

Symbiotic-Lung-10: a phase 2 trial of PD-1/VEGF bispecific antibody, PF-08634404, as monotherapy or in combination in NSCLC

Tina Cascone,¹ Heather Wakelee,² Lei Deng,³ Rafael Perez Casellas,⁴ Srilata Gundala,⁵ Luis Paz-Ares,⁶ Aakash Desai,⁷ Mariano Provencio Pulla,⁸ Yi-Long Wu,⁹ Ardy Davarifar,¹⁰ Jin-Yuan Shih,¹¹ Rachel Roberts-Thomson,¹² Chao-Hua Chiu,¹³ Hui Wang,¹⁴ Sabine Bohnet,¹⁵ Alexandre Martinez Marti,¹⁶ Federico Cappuzzo,¹⁷ Yu-Chung Huang,¹⁸ Ricky Philipossian,¹⁸ Xuesong Yu,¹⁸ Patrick Forde¹⁹

¹MD Anderson Cancer Center, Houston, TX, USA; ²Stanford University, Stanford Cancer Institute, Stanford, CA, USA; ³University of Washington/Fred Hutchinson Cancer Center, Seattle, WA, USA; ⁴Pan American Center for Oncology Trials, LLC, Manati, PR, USA; ⁵Hope and Healing Cancer Services, Hinsdale, IL, USA; ⁶Hospital Universitario 12 de Octubre, Madrid, Spain; ⁷O'Neal Comprehensive Cancer Center/University of Alabama Birmingham, Birmingham, AL, USA; ⁸Hospital Universitario Puerta de Hierro, Madrid, Spain; ⁹Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital, Guangzhou, China; ¹⁰University of Tennessee Medical Center, Knoxville, TN, USA; ¹¹National Taiwan University Hospital, Taipei, Taiwan; ¹²The Queen Elizabeth Hospital, Central Adelaide Local Health Network, Adelaide, SA, Australia; ¹³Taipei Medical University Hospital, Taipei, Taiwan; ¹⁴Hunan Province Cancer Hospital, Hunan, China; ¹⁵Universitätsklinikum Schleswig-Holstein, Lübeck, Germany; ¹⁶Hospital Universitario Vall d'Hebron, Barcelona, Spain; ¹⁷National Cancer Institute Regina Elena, Rome, Italy; ¹⁸Pfizer, New York, NY, USA; ¹⁹Trinity College Dublin, Dublin, Ireland



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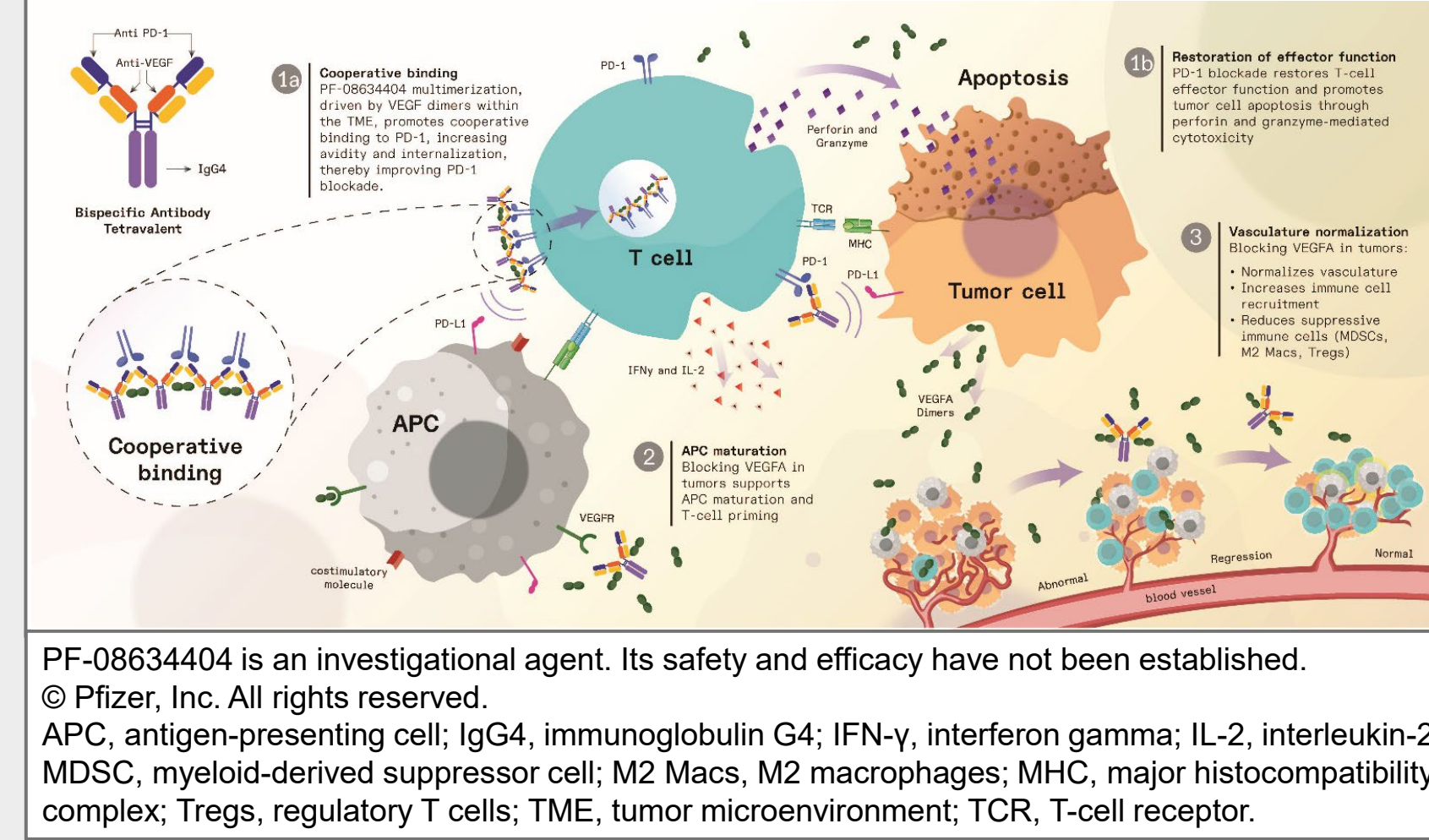
Correspondence: Tina Cascone, tcascone@mdanderson.org

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Background

- Despite advances in the detection and treatment for early-stage and locally advanced non-small cell lung cancer (NSCLC), recurrence rates remain high and long-term outcomes remain suboptimal, indicating a continued need for novel treatments¹
- PF-08634404 (PF'4404) is a fully human immunoglobulin G4 (IgG4) bispecific antibody that simultaneously targets programmed death 1 (PD-1) and vascular endothelial growth factor (VEGF)^{2,3} (**Figure 1**)
- Phase 2 studies have shown clinically meaningful efficacy and manageable safety with PF'4404 as monotherapy⁴ and in combination with platinum-based chemotherapy⁵ as first-line (1L) treatment in locally advanced or metastatic NSCLC (**Table 1**)
- The Symbiotic-Lung-10 study is evaluating PF'4404 as monotherapy or in combination with chemotherapy in patients with early-stage resectable and unresectable NSCLC (NCT07489066)

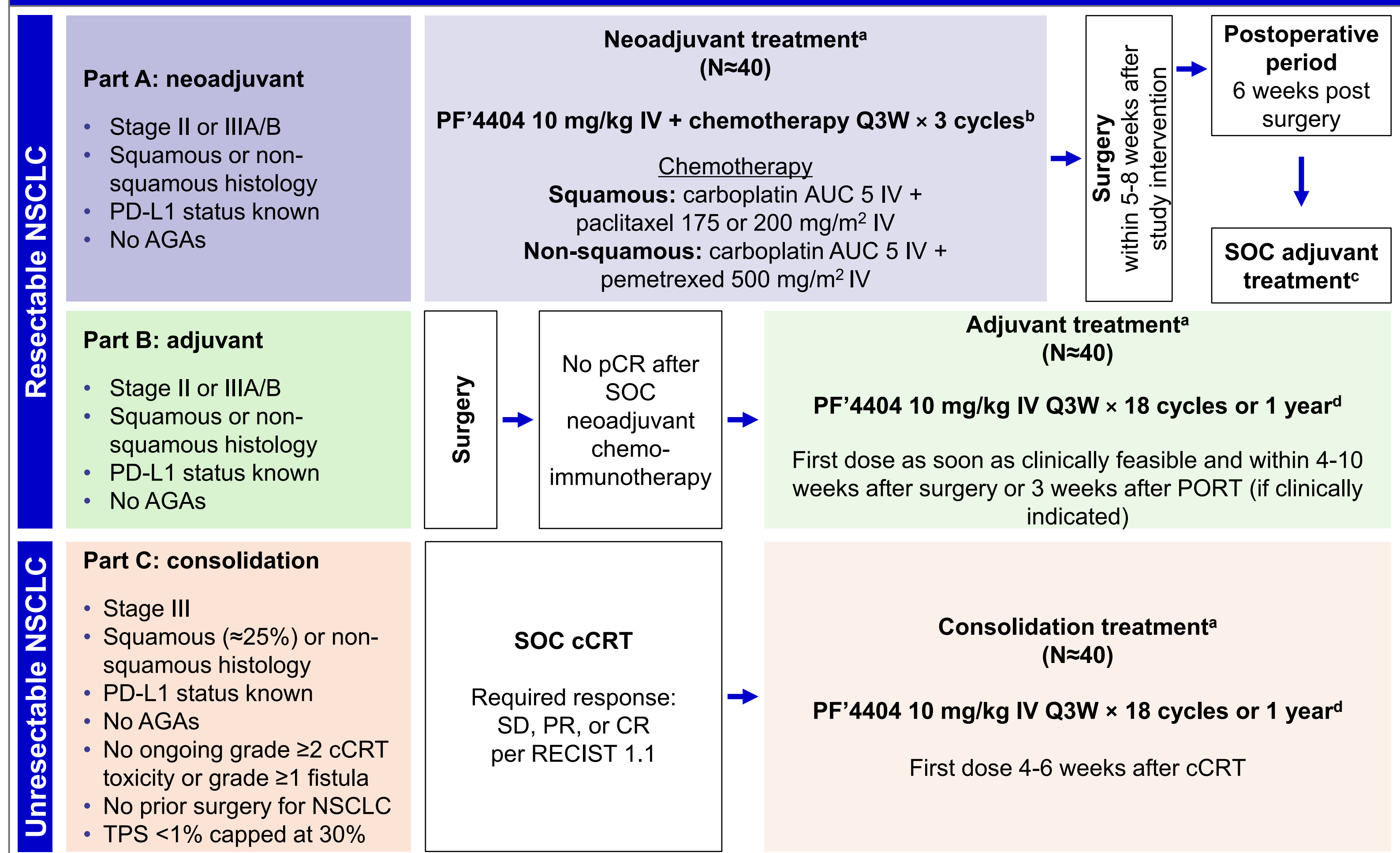
Figure 1. Proposed mechanism of action of PF'4404, a bispecific antibody targeting PD-1 and VEGF



Trial design

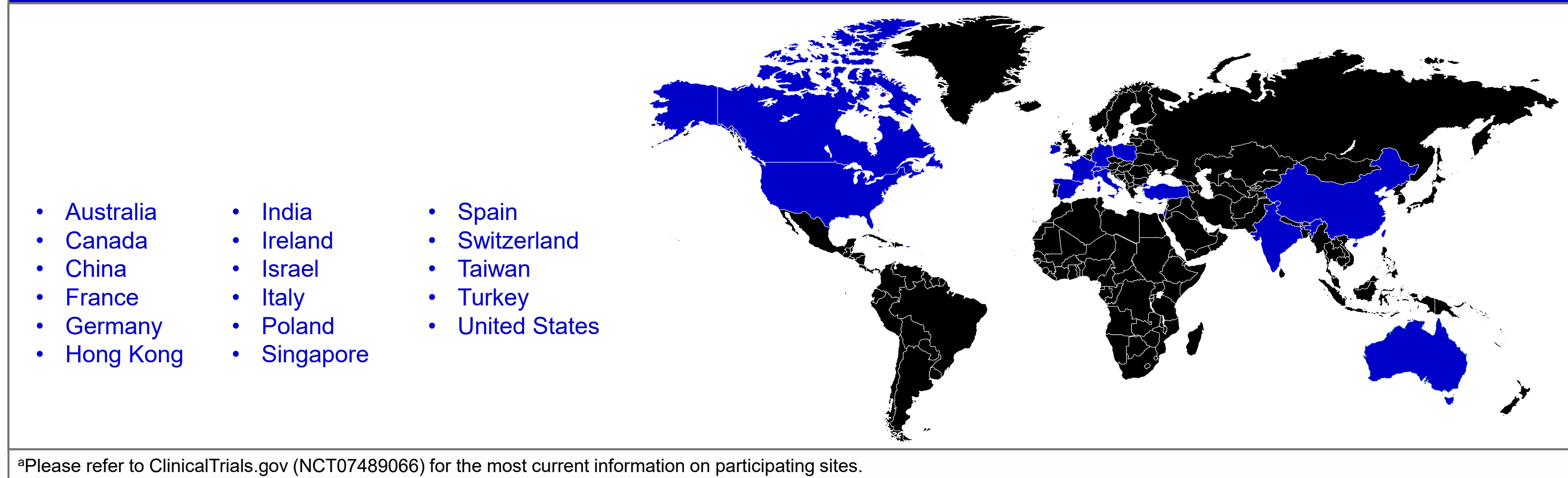
- Symbiotic-Lung-10 (**Figure 2**) is a multicenter, open-label, multi-arm phase 2 trial in adults with squamous and non-squamous NSCLC without actionable genomic alterations (AGAs), regardless of tumor programmed death ligand 1 (PD-L1) expression (**Table 2**)
- The study is evaluating PF'4404 as monotherapy and in combination regimens in the neoadjuvant and adjuvant settings for patients with resectable NSCLC as well as in consolidation therapy for patients with unresectable NSCLC. The study comprises 3 independent parts with simultaneous enrollment
 - Part A:** PF'4404 combined with platinum doublet chemotherapy in the neoadjuvant setting in patients with treatment-naïve, early-stage or locally advanced, resectable stage II or IIIA/B NSCLC
 - Part B:** PF'4404 monotherapy in the adjuvant setting in patients with completely resected, early-stage or locally advanced stage II or IIIA/B NSCLC who did not achieve a pathological complete response (pCR) after standard-of-care (SOC) neoadjuvant chemioimmunotherapy
 - Part C:** PF'4404 consolidation therapy in patients with locally advanced, unresectable stage III NSCLC who did not have progressive disease after definitive, platinum-based concurrent chemoradiotherapy (cCRT)
- Study endpoints are described in Table 3 and will be analyzed separately in each part
- The study is enrolling approximately 120 patients overall, with approximately 40 patients in each part
- Enrollment is active and began in March 2026 (**Figure 3**)

Figure 2. Symbiotic-Lung-10 trial design: early-stage NSCLC



^aIf PF'4404 10 mg/kg is not tolerated as determined by the safety committee, the dose may be de-escalated to 5 mg/kg Q3W. ^bWith an optional fourth cycle for patients deriving clinical benefit. ^cAt investigator discretion. ^dUntil confirmed disease progression, intolerable toxicity, or other protocol-specified criteria for treatment discontinuation. AGAs, actionable genomic alterations; AUC, area under curve; CR, complete response; IV, intravenous; PORT, postoperative radiation therapy; PR, partial response; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

Figure 3. Enrollment sites^a



^aPlease refer to ClinicalTrials.gov (NCT07489066) for the most current information on participating sites.

Table 1. Phase 2 studies in NSCLC with PF'4404			
	PF'4404 monotherapy ^a (NCT06361927) ¹	PF'4404 ^a plus platinum-based chemotherapy ^b (NCT06412471) ⁵	
Patient population	TPS ≥1% NSCLC (n=34)	Any TPS NSCLC	
		Squamous (n=24)	Non-squamous (n=29)
Data cutoff	February 28, 2026	July 4, 2025	
Median follow-up (95% CI), months	18.2 (17.3-19.3)	7.9 (7.0-8.7)	6.1 (4.6-7.0)
Confirmed ORR (95% CI), %	67.6 (49.5-82.6)	75.0 (53.3-90.2)	58.6 (38.9-76.5)
Median PFS (95% CI), months	12.4 (8.2-NE)	Not available	
^a At a dose of 10 mg/kg. ^b Carboplatin + paclitaxel in squamous NSCLC and carboplatin + pemetrexed in non-squamous NSCLC. NE, not estimable; ORR, objective response rate; PFS, progression-free survival; TPS, tumor proportion score.			



Table 2. Key patient inclusion and exclusion criteria

Key inclusion criteria	Key exclusion criteria
Part A only - Newly diagnosed, previously untreated, pathologically confirmed early-stage or locally advanced (stage II or IIIA/B) squamous or non-squamous NSCLC that is considered resectable Part B only - Pathologically confirmed early-stage or locally advanced (stage II or IIIA/B) squamous or non-squamous NSCLC and have undergone complete surgical resection - Did not achieve pCR with SOC neoadjuvant chemoimmunotherapy Part C only - Pathologically confirmed locally advanced unresectable (stage III) squamous or non-squamous NSCLC - Received ≥60 Gy of radiation and ≥2 cycles of definitive, platinum-based concurrent chemotherapy within 4-6 weeks before first dose and achieved SD or better per RECIST 1.1 - PD-L1 status known - ECOG performance status of 0 or 1 - Life expectancy ≥12 weeks - Adequate organ function - Submission of sufficient tumor tissue, if available	Parts A, B and C - Known <i>EGFR</i> or <i>ALK</i> AGAs; documented negative results required for patients with non-squamous histology - Known CNS lesions, including leptomeningeal metastases, brainstem, meningeal, or spinal cord metastases or compression - Clinically significant risk of hemorrhage or fistula - History of another malignancy ≤3 years before the first dose of study intervention, or any evidence of residual disease from a previously diagnosed malignancy - Active autoimmune diseases requiring systemic treatment within the past 2 years - Evidence of noninfectious or drug-induced ILD or pneumonitis - Any grade ≥3 pulmonary disease unrelated to underlying malignancy - Pleural effusion, pericardial effusion, or ascites - Major surgery or severe trauma ≤4 weeks prior to first dose of study intervention - History of severe bleeding tendency or coagulation dysfunction - History of esophageal varices, severe ulcers, unhealed wounds, GI perforation, GI obstruction, intra-abdominal abscess, or acute GI bleeding within 6 months of first dose - Unresolved toxicities from prior antitumor therapy that did not recover to NCI CTCAE v5.0 grade 0 or 1 Part A only - Previous systemic antitumor therapy, including chemotherapy, radiotherapy, or any other systemic therapy for NSCLC Part B only - Previous systemic antitumor therapy, including chemoradiotherapy, nonspecific immunomodulatory therapy within 2 weeks of first dose, or systemic anti-angiogenic therapy - For patients previously exposed to PD-(L)1 inhibitors - History of grade ≥3 irAEs caused by immunotherapy, irAEs leading to permanent discontinuation of treatment, grade 2 immune-related cardiotoxicity, or irAEs of any grade affecting nervous system or eyes - AEs from prior immunotherapy that have not completely resolved - History of AEs requiring treatment with immunosuppressants other than corticosteroids Part C only - Previous systemic antitumor therapy, including immunotherapy, nonspecific immunomodulatory therapy within 2 weeks of first dose, systemic anti-angiogenic therapy, or curative intent surgery for NSCLC - Unresolved fistula due to chemoradiotherapy that did not recover to NCI CTCAE v5.0 grade 0 - Clinically significant risk of hemorrhage or fistula, including but not limited to the following: - History of clinically significant hemoptysis with high risk of future serious hemoptysis event (eg, hemoptysis requiring transfusion/other invasive procedure) - Presence of radiographic or other evidence of tumor invasion through vascular wall - Mediastinal lymph node metastasis with invasion of the trachea, main bronchi, or esophagus
AE, adverse event; CNS, central nervous system; CTCAE, Common Terminology Criteria for Adverse Events; ECOG, Eastern Cooperative Oncology Group; GI, gastrointestinal; ILD, interstitial lung disease; irAE, immune-related AE; NCI, National Cancer Institute.	

Table 3. Study endpoints

	Part A	Part B	Part C
Primary endpoints	- Incidence of AEs - Proportion of patients undergoing surgery - Proportion of patients with complications after surgery - pCR rate by central pathology review	Incidence of AEs	Incidence of AEs
Secondary endpoints	- MPR rate by central pathology review and by investigator - pCR rate by investigator - EFS per RECIST 1.1 by investigator - OS - ORR per RECIST 1.1 by investigator after neoadjuvant therapy - ctDNA reduction or clearance - Laboratory abnormalities - Predose and/or postdose concentrations (PK) - Incidence of anti-drug antibodies	- DFS per RECIST 1.1 by investigator - OS - ctDNA reduction or clearance - Laboratory abnormalities - Predose and/or postdose concentrations (PK) - Incidence of anti-drug antibodies	- Confirmed ORR per RECIST 1.1 by investigator - PFS per RECIST 1.1 by investigator - OS - ctDNA reduction or clearance - Laboratory abnormalities - Predose and/or postdose concentrations (PK) - Incidence of anti-drug antibodies
Exploratory endpoints	- Patient-reported outcomes per EORTC QLQ-C30, EORTC QLQ-LC13, and FACT GP-5 - Measurements of biomarkers	- Patient-reported outcomes per EORTC QLQ-C30, EORTC QLQ-LC13, and FACT GP-5 - Measurements of biomarkers	- Patient-reported outcomes per EORTC QLQ-C30, EORTC QLQ-LC13, and FACT GP-5 - Measurements of biomarkers
ctDNA, circulating tumor DNA; DFS, disease-free survival; EFS, event-free survival; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EORTC QLQ-LC13, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Lung Cancer 13; FACT GP-5, Functional Assessment of Cancer Therapy Physical Well-Being Item GP5; MPR, major pathological response; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics.			