

A Phase 1, first-in-human study of DS3610, a stimulator of interferon genes (STING) agonist antibody–drug conjugate, in patients with advanced/metastatic solid tumors

Shigehiro Koganemaru,¹ Justin Han,² Sofia Buckley,² Nagisa Kaneko,² Yoshihiro Ohue,² John Toso,^{2*} Noboru Yamamoto³

¹National Cancer Center Hospital East, Kashiwa, Japan; ²Daiichi Sankyo, Inc., Basking Ridge, NJ, USA; ³National Cancer Center Hospital, Tokyo, Japan.

*At the time of the study design.

PLAIN LANGUAGE SUMMARY

Why perform this study?

- Many cancers are now treated using immunotherapy, which helps the body's immune system to locate and attack cancer cells¹
- Although immunotherapy provides benefits for people with cancer, the effects are not always long lasting, and the cancer may stop responding to these therapies²
- New types of treatment are needed to help prevent cancer from progressing and improve patient outcomes^{1,2}

What will this study determine?

- The aim is to find out which doses of a potential new treatment called **DS3610** can be given safely to people with cancer
- This will help determine the best dose of **DS3610** to use in future clinical studies³

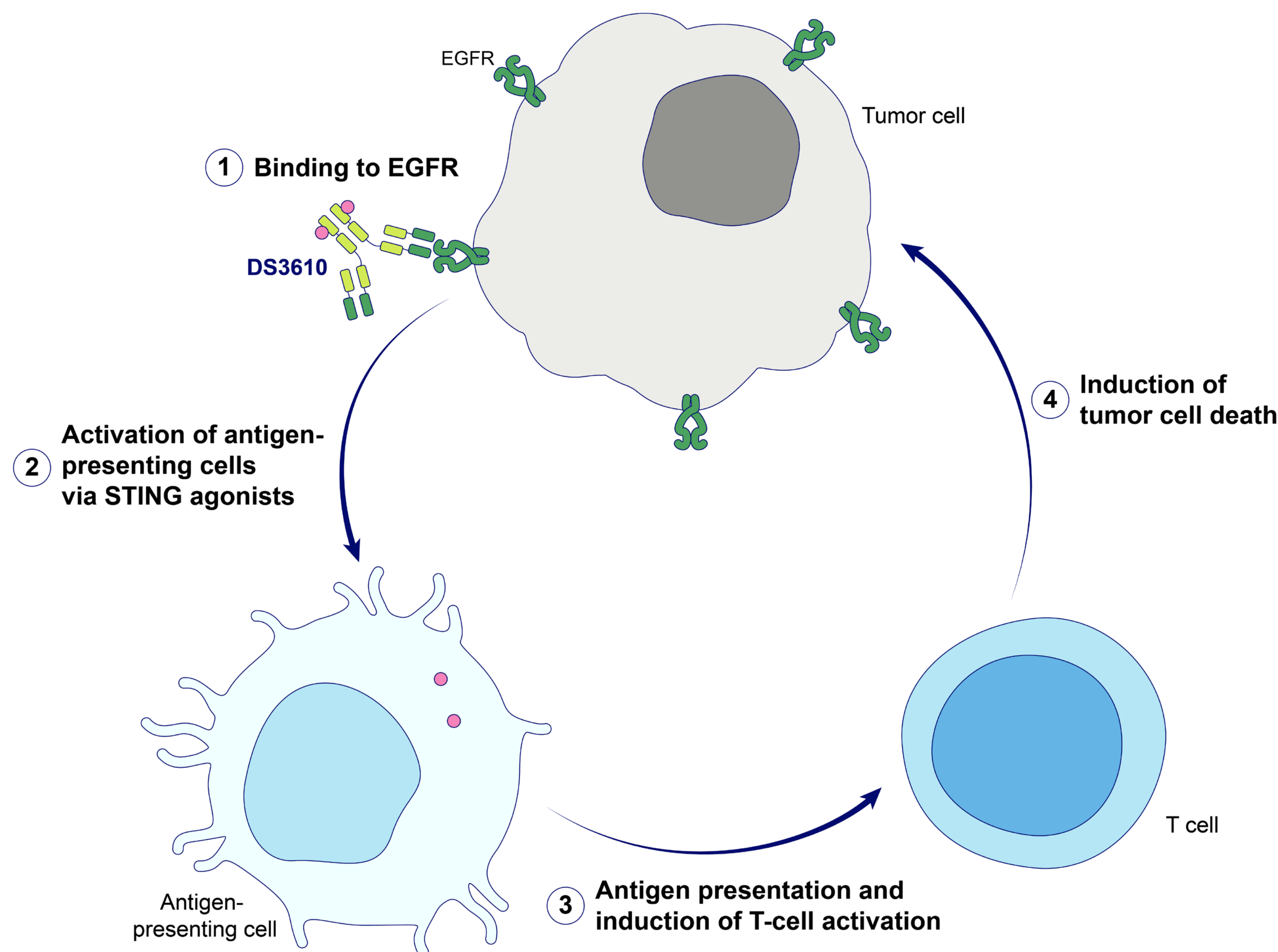
How will this study be performed?

- People with advanced cancer or cancer that has spread to other parts of the body and who cannot have standard treatments will be given **DS3610** at steadily increasing doses³
- At each dose level, the researchers will check if patients have any side effects before deciding whether to test the next higher dose³

BACKGROUND

- Although immunotherapies have improved treatment for patients with advanced/metastatic solid tumors, there remains a need for novel therapies that can overcome resistance to existing therapies, enhance antitumor activity, and delay disease progression^{1,2}
- Promoting the innate immune response through activation of the endoplasmic reticulum adaptor protein STING has been associated with antitumor activity^{4,5}
- EGFR is a transmembrane receptor tyrosine kinase that is overexpressed in a broad range of solid tumors^{6,7}
- **DS3610** is an ADC comprising an anti-EGFR monoclonal antibody attached to a STING agonist immunomodulatory payload
 - **DS3610** is designed to deliver the STING agonist payload directly to the tumor microenvironment, activating immune cells, such as antigen-presenting cells and T cells, and inducing immune targeting of cancer cells (**Figure 1**)
 - The antibody component has novel Fc modifications designed to reduce the risk of class-specific AEs, such as systemic cytokine release

Figure 1. DS3610 proposed mechanism of action



- The antibody component of **DS3610** targets EGFR, a cancer antigen, on the tumor cell surface
- Antigen engagement facilitates delivery of the STING agonist payload to the tumor microenvironment
- Local immune cells, such as antigen-presenting cells and T cells, are activated and trigger an adaptive immune response
- Effector immune cells target the tumor cells, inducing cell death

METHODS

- **DS3610-071** (NCT07159126) is a Phase 1, **first-in-human**, open-label, global dose-escalation study of **DS3610**³
- Adults with advanced or metastatic solid tumors who are intolerant to, refractory to, or whose disease progressed on SOC therapies are eligible (**Table 1**)
 - Tumor types include non-small cell lung cancer, head and neck cancer, renal cell carcinoma, urothelial carcinoma, colorectal cancer, gastric cancer, pancreatic cancer, esophageal cancer, biliary tract cancer, and uterine cancer
- Approximately 70 patients will be enrolled to receive **DS3610** at escalating doses until radiographic PD by investigator assessment per RECIST 1.1, unacceptable toxicity, withdrawal of consent, or discontinuation for other reasons (**Figure 2**)
- Primary objectives are to assess the safety and tolerability of **DS3610** and to determine the recommended dose(s) for expansion for further evaluation of **DS3610**
- Study endpoints are summarized in **Table 2**

Table 1. Key eligibility criteria

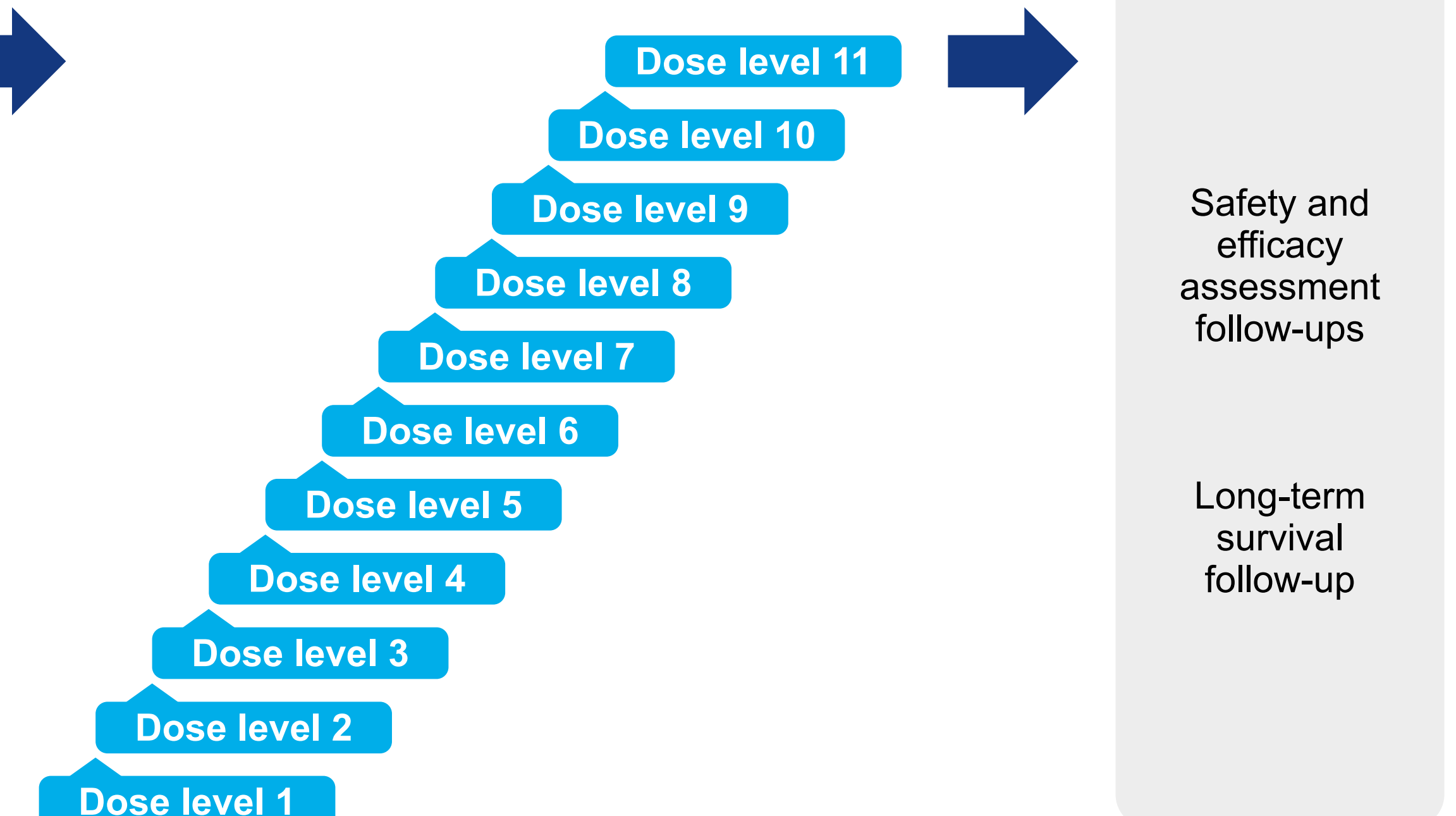
Key inclusion criteria	Key exclusion criteria
Adults (aged ≥18 years)	Prior treatment with a STING or TLR agonist (ADC or not)
Histologically documented advanced, metastatic, or unresectable solid tumors	Known symptomatic CNS metastases, leptomeningeal disease, or cord compression (patients with asymptomatic or adequately treated CNS metastases, who are neurologically stable per investigator, are eligible)
Disease relapsed or refractory to SOC, or patient unable to tolerate SOC	Uncontrolled or clinically significant cardiovascular disease
Willing and able to provide an adequate pretreatment or archival tumor tissue sample	History of, current, or suspected (noninfectious) ILD/pneumonitis
Measurable disease based on local CT/MRI imaging per RECIST 1.1	Clinically severe pulmonary compromise
ECOG PS 0–2	Active or uncontrolled HBV, HCV, or HIV infection
Adequate organ and bone marrow function	Prior immunotherapy with a Grade ≥3, or any unresolved Grade ≥2, irAE
	Other active malignancy within 3 years prior to enrollment

Figure 2. DS3610-071 study design

Dose escalation, N≈70

- Advanced/metastatic solid tumors
- Independent of EGFR level

DS3610 at escalating doses^a



^aAn accelerated titration design with single-patient cohorts will be implemented at lower dose levels. In the event of a Grade ≥2 AE, the dose escalation will transition to BOIN design to determine the MTD. Dose escalation will stop if 9 patients are treated at a given dose and the recommendation is to stay at that dose. Additional patients may be enrolled in some cohorts to allow for collection of additional safety, efficacy, and biomarker data.

Table 2. Study endpoints

Primary endpoints
Safety, including DLTs, TEAEs, and SAEs
Secondary endpoints
Pharmacokinetics
Immunogenicity
Exploratory endpoints
Efficacy of DS3610
Biomarkers associated with clinical benefit

Study status

- Enrollment began in October 2025 and is ongoing at sites in Japan (Chūō-ku and Kashiwa), with plans for enrollment to open in additional sites and countries

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ABBREVIATIONS

ADC, antibody–drug conjugate; AE, adverse event; BOIN, Bayesian optimal interval; CNS, central nervous system; CT, computed tomography; DLT, dose-limiting toxicity; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Fc, fragment crystallizable; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; ILD, interstitial lung disease; irAE, immune-related adverse event; MRI, magnetic resonance imaging; MTD, maximum tolerated dose; PD, progressive disease; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1; SAE, serious adverse event; SOC, standard of care; STING, stimulator of interferon genes; TEAE, treatment-emergent adverse event; TLR, Toll-like receptor.

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DISCLOSURES

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