FPN 150TiP

# A phase 1b/2 trial of a PD-1/VEGF bispecific antibody (PF-08634404) in combination with anticancer agents in first-line for advanced solid tumors (Symbiotic-Lung-20)

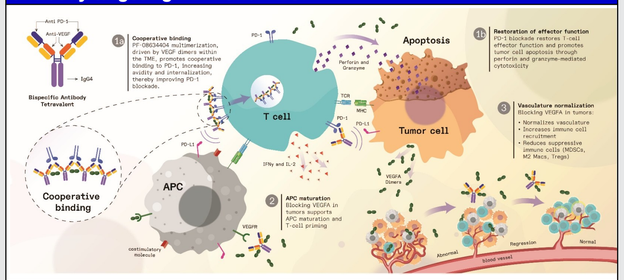

Enriqueta Felip,[1] Federico Cappuzzo,[2] Renato Martins,[3] Bo Wang,[4] Eric S. Schaefer,[5] Stefanie Gröpper,[6] Yung Lyou,[7] Ronald Tang,[8] Haiying Cheng,[9] Toshio Shimizu,[10] Kazushige Wakuda,[11] Jun Zhao,[12] Madeena Siddiqui,[13] Kevin Kim,[14] Shun Lu[15]

[1]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [2]National Cancer Institute Regina Elena, Rome, Italy; [3]Virginia Commonwealth University Medical Center, Richmond, VA, USA; [4]Sarah Cannon Research Institute at Willamette Valley Cancer Institute and Research Center, Eugene, OR, USA; [5]Highlands Oncology Group, Fayetteville, AR, USA; [6]Marien Hospital Düsseldorf, Düsseldorf, Germany; [7]Providence Medical Foundation, Fullerton, CA, USA; [8]Los Angeles Hematology Oncology Medical Group, Los Angeles, CA, USA; [9]Montefiore Medical Center, Bronx, NY, USA; [10]Kansai Medical University Hospital, Osaka, Japan; [11]Shizuoka Cancer Center, Shizuoka, Japan; [12]Beijing Cancer Hospital, Beijing, China; [13]Pfizer, San Francisco, CA, USA; [14]Pfizer, New York, NY, USA; [15]Shanghai Chest Hospital, Shanghai, China


## Background

- Current first-line (1L) treatment options for metastatic non-small cell lung cancer (NSCLC) for patients without actionable genomic alterations (AGAs) include programmed death-1 (PD-1) or programmed death ligand-1 (PD-L1) inhibitors with or without platinum-based chemotherapy[1]
  - However, most patients who receive PD-(L)1–based regimens in the 1L setting experience disease progression within 2-3 years, underscoring the need for more effective regimens to optimize outcomes in the 1L[2]
- PF-08634404 is a fully human immunoglobulin G4 bispecific antibody that simultaneously targets PD-1 and vascular endothelial growth factor (VEGF)[3,4] (**Figure 1**)
- Phase 2 studies have shown promising efficacy and manageable safety with PF-08634404 (SSGJ-707) as monotherapy (NCT06361927)[3] and in combination with platinum-based chemotherapy (NCT06412471)[5] as 1L treatment in advanced NSCLC
- Based on the results of these studies, Symbiotic-Lung-20, a phase 1b/2 trial was initiated to evaluate PF-08634404 in combination with different anticancer agents in advanced solid tumors including 1L treatment of NSCLC (NCT07227298)
- Sigvotatug vedotin (SV), an integrin beta-6 directed antibody-drug conjugate (ADC), has shown promising antitumor activity and manageable safety as monotherapy in patients with heavily pretreated advanced NSCLC[6] and in combination with pembrolizumab in 1L treatment of advanced NSCLC regardless of PD-L1 expression[7]
- PF-08046054 (PDL1V), a PD-L1–directed vedotin ADC, has also shown promising antitumor activity and manageable safety as monotherapy in patients with relapsed or refractory PD-L1–positive NSCLC[8]
- Based on these findings, PF-08634404 in combination with SV or PDL1V is being assessed as 1L therapy in patients with advanced NSCLC

## Figure 1. Proposed mechanism of action of PF-08634404, a bispecific antibody targeting PD-1 and VEGF




PF-08634404 is an investigational agent. Its safety and efficacy have not been established. © Pfizer, Inc. All rights reserved.
APC, antigen-presenting cell; IgG4, immunoglobulin G4; IFN-γ, interferon-gamma; IL-2, interleukin-2; MDSC, myeloid-derived suppressor cells; M2 Macs, M2 macrophages; MHC, major histocompatibility complex; Tregs, regulatory T-cells; TME, tumor microenvironment; TCR, T-cell receptor.

## Trial Design

- Symbiotic-Lung-20 is a prospective, open-label, multicenter, phase 1b/2 study designed to evaluate the safety, preliminary antitumor activity, pharmacokinetics (PK), and pharmacodynamics (PD) of PF-08634404 in combination with different anticancer agents in adults with advanced solid tumors
  - In part A, combination of PF-08634404 plus SV will be evaluated in patients with treatment-naïve locally advanced or metastatic NSCLC without AGAs
  - In part B, combination of PF-08634404 plus PDLV1 will be evaluated in patients with treatment-naïve locally advanced or metastatic PD-L1–positive NSCLC without AGAs
- Each part will be assessed in 2 phases (**Figure 2**):
  - The phase 1b safety run-in portion will evaluate safety, tolerability, PK, and preliminary antitumor activity to determine up to 2 recommended combination doses for each combination
    - Approximately 42 patients will be enrolled, with ≥3 patients per dose level
  - The phase 2 dose optimization portion will evaluate the 2 recommended combination doses from phase 1b to assess safety, tolerability, PK, PD, and antitumor activity
    - Approximately 40 patients each will be randomized 1:1 to receive the recommended combination doses
    - Upon selection of the recommended dose for expansion (RDE), 20 additional patients will be enrolled in each part of the phase 2 dose-expansion portion
- Inclusion and exclusion criteria are summarized in **Table 1**
- Study endpoints are summarized in **Table 2**
- Future cohorts may investigate other PF-08634404 combinations and tumor types
- Enrollment has begun in several countries (**Figure 3**)

## Table 1. Key patient inclusion and exclusion criteria

| Key inclusion criteria | Key exclusion criteria |
|---|---|
| • Age ≥18 years<br>• Pathologically confirmed locally advanced (stage IIIB/IIIC) or metastatic (stage IV) squamous or non-squamous NSCLC and not a candidate for complete surgical resection and curative concurrent/sequential chemoradiotherapy<br>• PD-L1 status available<br>– Part A: any PD-L1 TPS level<br>– Part B: only: PD-L1 ≥ TPS 1%<br>• Measurable disease based on RECIST 1.1 per investigator<br>• ECOG PS of 0 or 1<br>• Life expectancy ≥3 months<br>• Adequate organ function | • Previous systemic antitumor therapy for locally advanced, unresectable, or metastatic NSCLC<br>• Previous treatment with immunotherapy (exception is (neo)adjuvant anti–PD-(L)1), ADCs containing MMAE payload, systemic anti-angiogenic therapy, or prior radiotherapy to the lung within 6 months of first dose of study intervention<br>• For patients previously exposed to PD-(L)1 inhibitors<br>– 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<br>– AEs from prior immunotherapy not completely resolved<br>– History of AEs requiring treatment with immunosuppressants other than corticosteroids<br>• Participants with known AGAs with approved 1L therapies including *EGFR*, *ALK*, *ROS1*, *NTRK*, *BRAF*, *RET*, and *MET*<br>• Known active CNS lesions, including brainstem, meningeal, or spinal cord metastases or compression<br>• Clinically significant risk of hemorrhage or fistula<br>• History of another malignancy within 3 years before first dose of study intervention, or any evidence of residual disease from previously diagnosed malignancy<br>• Active autoimmune diseases requiring systemic treatment within past 2 years<br>• Evidence of noninfectious or drug-induced ILD or pneumonitis<br>• Any grade ≥3 pulmonary disease unrelated to underlying malignancy<br>• Uncontrolled hypertension<br>• Major surgery or severe trauma ≤4 weeks prior to first dose of study intervention<br>• History of severe bleeding tendency or coagulation dysfunction |

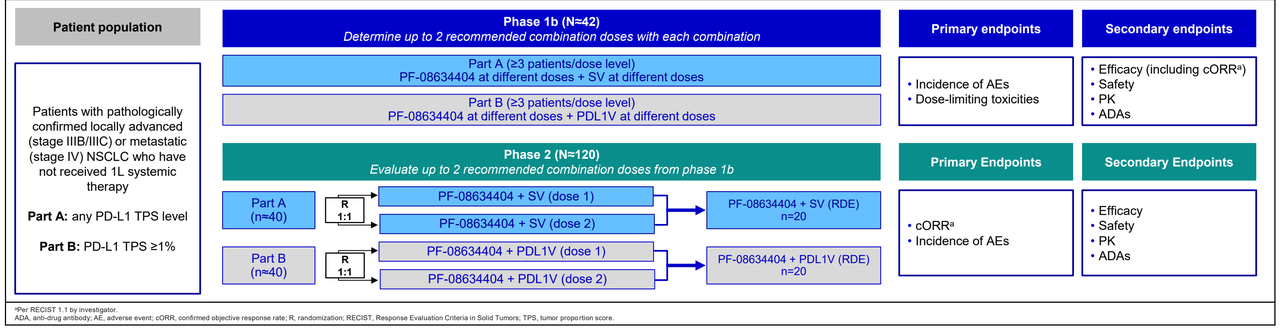
*ALK*, anaplastic lymphoma kinase; *BRAF*, v-raf murine sarcoma viral oncogene homolog B1; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; ILD, interstitial lung disease; irAE, immune-related adverse event; *MET*, mesenchymal-epithelial transition; MMAE, monomethyl auristatin E; NTRK, neurotrophic tyrosine receptor kinase; *RET*, rearranged during transfection; ROS1, repressor of silencing 1.

## Table 2. Study endpoints

| | Phase 1b | Phase 2 |
|---|---|---|
| **Primary endpoints** | • Incidence of AEs<br>• Dose-limiting toxicities | • Confirmed ORR per RECIST 1.1 by investigator<br>• Incidence of AEs |
| **Secondary endpoints** | • Confirmed ORR per RECIST 1.1 by investigator<br>• DCR per RECIST 1.1 by investigator<br>• DOR per RECIST 1.1 by investigator<br>• PFS per RECIST 1.1 by investigator<br>• OS<br>• Laboratory abnormalities<br>• Predose and/or postdose concentrations (PK)<br>• Incidence of ADAs | • DOR per RECIST 1.1 by investigator<br>• DCR per RECIST 1.1 by investigator<br>• PFS per RECIST 1.1 by investigator<br>• OS<br>• Laboratory abnormalities<br>• Predose and/or postdose concentrations (PK)<br>• Incidence of ADAs |
| **Exploratory endpoints** | • Measurements of biomarkers | • Mean score and change from baseline per EORTC QLQ-C30<br>• Mean score and change from baseline per EORTC QLQ-LC13<br>• Descriptive statistics per FACT GP5<br>• Measurements of biomarkers |

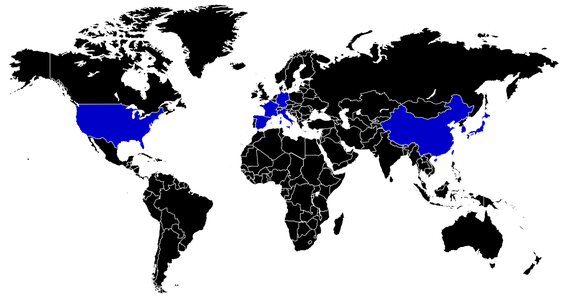
DCR, disease control rate; DOR, duration of response; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EORTC QLQ-LC13, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Lung Cancer 13; FACT, Functional Assessment of Cancer Therapy; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

## Figure 2. Symbiotic-Lung-20 trial design




[a]Per RECIST 1.1 by investigator.
ADA, anti-drug antibody; AE, adverse event; cORR, confirmed objective response rate; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors; TPS, tumor proportion score.

## Figure 3. Enrollment sites



- China
- France
- Germany
- Italy
- Japan
- South Korea
- Spain
- Taiwan
- United States

[a]Please refer to ClinicalTrials.gov (NCT07227298) for the most current information on participating sites.

**Electronic Poster**
Copies of this poster obtained through Quick Response code are for personal use only and may not be reproduced without permission from the authors of this poster. If you don't have a smartphone, access the poster via the internet at: https://scientificpubs.congressposter.com/p/g353m2ivqlv6zkwv


**References: 1.** Hendriks LE, et al. *Ann Oncol.* 2023;34(4):358-376. **2.** Garassino MC, et al. *J Clin Oncol.* 2023;41(11):1992-1998. **3.** Wu L, et al. *J Clin Oncol*. 2025. 43(suppl 16):Abstract 8543. **4.** Pfizer. Data on file. **5.** Wu L, et al. *J ImmunoTher Cancer.* 2025;13(suppl 3):Abstract 1328. **6.** Peters S, et al. *J Clin Oncol.* 2024;42(suppl 16):Abstract 8521. **7.** Seghal K, et al. *J Clin Oncol.* 2025;43(suppl 16):Abstract 3010. **8.** Oliva Bernal M, et al. *Ann Oncol.* 2025;36(suppl 2):S586-S587.



**Acknowledgments:** The authors thank the participating patients and their families, investigators, sub-investigators, research nurses, study coordinators, and operations staff. Editorial and medical writing support was provided by Rebecca Yao, PhD, of Nucleus Global and was funded by Pfizer.

This study is sponsored by Pfizer.


**Disclosures:** Dr Felip reports advisory board roles for AbbVie, Amgen, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Genentech, GlaxoSmithKline, Johnson & Johnson, Merck Sharpe & Dohme, Regeneron, Pfizer, Daiichi Sankyo, iTeos Therapeutics, Pierre-Fabre, PharmaM, Seagen, Tubulis, Moderna, and Ellipses Pharma; invited speaker roles for Amgen, Daiichi Sankyo, Merck Sharpe & Dohme, Pfizer, Eli Lilly, Roche-Genentech, Gilead, Johnson & Johnson, Medical Trends, Medscape, and PeerVoice; principal investigator roles for AstraZeneca, AbbVie, Amgen, Bayer, Beigene, Boehringer, Bristol Myers Squibb, Daiichi Sankyo, Exelixis Inc., F. Hoffmann-La Roche, Genentech, GlaxoSmithKline, Janssen, Merck Sharpe & Dohme, Merck KG, Novartis, Pfizer, Takeda, and Nuvalent; a leadership role for SEOM; membership in ETOP and CAC; and serves on the board of directors for Grifols.


**Contact:** Enriqueta Felip, efelip@vhio.net



Presented at the European Lung Cancer Congress 2026 | March 25-28, 2026 | Copenhagen, Denmark