
A Phase II Study to Determine the Safety and Efficacy of INCB024360 in Patients with Myelodysplastic Syndromes	Myelodysplastic Syndrome	II	H. Lee Moffitt Cancer Center and Research Institute Incyte	INCB-24360	IDO-1 inhibitor		Closed	Jul-12	Incyte press releases; NCT01822691
A Pilot Study of the Immunological Effects of Neo-adjuvant INCB024360 in Patients With Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Carcinoma	Newly Diagnosed Stage III-IV Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer	II	NIH/NCI	INCB-24360	IDO-1 inhibitor	Surgical intervention	Open	Dec-12	NCT02042430
A Phase II Pilot Trial of an Indoleamine 2,3, Dioxygenase-1 (IDO1) Inhibitor (INCB024360) Plus a Muropeptide Melanoma Vaccine (MELITAC 12.1) in Patients With Advanced Melanoma	Melanoma	II	Fred Hutchinson Cancer Research Center, Incyte, NIH/NCI University of Virginia	INCB-24360	IDO-1 inhibitor	MELITAC 12.1	Open	Sept-12	Incyte press releases; NCT01961115
A Phase I/II Study of Nivolumab in Combination with INCB24360 in Patients with Multiple Tumor Types	Multiple Tumor Types	I/II	Bristol-Myers Squibb Incyte	INCB-24360	IDO-1 inhibitor	nivolumab	Planned	Dec-14	Incyte press releases; TrialTrove
A Phase I/II Study Exploring the Safety, Tolerability, and Efficacy of MK-3475 in Combination With INCB024360 in Subjects With Selected Solid Tumors (Phase I) Followed by a Randomized, Double-Blind, Placebo-Controlled Study in Subjects With Advanced NSCLC (Phase II)	Cancer, Solid Tumor; Phase II will include patients with advanced NSC	I/II	Incyte Merck & Co.	INCB-24360	IDO-1 inhibitor	pembrolizumab	Open	June-14	Incyte & Merck press releases; NCT02178722

A Safety, Tolerability and Efficacy Study of INCB24360 in Combination with MPDL3280A in Patients with Non-Small Cell Lung Cancer	Lung, Non-Small Cell	II	Incyte Roche/Genentech	INCB-24360	IDO-1 inhibitor	MPDL3280A	Planned		Incyte press releases; NCT02298153
A Phase I Study of NLG-919 for Adult Patients with Recurrent Advanced Solid Tumors	Breast, Lung, Non-Small Cell, Pancreas, Unspecified Solid Tumor	I	NewLink Genetics	NLG-919	IDO-1 inhibitor		Open	Dec-13	Khleif <sup>3</sup> , 2014; NCT02048709
Phase I Multiple-Dose Safety, Pharmacokinetic and Pharmacodynamic Clinical Study of Nitric Oxide Releasing Aspirin (NCX 4016)	Colorectal Cancer	I	Stony Brook University NCI	NCX 4016	arginase I/iNOS dual inhibitor		Completed	Jul-06	NCT00331786
Phase I Trial of Chemoimmunotherapy and Hypofractionated Radiation Therapy for Borderline Resectable and Locally Advanced Pancreatic Adenocarcinoma	Pancreas	I	Providence Health & Services / Eli Lilly and Company	Gemcitabine-HCl radiation therapy tadalafil (tablet)	PDE 5 inhibitor	Surgical intervention	Closed	Jul-13-	NCT01903083
Exploratory Trial of Immunochemoradiotherapy for Locally Advanced Pancreatic Adenocarcinoma	Pancreas	I	Providence Health & Services / Earle A. Chiles Research Institute	GV-1001 (ID) sargramostim (ID) tadalafil	PDE 5 inhibitor	Gemcitabine radiation therapy surgical intervention	Closed	Jan-11	Crocenzi <sup>4</sup> , 2013; NCT01342224
Randomized Phase II Study of Autologous Stem Cell Transplantation With Tadalafil and Lenalidomide Maintenance With or Without Activated Marrow Infiltrating Lymphocytes (MILs) in High Risk Myeloma	Multiple Myeloma	II	Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins	Activated infiltrating lymphocytes, tadalafil	PDE 5 inhibitor	Prevnar vaccine	Open	Sept-13	Johns Hopkins press releases; NCT01858558
Pilot Study of Phosphodiesterase-5 Inhibitor Tadalafil (Cialis) as an Immunomodulator in Patients With Oral Cavity and Oropharyngeal Squamous Cell Carcinoma	Head/Neck	II	Sylvester Cancer Center, University of Miami	Tadalafil	PDE 5 inhibitor	Surgical intervention	Closed, results published	Sept-08	Weed <sup>5</sup> , 2015; NCT00843635
Administration of an Oral PDE5 Inhibitor, Tadalafil in Conjunction With Lenalidomide and Dexamethasone in Patients With Multiple Myeloma	Multiple Myeloma	II		Tadalafil (tablet)	PDE 5 inhibitor	Clarithromycin, Abbott dexamethasone lenalidomide	Terminated	Mar-12	Ghosh <sup>6</sup> , 2013; NCT01374217

A Phase II Trial of Tadalafil in Patients With Squamous Cell Carcinoma of the Upper Aero Digestive Tract	Head/Neck	II	Sidney Kimmel Comprehensive Cancer Center / National Institute of Dental and Craniofacial Research	tadalafil (tablet)	PDE 5 inhibitor	Undisclosed chemotherapy	Closed, results published	Jan-09	Califano <sup>7</sup> , 2015; NCT00894413
A Pilot Study to Determine the Safety of the Combination of Stable-Emulsion Formulation of Glucopyranosyl Lipid A (GLA-SE) with Radiation in Patients with Metastatic Sarcoma	Soft Tissue Sarcoma	I	Fred Hutchinson Cancer Research Center / NCI	GLA	TLR4	Radiation therapy	Open	Oct-14	NCT02180698
Phase One Study With Direct Individual Benefit: Effects of OM-174 in Adult Patients With Solid Tumors	Solid tumors	I	Centre Hospitalier Universitaire Dijon	OM-174	TLR4		Completed	Mar-07	Isambert <sup>8</sup> , 2013; NCT01800812
Pilot Phase II, Open Label, Multicenter, Efficacy and Safety Study of 852A Administered Intravenously to Subjects With Unresectable Metastatic Cutaneous Melanoma	Unresectable Metastatic Cutaneous Melanoma	II	Pfizer	852A <sup>†</sup>	TLR7		Completed	Feb-05	NCT00189332
A Randomized, Double-Blind, Placebo-Controlled Study of Chemotherapy Plus Cetuximab in Combination With VTX 2337 in Patients With Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck	Carcinoma, Squamous Cell of Head and Neck	II	VentiRx Pharmaceuticals Inc	VTX-2337 <sup>*</sup>	TLR8	Cetuximab, Carboplatin, Cisplatin, 5-fluorouracil	Open	Jul-13	NCT01836029
A Randomized, Double-Blind, Placebo-Controlled Phase II Study of VTX-2337 in Combination With Pegylated Liposomal Doxorubicin (PLD) in Patients With Recurrent or Persistent Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancer	Epithelial Ovarian Cancer Fallopian Tube Cancer Primary Peritoneal Cancer	II	VentiRx Pharmaceuticals Inc. Gynecologic Oncology Group	VTX-2337 <sup>*</sup>	TLR8	Pegylated liposomal doxorubicin	Open	Oct-12	NCT01666444
Open-Label Phase I b Study of Erlotinib Plus Bevacizumab and IMO-2055 in Patients With Non-Small Cell Lung Cancer Who Have Progressed Following Initial Chemotherapy for Advanced or Metastatic Disease	Lung, Non-Small Cell	I	Idera Pharmaceuticals Merck KGaA/EMD Serono	IMO-2055 (EMD1201081) <sup>#</sup>	TLR9	Bevacizumab erlotinib	Completed	Nov-07	Smith <sup>9</sup> , 2014; NCT00633529

A Phase II, Multi-Center, Randomized, Open-Label Study of Two Dose Levels of IMOxine (IMO-2055 for Injection) in Patients With Metastatic or Locally Recurrent Clear Cell Renal Carcinoma.	Renal Cell Carcinoma	II	Idera Pharmaceuticals	IMO-2055 (EMD1201081) <sup>#</sup>	TLR9		Completed	Oct-04	Idera Pharmaceuticals press releases; NCT00729053
A Phase II, Open-label, 1:1 Randomized, Controlled Trial Exploring the Efficacy of EMD 1201081 in Combination With Cetuximab in Second-Line Cetuximab-Naive Subjects With Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck (R/M SCCHN)	Head/Neck	II	Bayer AG Idera Pharmaceuticals Merck & Co./Merck Sharp & Dohme (MSD) Merck KGaA/Merck Serono	IMO-2055 (EMD1201081) <sup>†</sup>	TLR9	Cetuximab	Completed	Dec-09	Ruzsa <sup>10</sup> , 2014; NCT01040832
A Phase I/II Study of Intratumoral Injection of SD-101, an Immunostimulatory CpG, and Intratumoral Injection of Ipilimumab, an Anti-CTLA4 Monoclonal Antibody, in Combination With Local Radiation in Low-Grade B-Cell Lymphomas	Lymphoma, Non-Hodgkin's	I/II	National Institutes of Health/National Cancer Institute Stanford University Medical Center	SD-101	TLR9	Radiation therapy, ipilimumab	Open	Sept-14	Dynavax press releases; NCT02254772
Intratumoral Injection of an Immunostimulatory CpG, SD-101, Combined With Local Radiation for the Treatment of Recurrent or Progressive Lymphoma After Allogeneic Hematopoietic Cell Transplantation	Lymphoma, Hodgkin's Lymphoma, Non-Hodgkin's	I	Stanford University Medical Center	SD-101	TLR9	Radiation therapy	Open	Aug-08	Stanford press releases; NCT01745354
A Phase 1/2, Non-randomized, Open-label, Multicenter, Dose Escalation and Expansion Study of Intratumoral Injections of SD-101 in Combination With Localized Low-dose Radiation in Patients With Untreated Low-grade B-cell Lymphoma	B-cell Lymphoma	I/II	Dynavax Technologies Corporation	SD-101	TLR9	Radiation therapy	Open	Oct-14	NCT02266147
A Single Arm, Preoperative, Pilot Study to Evaluate the Safety and Biological Effects of Orally Administered Reparixin in Early Breast Cancer Patients Who Are Candidates for Surgery	Breast Cancer	II	Dompe Farmaceutici	Reparixin/H Y-15251	CXCR2		Open	Feb-13	NCT01861054
Phase IB Study of FOLFIRINOX Plus PF-04136309 in Patients With Borderline Resectable and Locally Advanced Pancreatic Adenocarcinoma	Pancreatic Neoplasms	IB	Washington University School of Medicine / NCI	PF-04136309	CCR2	FOLFIRINOX (Oxaliplatin, Irinotecan, Leucovorin, Fluorouracil)	Open	Apr-12	NCT01413022

Phase 1 Study to Determine the Immunomodulatory Activity of LY2157299 Monohydrate in Patients With Solid Tumors	Neoplasm	I	Eli Lilly and Company	LY2157299 **	ALK5 inhibitor		Open	Dec-14	NCT02304419
First-in-Human Dose-Escalation Study of TEW-7197 Monotherapy in Subjects With Advanced Stage Solid Tumors	Advanced Stage Solid Tumors	I	MedPacto, Inc./ National OncoVenture	EW-7179	ALK5 inhibitor		Open	Jun-14	NCT02160106
An Open Label Phase 1b/2 Study of Orally Administered PLX3397 in Combination With Radiation Therapy and Temozolomide in Patients With Newly Diagnosed Glioblastoma	Newly Diagnosed Glioblastoma	IB/II	Plexxikon	PLX3397§	CSF-1 inhibitor	Radiation Therapy Temozolomide	Open	Aug-13	NCT01790503

In the selection of agents included in this table we have endeavored to select those clinical trials for which the drug is being evaluated for its ability to stimulate the immune response or reverse immune tolerance to treat malignancies. For trials which do not appear criteria or for which the agent is being employed as an adjuvant in a vaccine, we have chosen to list the additional trial numbers at the end of the table.

\* Only the largest two trials are listed for VTX-2337. There are 5 additional smaller trials listed for VTX-2337 in [clinicaltrials.gov](http://clinicaltrials.gov)- NCT01334177, NCT01289210, NCT00688415, NCT01294293, NCT02124850

† Listed for IMO-2055 (HYB2055, EMD1201081). There are 2 additional smaller trials listed for IMO-2055 in [clinicaltrials.gov](http://clinicaltrials.gov) (NCT00719199, NCT01360827) and two publications of early trial results, Hwang, 2004 and Sullivan, 2004.

‡ Listed is a Phase II trial by Pfizer for 852A. There are 5 additional trials listed for 852A in [clinicaltrials.gov](http://clinicaltrials.gov)- NCT00276159, NCT00319748, NCT00095160, NCT00386594, NCT00091689

§ Trial listed for PLX3397 in GBM with in line with data from Pyontek, 2013. There are 10 additional cancer trials listed for PLX3397 in [clinicaltrials.gov](http://clinicaltrials.gov)- NCT01525602, NCT02071940, NCT01596751, NCT01499043, NCT01826448, NCT01349049, NCT01090570, NCT01349036, NCT01217229, NCT01004861

\*\* There are 12 additional trials listed for LY2157299 in [clinicaltrials.gov](http://clinicaltrials.gov) - NCT02240433, NCT02154646, NCT01965808, NCT01746004, - NCT01722825, NCT02178358, NCT02008318, NCT01246986, NCT01220271, NCT01582269, NCT01373164, NCT01682187.

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