The study design has been described previously and is summarized below (scan QR code to read full study methods).

In this RATIONALE-303 trial subanalysis among patients with non-sq locally advanced or metastatic NSCLC previously treated with platinum-based chemotherapy:

- Tislelizumab prolonged OS vs docetaxel in patients with non-sq NSCLC
- Tislelizumab improved PFS rate at 12 months and ORR, and prolonged DoR vs docetaxel in patients with non-sq NSCLC
- Tislelizumab had a generally tolerable and manageable safety profile, in line with the profile of other PD-1/L1 inhibitors, with a lower occurrence of Grade 3 TEAEs vs docetaxel

Results were generally consistent with those in the overall ITT population.

### Methods

The study design has been described previously and is summarized below (scan QR code to read full study methods).

In the multivariate Cox proportional hazards regression model, in line with the profile of other PD-1/L1 inhibitors, with a lower occurrence of Grade 3 TEAEs vs docetaxel

Results were generally consistent with those in the overall ITT population.

### Results

### Background

- **Tislelizumab** is a humanized immunoglobulin G4 programmed cell death protein 1 (PD-1) inhibitor with high affinity and binding specificity for PD-1, and was engineered to minimize antibody-dependent cellular cytotoxicity, and complement-dependent cytotoxicity by T cells.

- The multicenter, randomized, open-label, Phase 3 RATIONALE-303 study (NCT03358875) investigated the efficacy and safety of tislelizumab vs docetaxel in patients with squamous (sq) or non-sq locally advanced or metastatic NSCLC with programmed death-ligand 1 (PD-L1) expression.

- In a pre-specified interim analysis in the overall intent-to-treat (ITT) population, tislelizumab was found to significantly improve overall survival (OS) vs docetaxel (median OS 17.2 vs 11.9 months, respective hazard ratio [HR] 0.65 [95% confidence interval (CI) 0.53, 0.81] vs 0.001), with a manageable safety profile.

- Given disease characteristics, standard of care, and prognosis differ between subtypes of NSCLC, the multicenter, randomized, open-label, Phase 3 RATIONALE-303 study (NCT03358875) investigated the efficacy and safety of tislelizumab vs docetaxel in patients with squamous (sq) or non-sq locally advanced or metastatic NSCLC with programmed death-ligand 1 (PD-L1) expression.

- Given disease characteristics, standard of care, and prognosis differ between subtypes of NSCLC, the study was conducted after 441 deaths had occurred (data cutoff: August 10, 2020).

- The primary endpoint was OS assessed in two ITT populations: the intention-to-treat (ITT) population and post-randomization ITT TUC (ITT TUC) population.

- Secondary endpoints included investigator (INV)-assessed objective response rate (ORR), duration of response (DoR), progression-free survival (PFS), and safety and tolerability.

- Exploratory endpoints included PD-L1 assessed disease control rate (DCR), clinical benefit rate and biometric, pharmacometrics, and immunogenicity analysis.

- The analysis was prespecified after 493 deaths (75% of planned events) and was ultimately concluded after a median follow-up duration of 16.0 months.

### Patient disposition

- In total, 287 patients were randomized to tislelizumab and 148 patients to docetaxel (the non-sq ITT population).

- Baseline characteristics were balanced between arms (Table 1), and broadly similar to the overall ITT population.

- At the date of cutoff (August 10, 2020):
  - Median follow-up was 20.6 months (IQR 18.3, 23.0) in the tislelizumab treatment arm and 16.7 months (IQR 14.2, 18.2) in the docetaxel treatment arm.

### Efficacy: OS

- Tislelizumab improved OS vs docetaxel (HR=0.70 [95% CI 0.54, 0.92]; p=0.0045) (Figure 1).

- Median OS was longer in the tislelizumab treatment arm than in the docetaxel arm (17.7 months vs 11.7 months, respectively; HR=0.70 [95% CI 0.54, 0.92]; p=0.0045) (Figure 1).

### Efficacy: PFS

- Treatment with tislelizumab resulted in a numerical improvement in PFS vs docetaxel (HR=0.84 [95% CI 0.68, 1.02]; p=0.0565) (Figure 2).

- While median OS was similar (17.7 months vs 11.7 months, respectively), patients remaining PFS event-free at 12 months was higher in the tislelizumab treatment arm than in the docetaxel arm (21.0% vs 17.5%, respectively) (Figure 2).

### Efficacy: Response rates

- ORR was greater with tislelizumab (23.9% vs docetaxel 14.2%) (Figure 3).

- DCR was exploratory endpoint and was similar in the two treatment arms.

- Median DoR was prolonged with tislelizumab (11.7 months [95% CI 8.8, 14.7]) vs docetaxel (6.2 months [95% CI 2.1, 7.2]) (Figure 4).

### Efficacy: Safety

- Fewer patients experienced Grade 3 treatment-emergent adverse events (TEAEs) with tislelizumab (30.9%) than docetaxel (41.0%) (Table 2).

- The most commonly reported Grade 3 TEAEs were lymphopenia (2.8% vs 4.2% with docetaxel) and neutropenia for docetaxel (22.5% vs 14.2% with tislelizumab).

- Table 2. Summary of TEAE incidence in the non- sq safety analysis population.

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### References