



# A phase I/II study to evaluate EP0031 (lunbotinib), a next-generation selective RET inhibitor, as monotherapy and in combination with chemotherapy, in patients with advanced *RET* fusion-positive NSCLC

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## INTRODUCTION

### About EP0031

EP0031 (lunbotinib, A400), a first-in-class, next-generation selective RET inhibitor (SRI), has broad potency against common *RET* alterations, including resistance mutations<sup>1</sup>

- It has greater potency, antitumour activity, and central nervous system penetration/activity compared with first-generation SRIs<sup>1,2</sup>
- Clinical data indicate that EP0031 is active in patients who are SRI-naïve or have received prior SRI treatment, including those with brain metastases and/or on-target *RET* resistance mutations, and has an acceptable safety and tolerability profile<sup>1-4</sup>
- A new drug application has been submitted by Kelun-Biotech in China, based on positive monotherapy data in patients with SRI-naïve *RET* fusion-positive advanced non-small cell lung cancer (NSCLC), with/without prior treatment<sup>5</sup>
- The study described here is enrolling patients in the UK, Europe, US, and UAE; to date, more than 500 patients globally have received EP0031

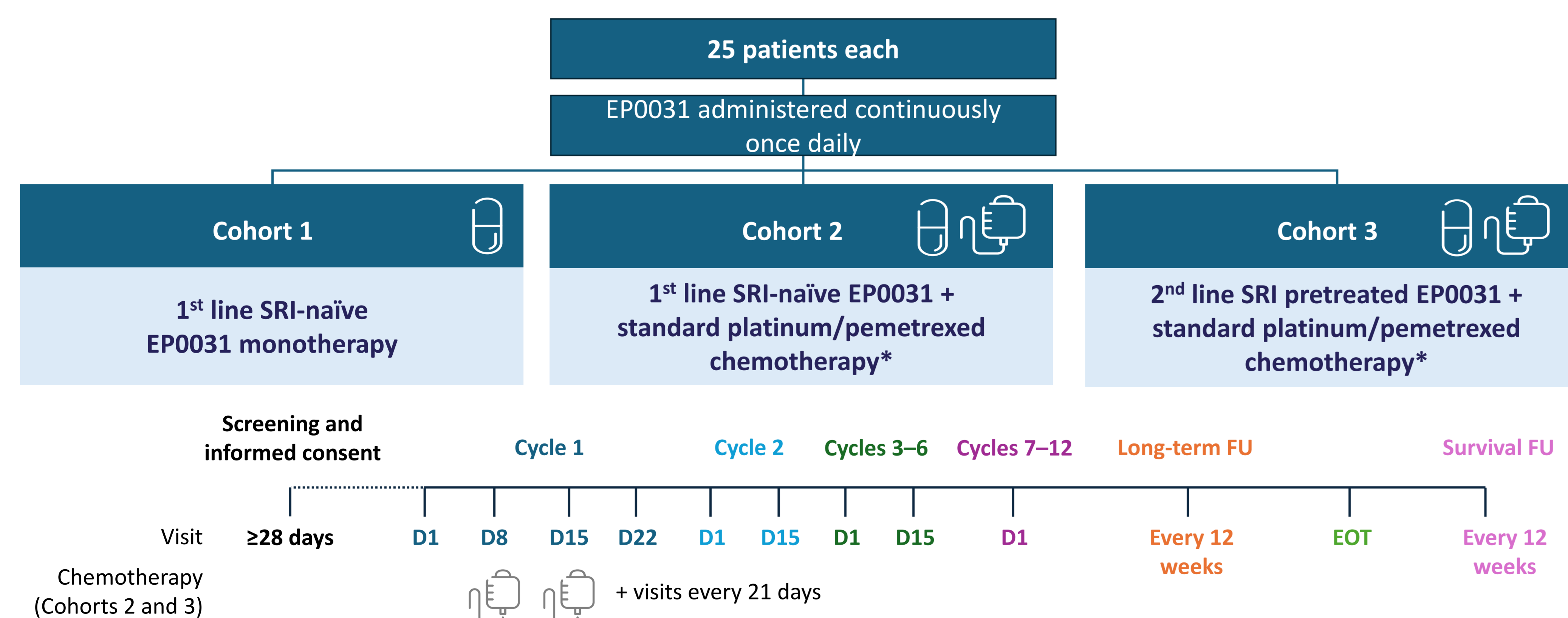
### Study rationale

- This is the first trial to evaluate SRI + chemotherapy in SRI-naïve and SRI pretreated settings
- Resistance to first-generation SRIs is heterogeneous and characterised by *RET*-dependent and -independent pathways
- Preclinical evidence indicates strong synergy between EP0031 and different chemotherapy agents
- There is growing evidence that *RET* fusion-positive NSCLC is sensitive to pemetrexed-based chemotherapy
- SRI + chemotherapy may represent a promising strategy to address underlying disease heterogeneity

## STUDY DESIGN

- EP0031-101 (NCT05443126) is an ongoing, modular phase I/II trial of EP0031 in patients with *RET* fusion-positive advanced NSCLC with three ongoing phase II cohorts (Figure)

Figure. Study design



\*Patients will receive chemotherapy doublet every 21 days for four cycles followed by pemetrexed maintenance; each combination cohort included a 3+3 safety run-in before expansion at the combination RP2D.

D, day; EOT, end of treatment; FU, follow-up; RP2D, recommended phase II dose; SRI, selective RET inhibitor.

## STUDY DESIGN

### Objectives

Phase II objectives include to investigate safety, tolerability, and efficacy of EP0031:

- Given as monotherapy in patients with no prior SRI therapy
- Given in combination with standard of care (SoC) chemotherapy in patients who have received a first-generation SRI or with no prior SRI therapy

Table. EP0031-101 study endpoints

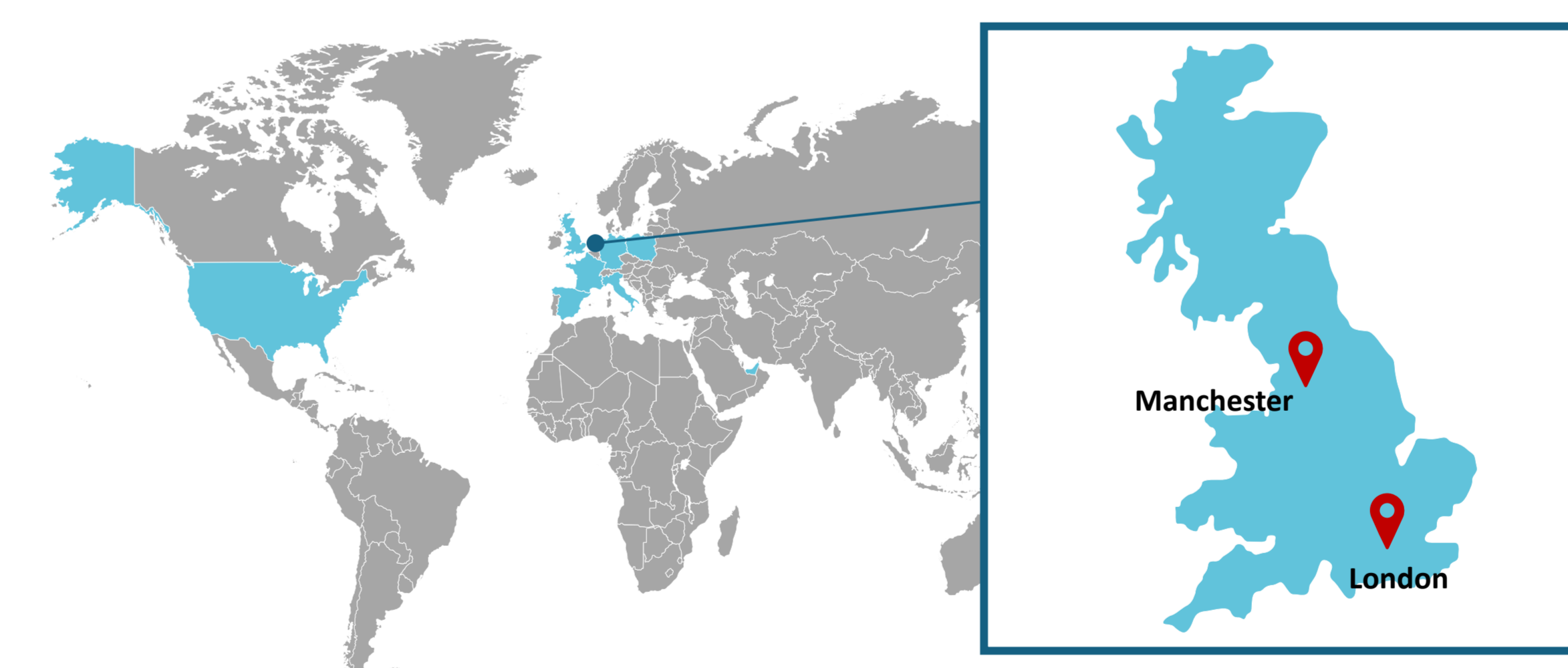
<b>Safety and tolerability</b>	Incidence of dose-limiting toxicities, adverse events (AE), serious AEs, and changes in laboratory parameters, physical examination, vital signs, and electrocardiogram
<b>Efficacy</b>	Tumour response as per RECIST v1.1 (objective response rate, best overall response, duration of response, time to response, change in tumour size), progression-free survival, and overall survival

### Key eligibility criteria

- ≥18 years of age
- Eastern Cooperative Oncology Group (ECOG) performance status ≤1
- Life expectancy >3 months at screening
- RET* fusion-positive NSCLC measurable by RECIST v1.1
- Brain metastases are permitted if stable following definitive treatment or asymptomatic and not requiring immediate definitive treatment
- No known major driver gene alterations other than *RET*
- One cycle of chemotherapy permitted prior to inclusion (1<sup>st</sup> line cohorts)

## STUDY CENTRES

- The study is currently recruiting with trial sites in France, Germany, Italy, Poland, Spain, UAE, UK, and US



### UK study sites:

- London**
  - University College London Hospital
  - Guy's and St Thomas' Hospital
  - The Royal Marsden NHS Foundation Trust
- Manchester**
  - The Christie NHS Foundation Trust

### EP0031:

- EP0031-101 is a phase I/II trial currently recruiting patients with *RET* fusion-positive advanced NSCLC
- EP0031, a next-generation SRI, is being investigated as monotherapy and in combination with SoC chemotherapy
- Safety run in completed for both cohorts 2 and 3 and expansions ongoing
- There are 40 study sites worldwide, including four study sites recruiting across the UK

### References

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