

## **Supplementary material**

### **Annual rate of decline in FVC and frequency of acute exacerbations across TOMORROW periods 1 and 2**

The adjusted annual rates of decline in FVC over TOMORROW periods 1 and 2 were -95.9 mL/year (95% CI: -153.2, -38.6) in the nintedanib 150 mg bid group and -189.7 mL/year (95% CI: -229.8, -149.6) in the comparator group. Over TOMORROW periods 1 and 2, the proportions of patients with  $\geq 1$  acute exacerbation were 4.7% in the nintedanib 150 mg bid group and 19.5% in the comparator group.

### **Annual rate of decline in FVC and frequency of acute exacerbations across TOMORROW periods 1 and 2, and across TOMORROW periods 1 and 2 and the open-label extension trial, including only patients who entered period 2 and the open-label extension trial, respectively**

The adjusted annual rate of decline in FVC over TOMORROW periods 1 and 2 including only patients who entered period 2 was -91.1 mL/year (95% CI: -144.9, -37.3) in the nintedanib 150 mg bid group (n=48) and -159.5 mL/year (95% CI: -209.7, -109.3) in the comparator group (n=54). The adjusted annual rate of decline in FVC over TOMORROW periods 1 and 2 and the open-label extension trial including only patients who entered the open-label extension trial was -134.8 mL/year (95% CI: -172.6, -97.0) in the nintedanib 150 mg bid group (n=35) and -149.3 mL/year (95% CI: -186.6, -112.0) in the comparator group (n=37). Over TOMORROW periods 1 and 2 and the open-label extension, the proportion of patients with  $\geq 1$  acute exacerbation including only patients who entered the open-label extension trial was 20.0% and 16.2% in the nintedanib 150 mg bid and comparator groups, respectively.

## Supplementary Tables

## Supplementary Figures

Figure S1. Design of TOMORROW periods 1 and 2 and the open-label extension trial

R, randomisation

Visits in period 2 occurred at 2, 4, 12 and 24 weeks after visit 9 and every 6 months thereafter. An end-of-treatment visit was completed by patients if they discontinued treatment, with a follow-up visit 2 weeks later. In period 2, patients treated with nintedanib in period 1 continued their dose, and placebo-treated patients were switched to nintedanib 50 mg qd in a blinded manner.

\*Patients entered the extension trial on the dose that they were receiving at the end of period 2, but had the option to increase dose to nintedanib 150 mg bid. Dose reduction from 150 mg bid to 100 mg bid and treatment interruption were permitted for the management of adverse events.

†Data are presented for the nintedanib 150 mg bid group and a comparator group comprising patients who received placebo in TOMORROW period 1, nintedanib 50 mg qd in TOMORROW period 2, and nintedanib at a range of doses between 50 mg qd and 150 mg bid in the open-label extension trial.

## Figure S2. Patient disposition

\*Patients entered the extension trial on the dose that they were receiving at the end of period 2, but had the option to increase dose to nintedanib 150 mg bid. Dose reduction from 150 mg bid to 100 mg bid and treatment interruption were permitted for the management of adverse events.

†Data are presented for the nintedanib 150 mg bid group and a comparator group comprising patients who received placebo in TOMORROW period 1, nintedanib 50 mg qd in TOMORROW period 2, and nintedanib at a range of doses between 50 mg qd and 150 mg bid in the open-label extension trial.

Data from the open-label extension trial are based on the database lock for the final analysis conducted on 15 October 2015. At the time of this analysis, 10 patients in the nintedanib 150 mg bid group and 5 patients in the comparator group remained in the trial (of whom 10 and 4 were still on trial medication).

The most common reason for discontinuation of trial medication in the extension trial in these groups was adverse events (17 of 25 patients in the nintedanib 150 mg bid group and 25 of 33 patients in the comparator group).