Bristol Myers Squibb & BioNTech
Independent Medical Education
Request for Educational Support (RFE)

Date	
RFE Requestor Information	Name: Maria Deutsch Title: Global Medical Oncology, Medical Education E-mail: maria.deutsch@bms.com Name: Fiona Zhu Title: Senior Director, Medical Excellence E-mail: fiona.zhu@biontech.de
RFE Code	RFE-26-ONC-102
Therapeutic Area	Oncology – Lung
Area of Interest	Novel regimens with emerging bispecific antibodies for the treatment of lung cancer
Educational Design	Bristol Myers Squibb & BioNTech are interested in supporting innovative, comprehensive educational initiatives that include the following (please submit as separate activities/grant proposals): • Live satellite symposium with simulcast + enduring activity at the World Conference on Lung Cancer (WCLC) 2026 in the Republic of Korea. The enduring activity should include translations into English, Mandarin, French, Spanish, Italian, and German. • A standalone on-demand, web-based enduring activity translated in English, Mandarin, French, Spanish, Italian, and German. Knowledge and competency-based objective outcome measures according to Moore's Level 4 are required. *Performance-based Level 5 outcomes are highly preferred.*
Intended Audience (may include, but not limited to)	Targeted to medical oncologists, pulmonologists, nurses, NPs, PAs, pharmacists, and other healthcare professionals involved in the care of patients with lung cancer.
Budget/Budget Range	The anticipated programs are expected to be achieved with a budget of no more than: • $425,000 for the live satellite symposium + enduring activity at the World Conference on Lung Cancer (WCLC) 2026 ***Please note: Korean HCPs are restricted from symposia that offer meals or refreshments. Proper signage must be put in place.***

	• $175,000 for the standalone on-demand, web-based enduring activity Single and multi-supported initiatives will be considered. *Significant or major updates to the medical content (e.g., regulatory status changes, primary data releases, etc.) are expected for enduring online activities outlined in this RFE.
Accreditation	ACCME, ACPE, CCNE, ECCME, and others as appropriate to the audience(s) of various countries and learners being educated. All activities and content must follow the IFPMA code and the EFPIA code. Please follow local accredited continuing medical education guidance and compliance. Please include in the grant proposal each country's HCP accreditation requirements.
Geographic Coverage	United States Ex-US regions: Korea, China, France, Spain, Italy, and Germany
Deadline for Submission (Date and Time)	02/27/2026 EOB 5pm EST

Background:

Major advances have been made in the last decade with oncology treatments, with innovation supporting the development of novel mechanisms and better patient outcomes.[1] However, there remains a significant unmet need, including in certain solid tumors.[1] Often, solid tumors exhibit substantial heterogeneity in antigen expression, leading to resistance against single-targeted therapies.[2] Bispecific antibodies (BsAbs) are able to simultaneously target two distinct antigens, overcoming tumor heterogeneity and providing broader tumor coverage.[2]

Mechanism of Action and Rationale of PD-(L)1 x VEGF Targeting Bispecific Antibodies

BsAb T-cell engagers represent a novel class of therapeutic agents that have two distinct target-binding sites, allowing simultaneous engagement with two different targets. This enables them to bridge tumor and immune cells or block two signals at once, providing a multifaceted approach to cancer treatment.[2,4,5] Their mechanisms of action are diverse and go beyond simple dual targeting, as BsAbs can disrupt multiple signaling cascades at once, thereby preventing tumor escape mechanisms and offering more durable responses compared to conventional monoclonal antibodies (mAbs), which are often limited by tumor heterogeneity and resistance.[2]

Programmed cell death protein 1 (PD-1) and its ligand (PD-L1) are immune checkpoint molecules that suppress the activity of cytotoxic T cells, enabling cancer cells to evade detection and destruction by the immune system.[6] Inhibiting this pathway with immune checkpoint inhibitors has led to significant advances in cancer immunotherapy, producing durable responses in a subset of patients.[6] Suboptimal outcomes to the PD-1/PD-L1 blockade may be driven by the complex and immunosuppressive tumor microenvironment (TME).[6] Vascular endothelial growth factor (VEGF), particularly the VEGFA isoform, plays a pivotal role in tumor angiogenesis, as it stimulates the formation of new blood vessels that support tumor growth, metastasis, and sustain the immunosuppressive TME.[6] VEGF also actively impairs antitumor immune responses by inhibiting dendritic cell maturation and cytotoxic T-cell function, thereby promoting immune evasion.[6]

Both PD-(L)1 and VEGF are frequently co-expressed within the TME of solid tumors, and their pathways contribute to tumor progression through immune suppression and angiogenesis.[6] Targeting them together can disrupt these processes more effectively than inhibiting either pathway alone.[6] A bispecific antibody (BsAb) designed to simultaneously block PD-(L)1 and VEGF offers several advantages: it can enhance antitumor activity by reviving immune responses and shutting down tumor-driven vascular support; it may also simplify treatment regimens by minimizing issues related to dosage, pharmacokinetics, and overlapping toxicities commonly encountered with conventional combination therapies.[6] Ultimately, dual targeting with BsAbs, either in combination with chemotherapy or as monotherapy, holds promise for more comprehensive tumor control and improved clinical outcomes.[6,9]

Current Landscape for PD-(L)1 x VEGF Targeting Bispecific Antibodies in Lung Cancer

Efficacy data for emerging BsAbs that target the PD-(L)1 x VEGF/angiogenesis pathways are promising and demonstrate an improvement in patient outcomes, as reported in multiple Phase 2 and 3 lung clinical trials.[5]

SSGJ-707 is a bispecific antibody targeting VEGF x PD-1.[7] The compound is currently undergoing clinical trials globally for multiple indications, including non-small cell lung cancer (NSCLC), metastatic colorectal cancer, and gynecological tumors.[8,14] In a phase 2 randomized study, the safety and efficacy of SSGJ-707 combined with platinum-based chemotherapy was compared to tislelizumab plus chemotherapy in patients with advanced NSCLC.[7] At the data cutoff, 244 patients with advanced NSCLC had received either SSGJ-707 (10 mg/kg) with chemotherapy or tislelizumab with chemotherapy.[7] SSGJ-707 achieved higher confirmed objective response rates (ORRs)—58.6% in the nonsquamous cohort and up to 75.0% in the squamous cohort—

compared to ORRs of 38.7% (nonsquamous) and 47.6% (squamous) with tislelizumab.[7] Grade ≥3 treatment-related adverse events occurred in 39.0% of patients on SSGJ-707 versus 32.8% with tislelizumab.[7] These findings indicate superior efficacy and manageable safety for SSGJ-707 compared to tislelizumab in both nonsquamous and squamous NSCLC.[7] Additionally, a phase 2 study of SSGJ-707 monotherapy in treatment-naïve advanced NSCLC demonstrated overall response rates of up to 72% and a disease control rate of 100% at the 10 mg/kg dose, supporting further investigation in ongoing trials.[18]

Pumitamig is a bispecific antibody targeting PD-L1 x VEGF-A that is being evaluated in multiple phase 2 and 3 clinical trials across solid tumor indications.[10] In an interim analysis of a global phase 2 trial involving 43 patients with treatment-naïve ES-SCLC, pumitamig (20 mg/kg or 30 mg/kg) plus chemotherapy delivered a confirmed overall response rate (ORR) of 76.3% (85.0% at 20 mg/kg and 66.7% at 30 mg/kg), and among 38 efficacy-evaluable patients, a disease control rate of 100% was reported.[9,16] Median progression-free survival was 6.8 months overall (6.3 months at 20 mg/kg; 7.0 months at 30 mg/kg), while median overall survival was not mature at data cutoff.[9,16] Pumitamig demonstrated a manageable safety profile, with grade ≥3 adverse events observed in six patients (one at 20 mg/kg and five at 30 mg/kg).[9] Overall, pumitamig plus etoposide/carboplatin showed promising efficacy and acceptable safety in first-line ES-SCLC, supporting this therapy and mechanism of action as a promising option in a setting with significant unmet need.[9] These data supported dose selection for the ongoing global pivotal Phase 3 ROSETTA LUNG-01 trial evaluating pumitamig in first-line SCLC.[9] Additionally, a phase Ib/IIa trial evaluating the safety and efficacy of pumitamig monotherapy demonstrated antitumor activity and acceptable safety in patients with advanced NSCLC, supporting rationale for the Phase 2/3 ROSETTA LUNG-02 trial evaluating pumitamig in combination with chemotherapy and other investigational agents in first-line NSCLC.[10,17]

Ivonescimab is a bispecific antibody targeting PD-1 x VEGF, approved by China's NMPA as monotherapy for first-line treatment of NSCLC patients with positive PD-L1 expression.[11] In the phase 3, randomized, double-blind HARMONi-2 study conducted in China, 398 adults with locally advanced or metastatic PD-L1-positive NSCLC were randomized to receive intravenous ivonescimab (20 mg/kg) or pembrolizumab (200 mg) every three weeks.[12] Interim analysis demonstrated that median progression-free survival was significantly longer with ivonescimab compared to pembrolizumab (11.1 vs. 5.8 months; one-sided $p<0.0001$), with consistent benefit across all prespecified subgroups, including by PD-L1 tumor proportion score.[12] Grade ≥3 treatment-related adverse events were reported in 29% of ivonescimab patients and 16% of pembrolizumab patients, while grade ≥3 immune-related events were similar between arms.[12] These results indicate that ivonescimab significantly improves PFS compared to pembrolizumab for previously untreated, PD-L1-positive advanced NSCLC, supporting its use as a first-line

treatment option.[12] Additionally, in the phase 3 HARMONi-6 trial, patients with squamous NSCLC were randomized to receive ivonescimab (20 mg/kg) or tislelizumab (200 mg), plus chemotherapy followed by respective monotherapy.[15] Ivonescimab plus chemotherapy achieved a median PFS of 11.1 months compared to 6.9 months with tislelizumab plus chemotherapy, demonstrating a statistically significant benefit regardless of PD-L1 status.[15]

Education Needs:

Medically accurate, fair-balanced learning programs are required to maximize transparency and minimize clinician bias in the provision of medical education. Applying evidence-based scientific knowledge significantly contributes to professional competencies of HCPs and improves patient outcomes.

These activities will ensure timely and effective communication of the latest science and clinical trial data.

The following educational needs should be addressed through this educational program:

- Describe the current unmet needs in lung cancer and how bispecific antibodies, particularly those targeting PD-(L)1 x VEGF, may address these challenges
- Explain the mechanism of action of PD-(L)1 x VEGF bispecific antibodies and review the latest clinical evidence on their safety and efficacy in lung cancer
- Compare the therapeutic benefits and challenges of bispecific antibodies versus conventional monoclonal antibody therapies (e.g., PD-(L)1-based therapies), and identify key considerations for their clinical integration, including safety, efficacy, and patient selection

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