Table S1. Summary of phase 3 pegvaliase ELISA performance

Key Assay Parameter	Validation Results
Intra-Assay Accuracy and Precision (QCs, LOQs)	|%RE| ≤7.1%, 3.0% at LOQs %CV ≤7.8%, 13.4% at LOQs %TE ≤14.9%, 16.4% at LOQs
Inter-Assay Accuracy and Precision (QCs, LOQs)	|%RE| ≤7.1%, 3.0% at LOQs %CV ≤15.7%, 21.0% at LOQs %TE ≤22.8%, 24.0% at LOQs
Standard Curve	Mean 5PL curve fit R^2 ≥0.996 Absolute %RE ≤2.9%, ≤3.6% at LOQs %CV ≤7.9%, ≤10.1% at LOQs
Specificity	rAvPAL: tolerant up to 78 ng/mL; %CV ≤13.8%, mean |%RE| ≤9.7% PEG: tolerant up to 8 µg/mL; %CV ≤20.6%, mean |%RE| ≤22% Anti-rAvPAL: tolerance up to 2.5 µg/mL; %CV ≤6.6%, mean |%RE| ≤24.7% Anti-PEG: tolerance up to 50 µg/mL; %CV ≤5.8%, mean |%RE| ≤11.0% Non-specific analyte in Blank Matrix: 100% tested BLQ

5PL, 5-parameter logistic regression; BLQ, below limit of quantitation; %CV, coefficient of variation; ELISA, enzyme-linked immunosorbent assay; IgG, immunoglobulin G; LOQ, limit of quantitation; PEG, polyethylene glycol; QC, quality control; rAvPAL, recombinant *Anabaena variabilis* phenylalanine [Phe] ammonia lyase; %RE, percent relative error; ROQ, range of quantitation; %TE, percent total error. Tolerance limits denote concentrations of potentially interfering substances in plasma samples that did not interfere with precise and accurate quantitation of pegvaliase during method validation assessments. Tolerant up to 78 ng/mL indicates that quality control samples containing known pegvaliase concentrations could be precisely and accurately measured in the presence of up to 78 ng/mL rAvPAL.

Table S2. Mean (relative standard error) of pharmacodynamic parameters, by dietary phenylalanine intake quartile

Dietary Phe Intake Quartile	E_0 (µmol/L)	IC_{50} (ng/mL)	I_{max} (µmol/L)	Gamma
Q1 (0–1,042.3 mg)	764 (1.95%)	367 (8.61%)	765 (2.04%)	1.98 (10.7%)
Q2 (1,042.3–1,695.0 mg)	898 (1.81%)	403 (7.15%)	902 (1.87%)	1.57 (7.00%)
Q3 (1,695.0–2,711.3 mg)	1,322 (1.35%)	938 (5.61%)	1,309 (1.43%)	1.42 (5.66%)
Q4 (2,711.3–10,903.3 mg)	1,353 (1.55%)	1,045 (4.11%)	1,352 (1.57%)	2.74 (5.70%)

E_0, blood Phe level when plasma pegvaliase concentration is 0; I_{max}, maximum change in blood Phe level due to drug effect; IC_{50}, plasma concentration of drug required to obtain 50% of the maximum drug effect; Gamma, Hill coefficient; Phe, phenylalanine; Q, quartile.

Figure S1. Relationship between pegvaliase clearance and patient body weight in PRISM-2. CL/F, apparent clearance.