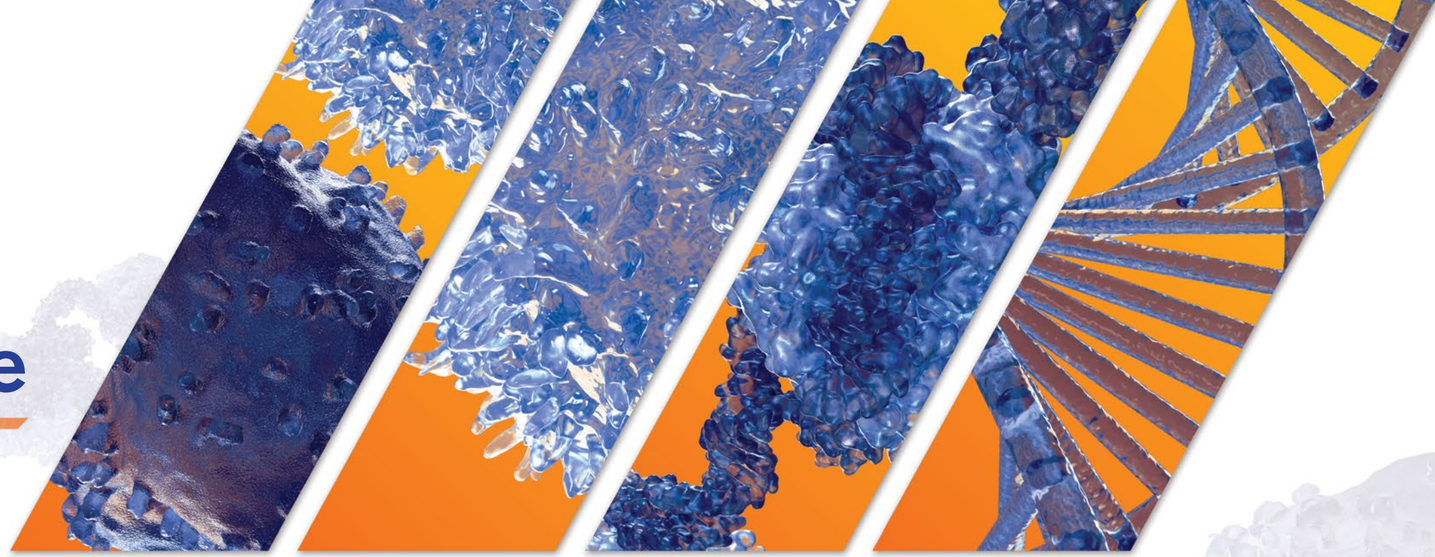
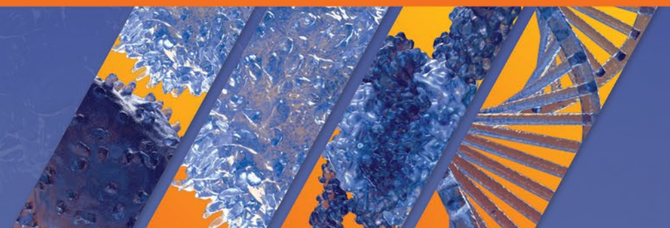
GSK oncology pipeline

Driving toward transformative medicine





This brochure is designed to foster collaboration with the research community by highlighting study molecules in our GSK oncology pipeline. This brochure includes ongoing clinical trials for both approved and investigational compounds. Some agents are approved in select indications. Inclusion in this brochure does not imply regulatory approval for these compounds or all indications. For more information on GSK compounds currently in clinical trials, please go to www.clinicaltrials.gov.

Our approach

AXEL HOOS, MD, PhD
SVP, Therapeutic Area Head, Oncology R&D

PATIENT-DRIVEN SCIENCE. TRAILBLAZING RESEARCH.

GSK oncology is committed to the discovery and development of new oncology compounds that leverage patient-driven science to deliver improved outcomes for more patients.

We have prioritized our research efforts into four key areas that we believe offer the greatest potential for transformational medicines that can help patients diagnosed with cancer.

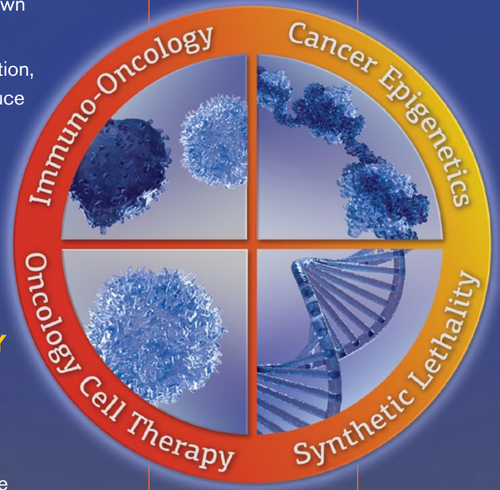
SEEKING ANSWERS TO SOME OF THE MOST CHALLENGING QUESTIONS IN CANCER RESEARCH

IMMUNO-ONCOLOGY

- How can we harness the body's own immune system to attack cancer?
- Which drugs, alone or in combination, have the greatest potential to reduce treatment resistance and provide the most durable response?

ONCOLOGY CELL THERAPY

- Can a patient's own immune cells be modified with redirected specificity to treat their cancer?
- Which targeted receptors have the most potential impact on tumor cells?



CANCER EPIGENETICS

- How can we target specific epigenetic pathways to treat cancer?
- What epigenetic changes drive cancer development and progression?

SYNTHETIC LETHALITY

- Which pathways are required for detection, repair, and bypass of DNA damage in cancer cells?
- How can we interfere with maladaptive DNA repair processes to inhibit tumor growth?

Immuno-Oncology

HARNESSING THE BODY'S IMMUNE SYSTEM

The growing understanding of tumor cells' ability to evade immune surveillance has led to advances in the field of immuno-oncology.[1] Malignant cells manipulate a variety of physiological mechanisms involved in antigenicity, immune activation, T-cell priming and recruitment, and upregulation of checkpoint molecules.[1] Many of these mechanisms may be impacted simultaneously to promote tumor cell survival.[1] Immunotherapies harness the body's own immune system to fight cancer by using different immunological pathways to enhance antitumor responses.[1,2] GSK is exploring different clinical assets aimed at augmenting the immune response, reducing immune suppression, and modulating the tumor microenvironment.[3,4]

IN CLINICAL DEVELOPMENT

Belantamab mafodotin-blmf | anti-BCMA antibody-drug conjugate*

Belantamab mafodotin-blmf is an antibody-drug conjugate (ADC). The antibody component is an afucosylated immunoglobulin G1 (IgG1) directed against B-cell maturation antigen (BCMA), a protein expressed on normal B lymphocytes and multiple myeloma cells. The small molecule component is monomethyl auristatin F (MMAF), a microtubule inhibitor. Upon binding to BCMA, belantamab mafodotin-blmf is internalized followed by release of MMAF via proteolytic cleavage. The released MMAF intracellularly disrupts the microtubule network, leading to cell cycle arrest and apoptosis.[5]

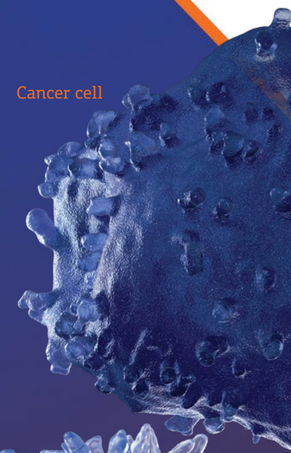
Belantamab mafodotin-blmf had antitumor activity in multiple myeloma cells and mediated killing of tumor cells through MMAF-induced apoptosis, as well as by tumor cell lysis through antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP).[5]

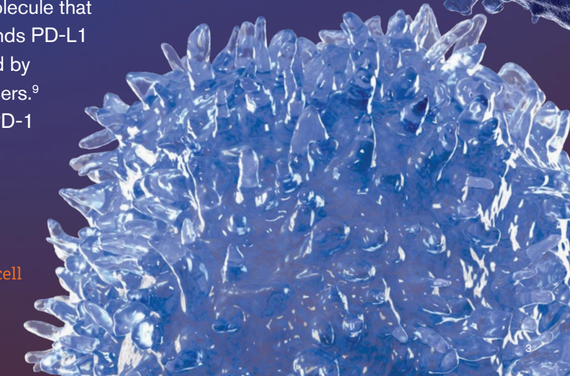
GSK3174998 | OX40 agonist antibody*

Tumor necrosis factor receptor superfamily, member 4 (OX40 [CD134]) is expressed by T cells during antigen-specific priming.[6] GSK3174998 is a humanized IgG1 OX40 agonist antibody that can enhance the proliferation and survival of CD4+ and CD8+ T cells and deplete tumor-infiltrating regulatory T cells via antibody-dependent cell cytotoxicity or phagocytosis.[6,7] GSK3174998 is being investigated in combination with other anticancer agents in multiple tumor types.[8]

Dostarlimab | anti–PD-1 antibody

Programmed cell death protein 1 (PD-1) is an immune checkpoint molecule that interacts with the PD-1 ligands PD-L1 and PD-L2 to limit T-cell–mediated immune responses.[9] PD-L1 is expressed by many tumor types and is linked to poor clinical outcomes in a variety of cancers.[9] Dostarlimab is a humanized anti–PD-1 mAb that binds with high affinity to PD-1 and effectively blocks interactions with PD-L1 and PD-L2.[8] Dostarlimab is being investigated as a monotherapy in DNA mismatch repair–deficient cancers, including endometrial cancer, and in unselected populations in combination with other therapies.[8]





*In-license or other partnership with third party.
Belantamab mafodotin-blmf is being investigated in various multiple myeloma settings.

Please see pages 9-11 for ongoing clinical studies.

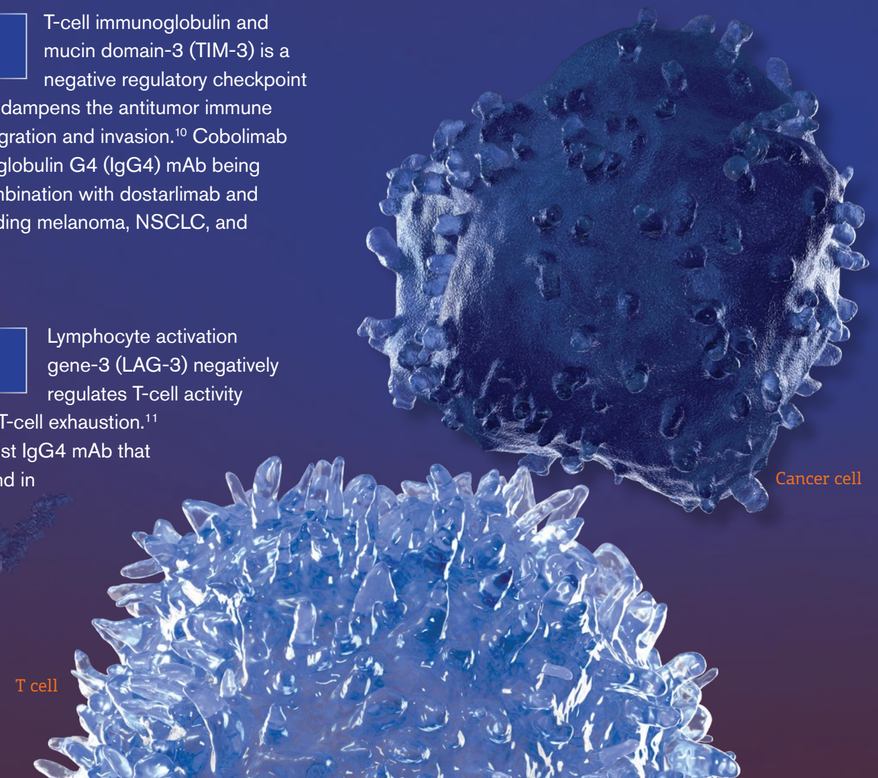
Immuno-Oncology (cont'd)

Cobolimab | TIM-3 antagonist antibody

T-cell immunoglobulin and mucin domain-3 (TIM-3) is a negative regulatory checkpoint molecule that regulates T-cell exhaustion, dampens the antitumor immune response, and may promote tumor cell migration and invasion.[10] Cobolimab is a humanized TIM-3 antagonist immunoglobulin G4 (IgG4) mAb being investigated as a monotherapy and in combination with dostarlimab and TSR-033 in advanced solid tumors, including melanoma, NSCLC, and colorectal cancer.[8]

TSR-033 | LAG-3 antagonist IgG4 antibody

Lymphocyte activation gene-3 (LAG-3) negatively regulates T-cell activity and, in combination with PD-1, mediates T-cell exhaustion.[11] TSR-033 is a humanized LAG-3 antagonist IgG4 mAb that is being investigated as a monotherapy and in combination with anti–PD-1 therapy in advanced solid tumors.[8]



GSK3745417 | STING agonist

Stimulator of interferon genes (STING) is a key adapter molecule that mediates sensing of cytosolic DNA and activates T-cell–dependent tumor immunity.[12] GSK3745417 is a synthetic STING agonist that is being investigated as a monotherapy and in combination with pembrolizumab in relapsed/refractory solid tumors.[8]

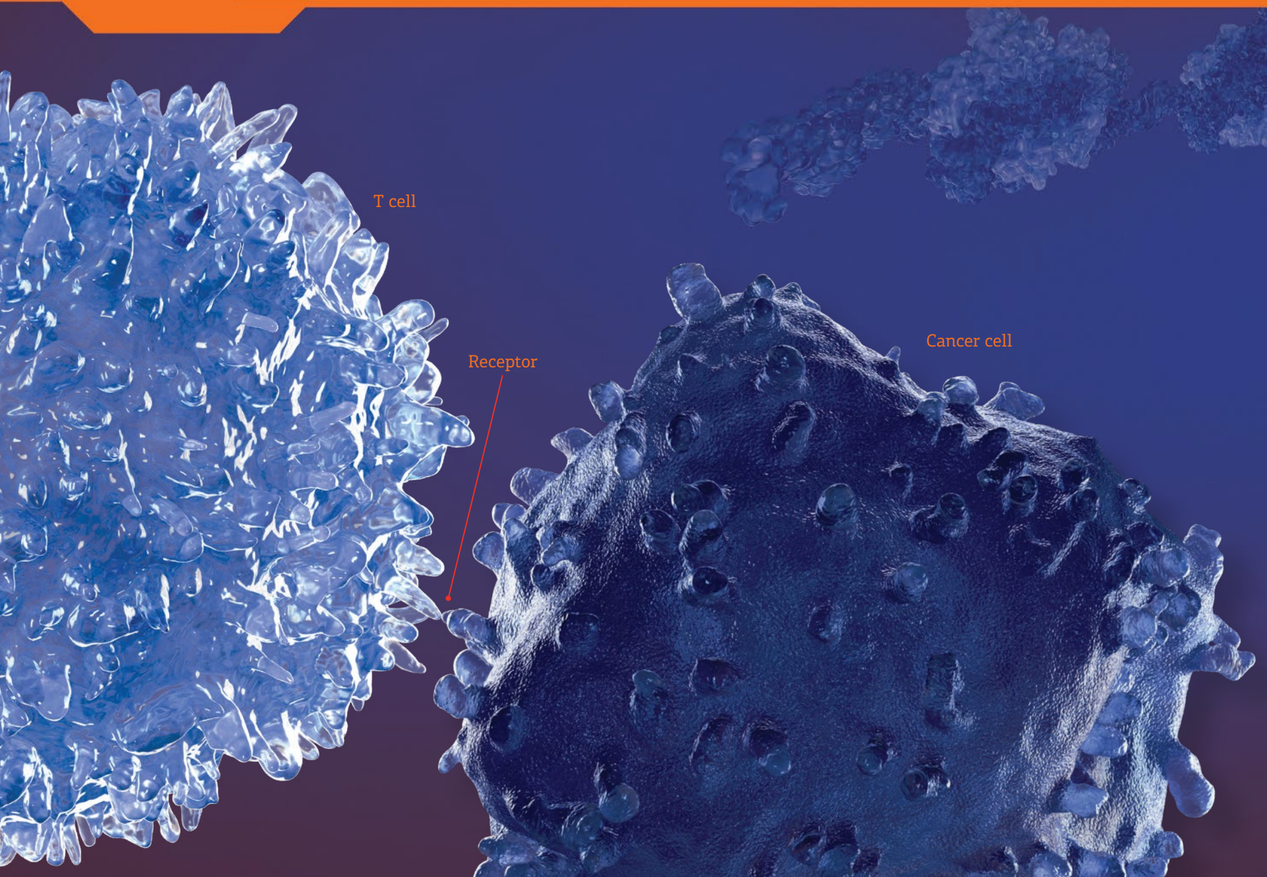
Feladilimab | ICOS agonist IgG4 antibody*

Activation of inducible T-cell costimulator (ICOS) supports proliferation and functional activity of effector T cells and expands memory T-cell populations, which promote durable anti-tumor responses.[13] Feladilimab is an IgG4 ICOS agonist antibody that is designed to enhance T-cell function and enable antitumor responses without depletion of ICOS-expressing cells.[14,15] Feladilimab is being actively evaluated in a number of clinical trials in solid tumors, including head and neck squamous cell carcinoma and NSCLC, both as monotherapy and in combination with currently available immunomodulatory agents and anticancer therapies.[8]

*In-license or other partnership with third party.

Please see pages 9-11 for ongoing clinical studies.

Immuno-Oncology (cont'd)



Bintrafusp alfa | bifunctional TGF-β "trap"/anti–PD-L1 fusion protein*

Bintrafusp alfa is a bifunctional fusion protein composed of the extracellular domain of the human transforming growth factor β receptor II (TGF-βRII or TGF-β "trap") fused via a flexible linker to the C-terminus of each heavy chain of an IgG1 antibody blocking PD-L1. Bintrafusp alfa is designed to allow for targeting tumor cells via two nonredundant immunostimulatory mechanisms—the TGF-β and PD-L1 pathways.[4,16] It is being investigated as monotherapy and in combination with other anticancer agents in various malignancies.[8]

NY-ESO-ImmTAC® (IMCnyeso)†

New York esophageal squamous cell carcinoma 1 (NY-ESO-1) and cancer-testis antigen 2 (LAGE-1a) are immunogenic cancer-testis antigens that can elicit humoral and cellular immune responses in cancer patients.[17,18] NY-ESO-1 and LAGE-1a are widely expressed in diverse tumor types, with restricted expression in normal tissues.[17] NY-ESO-ImmTAC (immune mobilizing monoclonal TCR against cancer [IMCnyeso]) is a bifunctional soluble high-affinity T-cell receptor (TCR) specific for NY-ESO-1 that also engages the CD3 receptor on T cells.[19] It is being studied as a monotherapy in advanced NY-ESO-1– and/or LAGE-1a–positive cancers.[8]

GSK6097608 | anti-CD96 antibody‡

CD96 is an immune checkpoint protein expressed on T cells and natural killer (NK) cells in multiple tumor types. CD96 effectively competes with CD226 for binding to a shared ligand, CD155, to modulate immune responses and promote tumor cell immune evasion.[20-22] GSK6097608 inhibits the binding of CD96 to CD155 and activates T cells and NK cells, which enhances antitumor activity.[20,22] GSK6097608 is a first-in-class anti-CD96 IgG1 monoclonal antibody being investigated as a monotherapy and in combination with dostarlimab (anti–PD-1 antibody) in advanced solid tumors.[8]

*Being developed in a strategic global alliance between GSK and Merck KGaA, Darmstadt, Germany.
†Option-based alliance with Immunocore Ltd. ImmTAC is a registered trademark of Immunocore Ltd.
‡In collaboration with 23andMe.

Please see pages 9-11 for ongoing clinical studies.

Oncology Cell Therapy

T cell

ENGINEERING IMMUNE CELLS TO TARGET CANCER

The physiologic role of central and peripheral tolerance mechanisms is to limit unchecked immune responses that can lead to autoimmunity.[23] In cancer, these mechanisms are major limitations to effective T cell–mediated antitumor immunity.[23] T-cell immunotherapy that uses autologous genetically modified T cells may mediate improved antitumor effects. T cells are isolated from the patient, modified to express a TCR with greater affinity for a specific cancer antigen—alone or in combination with other modifications to T-cell function—and then reintroduced into the patient.[23,24] This innovative approach generates T cells that may be more efficient at recognizing cancer cells and overcoming the barriers of tolerance mechanisms.[24] GSK is developing a platform of investigational TCR T-cell immunotherapies designed to target a tumor-specific antigen and eliminate malignant cells in solid tumors and hematologic malignancies.[8]

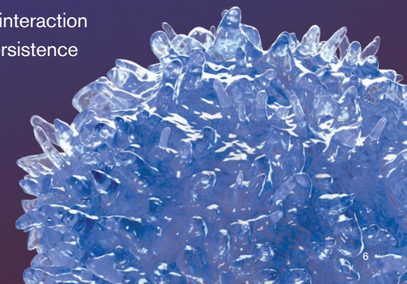
IN CLINICAL DEVELOPMENT

Letetresgene autoleucel | NY-ESO-1 TCR T cell*

NY-ESO-1 and LAGE-1a are homologous highly immunogenic cancer-testis antigens that can elicit humoral and cellular immune responses in cancer patients.[17,18] NY-ESO-1 and LAGE-1a are expressed in a wide range of tumor types, with restricted expression in normal tissues.[17] Letetresgene autoleucel (lete-cel; GSK3377794) is a genetically modified autologous T cell that expresses a TCR with greater affinity for NY-ESO-1.[17] Lete-cel is being investigated as a monotherapy and in combination with pembrolizumab in NY-ESO-1– and/or LAGE-1a–positive solid tumors, including NSCLC and synovial sarcoma.[8]

GSK3901961 and GSK3845097 | NY-ESO-1 TCR T cells

GSK3901961 incorporates the expression of the CD8α chain to induce stabilization of TCR-HLA class I interaction on CD4+ T cells to enhance proliferation and persistence of TCR T cells, increase helper functions including the Type 1 T-helper antitumor response, and potentially enhance activity of tumor-specific effector cells.[25,26] GSK3845097 further genetically modifies autologous NY-ESO-1–targeted TCR T cells by incorporating the expression of the dnTGF-βRII chain, which makes T cells resistant to the inhibitory signaling of TGF-β.[26,27]



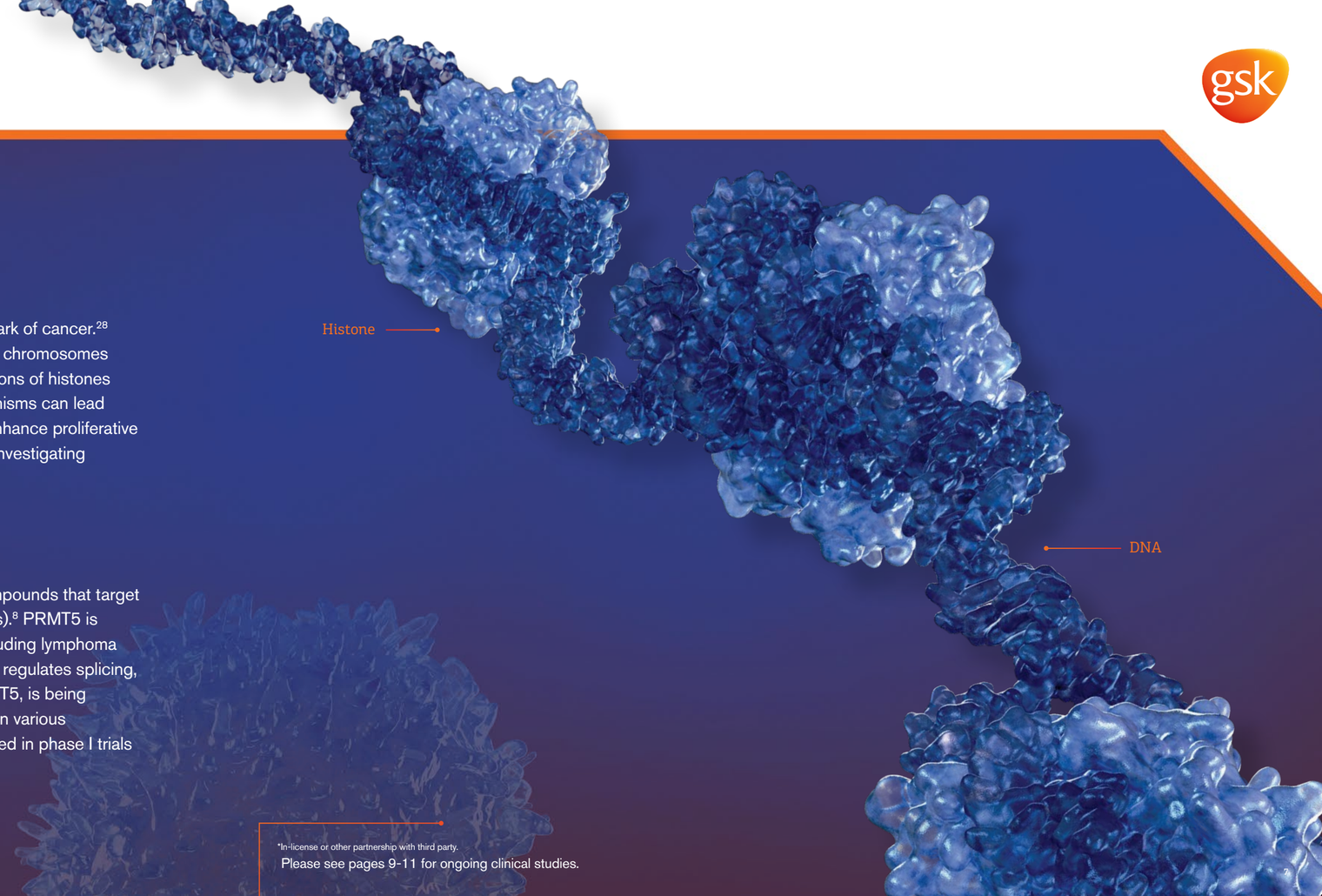
*In-license or other partnership with third party.

Please see pages 9-11 for ongoing clinical studies.

Cancer Epigenetics

ADDRESSING A HALLMARK OF CANCER

Aberrant gene expression, regulated in large part by epigenetic mechanisms, is a hallmark of cancer.[28] "Epigenetics" refers to heritable changes in gene expression that arise from changes in chromosomes without altering the DNA sequence.[29] DNA methylation and posttranslational modifications of histones play key roles in regulating gene expression.[28] Deregulation of these epigenetic mechanisms can lead to aberrant expression of oncogenes and tumor suppressors in cancer cells that can enhance proliferative signals, impair cell death, promote angiogenesis, and facilitate metastasis.[28,29] GSK is investigating compounds that work by altering these epigenetic pathways.[8]



IN CLINICAL DEVELOPMENT

GSK3326595 | PRMT5 inhibitor* and GSK3368715 | Type 1 PRMT inhibitor*

GSK is investigating the activity of two compounds that target protein arginine methyltransferases (PRMTs).[8] PRMT5 is overexpressed in multiple tumor types, including lymphoma and breast, lung, and bladder cancers, and regulates splicing, gene expression, and activation of p53.[30,31] GSK3326595, a selective inhibitor of PRMT5, is being investigated as a monotherapy in solid tumors and in combination with other therapies in various hematologic malignancies.[8] GSK3368715, a type 1 PRMT inhibitor, is being investigated in phase I trials for patients with diffuse large B-cell lymphoma and solid tumors.[8,32]

*In-license or other partnership with third party.

Please see pages 9-11 for ongoing clinical studies.

Synthetic Lethality

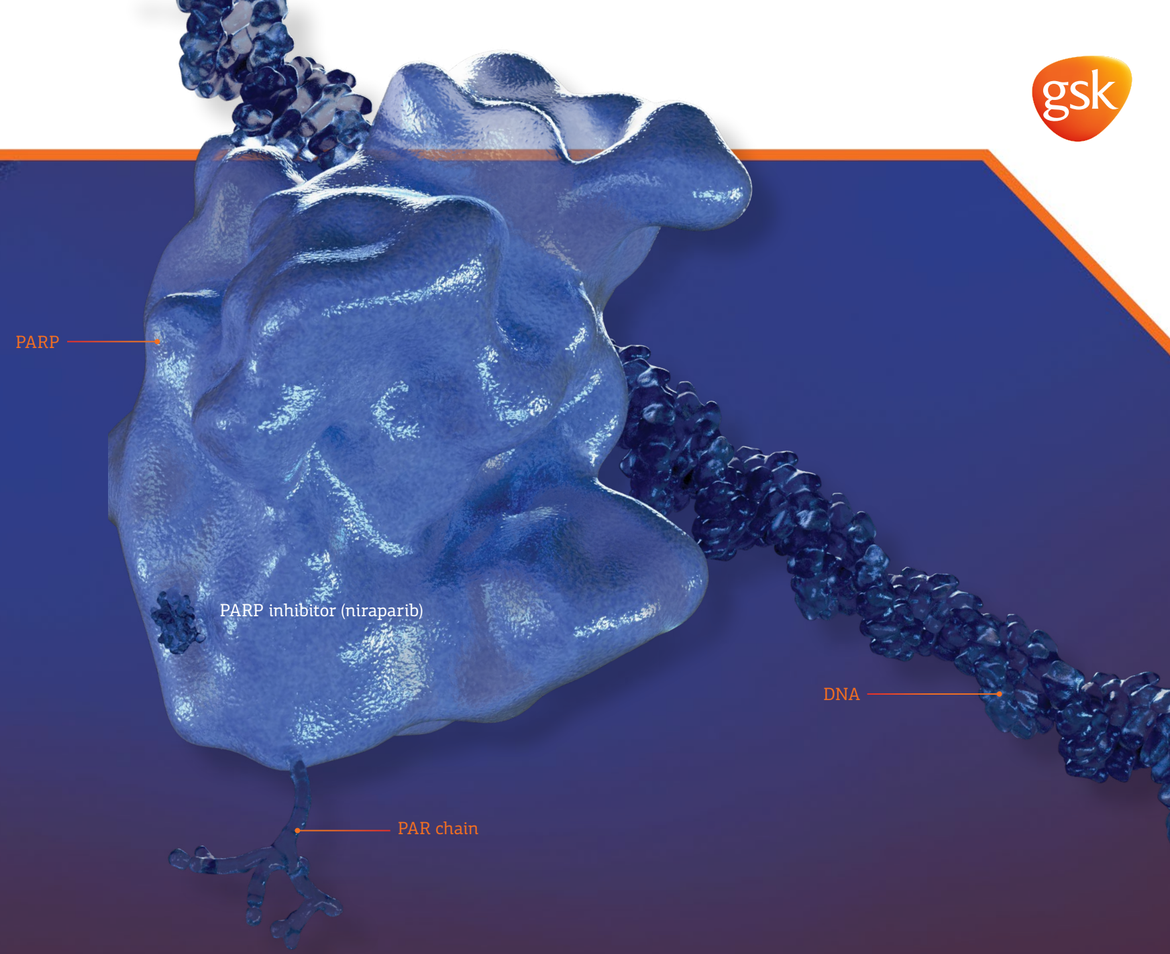
INHIBITING PATHWAYS THAT CONTRIBUTE TO ABERRANT DNA REPAIR

Accumulation of DNA damage and genomic instability are pervasive characteristics of human tumors and are caused by defects in DNA repair.[33,34] Deficiencies in essential DNA damage repair in cancer cells may increase dependency on an alternate repair pathway for cell survival.[34] Synthetically lethal therapies aim to combine pharmacologic inhibition of these alternate repair pathways with inherent defects in DNA damage repair to selectively kill tumor cells while sparing healthy tissue.[34-36] GSK is investigating a clinical asset that utilizes the power of synthetically lethal interactions to fight malignant cells in a variety of cancers.[8]

IN CLINICAL DEVELOPMENT

Niraparib | PARP inhibitor

Poly ADP ribose polymerases (PARPs) are a family of enzymes involved in many functions, including DNA repair, gene expression, cellular signaling, and base excision repairs. PARP inhibition induces cell death through synthetic lethality.[37] Niraparib is a selective PARP1/2 inhibitor being investigated as a monotherapy and in combination with other anticancer agents, including dostarlimab, in breast cancer, ovarian cancer, and advanced NSCLC.[8,38,39]



Please see pages 9-11 for ongoing clinical studies.

GSK-sponsored clinical trials

IMMUNO-ONCOLOGY

		PHASE
Anti-BCMA antibody-drug conjugate belantamab mafodotin-blmf*	DREAMM-3: relapsed/refractory multiple myeloma alone vs pomalidomide/dexamethasone	III
	DREAMM-7: relapsed/refractory multiple myeloma in combination with bortezomib and dexamethasone vs daratumumab/bortezomib/dexamethasone	III
	DREAMM-8: relapsed/refractory multiple myeloma in combination with pomalidomide and dexamethasone vs pomalidomide/bortezomib/dexamethasone	III
	NCT04549363: companion study of belantamab mafodotin-blmf	III†
	DREAMM-4: relapsed/refractory multiple myeloma in combination with pembrolizumab	I/II
	DREAMM-5: relapsed/refractory multiple myeloma alone and in combination with GSK3174998 (OX40 agonist antibody) or feladilimab (ICOS agonist IgG4 antibody)	I/II
	DREAMM-6: relapsed/refractory multiple myeloma in combination with lenalidomide plus dexamethasone or in combination with bortezomib plus dexamethasone	I/II
	NCT03828292: relapsed/refractory multiple myeloma in Japanese patients	I
	NCT04177823: relapsed/refractory multiple myeloma in Chinese patients	I
	DREAMM-9: newly diagnosed multiple myeloma in combination with bortezomib, lenalidomide, and dexamethasone	I
	DREAMM-12: relapsed/refractory multiple myeloma in normal or varying degrees of impaired renal function	I
	DREAMM-13: relapsed/refractory multiple myeloma in normal or varying degrees of impaired hepatic function	I†
	NCT03763370: US expanded access program in relapsed/refractory multiple myeloma	N/A

		PHASE
Anti–PD-1 antibody dostarlimab	RUBY: recurrent or primary advanced endometrial cancer (EC) in combination with chemotherapy	III
	NCT04581824: metastatic nonsquamous NSCLC in combination with chemotherapy	II†
	GARNET: mismatch repair deficient (dMMR)/microsatellite instability high (MSI-H) non-EC solid tumors, EC,‡ ovarian cancer, and non-small cell lung cancer (NSCLC)	I
	IOLite: advanced NSCLC and solid tumors in combination with niraparib (PARP inhibitor), cobolimab (TIM-3 antagonist antibody), bevacizumab, and/or platinum-based doublet chemotherapy	I
ICOS agonist IgG4 antibody feladilimab*	INDUCE-3: recurrent/metastatic head and neck squamous cell carcinoma (HNSCC) in combination with pembrolizumab	II/III
	INDUCE-4: recurrent/metastatic HNSCC in combination with pembrolizumab and 5-FU platinum chemotherapy	II/III
	ENTRÉE-Lung: advanced NSCLC in combination with docetaxel	II
	INDUCE-2: advanced solid tumors in combination with tremelimumab	I/II
	INDUCE-1: advanced solid tumors alone and in combination with pembrolizumab, chemotherapy, or GSK3174998	I
TIM-3 antagonist antibody cobolimab	AMBER: melanoma, NSCLC, and colorectal cancer alone and in combination with dostarlimab (anti–PD-1 antibody)	I
LAG-3 antagonist IgG4 antibody TSR-033	CITRINO: advanced solid tumors alone and in combination with dostarlimab	I

Pivotal trials.

5-FU, 5-fluorouracil; BCMA, B-cell maturation antigen; ICOS, inducible T-cell costimulator; IgG4, immunoglobulin G4; LAG-3, lymphocyte activation gene-3; N/A, not applicable; OX40, tumor necrosis factor receptor superfamily, member 4; PARP, poly ADP ribose polymerase; PD-1, programmed cell death protein 1; TIM-3, T-cell immunoglobulin and mucin domain-3.

This information is intended for healthcare professionals only. This brochure includes ongoing clinical trials for both approved and investigational compounds. Some agents are approved in select indications. Inclusion in this brochure does not imply regulatory approval for these compounds or all indications. Information about all GSK-sponsored trials can be found at www.clinicaltrials.gov.

*In-license or other partnership with third party.
†Not yet recruiting as of October 29, 2020.
‡The trial is no longer enrolling patients with endometrial cancer.

GSK-sponsored clinical trials (cont'd)

IMMUNO-ONCOLOGY

		PHASE
Bifunctional TGF-β "trap"/ anti–PD-L1 fusion protein Bintrafusp alfa*	INTR@PID SOLID TUMOR 001: locally advanced/metastatic solid tumors	I
	INTR@PID SOLID TUMOR 008: locally advanced/metastatic solid tumors	I
	INTR@PID LUNG 037: first-line treatment in stage IV, PD-L1–high NSCLC	III
	INTR@PID BTC 047: second-line locally advanced/metastatic biliary tract cancer (BTC)	II
	INTR@PID LUNG 005: unresectable stage III NSCLC in combination with concurrent chemoradiation therapy	II
	INTR@PID LUNG 024: stage IV NSCLC in combination with chemotherapy	I/II
	INTR@PID BTC 055: first-line treatment in combination with gemcitabine plus cisplatin in locally advanced/metastatic BTC	II/III
	INTR@PID CERVICAL 017: advanced, unresectable cervical cancer that progressed during or after platinum-containing chemotherapy	II
	INTR@PID UROTHELIAL 152: locally advanced/metastatic urothelial cancer that progressed or recurred after platinum-containing chemotherapy	I‡
	INTR@PID BREAST 020: TNBC with high levels of HMGA2 that progressed on at least one line of systemic therapy	II†
	INTR@PID CERVICAL 046: locally advanced or advanced cervical cancer in combination with other anticancer therapies	I†

		PHASE
STING agonist GSK3745417	NCT03843359: advanced solid tumors alone and in combination with pembrolizumab	I
NY-ESO-ImmTAC* IMCnyeso§	NCT03515551: advanced NY-ESO-1– and/or LAGE-1a–positive solid tumors	I/II
Anti-CD96 antibody GSK6097608‖	NCT04446351: advanced solid tumors alone and in combination with dostarlimab	I

CD96, cluster of differentiation 96; HMGA2, high-mobility group AT-hook 2; ImmTAC, immune mobilizing monoclonal TCR against cancer; LAGE-1a, cancer-testis antigen 2; NSCLC, non-small cell lung cancer; NY-ESO-1, New York esophageal squamous cell carcinoma 1; PD-L1, programmed cell death ligand 1; STING, stimulator of interferon genes; TCR, T-cell receptor; TGF-β, transforming growth factor β; TNBC, triple-negative breast cancer.

This information is intended for healthcare professionals only. This brochure includes ongoing clinical trials for both approved and investigational compounds. Some agents are approved in select indications. Inclusion in this brochure does not imply regulatory approval for these compounds or all indications. Information about all GSK-sponsored trials can be found at www.clinicaltrials.gov.

Bintrafusp alfa is under clinical investigation and has not been proven to be safe and effective. There is no guarantee that bintrafusp alfa will be approved in the sought-after indication by any health authority worldwide.

*Being developed in a strategic global alliance between GSK and Merck KGaA, Darmstadt, Germany.
†Not yet recruiting as of October 29, 2020.
‡GSK identifier: 213152.
§Option-based alliance with Immunocore Ltd. ImmTAC is a registered trademark of Immunocore Ltd.
‖In collaboration with 23andMe.

GSK-sponsored clinical trials (cont'd)

ONCOLOGY CELL THERAPY

		PHASE
NY-ESO-1 TCR T cell letetresgene autoleucel*	IGNYTE-ESO: master protocol–advanced NY-ESO-1– and/or LAGE-1a–positive synovial sarcoma and solid tumors	II
	NCT03168438: relapsed/refractory NY-ESO-1– and/or LAGE-1a–positive multiple myeloma alone and in combination with pembrolizumab	II
	NCT02992743: advanced myxoid/round cell liposarcoma	II
	NCT03709706: advanced NY-ESO-1– and/or LAGE-1a–positive NSCLC alone and in combination with pembrolizumab	I/II
	NCT03391778: long-term follow-up from previous letetresgene autoleucel studies	I
NY-ESO-1 TCR T cell GSK3901961	NCT04526509: master protocol–GSK3901961 and GSK3845097 alone and in combination with other anticancer agents in NY-ESO-1–positive advanced tumors	I†
NY-ESO-1 TCR T cell GSK3845097	NCT04526509: master protocol–GSK3901961 and GSK3845097 alone and in combination with other anticancer agents in NY-ESO-1–positive advanced tumors	I†

CANCER EPIGENETICS

		PHASE
PRMT5 inhibitor GSK3326595*	NCT03614728: relapsed/refractory myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), and chronic myelomonocytic leukemia (CMML)	I/II
	METEOR-1: solid tumors and non-Hodgkin's lymphoma (NHL)	I
Type 1 PRMT inhibitor GSK3368715*	NCT03666988: relapsed/refractory solid tumors and diffuse large B-cell lymphoma (DLBCL)	I

SYNTHETIC LETHALITY

		PHASE
PARP inhibitor niraparib	FIRST†: ovarian cancer maintenance in combination with or without dostarlimab and bevacizumab following first-line treatment with platinum-based chemotherapy with or without dostarlimab and bevacizumab	III
	ZEAL-1L: NSCLC maintenance in combination with pembrolizumab vs pembrolizumab and placebo following first-line treatment with platinum-based chemotherapy and pembrolizumab	III†
	OVARIO: ovarian cancer first-line maintenance in combination with bevacizumab following response on front-line platinum-based chemotherapy plus bevacizumab	II
	OPAL: platinum-resistant ovarian cancer treatment in combination with dostarlimab and bevacizumab	II
	MOONSTONE: platinum-resistant ovarian cancer treatment in combination with dostarlimab	II§
	NCT04544995: dose-escalation and cohort-expansion study of niraparib and dostarlimab in pediatric participants with solid tumors	I†
	NCT03359850: pharmacokinetics and safety in advanced solid tumors with normal hepatic function or moderate hepatic impairment	I
	NCT03329001: crossover bioavailability study of niraparib tablet compared to niraparib capsule in advanced solid tumors	I

Pivotal trials.

1L, first line; LAGE-1a, cancer-testis antigen 2; NSCLC, non-small cell lung cancer; NY-ESO-1, New York esophageal squamous cell carcinoma 1; PARP, poly ADP ribose polymerase; PRMT, protein arginine methyltransferase; PRMT5, protein arginine methyltransferase 5; TCR, T-cell receptor.

This information is for healthcare professionals only. This brochure includes ongoing clinical trials for both approved and investigational compounds. Some agents are approved in select indications. Inclusion in this brochure does not imply regulatory approval for these compounds or all indications. Information about GSK-sponsored trials can be found at www.clinicaltrials.gov.

*In-license or other partnership with third party.
†Not yet recruiting as of October 29, 2020.
‡In collaboration with ENGOT, the European Network for Gynaecological Oncological Trial groups.
§This study has temporarily suspended recruitment activities.

Our partnerships

WE WELCOME COLLABORATION

If you are interested in collaborating with GSK on our investigational agents in hematologic malignancies and solid tumors, please contact us by visiting https://iss.gsk.com.

JOIN OUR WORLD-CLASS COLLABORATIVE TEAMS AS WE FOCUS ON FOUR KEY AREAS OF ONCOLOGY RESEARCH

IMMUNO-ONCOLOGY
ONCOLOGY CELL THERAPY
CANCER EPIGENETICS
SYNTHETIC LETHALITY

This fourfold strategy has helped us develop a diverse pipeline of innovative agents with the transformational potential of becoming the next breakthrough therapies in the treatment of cancer. Together, we can make a difference.

"GSK oncology is committed to discovering and developing new medicines for patients with cancer. Join us."

TANIA SMALL, MD
VP, Global Medical Oncology Franchise Head

References

1. Allard B, Aspeslagh S, Garaud S, et al. Immuno-oncology-101: overview of major concepts and translational perspectives. *Semin Cancer Biol*. 2018;52(pt 2):1-11. doi:10.1016/j.semcancer.2018.02.005.
2. PhRMA. Medicines in development for immuno-oncology 2017 report. https://www.phrma.org/medicines-in-development-immuno-oncology. Accessed January 30, 2019.
3. Tai Y-T, Anderson KC. Targeting B-cell maturation antigen in multiple myeloma. *Immunotherapy*. 2015;7(11):1187-1199.
4. Knudson KM, Hicks KC, Luo X, Chen J-Q, Schlom J, Gameiro SR. M7824, a novel bifunctional anti-PD-L1/TGF trap fusion protein, promotes anti-tumor efficacy as monotherapy and in combination with vaccine. *Oncoimmunology*. 2018;7(5):e1426519. doi:10.1080/2162402X.2018.1426519.
5. BLENREP [package insert]. Research Triangle Park, NC: GlaxoSmithKline; 2020.
6. Linch SN, McNamara MJ, Redmond WL. OX40 agonists and combination immunotherapy: putting the pedal to the metal. *Front Oncol*. 2015;5:34. doi:10.3389/fonc.2015.00034.
7. Aspeslagh S, Postel-Vinay S, Rusakiewicz S, Soria JC, Zitvogel L, Marabelle A. Rationale for anti-OX40 cancer immunotherapy. *Eur J Cancer*. 2016;52:50-66.
8. ClinicalTrials.gov. https://clinicaltrials.gov/. Accessed October 29, 2020.
9. Dyck L, Mills KHG. Immune checkpoints and their inhibition in cancer and infectious diseases. *Eur J Immunol*. 2017;47(5):765-779.
10. Das M, Zhu C, Kuchroo VK. Tim-3 and its role in regulating anti-tumor immunity. *Immunol Rev*. 2017;276(1):97-111.
11. Andrews LP, Marciscano AE, Drake CG, Vignali DAA. LAG3 (CD223) as a cancer immunotherapy target. *Immunol Rev*. 2017;276(1):80-96.
12. Corrales L, McWhirter SM, Dubensky TW Jr, Gajewski TF. The host STING pathway at the interface of cancer and immunity. *J Clin Invest*. 2016;126(7):2404-2411.
13. Amatore F, Gorvel L, Olive D. Inducible Co-Stimulator (ICOS) as a potential therapeutic target for anti-cancer therapy. *Expert Opin Ther Targets*. 2018;22(4):343-351.
14. Angevin E, Barnette MS, Bauer TM, et al. INDUCE-1: a phase I open-label study of GSK3359609, an ICOS agonist antibody, administered alone and in combination with pembrolizumab in patients with advanced solid tumors. *J Clin Oncol*. 2017;35(15)(suppl). doi:10.1200/JCO.2017.35.15_suppl.TPS3113.
15. Brett S, Yadavilli S, Seestaller-Wehr L, et al. Nonclinical evaluation of a non-depleting, first-in-class humanized IgG4 agonist anti-ICOS antibody. Poster presented at: The European Society for Medical Oncology Annual Congress; October 19-23, 2018; Munich, Germany: Poster 1840P.
16. Lan Y, Zhang D, Xu C, et al. Enhanced preclinical antitumor activity of M7824, a bifunctional fusion protein simultaneously targeting PD-L1 and TGF-ß. *Sci Transl Med*. 2018;10(424):eaan5488. doi:10.1126/scitranslmed.aan5488.
17. Thomas R, Al-Khadairi G, Roelands J, et al. NY-ESO-1 based immunotherapy of cancer: current perspectives. *Front Immunol*. 2018;9:947. doi:10.3389/fimmu.2018.00947.
18. Rapoport AP, Stadtmauer EA, Binder-Scholl GK, et al. NY-ESO-1–specific TCR–engineered T cells mediate sustained antigen-specific antitumor effects in myeloma. *Nat Med*. 2015;21(8):914-921.
19. McCormack E, Adams KJ, Hassan NJ, et al. Bi-specific TCR-anti CD3 redirected T-cell targeting of NY-ESO-1- and LAGE-1-positive tumors. *Cancer Immunol Immunother*. 2013;62(4):773-785.
20. Blake SJ, Stannard K, Liu J, et al. Suppression of metastases using a new lymphocyte checkpoint target for cancer immunotherapy. *Cancer Discov*. 2016;6(4):446-459.
21. Georgiev H, Ravens I, Papadogianni G, Bernhardt G. Coming of age: CD96 emerges as modulator of immune responses. *Front Immunol*. 2018;9:1072. doi:10.3389/fimmu.2018.01072.
22. Mittal D, Lepletier A, Madore J, et al. CD96 is an immune checkpoint that regulates CD8+ T-cell antitumor function. *Cancer Immunol Res*. 2019;7(4):559-571.
23. Perica K, Varela JC, Oelke M, Schneck J. Adoptive T cell immunotherapy for cancer. *Rambam Maimonides Med J*. 2015;6(1):e0004. doi:10.5041/RMMJ.10179.
24. Sharpe M, Mount N. Genetically modified T cells in cancer therapy: opportunities and challenges. *Dis Model Mech*. 2015;8(4):337-350.
25. Li Y, Yin Y, Mariuzza RA. Structural and biophysical insights into the role of CD4 and CD8 in T cell activation. *Front Immunol*. 2013; 4:206. doi.org/10.3389/fimmu.2013.00206.
26. Reid R, Pradas DC, Dow D, et al. Arming TCR-T cell therapy for efficacy enhancement. Poster presented at: CAR TCR Summit; September 4-7, 2018; Boston, MA.
27. Catchpole I, Brett S, Sheppard NC, et al. Engineering T-cells for adoptive cell therapy to overcome TGF-ß-mediated immunosuppression in the tumour microenvironment. Poster presented at: The European Society for Medical Oncology Annual Congress; September 8-12, 2017; Madrid, Spain. Poster 100P.
28. Kanwal R, Gupta S. Epigenetic modifications in cancer. *Clin Genet*. 2012;81(4):303-311.
29. Nebbioso A, Tambaro FP, Dell'Aversana C, Altucci L. Cancer epigenetics: moving forward. *PLoS Genet*. 2018;14(6):e1007362. doi:10.1371/journal.pgen.1007362.
30. Smith E, Zhou W, Shindiapina P, Sif S, Li C, Baiocchi RA. Recent advances in targeting protein arginine methyltransferase enzymes in cancer therapy. *Expert Opin Ther Targets*. 2018;22(6):527-545.
31. Poulard C, Corbo L, Le Romancer M. Protein arginine methylation/demethylation and cancer. *Oncotarget*. 2016;7(41):67532-67550.
32. Fedoriw A, Rajapurkar SR, O'Brien S, et al. Anti-tumor activity of the type I PRMT inhibitor, GSK3368715, synergizes with PRMT5 inhibition through MTAP loss. *Cancer Cell*. 2019;36(1):100-114.
33. Lord CJ, Ashworth A. The DNA damage response and cancer therapy. *Nature*. 2012;481(7381):287-294.
34. O'Connor MJ. Targeting the DNA damage response in cancer. *Mol Cell*. 2015;60(4):547-560.
35. Kelley MR, Logsdon D, Fishel ML. Targeting DNA repair pathways for cancer treatment: what's new? *Future Oncol*. 2014;10(7):1215-1237.
36. O'Neil NJ, Bailey ML, Hieter P. Synthetic lethality and cancer. *Nat Rev Genet*. 2017;18(10):613-623.
37. Gupte R, Liu Z, Kraus WL. PARPs and ADP-ribosylation: recent advances linking molecular functions to biological outcomes. *Genes Dev*. 2017;31(2):101-126.
38. Zejula [summary of product characteristics]. Stockley Park West, Uxbridge, Middlesex, UK: GlaxoSmithKline (Ireland) Ltd; 2020.
39. ZEJULA [package insert]. Research Triangle Park, NC: GlaxoSmithKline; 2020.

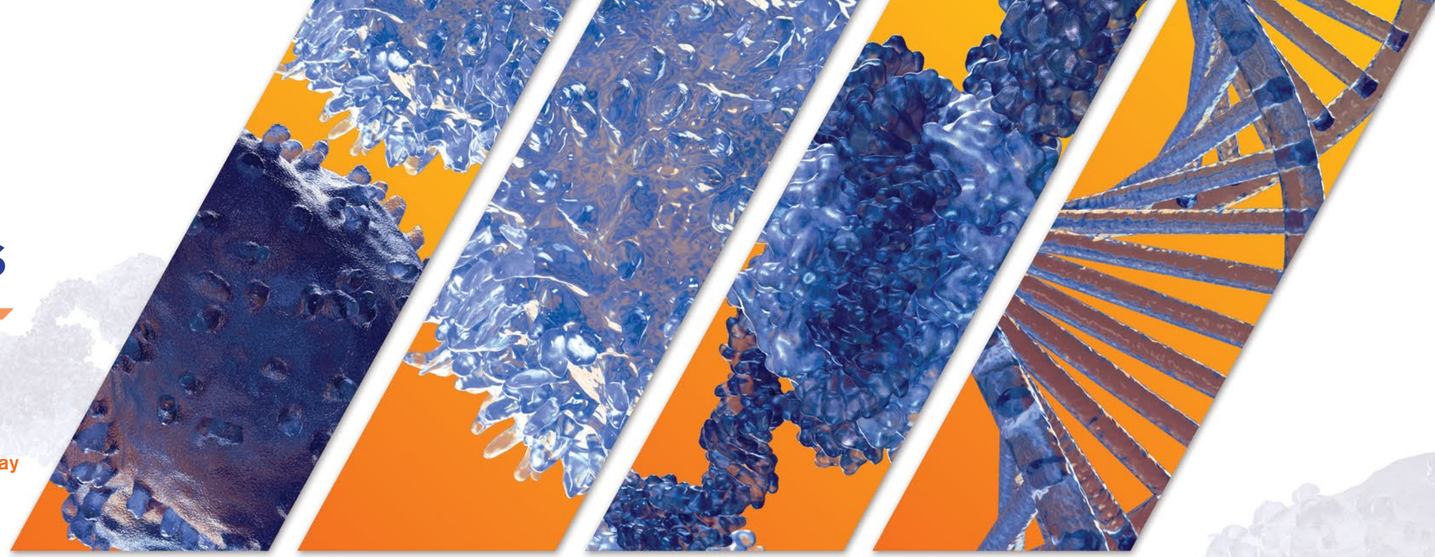
GSK oncology clinical pipeline

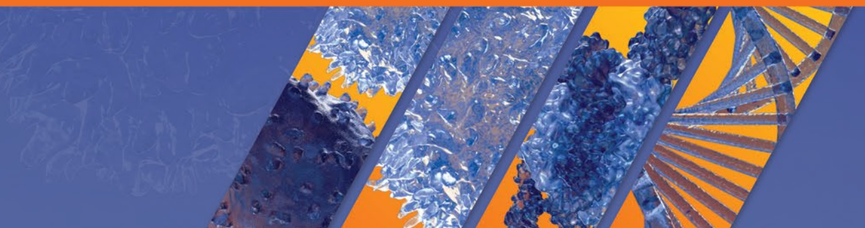
Innovation to discover transformational medicines

4 key areas of cancer research

16* clinical assets

50+ GSK-sponsored clinical trials currently underway





This information is intended for healthcare professionals only. This brochure includes ongoing clinical trials for both approved and investigational compounds. Some agents are approved in select indications. Inclusion in this brochure does not imply regulatory approval for these compounds or all indications. Information about all GSK-sponsored trials can be found at www.clinicaltrials.gov. All information for clinical trials verified as of October 29, 2020.

*Includes an asset being developed in a strategic global alliance between GSK and Merck KGaA, Darmstadt, Germany.

Electronic Certificate

Version: 0 . 4

Document Number: SE-GBL-ON-BROC-200010

Document Name: ASH Pipeline Brochure

Country: Global

Product: ACROSS ONCOLOGY

Type: Scientific Engagement

Role	Signature
Paul OGrady - Medical (paul.i.ogrady@gsk.com)	It is approved that this material has been examined and is believed to be in accordance with the relevant Code of Practice and any other relevant regulations, policies and SOPs. Date: 16-Nov-2020 15:59:50 GMT+0000