Cancer takes. Takes away time. Takes away loved ones. At Boehringer Ingelheim Oncology, we are giving patients new hope, by taking cancer on.

We are dedicated to collaborating with the oncology community on a shared journey to deliver leading science.

Our goal is treatment breakthroughs that can transform the lives of patients and help win the fight against cancer.

To learn more about the Boehringer Ingelheim Oncology Clinical Development Pipeline, please speak to your local Boehringer Ingelheim contact.
These compounds are investigational agents and have not been approved for use by any regulatory authority. Their efficacy and safety have not been established.
**Xentuzumab**

A humanized IgG1 monoclonal antibody against IGF-1 and IGF-2 ligands

**Mode of action**

Xentuzumab is a humanized IgG1 monoclonal antibody that binds to IGF-1 and IGF-2 with high affinity, preventing activation of IGF-1R and IR-A, respectively.1–3

Increased expression of IGF-1 and IGF-2 is implicated in tumor proliferation, migration and invasion; high IGF and IGF receptor expression is observed in both solid tumors and hematological malignancies.4–6

**Key information**

Xentuzumab has shown potent anti-proliferative effects (low nmol/L EC50) against a range of cancer cell lines, including NSCLC, SCLC, and multiple myeloma.3

**Clinical development**

Ongoing clinical trials are evaluating xentuzumab for the treatment of patients with breast cancer and NSCLC.

Scan for more information on these trials from ClinicalTrials.gov

**References**


This compound is an investigational agent and has not been approved for use by any regulatory authority. The safety and efficacy have not been established.
mRNA vaccine
BI 1361849: an mRNA-based vaccine with six mRNAs

Mode of action

BI 1361849 is an mRNA-based immunotherapeutic cancer vaccine that might have the potential to mobilize the patient’s immune system to fight tumors.1

BI 1361849 consists of six mRNAs that code for six different antigens, which are frequently expressed in NSCLC: NY-ESO-1, MAGE C1, MAGE C2, TPBG (ST4), survivin and MUC1.2 It is hypothesized that translation of encoded proteins and presentation to APCs may lead to expansion of antigen-specific T and B cells to give a balanced humoral cellular response to tumors.3

Key information

A Phase I/IIa trial with a BI 1361849 predecessor (NCT00923312, CV9201-003)4 demonstrated that antigen-specific immune responses occurred in 65% of patients.5

Clinical development

BI 1361849 is being investigated in combination with durvalumab and tremelimumab in a Phase I/II trial in NSCLC patients.

References

**Mode of action**

BI 836880 is a humanized bispecific nanobody comprising blocking domains for VEGF and Ang2 and an additional portion for extending the half-life. It potently and selectively inhibits VEGF and Ang2. Signaling via VEGF and Ang2 have different but complementary functions in tumor angiogenesis. Ang2 interrupts signaling via Tie2, allowing the destabilization of established blood vessels. This promotes remodeling and is a prerequisite for sprouting angiogenesis. Signaling via VEGF regulates endothelial cell proliferation and migration, and vessel sprouting.

**Key information**

Dual blockade of signaling via VEGF and Ang2 is itself a promising anti-angiogenic strategy for cancer therapy. Combined inhibition of VEGF, Ang2 and PD-1 has potential for complementary antitumor effects, namely increasing vascular normalization and promoting an antitumor immune response. BI 836880 showed tumor growth inhibition and inhibition of angiogenesis in vivo.

**Clinical development**

BI 836880 is being investigated in clinical studies as a monotherapy and in combination with the PD-1 inhibitor BI 754091.

**References**

BET inhibitor
BI 894999: a small molecule inhibitor of the BET protein family

Mode of action
BI 894999 is an oral, potent, and selective inhibitor of the BET family of bromodomain-containing proteins that bind to acetylated histones, inducing transcription.\(^1\)\(^-\)\(^3\)

Inhibition of BRD4, a member of the BET family that is considered a key epigenetic regulator, triggers suppression of target gene transcription, e.g. the oncogene Myc.\(^1\)\(^-\)\(^3\)

BRD4 deregulation is implicated in a number of hematological and solid tumors.\(^4\)\(^,\)\(^5\)

Key information
BI 894999 is highly active *in vitro* and *in vivo* in hematological malignancies and solid tumors.\(^1\)\(^,\)\(^2\)\(^,\)\(^6\)

Clinical development
BI 894999 is being investigated in a Phase I study as a single agent in patients with advanced solid tumors.

Scan for more information on this trial from ClinicalTrials.gov

References

This compound is an investigational agent and has not been approved for use by any regulatory authority. The safety and efficacy have not been established.
PD-1 inhibitor
BI 754091: a monoclonal antibody blocking the PD-1 receptor from interaction with its ligands PD-L1 and PD-L2

Mode of action
BI 754091 is a humanized PD-1-targeting monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2.\(^1\)

T cells are inactivated by the interaction of PD-1 and PD-L1. BI 754091 blocks the interaction of PD-1/PD-L1, leading to activation of T cells.\(^1\) Activated T cells can secrete, for example, perforin and granzyme B to kill tumor cells.\(^2\)

Key information
BI 754091 is a backbone combination partner for multiple immuno-oncology approaches to cancer treatment.

Clinical development
BI 754091 is being investigated as monotherapy and as a backbone combination partner for multiple immuno-oncology approaches.

References

Supporting citation: reference 1

These compounds are investigational agents and have not been approved for use by any regulatory authority. Their efficacy and safety have not been established.
LAG-3 inhibitor

BI 754111: a monoclonal antibody blocking the interaction between LAG-3 and MHC class II

Mode of action

BI 754111 is a humanized LAG-3-targeting monoclonal antibody that inhibits the interaction between LAG-3 and MHC class II.¹

LAG-3 is an immune checkpoint receptor located on the surface of T cells in the tumor microenvironment.² MHC class II molecules on the surface of tumors present antigens that are recognized by T-cell receptors, initiating a signaling pathway that promotes an adaptive immune response to the tumor.²

In the presence of an antigen, LAG-3 binds to the MHC class II molecule on the tumor cell, starting a signaling cascade that reduces T-cell activation and proliferation. LAG-3 inhibition may be able to restore T-cell activation, enabling an improved immune response to the tumor.²

Combined targeting of PD-1 and LAG-3 may have a synergistic effect, reactivating the T-cell response in the tumor microenvironment.

Clinical development

BI 754111 is being investigated in combination with the PD-1 inhibitor BI 754091 in patients with solid tumors, and in combination with the PD-1 inhibitor BI 754091 and the MDM2-p53 antagonist BI 907828.

References

SMAC mimetic

BI 891065: a small molecule that induces degradation of cIAP

Mode of action

SMAC is a pro-apoptotic mitochondrial protein that is released into the cytosol in response to cellular stress. SMAC binds directly to some members of the IAP family, and induces the degradation of other IAPs.

BI 891065 (a SMAC mimic) and BI 754091 (a PD-1 inhibitor) have been shown, in preclinical studies, to work together to re-activate and amplify the immune response to tumor cells. Together, the compounds initiate a 'virtuous cycle' consisting of a First and Second Punch.

First Punch: SMAC mimetics bind to cIAP, inducing degradation of cIAP proteins and activating caspase-8 provoking tumor cell death. This marks the first step in a set of events resulting in an anticancer immune response: the 'First Punch'.

Second Punch: T cells in the tumor microenvironment have been shown to express high levels of PD-1 and often exhibit an 'exhausted' phenotype, with an inability to control tumor growth.

Combined therapy with BI 754091, which blocks the interaction between PD-1 and its ligands, PD-L1, and PD-L2, has been shown to re-activate these T cells in preclinical studies. This reactivation enables potent T cell-mediated eradication of tumor cells, and delivers the 'Second Punch' of the immune response.

Clinical development

BI 891065 is being investigated in combination with the PD-1 inhibitor BI 754091 in Phase I studies in patients with solid tumors.

References


These compounds are investigational agents and have not been approved for use by any regulatory authority. Their efficacy and safety have not been established.
MDM2-p53 antagonist

BI 907828: a small molecule inhibiting the interaction between MDM2 and p53

Mode of action

BI 907828 is a small molecule MDM2-p53 antagonist that may promote p53-mediated cell cycle arrest and apoptosis.

In human cancers, the TP53 gene encoding the tumor suppressor p53 is frequently mutated or deleted, or the function of wild-type p53 is inhibited by high levels of MDM2, a negative regulator of p53, which leads to downregulation of the p53 pathway.

BI 907828 blocks the interaction between MDM2 and p53 by binding to free MDM2: p53 signaling contributes to the regulation of multiple cellular processes, including progression through the cell cycle, DNA repair, senescence, and apoptosis.

Key information

BI 907828 induced tumor regression in TP53 wild-type models of various tumor types (e.g. acute myeloid leukemia, osteosarcoma, dedifferentiated liposarcoma, NSCLC and brain tumors).

The pharmacological properties of BI 907828 allow for high-dose intermittent schedules that are expected to mitigate on-target thrombocytopenia (class effect). In preclinical models, BI 907828 penetrated the blood–brain barrier.

The immunomodulatory properties of MDM2-p53 antagonists support combination with PD-1 inhibitors.

Clinical development

BI 907828 is being investigated as a monotherapy in patients with TP53 wild-type-enriched solid tumors in a Phase I trial. A Phase I trial of BI 907828 in combination with the PD-1 inhibitor BI 754091 and the LAG-3 inhibitor BI 754111 in patients with advanced solid tumors is also ongoing.

Scan for more information on these trials from ClinicalTrials.gov

References


These compounds are investigational agents and have not been approved for use by any regulatory authority. Their efficacy and safety have not been established.
**LRP5/6 antagonist and LRP5 antagonist**

Humanized nanobodies consisting of blocking domains for the Wnt ligand co-receptors LRP5 and LRP6 (BI 905677) or LRP5 (BI 905681)

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**Mode of action**

BI 905677 and BI 905681 both act by inhibiting Wnt/β-catenin signaling.

BI 905677 is a humanized bispecific nanobody consisting of blocking domains for the Wnt ligand co-receptors LRP5 and LRP6. BI 905677 binds to LRP5 and LRP6 with high affinity, blocks binding of Wnt ligands, and inhibits Wnt ligand/β-catenin-driven cancer proliferation and survival.\(^1\)\(^3\) Wnt/β-catenin signaling activation was shown to drive resistance to checkpoint inhibitors through loss of dendritic cell function and T-cell exclusion, which is blocked by BI 905677.

**LRP5/6 antagonist (BI 905677): cancer cell-targeted mode of action\(^3\)\(^4\)**

- **Wnt/β-catenin signaling**
  - BI 905677
  - BI 905681
- **Cancer proliferation and survival**
  - BI 905677
  - BI 905681

BI 905681 is a humanized nanobody monotargeting LRP5 that blocks the binding of Wnt ligands to LRP5, thereby inhibiting Wnt ligand/β-catenin-driven tumor cell proliferation and survival.\(^1\)\(^2\)

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**Key information**

**RNF43**-inactivating mutations and R-spondin-3 fusion transcripts (genomic alterations driving ligand-dependent Wnt/β-catenin signaling activation) have been identified in a subset of solid tumors.\(^3\)\(^5\)

Preclinical data have shown that BI 905677 potently and selectively blocks ligand-dependent Wnt signaling and induces tumor growth inhibition in **RNF43** mutation-positive and R-spondin-3 fusion-positive tumors.\(^3\)

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**Clinical development**

BI 905667 and BI 905681 are currently undergoing clinical investigation as monotherapy in patients with advanced solid tumors.

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**References**

2. Boehringer Ingelheim. Data on file;

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*These compounds are investigational agents and have not been approved for use by any regulatory authority. Their efficacy and safety have not been established.*
**SOS1::KRAS inhibitor**

BI 1701963: A small molecule that binds to SOS1, reducing the formation of active, GTP-loaded KRAS

### Mode of action

KRAS functions as a molecular switch, existing in two states: the GDP-bound 'off' state and the GTP-bound 'on' state. Active KRAS-GTP activates downstream effector pathways, including the RAF/MEK/ERK pathway.¹

The KRAS GDP–GTP cycle is regulated by guanine nucleotide exchange factors (such as SOS1) which promote nucleotide exchange and formation of 'active' KRAS-GTP.¹

SOS1::KRAS inhibitors bind to SOS1 and inhibit the interaction between KRAS and SOS1 proteins, reducing the formation of GTP-loaded KRAS.¹ SOS1 inhibitors also antagonize the negative feedback relief induced by RAF/MEK/ERK pathway inhibitors.²

### Key information

The SOS1::KRAS inhibitor BI 1701963 is a first-in-class protein::protein interaction inhibitor, targeting a key interaction of the RAS GTpase.² Gain-of-function mutations in RAS genes have been identified in 27% of all human cancers.³

While SOS1 inhibition yields cytostasis in cancer cells addicted to KRAS signaling, the combination of a SOS1 inhibitor with a drug inhibiting the MAPK pathway results in a more profound blockade of KRAS signaling, induction of apoptosis, and tumor regression in preclinical mouse models of KRAS-driven cancers.² Hence, there is a strong rationale for development in combination with a MAPK pathway inhibitor.

### Clinical development

BI 1701963 is being investigated alone and in combination with a MAPK pathway inhibitor in patients with KRAS mutation-positive solid tumors.

**References**


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These compounds are investigational agents and have not been approved for use by any regulatory authority. Their efficacy and safety have not been established.
SIRPα antagonist
BI 765063: a monoclonal antibody blocking CD47/SIRPα interaction

Mode of action

BI 765063 is a first-in-class monoclonal antibody that blocks the interaction between SIRPα on the surface of myeloid cells and CD47.1 CD47 is a ‘don’t eat me’ signal that is expressed on the surface of tumor cells.2

The CD47/SIRPα axis is a regulator of macrophage and other myeloid cell activation, serving as a myeloid-specific immune checkpoint.3 CD47/SIRPα interaction inhibits phagocytosis of tumor cells.2,3 Blocking the interaction between CD47 and SIRPα restores the immune functions of myeloid cells in the tumor microenvironment, resulting in antigen uptake and presentation, and linking the innate and adaptive immune systems.2,3

Key information

The link between innate and adaptive immunity points to combination therapy with an adaptive immune checkpoint inhibitor.2,3 Preclinical studies in mouse tumor models have demonstrated benefit of SIRPα inhibitor monotherapy.3,4 These studies also indicate that clinical outcomes may be enhanced through combination therapy with a PD-1 inhibitor or with a costimulatory agent, such as an anti-4-1BB monoclonal antibody, which would provide dual activation of innate and acquired immunity.3,4

Clinical development

BI 765063 is being investigated as a single agent and in combination with the PD-1 inhibitor BI 754091 in patients with advanced solid tumors.

Scan for more information on this trial from ClinicalTrials.gov

Supporting citations: references 1, 3, 4

References


These compounds are investigational agents and have not been approved for use by any regulatory authority. Their efficacy and safety have not been established.
Mode of action

MEK is a component of the MAPK pathway, a signaling cascade also involving RAS and ERK that regulates gene expression, drives proliferation, and prevents apoptosis.1

BI 3011441 (LNP3794) is a small-molecule allosteric inhibitor that binds adjacent to the ATP pocket of MEK, resulting in inhibition of MEK activity.2 In tumor cells, treatment with BI 3011441 results in downregulated MAPK pathway signaling, reduced cell proliferation, and induction of apoptosis.2

MEK functions downstream of SOS1, KRAS, and RAF. MAPK pathway activity is strictly regulated by the gatekeeper ERK, which also mediates negative feedback loops within the MAPK pathway, for example by phosphorylation of upstream components such as receptor tyrosine kinases, SOS1, and RAF.3 Drugs that selectively inhibit MEK are able to block MAPK pathway activity, leading to reduced cell proliferation and cell death.

However, negative feedback resulting from MEK inhibition can lead to an increase in SOS1-mediated KRAS activation, which subsequently results in re-activation of the MAPK pathway.3

SOS1::KRAS inhibition reduces the formation of GTP-loaded, activated KRAS, and thereby inhibits MAPK pathway signaling.4 By simultaneously blocking the ERK-mediated negative feedback loop, SOS1::KRAS inhibition sensitizes KRAS-dependent cancers to MEK inhibition, resulting in complete blockade of the pathway and tumor regression in vivo.4

Clinical development

Further clinical studies of BI 3011441 in combination with a SOS1::KRAS inhibitor are expected to commence at the end of 2020.2

References


These compounds are investigational agents and have not been approved for use by any regulatory authority. Their efficacy and safety have not been established.
**STING agonist**
A small molecule agonist of the STING pathway

### Mode of action

Stimulator of interferon genes (STING) is a signaling molecule that plays a critical role in the cytosolic detection of tumor-derived DNA, i.e. in the sensing of a tumor by our innate immune system.\(^1,2\)

Once activated, the STING pathway induces transcription of Type I interferons by intratumoral dendritic cells. This in turn promotes tumor antigen-specific, T-cell priming and infiltration of cytotoxic T cells into the tumor microenvironment.\(^1\) STING is, therefore, a key precursor required for the activation of dendritic cells that link the innate and adaptive immune responses to cancer.\(^1,2\)

### Key information

This compound is a small molecule agonist of the STING pathway. Preclinical data show that intratumoral injection of a STING agonist activates dendritic cells and APCs in the tumor microenvironment, inducing a systemic antitumor immune response. These effects are increased in combination with an anti-PD-1 antibody.\(^3\)

### Clinical development

The first-in-human study of this compound as a single agent and in combination with the PD-1 inhibitor BI 754091 in patients with advanced solid tumors is planned to start in 2020.

Supporting citations: references 1, 4

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Supporting text: These compounds are investigational agents and have not been approved for use by any regulatory authority. Their efficacy and safety have not been established.

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**References**

TRAILR2/CDH17 antibody
BI 905711: a bispecific antibody consisting of TRAILR2 and CDH17 binding domains

Mode of action
This compound is a tetravalent bispecific antibody that cross-links the pro-apoptotic TRAILR2 receptor with CDH17, an anchor target in the tumor cell membrane. CDH17-dependent clustering of TRAILR2 permits BI 905711 to selectively induce apoptosis in CDH17-expressing tumor cells.1

TRAILR2 is a pro-apoptotic receptor of the extrinsic apoptotic pathway and is widely expressed on tumor cells.2,3 Clustering of TRAILR2 is required for activation and downstream signaling.4 CDH17 is a cell adhesion protein that was selected as the anchor target due to its restricted expression mostly on malignant cells and, in particular, a lack of expression in normal liver tissue that will potentially avoid the clinical hepatotoxicity associated with TRAILR2 agonism. This anchor protein makes this compound a targeted treatment strategy for CRC and other CDH17-positive tumors.1

Key information
This TRAILR2/CDH17 antibody has shown in-vivo efficacy in xenograft models of CRC, with tumor regression up to ~30 days. Reduction in tumor size correlated with changes in markers of apoptosis.1

Clinical development
BI 905711 is being investigated in patients with advanced gastrointestinal cancers.

Supporting citation: reference 1

References
KISIMA™ cancer vaccine (ATP-128)
A self-adjuvanting peptide vaccine built on the KISIMA® technology platform

**Mode of action**

This compound is a modular, self-adjuvanting, peptide-based cancer vaccine that has the potential to strengthen the capability of the patient’s immune system to recognize and kill tumor cells.\(^1\)\(^-\)\(^3\)

The cancer vaccine is engineered to induce an efficient immune response and promote immunological memory via activation of cytotoxic T cells and helper T cells.\(^1\)\(^-\)\(^3\) Designed using the KISIMA™ technology platform, the vaccine includes three components: a cell-penetrating peptide for antigen delivery, a multi-antigenic cargo that is tailored to raise an immune response against colorectal tumors, and a TLR peptide agonist as an adjuvant.\(^1\)\(^-\)\(^3\)

**Key information**

Preclinical evidence supports the immunogenicity of a previous generation of the cancer vaccine in an *in-vivo* model of CRC.\(^4\) This vaccine has been shown to induce highly potent helper and cytotoxic T-cell responses in several murine tumor models.\(^4\)

The cell-penetrating peptide and the TLR agonist components of the vaccine platform act together to elicit both CD8\(^+\) and CD4\(^+\) antigen-specific T-cell immune responses *in vivo*.\(^4\) This leads to immunological memory and high vaccine efficacy with increased intratumoral leukocyte infiltration.\(^4\)

Combination with PD-1 blockade has been shown to have an additive effect and to significantly increase the efficacy of the vaccine *in-vivo*.\(^4\) As the vaccine enhances T-cell infiltration, this could sensitize tumors that are resistant to PD-1 inhibition (some of which have been shown to have limited immune infiltration) to checkpoint inhibitors.\(^1\)\(^,\)\(^4\)

**Clinical development**

This self-adjuvanting peptide vaccine is being investigated as monotherapy and in combination with the PD-1 inhibitor BI 754091 in patients with histologically or cytologically confirmed Stage IV CRC.

**References**


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These compounds are investigational agents and have not been approved for use by any regulatory authority. Their efficacy and safety have not been established.
**DLL3/CD3 bispecific antibody**

**A bispecific T-cell engager directed against tumors expressing DLL3**

**Mode of action**

The DLL3/CD3 bispecific antibody functions as a T-cell engager, acting as a bridge between DLL3-expressing tumor cells and cytolytic T cells.\(^1,2\)

This compound has an extended half-life and directs activity of cytolytic T cells selectively to DLL3-expressing tumors.\(^1\)

The pharmacological effect of the DLL3/CD3 bispecific antibody depends on its simultaneous binding to both the CD3\(\varepsilon\) subunit of the T-cell receptor complex on T cells, as well as to DLL3 on cancer cells targeted for elimination.\(^1\)

**Key information**

DLL3 is an inhibitory Notch ligand that is expressed in tumors with a neuroendocrine origin, such as SCLC and glioblastoma multiforme, but not in normal adult tissue.\(^3-5\)

Preclinical studies demonstrate the antitumor activity of the DLL3/CD3 bispecific antibody in a variety of DLL3-positive tumor models.\(^2\)

The binding of the DLL3/CD3 bispecific antibody to CD3 may lead to PD-1 upregulation in activated T cells and PD-L1 upregulation on malignant cells.\(^2\)

Preclinical evidence supports the combination of the DLL3/CD3 bispecific antibody with PD-1 inhibitors in order to revert this upregulation.\(^1,2\)

**Clinical development**

The first-in-human study of the DLL3/CD3 bispecific antibody is planned to commence in 2020.\(^1\)

**References**


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This compound is an investigational agent and has not been approved for use by any regulatory authority. The safety and efficacy have not been established.
Abbreviations

4-1BB, receptor belonging to the tumor necrosis factor superfamily
AC, acetylation
Ang, angiopoietin
APC, antigen-presenting cell
ATP, adenosine triphosphate
BET, bromodomain and extra-terminal domain
BRD4, bromodomain protein 4
CD, cluster of differentiation
CDH, cadherin
CDK, cyclin-dependent kinase
cGAS, cyclic GMP-AMP synthase
cIAP, cellular inhibitor of apoptosis
CRC, colorectal cancer
CTD, C-terminal domain
CTL, cytotoxic T lymphocyte
DAMP, damage-associated molecular pattern
DLL3, delta-like ligand 3
DNA, deoxyribonucleic acid
ERK, extracellular signal-regulated kinase
GDP, guanosine diphosphate
GTP(ase), guanosine triphosphate (hydrolase)
IAP, inhibitor of apoptosis
IGF, insulin-like growth factor
IGF-1R, insulin-like growth factor-1 receptor
IgG, immunoglobulin G
IR-A/B, insulin receptor A/B
KRAS, Kirsten rat sarcoma
LAG-3, lymphocyte activation gene 3
LRP, low-density lipoprotein receptor-related protein
MAGE, melanoma-associated antigen
MAPK, mitogen-activated protein kinase
MDM2, murine double minute 2
MEK, mitogen-activated protein kinase
MHC, major histocompatibility complex
mRNA, messenger ribonucleic acid
MUC1, mucin 1
Myc, myelocytomatosis
NSCLC, non-small cell lung cancer
NY-ESO-1, New York esophageal squamous cell carcinoma 1
P, phosphate
PD-1, programmed cell death protein-1
PD-L1/2, programmed death-ligand 1/2
RAF, rapidly accelerated fibrosarcoma
RAS, rat sarcoma
RNA, ribonucleic acid
RNF, ribonucleic acid
RNF, ring finger protein
SCLC, small-cell lung cancer
SIRPa, signal regulatory protein alpha
SMAC, second mitochondria-derived activator of caspases
SOSI, Son of sevenless homolog 1
STING, stimulation of interferon genes
TCR, T-cell receptor
Tie, tyrosine kinase with immunoglobulin-like and epidermal growth factor-like domains
TLR, toll-like receptor
TP53, tumor protein p53
TPBG, trophoblast glycoprotein
TRAILR2, tumor necrosis factor-related apoptosis-inducing ligand receptor
Treg, regulatory T cell
VEGF(R), vascular endothelial growth factor (receptor)
Wnt, wingless/integrated