Supplemental Table 1. Summary of Ioflupane I123 Injection Exposure by Study – ITD Population

		Study A (*4*)	Study B (*5,6*)	Study Study C (*1*)[*]	Study D (*3,8*)	Study E (*2,7*)
Number of subjects dosed	n	220	326	102	78	122[†]
Number of Doses						
1	n (%)	220 (100%)	326 (100%)	3 (3%)	72 (92%)	122 (100%)
2	n (%)	0 (0%)	0 (0%)	2 (2%)	6 (8%)	0 (0%)
3	n (%)	0 (0%)	0 (0%)	97 (95%)	0 (0%)	0 (0%)
Net activity administered (MBq)	n	220	325	102	78	120
	Mean (SD)	161.9 (26.20)	184.2 (22.30)	471.2 (80.03)	178.1 (44.65)	171.10 (12.46)
	Min, Max	111, 204	121, 287	153, 551	114, 356	121, 203
	Median	164.8	178.5	509.2	173.5	172.8
Time of SPECT imaging initiation after ioflupane (^{123}I) (hrs)	n	220	326	102	78	120
	Mean (SD)	3.7 (0.68)	3.6 (0.53)	3.5 (0.34)	3.9 (0.48)	N/A[‡]
	Min, Max	2, 6	3, 6	3, 5	3, 5	3, 6
	Median	3.5	3.5	3.5	3.9	N/A

ITD = Intent to diagnosis; n = Number; SD = Standard deviation; Min = Minimum; Max = Maximum; SPECT = single-photon emission computed tomography; hrs = hours.

[*]Study C had multiple doses. The subjects were only counted once. The multiple doses were summed for each subject. The multiple time to SPECT imaging was averaged for each subject.

[†]Reported for n=122 safety population, not n=92 efficacy population. In spite of small differences in the sample size, the mean values for reported parameters are the same.

[‡]Different data points were collected for Study E – see Supplemental Table 3.

Supplemental Table 2. Summary of Ioflupane I123 Injection Exposure by Study – PP Population

		Study			
		Study A (4)	Study B (5,6)	Study C (1)[*]	Study D (3,8)
Number of subjects dosed	n	157	288	100	77
Number of Doses					
1	n (%)	157 (100%)	288 (100%)	3 (3%)	71 (92%)
2	n (%)	0 (0%)	0 (0%)	2 (2%)	6 (8%)
3	n (%)	0 (0%)	0 (0%)	95 (95%)	0 (0%)
Net activity administered (MBq)	n	157	287	100	77
	Mean (SD)	152.4 (23.33)	184.5 (22.47)	470.9 (80.35)	178.3 (44.91)
	Min, Max	111, 185	121, 287	153, 551	114, 356
	Median	151.0	178.4	509.2	173.7
Time of SPECT imaging initiation after ioflupane (^{123}I) (hrs)	n	157	288	100	77
	Mean (SD)	3.7 (0.64)	3.6 (0.54)	3.5 (0.34)	3.9 (0.48)
	Min, Max	3, 6	3, 6	3, 5	3, 5
	Median	3.5	3.5	3.5	3.9

PP = Per protocol; n = Number; SD = Standard deviation; Min = Minimum; Max = Maximum; SPECT = single-photon emission computed tomography; hrs = hours.

[*]Study C had multiple doses. The subjects were only counted once. The multiple doses were summed for each subject. The multiple time to SPECT imaging was averaged for each subject.

Study E exposure data for PP were similar to ITD population (not shown).

Supplemental Table 3. Summary of Ioflupane I123 Injection Exposure for Study E (*2,7*) – Safety Population

		Study E
Number of subjects dosed	n	122[*]
Total Volume Administered (mL)	n	117
	Mean (SD)	2.304 (0.6587)
	Min, Max	1.48, 4.99
	Median	2.360
Infusion duration (min) [†]	n	122
	Mean (SD)	2.0 (0.88)
	Min, Max	1, 5
	Median	2.0

n = Number; mL = milliliter; SD = Standard deviation; Min = Minimum; Max = Maximum; min = Minutes.

[*]Reported for n=122 safety population, not n=92 efficacy population. In spite of small differences in the sample size, the mean values for reported parameters are the same. Data shown are not included in the drug exposure Supplemental Table 1.

[†]Duration was calculated as administration stop time – administration start time + 1.

Supplemental Table 4. Sensitivity (PPA) and specificity (NPA) for individual blinded readers and on-site readers for subjects with expert clinical diagnosis of dementia with Lewy Bodies – ITD and PP populations

Study and Reader Design	ITD population		PP population	
	Sensitivity (%, 95% CI)	Specificity (%, 95% CI)	Sensitivity (%, 95% CI)	Specificity (%, 95% CI)
Study B (*5,6*)	N =326		N = 288	
Study B – Baseline SPECT vs. Baseline Diagnosis				
Reader A	79.7% (69.2, 88.0)	91.2% (85.2, 95.4)	79.7% (69.2, 88.0)	91.2% (85.2, 95.4)
Reader B	75.3% (64.2, 84.4)	88.5% (82.0, 93.3)	75.3% (64.2, 84.4)	88.5% (82.0, 93.3)
Reader C	80.2% (69.9, 88.3)	90.5% (84.3, 94.9)	80.2% (69.9, 88.3)	91.2% (85.1, 95.4)
On-site	88.3% (80.0, 94.0)	77.4% (69.7, 83.9)	87.5% (78.7, 93.6)	77.1% (69.3, 83.7)
Study B – Baseline SPECT vs. M12 Diagnosis				
Reader A	82.3% (72.1, 90.0)	95.0% (89.3, 98.1)	82.3% (72.1, 90.0)	95.0% (89.3, 98.1)
Reader B	74.4% (63.2, 83.6)	91.7% (85.3, 96.0)	74.4% (63.2, 83.6)	91.7% (85.3, 96.0)
Reader C	78.8% (68.2, 87.1)	91.6% (85.1, 95.9)	78.8% (68.2, 87.1)	92.4% (86.0, 96.5)
On-site	89.9% (81.7, 95.3)	81.6% (73.7, 88.0)	89.5% (81.1, 95.1)	81.5% (73.5, 87.9)

PPA = Positive percent agreement; NPA = Negative percent agreement; ITD = Intent to diagnose; PP = Per Protocol; CI = Confidence interval; N = Number; SPECT = single-photon emission computed tomography; vs. = Versus; M = Month.
Sensitivity/specificity for dementia with Lewy Bodies (DLB) is calculated based on Probable DLB vs. Non-DLB.

Supplemental Table 5. Sensitivity (PPA) and specificity (NPA) for individual blinded readers and on-site readers for subjects with expert clinical diagnosis of Parkinsonian Syndrome – ITD and PP populations

Study and Reader Design	ITD population		PP population	
	Sensitivity (%, 95% CI)	Specificity (%, 95% CI)	Sensitivity (%, 95% CI)	Specificity (%, 95% CI)
Study A (*4*)	N = 220		N = 157	
Study A – Baseline SPECT vs. Baseline Clinical Diagnosis				
Reader A	93.0% (87.9, 96.5)	93.5% (84.3, 98.2)	92.2% (85.7, 96.4)	92.9% (80.5, 98.5)
Reader B	96.8% (92.8, 99.0)	80.6% (68.6, 89.6)	97.4% (92.6, 99.5)	85.7% (71.5, 94.6)
Reader C	96.2% (91.9, 98.6)	91.9% (82.2, 97.3)	96.5% (91.3, 99.0)	95.2% (83.8, 99.4)
Reader D	92.4% (87.1, 96.0)	96.8% (88.8, 99.6)	92.2% (85.7, 96.4)	97.6% (87.4, 99.9)
Reader E	94.3% (89.5, 97.4)	91.9% (82.2, 97.3)	93.9% (87.9, 97.5)	90.5% (77.4, 97.3)
On-site	97.5% (93.6, 99.3)	98.4% (91.3, 100.0)	96.5% (91.3, 99.0)	100.0% (91.6, 100.0)
Study C (*1*)	N = 102		N = 100	
Study C – Baseline SPECT vs. M18 Diagnosis Clinical Expert Reader 1				
Reader A	67.0% (56.9, 76.1)	75.0% (55.1, 89.3)	65.6% (55.2, 75.0)	75.0% (55.1, 89.3)
Reader B	67.0% (56.7, 76.2)	75.0% (55.1, 89.3)	65.6% (55.0, 75.1)	75.0% (55.1, 89.3)
Reader C	67.7% (57.5, 76.7)	75.0% (55.1, 89.3)	66.3% (55.9, 75.7)	75.0% (55.1, 89.3)
On-site	71.0% (61.1, 79.6)	75.0% (55.1, 89.3)	69.8% (59.6, 78.7)	75.0% (55.1, 89.3)
Study C – Baseline SPECT vs. M18 Diagnosis Clinical Expert Reader 2				
Reader A	70.5% (60.3, 79.4)	83.3% (65.3, 94.4)	69.2% (58.7, 78.5)	83.3% (65.3, 94.4)
Reader B	69.6% (59.1, 78.7)	80.0% (61.4, 92.3)	68.2% (57.4, 77.7)	80.0% (61.4, 92.3)
Reader C	71.3% (61.0, 80.1)	83.3% (65.3, 94.4)	70.0% (59.4, 79.2)	83.3% (65.3, 94.4)
On-site	73.7% (63.6, 82.2)	80.0% (61.4, 92.3)	72.5% (62.2, 81.4)	80.0% (61.4, 92.3)
Study C – Baseline SPECT vs. M36 Diagnosis				
Reader A	77.5% (66.0, 86.5)	96.8% (83.3, 99.9)	76.8% (65.1, 86.1)	96.8% (83.3, 99.9)
Reader B	77.9% (66.2, 87.1)	96.8% (83.3, 99.9)	77.3% (65.3, 86.7)	96.8% (83.3, 99.9)
Reader C	78.6% (67.1, 87.5)	96.8% (83.3, 99.9)	77.9% (66.2, 87.1)	96.8% (83.3, 99.9)
On-site	80.3% (69.1, 88.8)	90.3% (74.2, 98.0)	79.7% (68.3, 88.4)	90.3% (74.2, 98.0)

Study and Reader Design	ITD population		PP population	
	Sensitivity (%, 95% CI)	Specificity (%, 95% CI)	Sensitivity (%, 95% CI)	Specificity (%, 95% CI)
Study C – M18 SPECT vs. M18 Diagnosis Clinical Expert Reader 1				
Reader A	68.4% (58.2, 77.4)	75.0% (55.1, 89.3)	67.0% (56.6, 76.4)	75.0% (55.1, 89.3)
Reader B	68.7% (58.6, 77.6)	75.0% (55.1, 89.3)	67.4% (57.0, 76.6)	75.0% (55.1, 89.3)
Reader C	69.7% (59.6, 78.5)	71.4% (51.3, 86.8)	68.4% (58.1, 77.6)	71.4% (51.3, 86.8)
On-site	72.4% (62.5, 81.0)	75.0% (55.1, 89.3)	71.3% (61.0, 80.1)	75.0% (55.1, 89.3)
Study C – M18 SPECT vs. M18 Diagnosis Clinical Expert Reader 2				
Reader A	71.3% (61.0, 80.1)	82.8% (64.2, 94.2)	70.0% (59.4, 79.2)	82.8% (64.2, 94.2)
Reader B	71.3% (61.0, 80.1)	80.0% (61.4, 92.3)	70.0% (59.4, 79.2)	80.0% (61.4, 92.3)
Reader C	74.5% (64.4, 82.9)	83.3% (65.3, 94.4)	73.3% (63.0, 82.1)	83.3% (65.3, 94.4)
On-site	75.3% (65.2, 83.6)	80.0% (61.4, 92.3)	74.2% (63.8, 82.9)	80.0% (61.4, 92.3)
Study C – M18 SPECT vs. M36 Diagnosis				
Reader A	77.5% (66.0, 86.5)	96.7% (82.8, 99.9)	76.8% (65.1, 86.1)	96.7% (82.8, 99.9)
Reader B	77.5% (66.0, 86.5)	93.5% (78.6, 99.2)	76.8% (65.1, 86.1)	93.5% (78.6, 99.2)
Reader C	81.7% (70.7, 89.9)	96.8% (83.3, 99.9)	81.2% (69.9, 89.6)	96.8% (83.3, 99.9)
On-site	81.4% (70.3, 89.7)	90.3% (74.2, 98.0)	80.9% (69.5, 89.4)	90.3% (74.2, 98.0)
Study C – M36 SPECT vs. M36 Diagnosis				
Reader A	75.0% (63.0, 84.7)	96.7% (82.8, 99.9)	74.2% (62.0, 84.2)	96.7% (82.8, 99.9)
Reader B	76.9% (64.8, 86.5)	96.7% (82.8, 99.9)	76.2% (63.8, 86.0)	96.7% (82.8, 99.9)
Reader C	77.9% (66.2, 87.1)	96.7% (82.8, 99.9)	77.3% (65.3, 86.7)	96.7% (82.8, 99.9)
On-site	83.8% (72.9, 91.6)	86.2% (68.3, 96.1)	83.3% (72.1, 91.4)	86.2% (68.3, 96.1)
Study D (3,8)	N = 78		N = 77	
Study D – Baseline SPECT vs. M24 Diagnosis				
On-site	97.9% (88.9, 99.9)	76.7% (57.7, 90.1)	97.9% (88.7, 99.9)	76.7% (57.7, 90.1)
Study E (2,7)			N=92 (Broad)/59 (Narrow)	
Study E – Baseline SPECT vs. M12 Diagnosis				
On-site – Broad[*]	N/A	N/A	93.9% (83.1, 98.7)	95.4% (84.2, 99.4)
On-site – Narrow[†]	N/A	N/A	95.2% (83.8, 99.4)	100% (80.5, 100)

PPA = Positive percent agreement; NPA = Negative percent agreement; ITD = Intent to diagnose; PP = Per Protocol; CI = Confidence interval; N = Number; SPECT = single-photon emission computed tomography; vs. = Versus; M = Month; N/A = Not applicable.

*The narrow PP population in study PDT409 included subjects who were diagnosed as having a specific diagnosis, either a specific Parkinsonian Syndrome (PS – Parkinson's Disease, multiple system atrophy, or progressive supranuclear palsy) or a specific non-parkinsonian syndrome (non-PS – essential tremor).

[†]The broad PP population included subjects both with the narrow (specific) diagnoses summarized above, and subjects with non-specific diagnoses, such as "PS, precise diagnosis not defined" and "non-PS, precise diagnosis not defined."

Supplemental Table 6. Summary of inter-reader agreement between each pair of ioflupane (^{123}I) image readers and blinded readers vs. on-site reads – ITD population

Reader Pair	N	Kappa Coefficient κ (95% CI)
Study A (*4*)		
Reader A vs. Reader B	220	0.84 (0.77, 0.92)
Reader A vs. Reader C	220	0.89 (0.83, 0.96)
Reader A vs. Reader D	220	0.89 (0.82, 0.95)
Reader A vs. Reader E	220	0.95 (0.90, 0.99)
Reader B vs. Reader C	220	0.88 (0.81, 0.95)
Reader B vs. Reader D	220	0.81 (0.73, 0.90)
Reader B vs. Reader E	220	0.83 (0.75, 0.91)
Reader C vs. Reader D	220	0.90 (0.84, 0.97)
Reader C vs. Reader E	220	0.90 (0.84, 0.96)
Reader D vs. Reader E	220	0.89 (0.83, 0.96)
Readers A, B, C, D, E[*]	220	0.88 (0.84, 0.92)
Reader A vs. On-site	220	0.87 (0.80, 0.94)
Reader B vs. On-site	220	0.82 (0.73, 0.90)
Reader C vs. On-site	220	0.89 (0.82, 0.96)
Reader D vs. On-site	220	0.88 (0.82, 0.95)
Reader E vs. On-site	220	0.88 (0.81, 0.95)

Reader Pair	N	Kappa Coefficient κ (95% CI)
Study C (*1*) – Baseline		
Reader A vs. Reader B	99	0.98 (0.94, 1.02)
Reader A vs. Reader C	101	0.98 (0.94, 1.02)
Reader B vs. Reader C	98	1.00 (1.00, 1.00)
Readers A, B, C*	98	0.99 (0.87, 1.10)
Reader A vs. On-site	102	0.92 (0.84, 1.00)
Reader B vs. On-site	99	0.94 (0.87, 1.01)
Reader C vs. On-site	101	0.94 (0.87, 1.01)
Study C – Month 18		
Reader A vs. Reader B	101	0.94 (0.87, 1.01)
Reader A vs. Reader C	101	0.94 (0.87, 1.01)
Reader B vs. Reader C	102	0.92 (0.84, 1.00)
Readers A, B, C*	101	0.93 (0.82, 1.05)
Reader A vs. On-site	100	0.90 (0.81, 0.98)
Reader B vs. On-site	101	0.88 (0.78, 0.97)
Reader C vs. On-site	101	0.92 (0.84, 1.00)

Reader Pair	N	Kappa Coefficient κ (95% CI)
Study C – Month 36		
Reader A vs. Reader B	94	0.96 (0.90, 1.02)
Reader A vs. Reader C	97	0.96 (0.90, 1.02)
Reader B vs. Reader C	95	1.00 (1.00, 1.00)
Readers A, B, C[*]	94	0.97 (0.85, 1.09)
Reader A vs. On-site	95	0.83 (0.72, 0.94)
Reader B vs. On-site	92	0.87 (0.77, 0.97)
Reader C vs. On-site	95	0.87 (0.77, 0.97)
Study B (5,6)		
Reader A vs. Reader B	282	0.82 (0.75, 0.89)
Reader A vs. Reader C	281	0.93 (0.88, 0.97)
Reader B vs. Reader C	280	0.86 (0.79, 0.92)
Readers A, B, C[*]	272	0.88 (0.81, 0.95)
Reader A vs. On-site	292	0.68 (0.60, 0.76)
Reader B vs. On-site	293	0.60 (0.51, 0.69)
Reader C vs. On-site	296	0.64 (0.55, 0.72)
Study D (3,8)/E (2,7)		
No Readers	NA	NA

ITD = Intent to diagnose; N = Number of images with non-missing values for the respective reader pair; CI = Confidence interval; vs. = Versus; NA = Not applicable.
[*] Multiple coefficient for all independent image readers.

Supplemental Table 7. Summary of inter-reader agreement between each pair of ioflupane (^{123}I) image readers and blinded readers vs. on-site reads – PP population

Reader Pair	N	Kappa Coefficient κ (95% CI)
Study A (*4*)		
Reader A vs. Reader B	157	0.86 (0.77, 0.95)
Reader A vs. Reader C	157	0.88 (0.79, 0.96)
Reader A vs. Reader D	157	0.85 (0.76, 0.94)
Reader A vs. Reader E	157	0.92 (0.86, 0.99)
Reader B vs. Reader C	157	0.89 (0.80, 0.97)
Reader B vs. Reader D	157	0.83 (0.73, 0.92)
Reader B vs. Reader E	157	0.84 (0.74, 0.93)
Reader C vs. Reader D	157	0.91 (0.84, 0.98)
Reader C vs. Reader E	157	0.89 (0.81, 0.97)
Reader D vs. Reader E	157	0.86 (0.78, 0.95)
Readers A, B, C, D, E*	157	0.87 (0.82, 0.92)
Reader A vs. On-site	157	0.88 (0.80, 0.96)
Reader B vs. On-site	157	0.89 (0.81, 0.97)
Reader C vs. On-site	157	0.94 (0.88, 1.00)
Reader D vs. On-site	157	0.91 (0.84, 0.98)
Reader E vs. On-site	157	0.89 (0.81, 0.97)
Study C (*1*) – Baseline		
Reader A vs. Reader B	97	0.98 (0.94, 1.02)
Reader A vs. Reader C	99	0.98 (0.94, 1.02)
Reader B vs. Reader C	96	1.00 (1.00, 1.00)
Readers A, B, C*	96	0.99 (0.87, 1.10)
Reader A vs. On-site	100	0.92 (0.84, 1.00)
Reader B vs. On-site	97	0.94 (0.87, 1.01)
Reader C vs. On-site	99	0.94 (0.87, 1.01)

Reader Pair	N	Kappa Coefficient κ (95% CI)
Study C – Month 18		
Reader A vs. Reader B	99	0.94 (0.87, 1.01)
Reader A vs. Reader C	99	0.94 (0.87, 1.01)
Reader B vs. Reader C	100	0.92 (0.84, 1.00)
Readers A, B, C[*]	99	0.93 (0.82, 1.05)
Reader A vs. On-site	98	0.90 (0.81, 0.98)
Reader B vs. On-site	99	0.88 (0.78, 0.97)
Reader C vs. On-site	99	0.92 (0.84, 1.00)
Study C – Month 36		
Reader A vs. Reader B	92	0.96 (0.90, 1.02)
Reader A vs. Reader C	95	0.96 (0.90, 1.02)
Reader B vs. Reader C	93	1.00 (1.00, 1.00)
Readers A, B, C[*]	92	0.97 (0.85, 1.09)
Reader A vs. On-site	93	0.83 (0.71, 0.94)
Reader B vs. On-site	90	0.86 (0.76, 0.97)
Reader C vs. On-site	93	0.87 (0.77, 0.97)
Study B (5,6)		
Reader A vs. Reader B	259	0.82 (0.75, 0.89)
Reader A vs. Reader C	258	0.92 (0.87, 0.97)
Reader B vs. Reader C	255	0.85 (0.78, 0.92)
Readers A, B, C[*]	249	0.88 (0.80, 0.95)
Reader A vs. On-site	269	0.68 (0.59, 0.76)
Reader B vs. On-site	268	0.59 (0.50, 0.68)
Reader C vs. On-site	272	0.63 (0.54, 0.72)
Study D (3,8)/E (2,7)		

Reader Pair	N	Kappa Coefficient κ (95% CI)
No Readers	NA	NA

PP = Per protocol; N = Number of images with non-missing values for the respective reader pair; CI = Confidence interval; vs. = Versus; NA = Not applicable.

[*] Multiple coefficient for all independent image readers.

Supplemental Table 8. Intra-reader agreement for each independent BIE Ioflupane (^{123}I) SPECT reader in Study B (*5,6*).

Reader	N	n	Cohen's Kappa (95% CI)
Reader A	26	26	1.00 (1.00, 1.00)
Reader B	24*	24*	1.00 (1.00, 1.00)
Reader C	26	26	1.00 (1.00, 1.00)

BIE SPECT = Blinded image evaluation single-photon emission computed tomography; N = number of images with non-missing value for SPECT visual assessment for the 2 respective reads; n = number of images with agreement; CI = Confidence interval.
*Reader B had 2 non-evaluable cases during the first read, so these 2 cases were removed from intra-reader analysis for this reader.