Phase 3 PRISM studies: Efficacy and safety of pegvaliase 60 mg dose in adult patients with phenylketonuria

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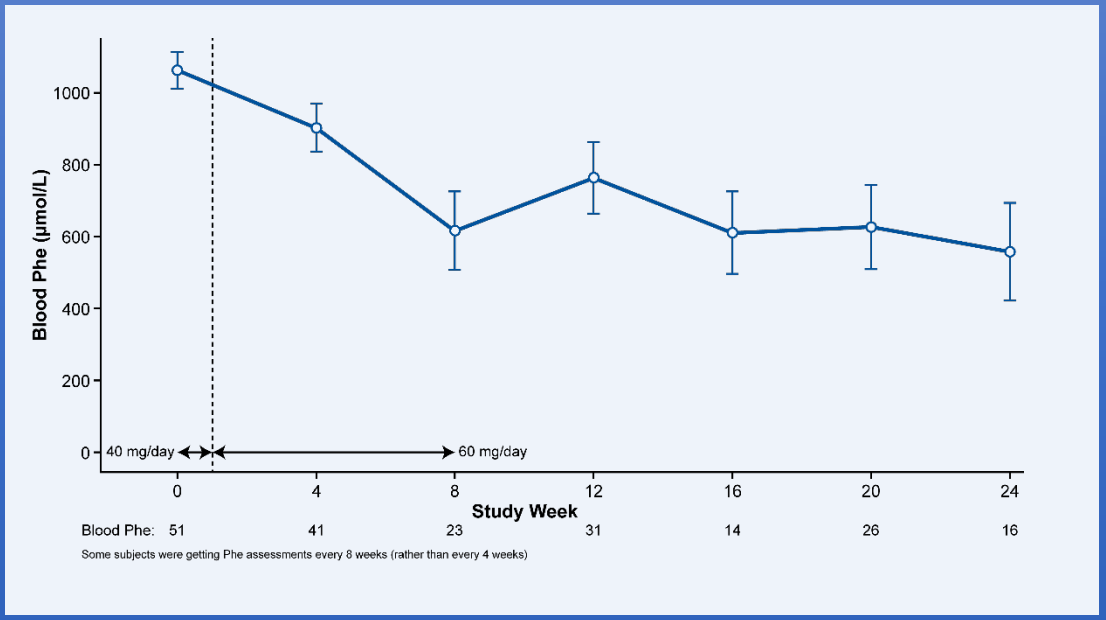
Objective

- **To report end of study (February, 2019) efficacy results for the Stable Pegvaliase 60 mg/day population (N=51), patients enrolled in PRISM-2 Part 4 on 60 mg/day for ≥4 weeks with ≥80% adherence, and report safety data for all patients receiving at least one dose of 60 mg in PRISM-2 Part 4**

- Pegvaliase (Palynziq®) is approved for PKU patients with uncontrolled blood Phe concentrations (>600 µmol/L) on existing management for adults at doses of up to 40 mg/day in the US and for patients ≥16 years old at doses of up to 60 mg/day in Europe
- PRISM-2 Part 4 was an open-label extension, in which subjects could titrate up to 60 mg/day if they had a total of >52 weeks of pegvaliase treatment and a minimum of 8 weeks at the 40 mg/day dosage in PRISM-2

Figure 1. Mean (SE) plot of blood Phe after dose titration from 40 mg/day to 60 mg/day in PRISM-2 Part 4



- Mean (SD) blood Phe was 1063 (372) µmol/L (n=51) on the 40 mg/day dose
- This decreased to 617 (528) µmol/L 8 weeks after increasing the dose increase to 60 mg/day (n=23)
- Kaplan-Meier estimates showed that 28%, 39%, and 57% of subjects reached blood Phe levels ≤360 µmol/L by 12, 24, and 48 weeks on 60 mg/day dose, respectively

Table 1. AEs occurring at or after 1 year of treatment were assessed by dose level

Number of subjects with event (%) Number of events (event rate per person-year)	Dosage on or prior to time of onset				
	<20 mg/day (n=202)	20 – <40 mg/day (n=202)	40 – <60 mg/day (n=193)	≥60 mg/day (n=98)	Any dose level (N=202)
Total treatment exposure person-years)[b]	67.8	99.9	238.6	94.7	501.8
AEs					
Any AE	55 (27.2%) 1343 (19.80)	89 (44.1%) 1884 (18.87)	164 (85.0%) 4106 (17.21)	58 (59.2%) 1413 (14.92)	199 (98.5%) 8762 (17.46)
AEs leading to study drug discontinuation	0	1 (0.5%) -	5 (2.6%) -	1 (1.0%) -	7 (3.5%) -
Any SAE	7 (3.5%) 8 (0.12)	5 (2.5%) 10 (0.10)	16 (8.3%) 25 (0.10)	6 (6.1%) 6 (0.06)	32 (15.8%) 49 (0.10)
AEs of special interest					
Acute systemic hypersensitivity reactions	0	1 (0.5%) -	3 (1.6%) -	0	4 (2.0%) -
Injection site reactions	9 (4.5%) 199 (2.93)	36 (17.8%) 279 (2.79)	90 (46.6%) 609 (2.55)	31 (31.6%) 216 (2.28)	127 (62.9%) 1304 (2.60)
Injection site skin reactions lasting ≥14 days	6 (3.0%) 57 (0.84)	14 (6.9%) 20 (0.20)	47 (24.4%) 88 (0.37)	17 (17.3%) 40 (0.42)	71 (35.1%) 205 (0.41)
Arthralgia	26 (12.9%) 136 (2.01)	39 (19.3%) 119 (1.19)	79 (40.9%) 294 (1.23)	32 (32.7%) 84 (0.89)	127 (62.9%) 633 (1.26)

- As AEs are more common in the first 6 months of treatment, when patients are on lower doses, AEs occurring at or after 1 year of treatment were assessed by dose level
- During this period, subjects who received at least one 60 mg dose of pegvaliase (n=98) had comparable/lower exposure-adjusted event rates at or after 1 year of treatment for AEs, SAEs, HAEs, injection site reactions, and arthralgia compared with subjects receiving lower doses
- No subjects experienced episodes of acute systemic hypersensitivity reactions after receiving 60 mg dose in Part 4 with a maximum of 274 weeks of follow-up

Conclusions

- **25% of subjects in Part 4 of PRISM-2 received stable doses of 60 mg/day**
- **Substantial blood Phe reduction was observed after dose increase to 60 mg/day, which was sustained over time**
- **Safety profile of 60 mg/day dose was consistent with the lower maintenance doses**