ONLINE SUPPLEMENTARY MATERIAL

Table S1. Exposure in the pooled nintedanib population and in nintedanib- and placebo-treated patients in the INPULSIS® trials

	Pooled population treated with nintedanib (n=1126)	INPULSIS®	
		Nintedanib (n=638)	Placebo (n=423)
Exposure, months			
Mean (SD)	27.7 (20.5)	10.3 (3.4)	10.8 (2.8)
Median	22.5	11.9	11.9
Maximum	93.1	12.7	13.1
Total exposure, patient–years	2599	548	383

Table S2. Exposure to nintedanib in individual trials

	TOMORROW (NCT00514683) (n=85)	TOMORROW open-label extension (NCT01170065) (n=35)	INPULSIS-1 (NCT01335464) (n=309)	INPULSIS-2 (NCT01335477) (n=329)	INPULSIS-ON open-label extension (NCT01619085) (n=734)	Phase IIIb trial (NCT01979952) (n=99)
Exposure, months						
Mean (SD)	14.3 (7.8)	33.9 (24.3)	10.3 (3.3)	10.3 (3.4)	28.8 (16.3)	10.3 (5.7)
Median	16.1	23.7	11.9	11.9	31.5	9.6
Maximum	25.9	69.1	12.5	12.7	56.2	19.1
Total exposure, patient–years	101	99	265	283	1765	85

Table S3. Adverse events leading to permanent dose reduction in the pooled nintedanib population and in nintedanib- and placebo-treated patients in the INPULSIS® trials

	Pooled population treated with nintedanib (n=1126)		INPULSIS®			
			Nintedanib (n=638)		Placebo (n=423)	
	Events, n	Event rate (per 100 patient exposure–years)	Events, n	Event rate (per 100 patient exposure–years)	Events, n	Event rate (per 100 patient exposure–years)
Diarrhoea	202	7.4	68	11.4	0	0.0
Nausea	27	1.0	11	1.8	0	0.0
Vomiting	19	0.7	7	1.2	0	0.0
Weight decreased	16	0.6	4	0.7	1	0.2

Adverse events leading to permanent dose reduction with event rate >0.5 per 100 patient exposure–years in the pooled population are shown.

Table S4. Adverse events leading to permanent treatment discontinuation in the pooled nintedanib population and in nintedanib- and placebo-treated patients in the INPULSIS® trials

	Pooled population treated with nintedanib (n=1126)		INPULSIS®			
			Nintedanib (n=638)		Placebo (n=423)	
	Events, n	Event rate (per 100 patient exposure–years)	Events, n	Event rate (per 100 patient exposure–years)	Events, n	Event rate (per 100 patient exposure–years)
Progression of IPF*	115	4.2	13	2.2	21	5.1
Diarrhoea	99	3.6	28	4.7	1	0.2
Nausea	26	1.0	13	2.2	0	0.0
Weight decreased	21	0.8	6	1.0	1	0.2
Decreased appetite	19	0.7	9	1.5	1	0.2
Vomiting	13	0.5	5	0.8	0	0.0
Pneumonia	11	0.4	6	1.0	1	0.2
Pulmonary embolism	10	0.4	2	0.3	2	0.5
Abdominal pain	9	0.3	5	0.8	1	0.2
Dyspnoea	8	0.3	0	0.0	1	0.2
Respiratory failure	8	0.3	0	0.0	1	0.2
Asthenia	7	0.3	4	0.7	0	0.0

Adverse events with event rate >0.25 per 100 patient exposure–years in the pooled population are shown. *Corresponds to MedDRA term 'IPF', which included disease worsening and acute exacerbations.

Table S5. Serious adverse events in the pooled nintedanib population and in nintedanib- and placebo-treated patients in the INPULSIS® trials

	Pooled population treated with nintedanib (n=1126)		INPULSIS®			
			Nintedanib (n=638)		Placebo (n=423)	
	Events, n	Event rate (per 100 patient exposure–years)	Events, n	Event rate (per 100 patient exposure–years)	Events, n	Event rate (per 100 patient exposure–years)
Progression of IPF*	229	8.4	46	7.7	47	11.4
Pneumonia	113	4.2	28	4.7	22	5.3
Pulmonary hypertension	67	2.5	11	1.8	10	2.4
Lung infection	56	2.1	3	0.5	0	0
Dyspnoea	49	1.8	3	0.5	6	1.5
Respiratory failure	46	1.7	2	0.3	9	2.2

Serious adverse events with event rate >1.5 per 100 patient exposure–years in the pooled population are shown. *Corresponds to MedDRA term 'IPF', which included disease worsening and acute exacerbations.

Table S6. Deaths in nintedanib-treated patients in the individual trials and in the pooled nintedanib population

	Number of deaths
TOMORROW trial (NCT00514683) and its open-label extension (NCT01170065)	22
INPULSIS-1* (NCT01335464)	18
INPULSIS-2 (NCT01335477)	30
INPULSIS-ON (NCT01619085)	179
Phase IIIb trial (NCT01979952)	4
Total	253

The pooled nintedanib population comprised 1126 patients. *One additional death, which occurred after lung transplant, was not taken into account in the survival models.

Table S7. Deaths in placebo-treated patients in the individual trials and in the pooled placebo population

	Number of deaths
TOMORROW trial (NCT00514683)	14
INPULSIS-1 (NCT01335464)	14
INPULSIS-2 (NCT01335477)	24
Phase IIIb trial (NCT01979952)	5
Total	57

The pooled placebo population comprised 565 patients.