APHENITY Topline Results

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Patient Living with PKU

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PTC THERAPEUTICS 25 YEARS

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APHENITY Topline Results Demonstrate Clinical and Statistically Significant Benefit

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Achieved primary endpoint in placebo-controlled portion of study with statistically significant ($p<0.0001$) blood phenylalanine (Phe) reduction

Demonstrated substantial Phe reduction in both the overall primary analysis population (63%) and the subset of classical PKU patients (69%)

Achieved Phe reduction sufficient to bring **84%** of study patients within US guidelines for Phe reduction <360 µmol/L

Well tolerated with no serious adverse events

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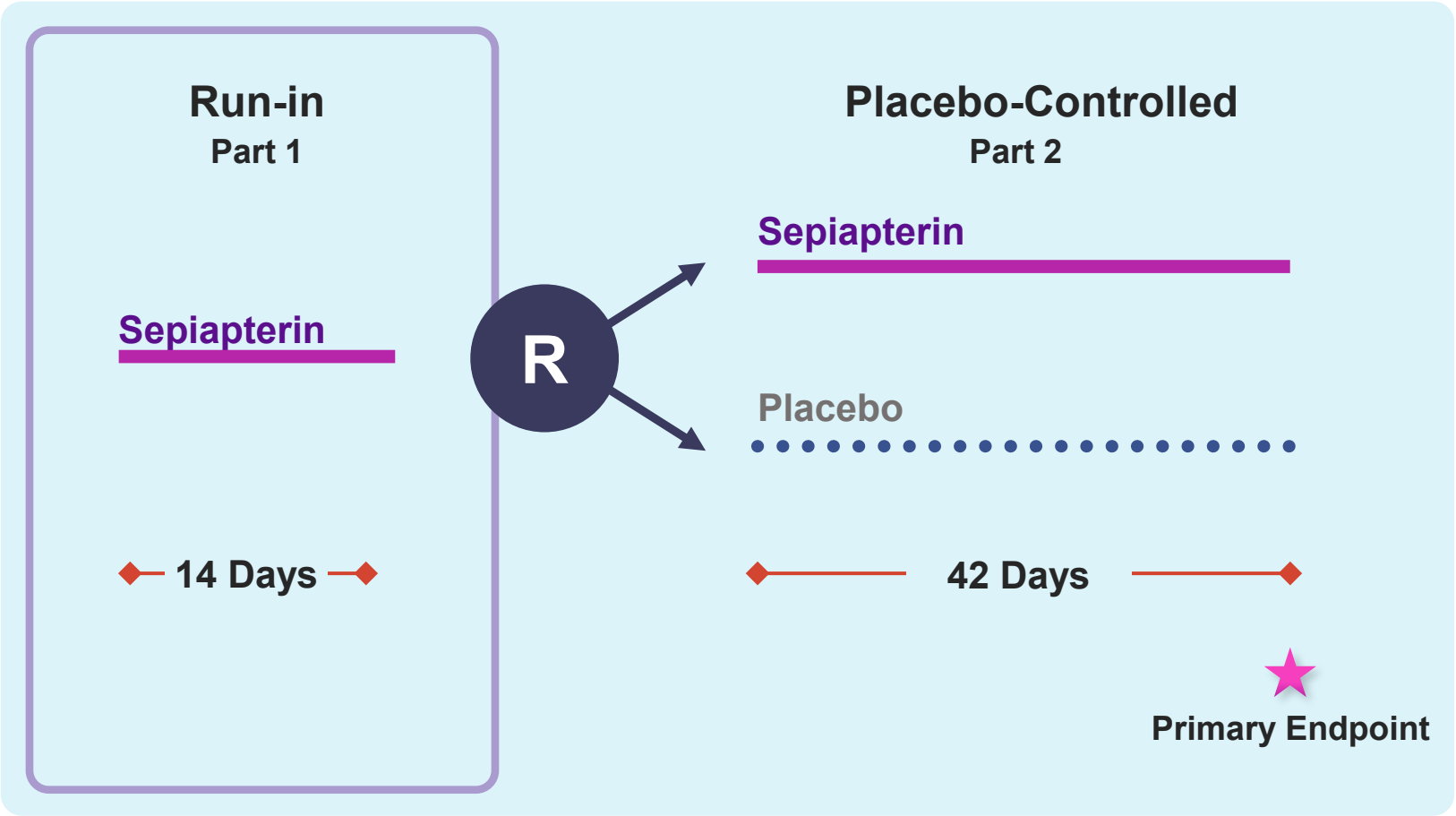
APHENITY Global Registration-Directed Trial of Sepiapterin Study Design



Primary Endpoint

Reduction in blood phenylalanine levels

APHENITY Part 1 Results Demonstrated Marked Blood Phe Reductions

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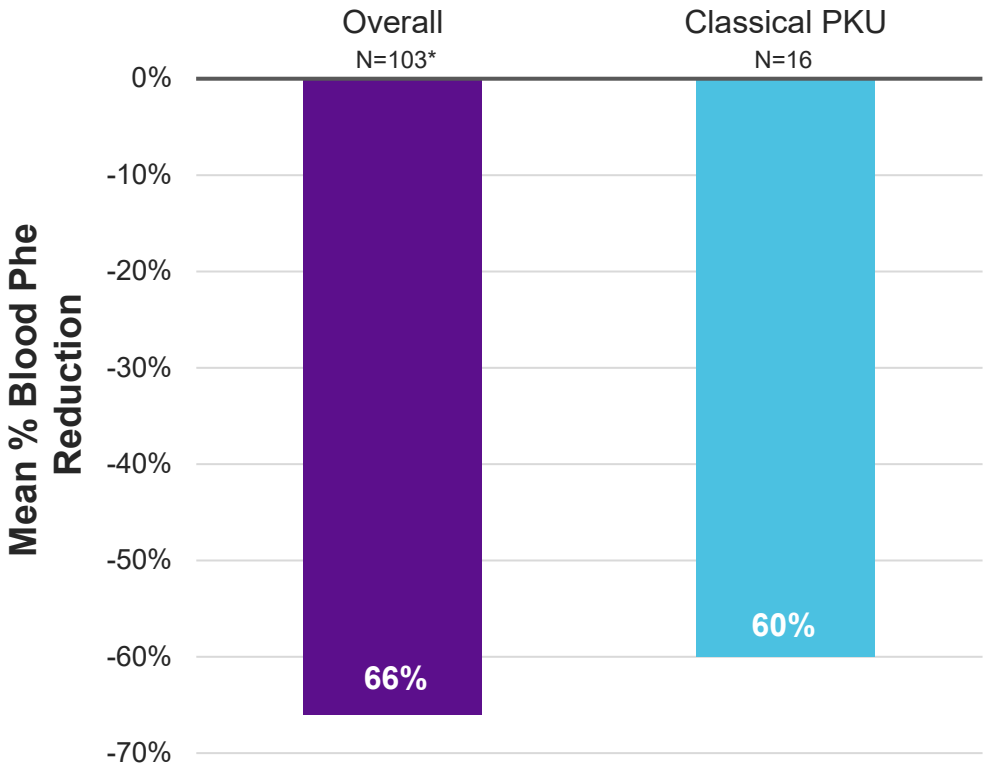
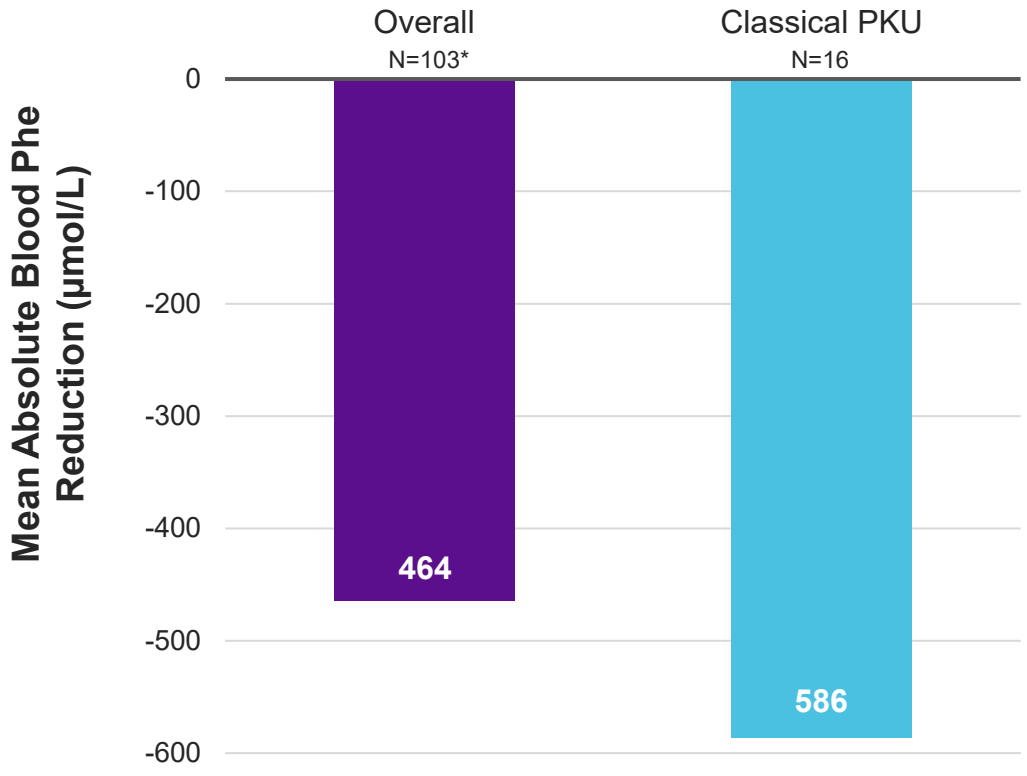
Mean % Blood Phe Reduction
≥30% responders



Mean Absolute Blood Phe Reduction (µmol/L)
≥30% responders



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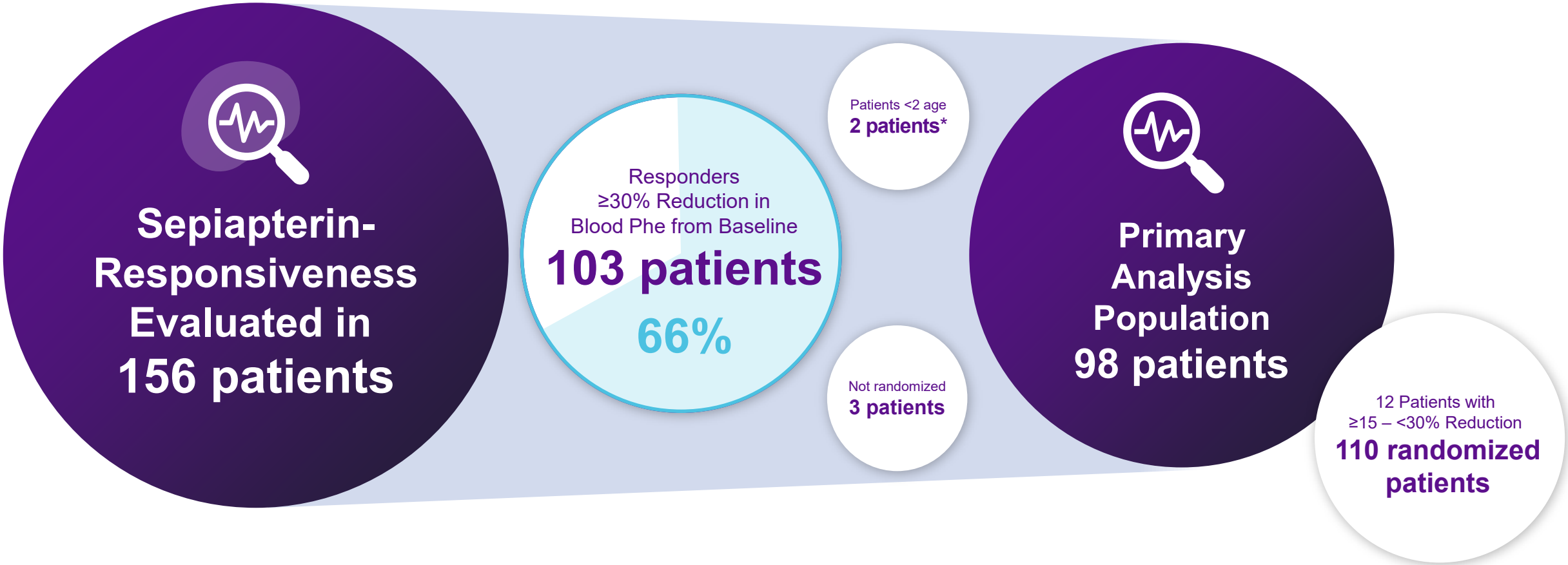
Baseline Phe Levels of Classical PKU Patients in Part 1

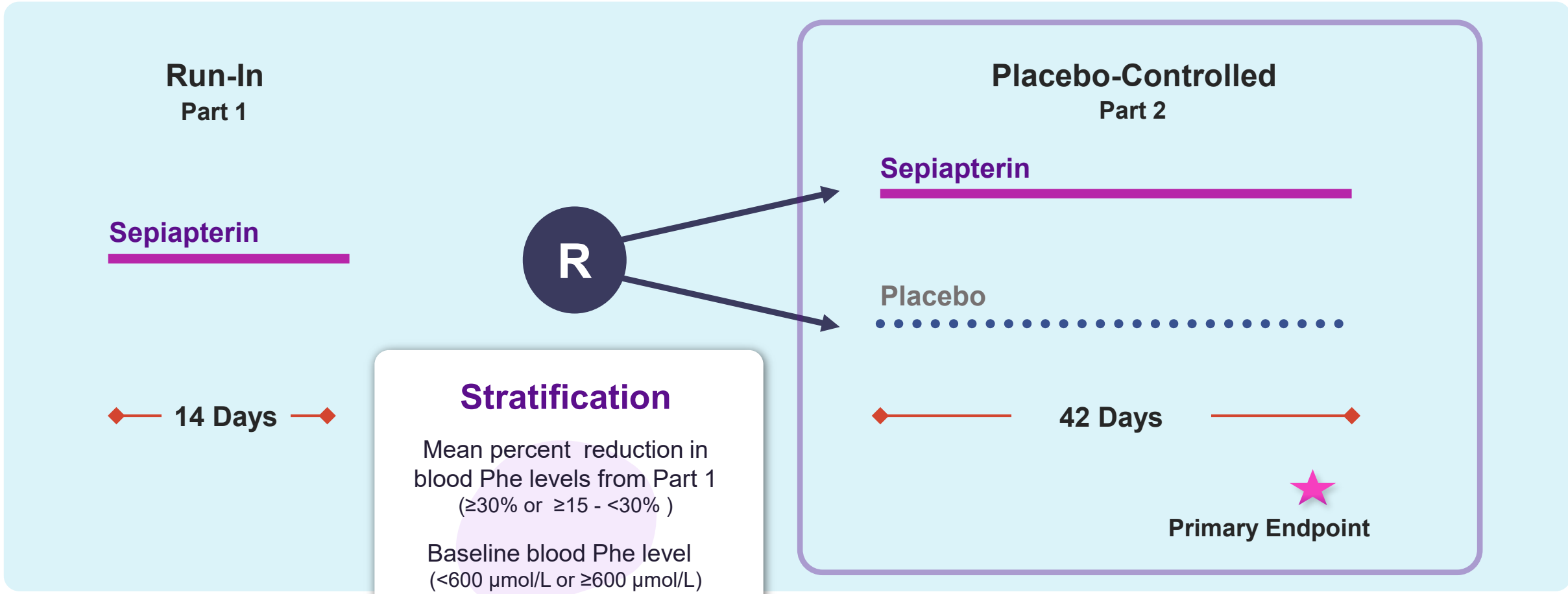
	Number of Patients	Baseline Phe (µmol/L)
>30% responders	16	978.6
15-30% responders	4	1,058.6
<15% responders	15	848.5
Total	35	928.6

APHENITY Study Population



*As per protocol this population entered directly into open label extension

APHENITY Global Registration-Directed Trial of Sepiapterin Study Design



APHENITY Primary Analysis Population Includes Full Spectrum of PKU Patients

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Baseline Characteristic	Sepiapterin (N=49)	Placebo (N=49)
Mean age at enrollment (yrs) [min, max]	16.3 [2, 47]	18.1 [4, 54]
2-17 (%)	34 (69.4)	31 (63.3)
≥18 years (%)	15 (30.6)	18 (36.7)
Sex: %F, %M	F: 46.9 M: 53.1	F: 55.1 M: 44.9
Mean Baseline Blood Phe (µmol/L) (min, max)	646.1 (179.5, 1350.0)	654.0 (289.5, 1650.0)
Mean Baseline Blood Phe in Classical PKU (µmol/L) (min, max)	761.25 (452.0, 1350.0)	771.56 (317.0, 1240.0)

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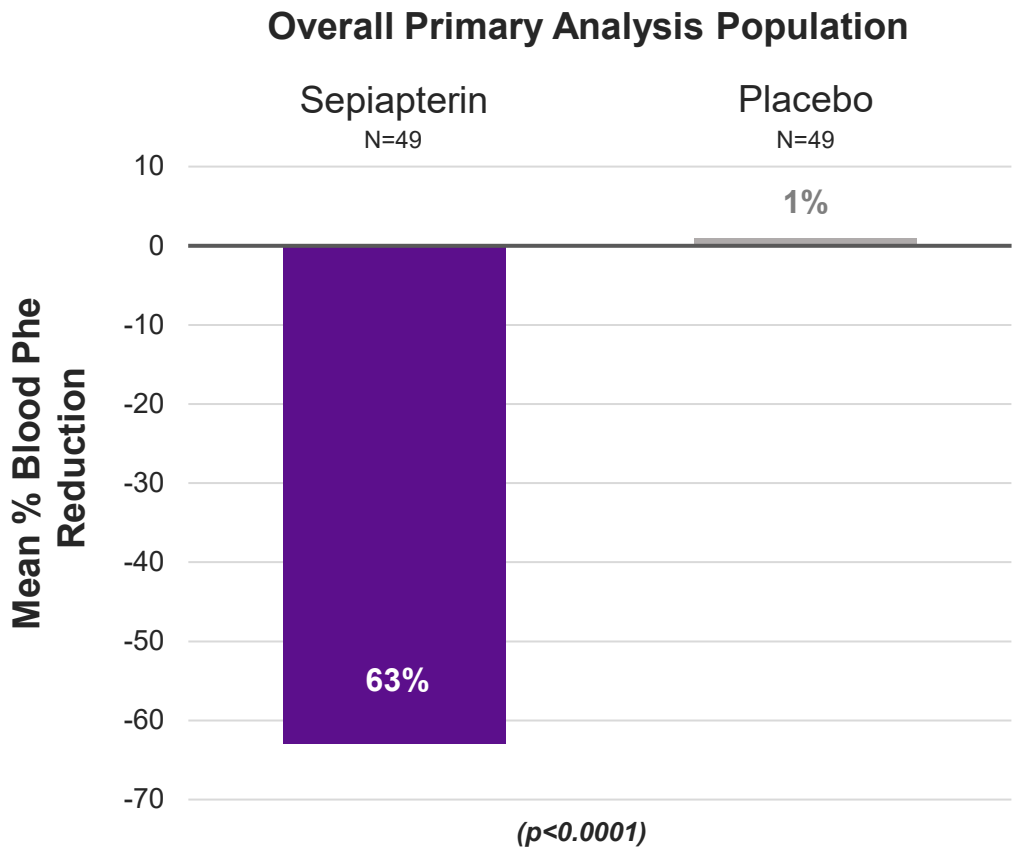
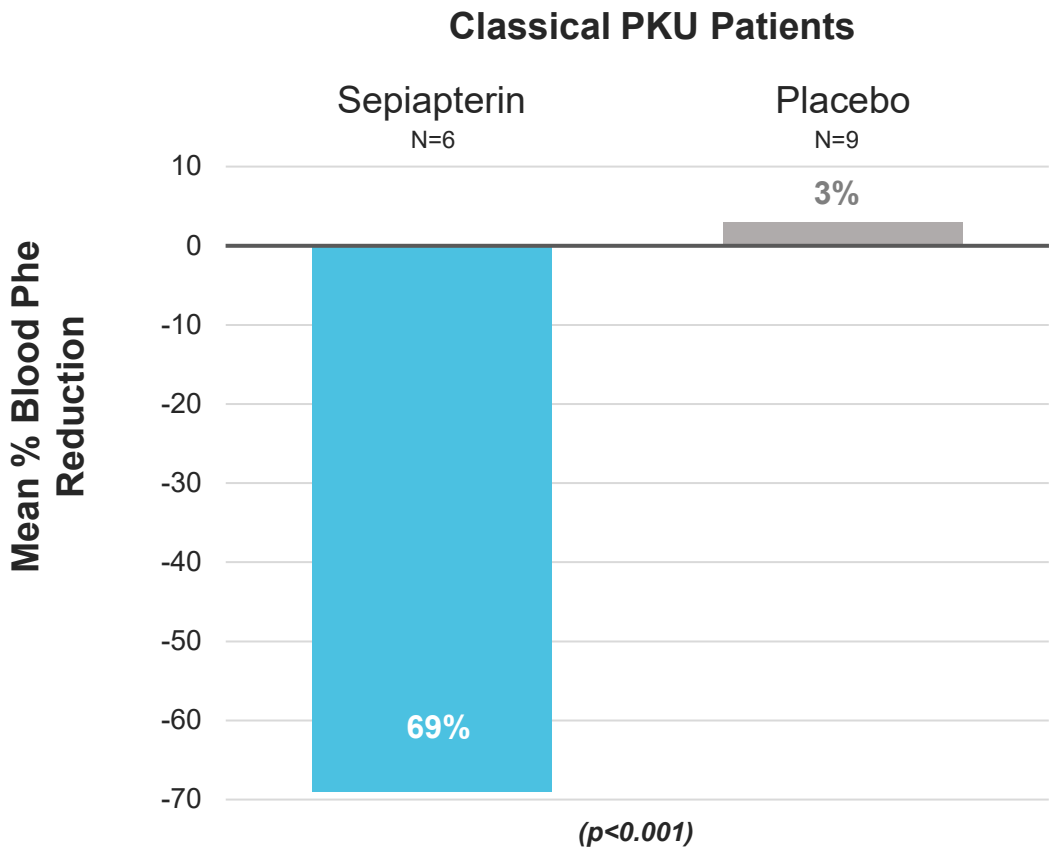
Sepiapterin Treatment Resulted in Clinically Significant Blood Phe Reduction

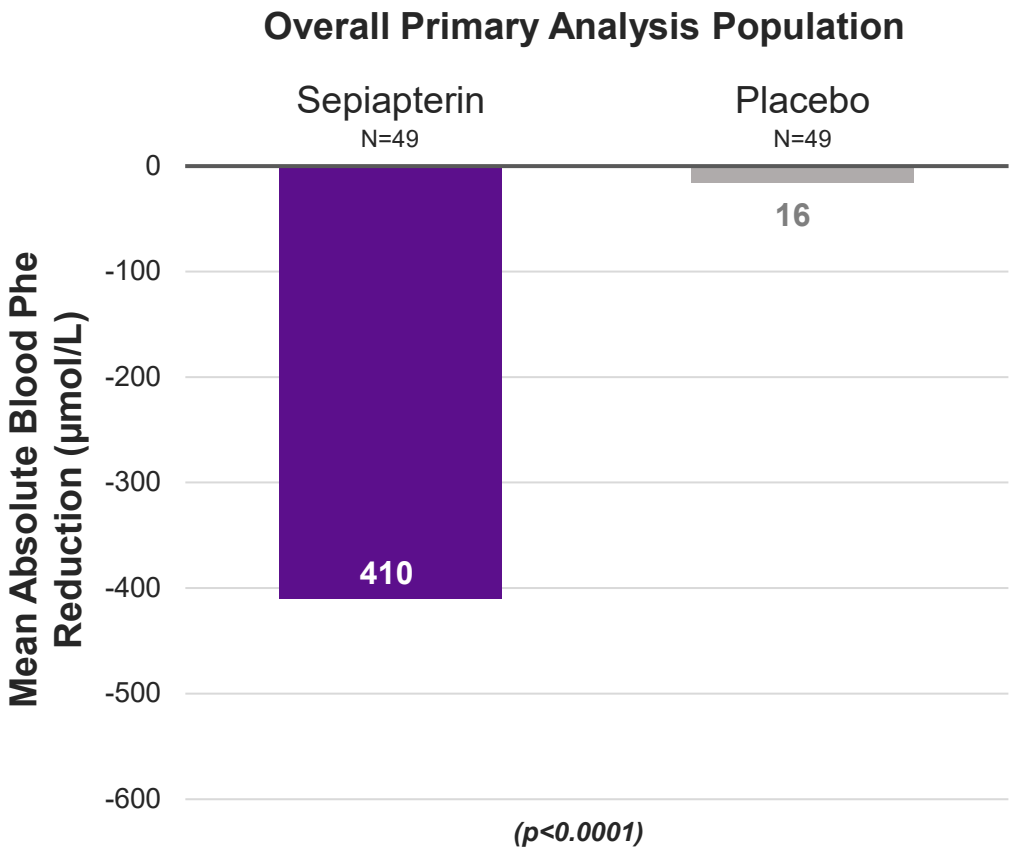
Mean % Blood Phe Reduction

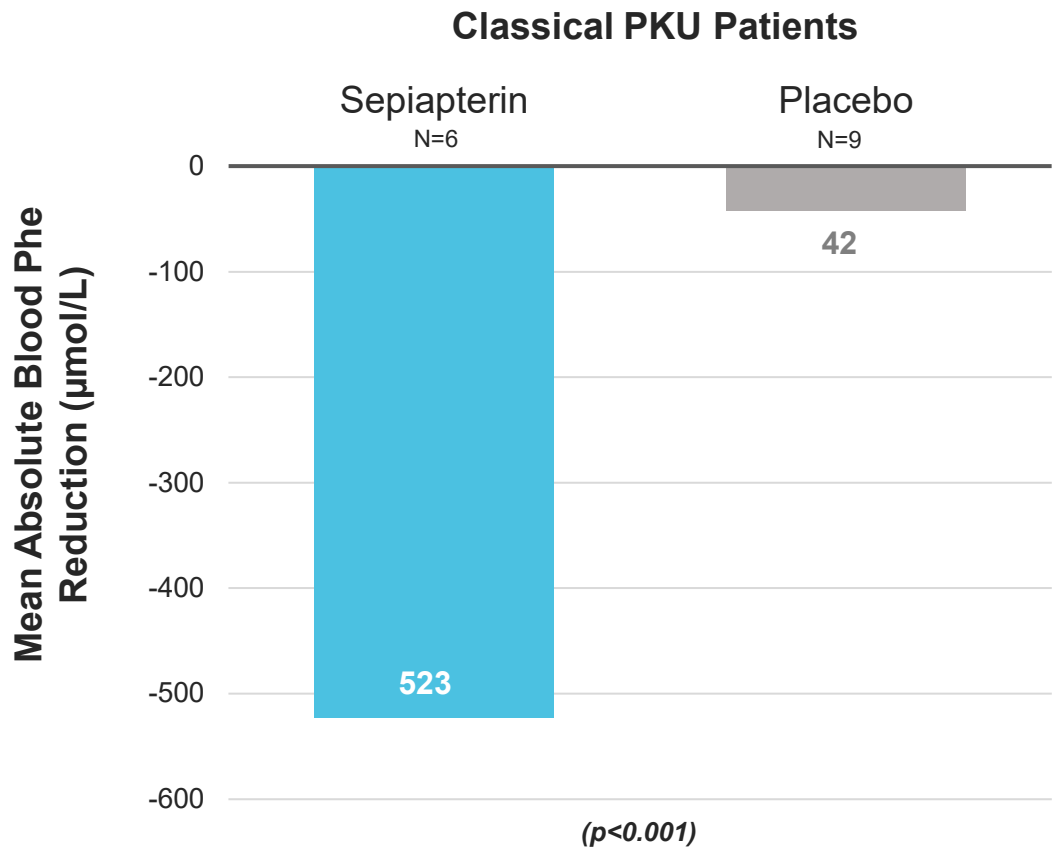




Sepiapterin Treatment Resulted in Clinically Significant Blood Phe Reduction

Mean Absolute Blood Phe Reduction (µmol/L)

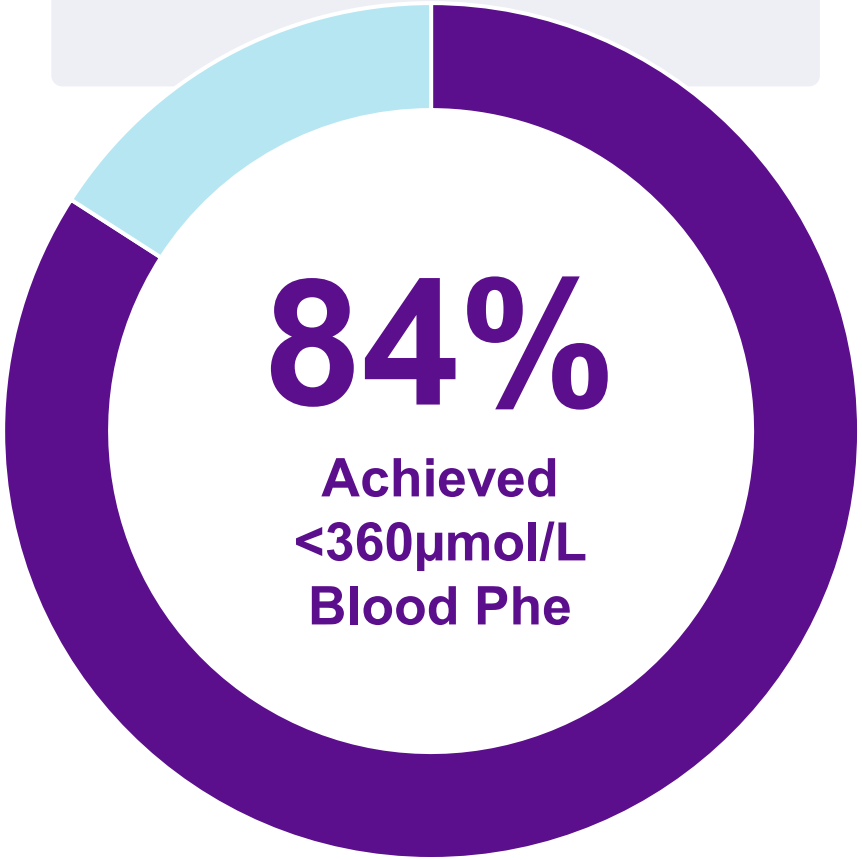




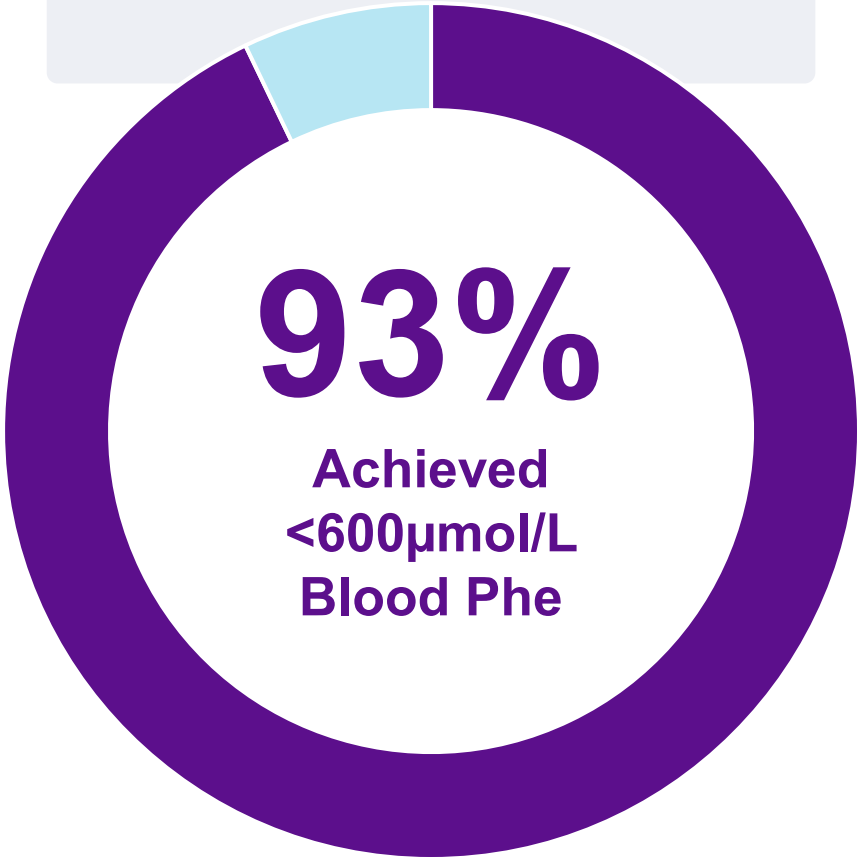
Vast Majority of Patients Achieved Guidelines Target Blood Phe Levels

US guidelines: all ages

EU guidelines: <12 years of age

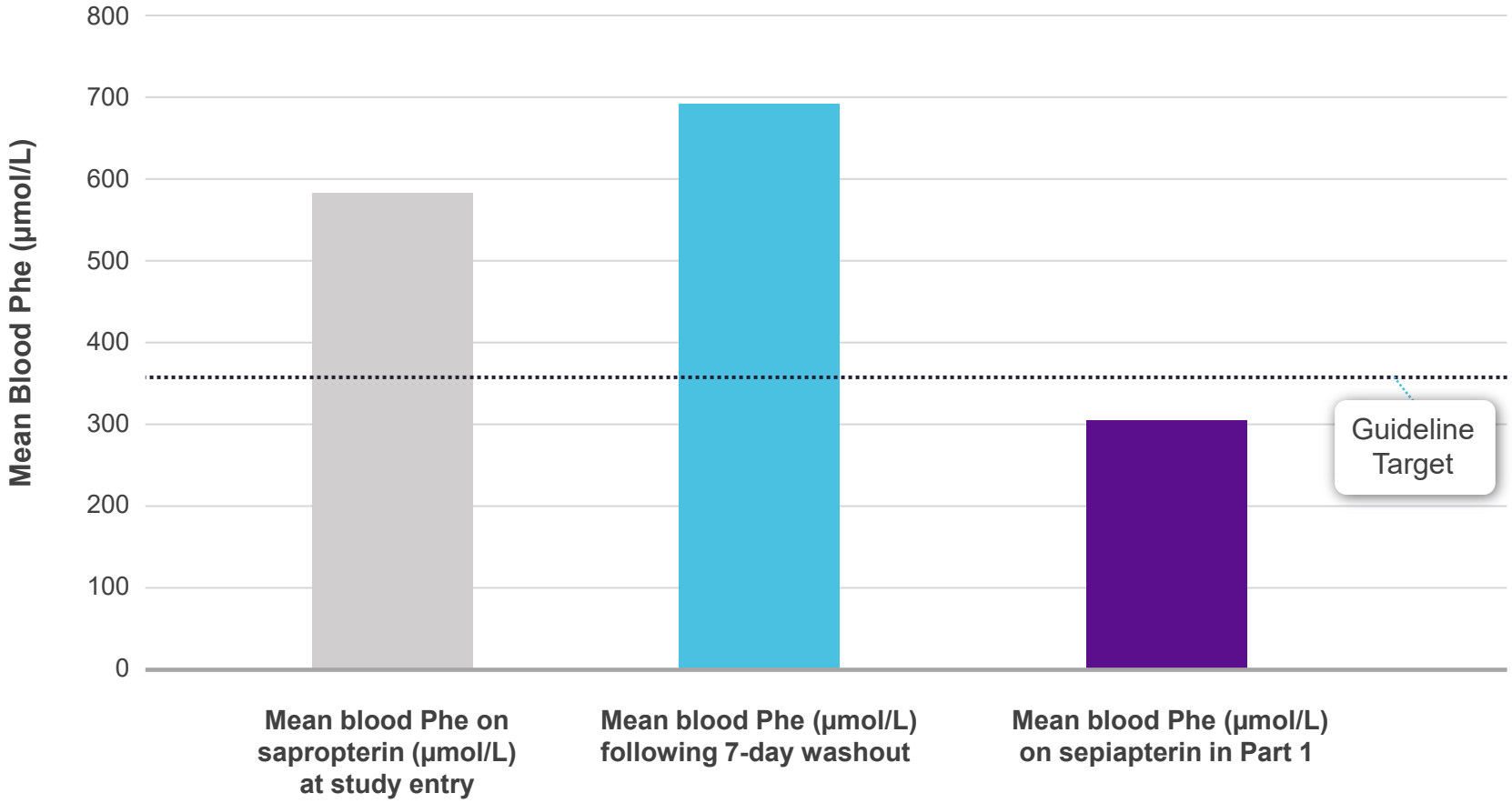


EU guidelines: ≥12 years of age



Sepiapterin Part 1 Treatment Effect in Patients Receiving Sapropterin at Study Entry

(N=27 patients)



48%

lower Phe levels following sepiapterin treatment in those patients receiving sapropterin at study entry

Sepiapterin Demonstrated to be Well Tolerated

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Sepiapterin was well tolerated with no serious adverse events

Similar related adverse event frequency between sepiapterin and placebo treatment groups

Most common adverse events were headache and diarrhea

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APHENITY Open-Label Extension Assesses Long Term Safety and Phe Tolerance

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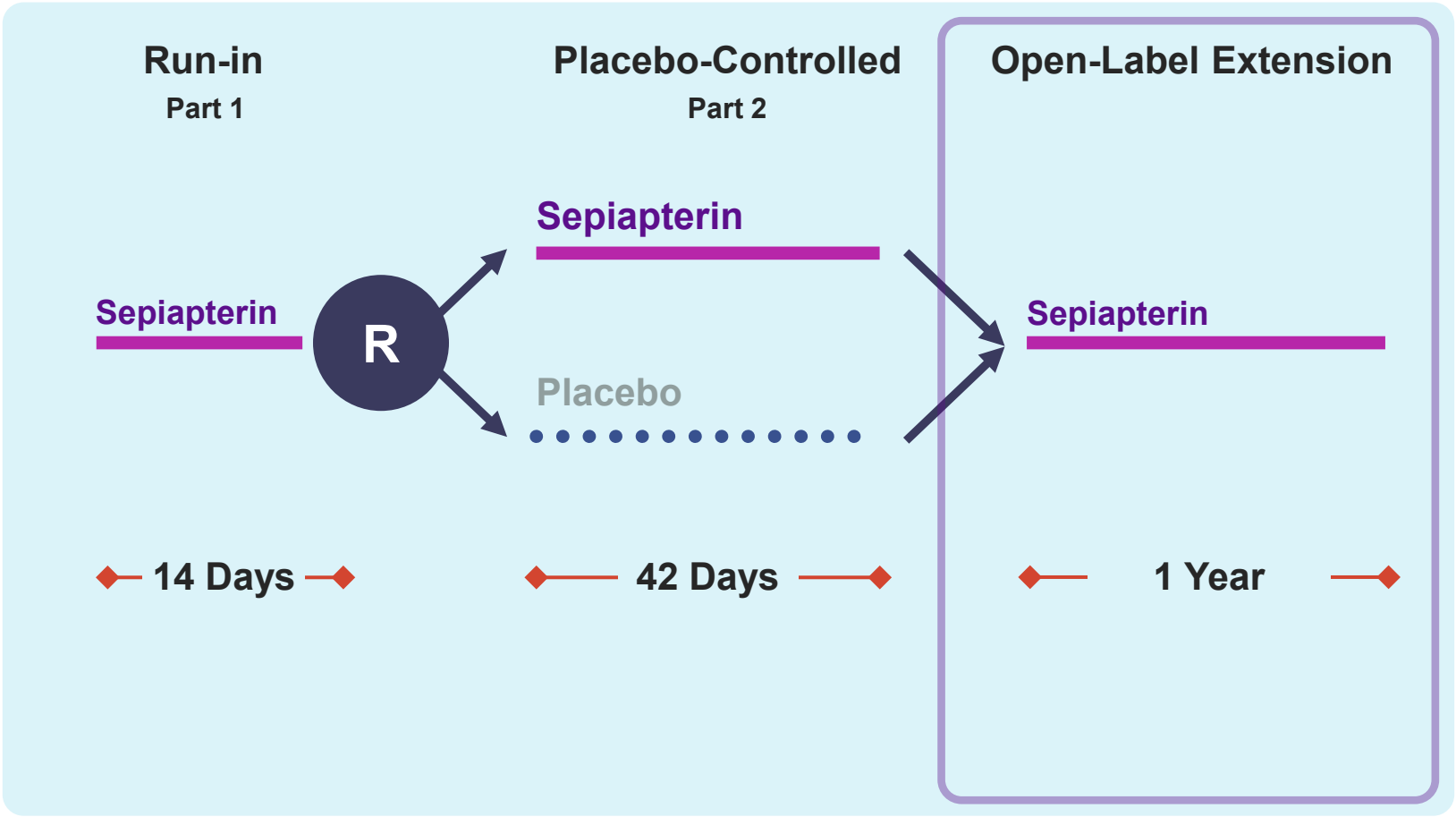

Study Objectives

Long-term safety

Change in dietary Phe/protein consumption

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Initial Phe Tolerance Data in Open-Label Extension

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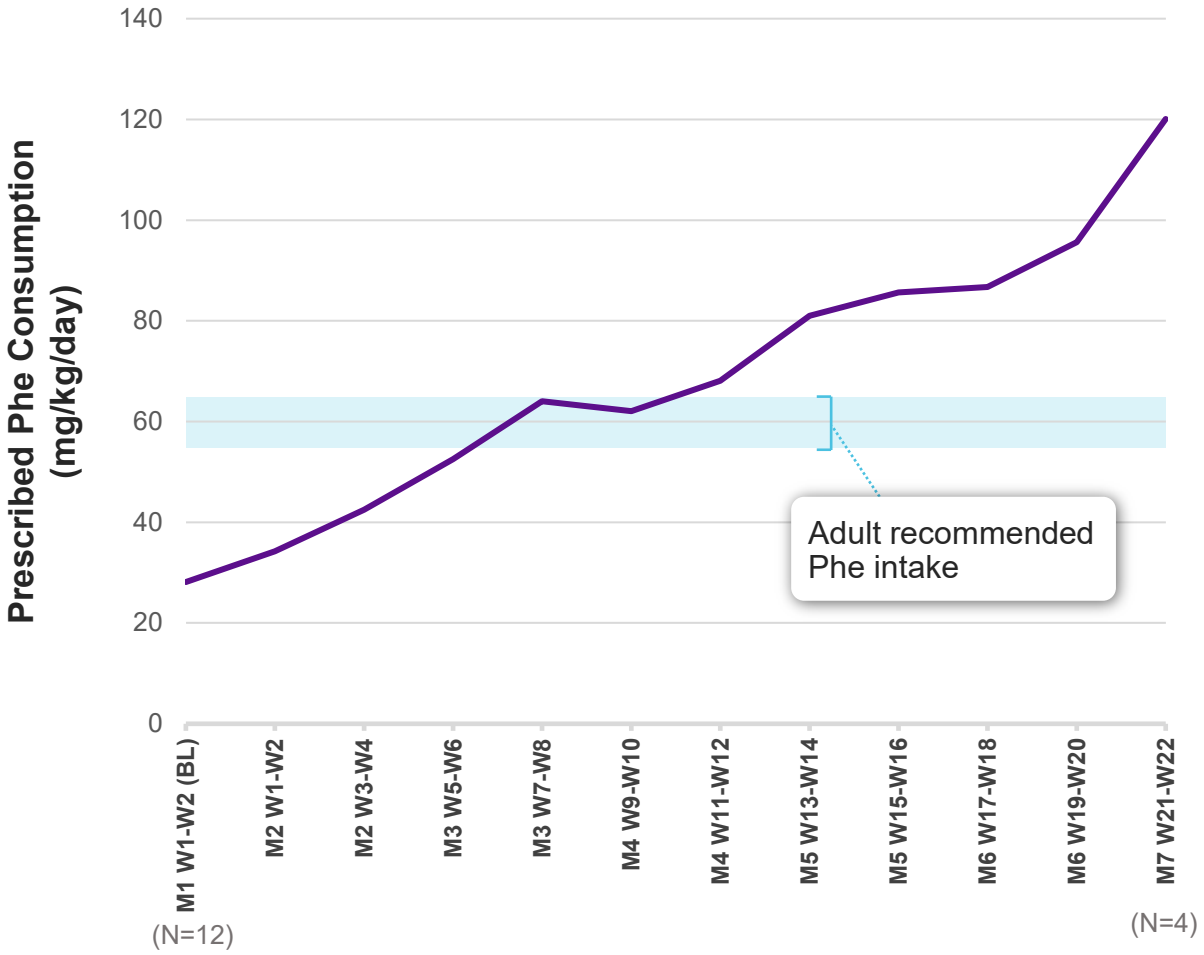
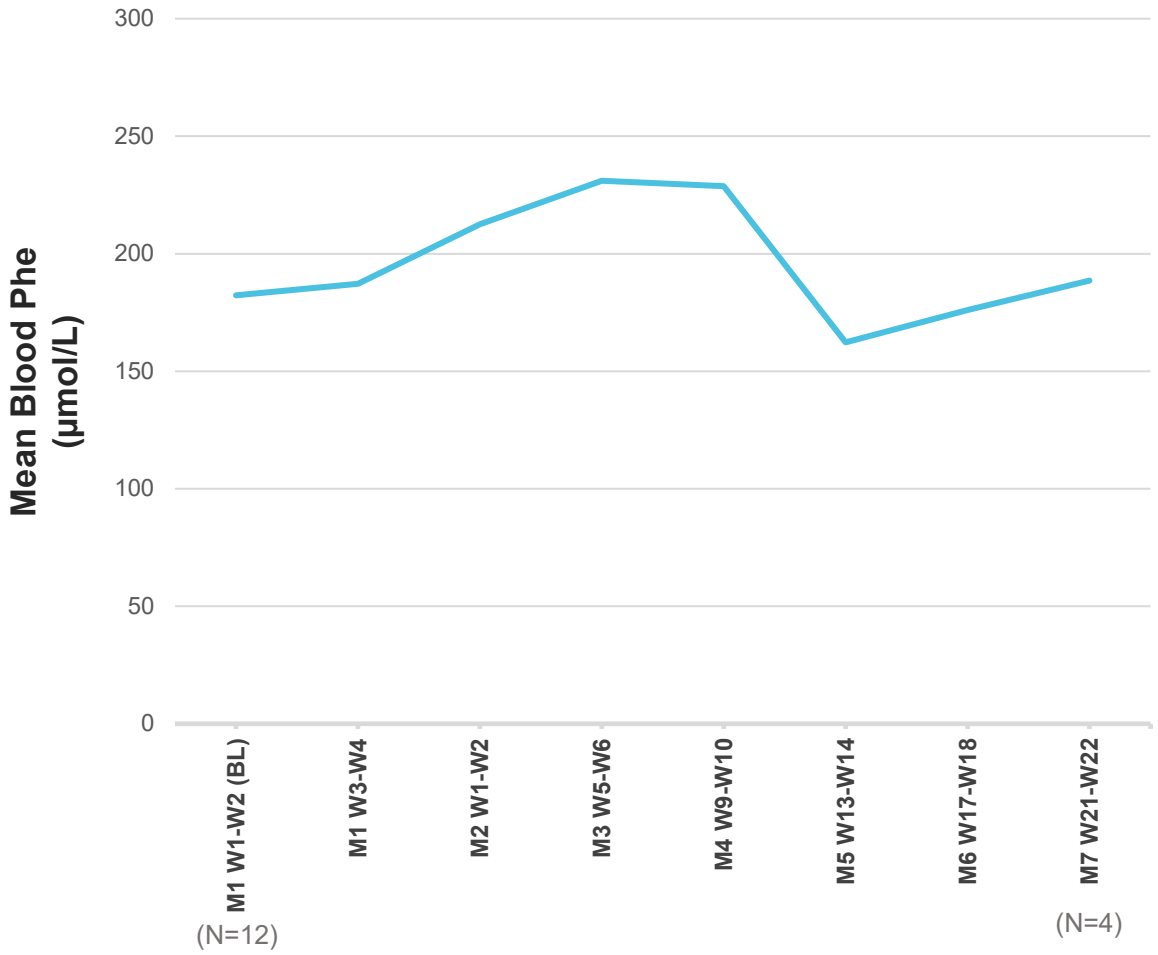
Increase in Dietary Phe Intake



Blood Phe Levels



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Commercial Pillars for Success Already Established

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Newborn screening with ~58,000 patients worldwide[1,2,3]

Well-known metabolic centers of excellence worldwide

Disease pathology well understood and documented

Connected and coordinated patient advocacy community

1. NPKUA; https://www.npkua.org/, 2. Shoraka et. Al, Clin Exp Pediatr. 2020; 63(2): 34–43., 3. Borrajo G., Acta Ped Mex. 2012; 33(6): 279-287.

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Overview of Treatment-Emergent Adverse Events

	Sepiapterin 20 mg/kg (N=56) N % m	Sepiapterin 40 mg/kg (N=56) N % m	Sepiapterin 60 mg/kg (N=55) N % m	Sepiapterin Overall (N=56) N % m	Placebo (N = 54) N % m
All TEAEs	20 (35.7%) 29	7 (12.5%) 10	15 (27.3%) 21	33 (58.9%) 60	18 (33.3%) 33
Treatment-Related TEAEs	5 (8.9%) 7	1 (1.8%) 3	1 (1.8%) 1	6 (10.7%) 11	6 (11.1%) 9
Serious TEAEs	0	0	0	0	0
CTCAE Grade 3 or Higher TEAEs	0	0	0	0	0
TEAEs Leading to Study Drug Withdrawal	0	0	0	0	0
TEAEs Leading to Study Discontinuation	0	0	0	0	0
Death	0	0	0	0	0

APHENITY Results Support Potential for Sepiapterin to Address Majority of PKU Segments

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Sepiapterin Market Opportunity

- Therapy Naive Patients Including Classical PKU
- Patients Who Have Failed on Current Therapies
- Patients Who Are Not Well Controlled

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PTC Global Commercial Infrastructure Will Allow for Rapid Worldwide Launch

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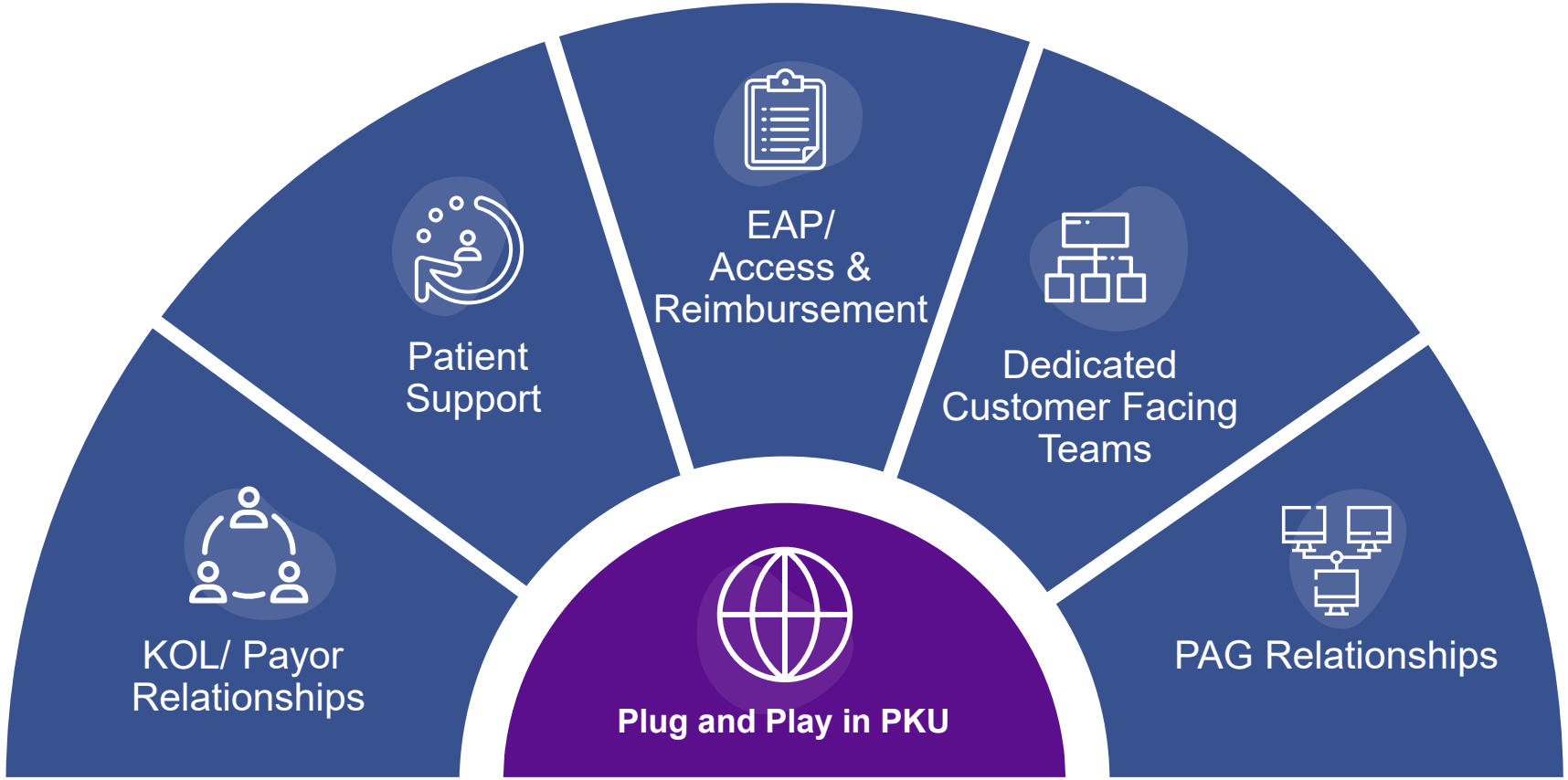

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APHENITY Results Support Next Steps in Regulatory Process and Commercial Planning

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Pre-Submission Meetings

Regulatory Submissions

Initiate Launch Preparation

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