

## PK Endpoints

1. PK parameter: Area under the plasma concentration-time curve from time 0 to infinity ( $AUC_{0-\infty}$ ) at Day1, Week 13, Week 26, Week 39, & Week 52
2. PK parameter: Apparent clearance ( $CL/F$ ) at Day 01, Week 13, Week 26, Week 39, & Week 52
3. PK parameter: Apparent volume of distribution ( $V_z/F$ ) at Day 01, Week 13, Week 26, Week 39, & Week 52
4. PK parameter: Elimination half-life ( $t_{1/2}$ ) at Day 01, Week 13, Week 26, Week 39, & Week 52

**Table 9.1.2.1: Mean Pharmacokinetic Parameters of BMN 111 By Dose And Visit For Cohort 2**

Cohort	VISIT	Dose ( $\mu\text{g/kg}$ )	Summary	$T_{\max}$ (min)	$C_{\max}$ (pg/ml)	$AUC_{0-4}$ (min*pg/ml)	$AUC_{0-120\text{min}}$ (min*pg/ml)	$AUC_{0-\infty}$ (min*pg/ml)	$CL/F$ (ml/min/kg)	$V_z/F$ (ml/kg)	$t_{1/2}$ (min)
Cohort 2	Day 1	15	N	3	3	3	3	1	1	1	1
			Mean	11.3	2840	65900	83100	102000	147	5550	26.1
			SD	6.35	1230	33600	48300				
			CV%	56	43.5	51	58.1				
			Min	4	1520	29100	29100	102000	147	5550	26.1
			Median	15	3030	73600	98300	102000	147	5550	26.1
			Max	15	3970	94900	122000	102000	147	5550	26.1
Cohort 2	Day 1	30	N	7	7	7	7	7	7	7	7
			Mean	12.9	14500	547000	525000	557000	65.9	3190	33.3
			SD	9.1	5950	279000	251000	278000	31.6	1790	8.41
			CV%	70.8	41.1	51	47.8	49.9	48	56.2	25.3
			Min	4	6270	256000	256000	264000	27.3	1440	25.2
			Median	14	15200	517000	500000	529000	56.7	2470	28.7
			Max	30	25400	1090000	1000000	1100000	114	6260	47
Cohort 2	Week 13	15	N	2	2	2	2	1	1	1	1
			Mean	6	5970	112000	115000	74500	201	7810	26.9
			SD	1.41	2390	62900	59300				
			CV%	23.6	40	56	51.6				
			Min	5	4280	67800	72900	74500	201	7810	26.9
			Median	6	5970	112000	115000	74500	201	7810	26.9
			Max	7	7660	157000	157000	74500	201	7810	26.9