Gout and Treatment with Uricases Approved and Under Development Made More Crystal Clear

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PRX-115

Phase 1 Top Line Results

Interim Analysis (Cohorts 1-7)

PB115-SAD-101; First in Human Phase 1 Trial

Study Title:

A double-blind, placebo-controlled, single ascending dose study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics properties of PRX-115 in adult volunteers with elevated uric acid levels

Primary Objective:

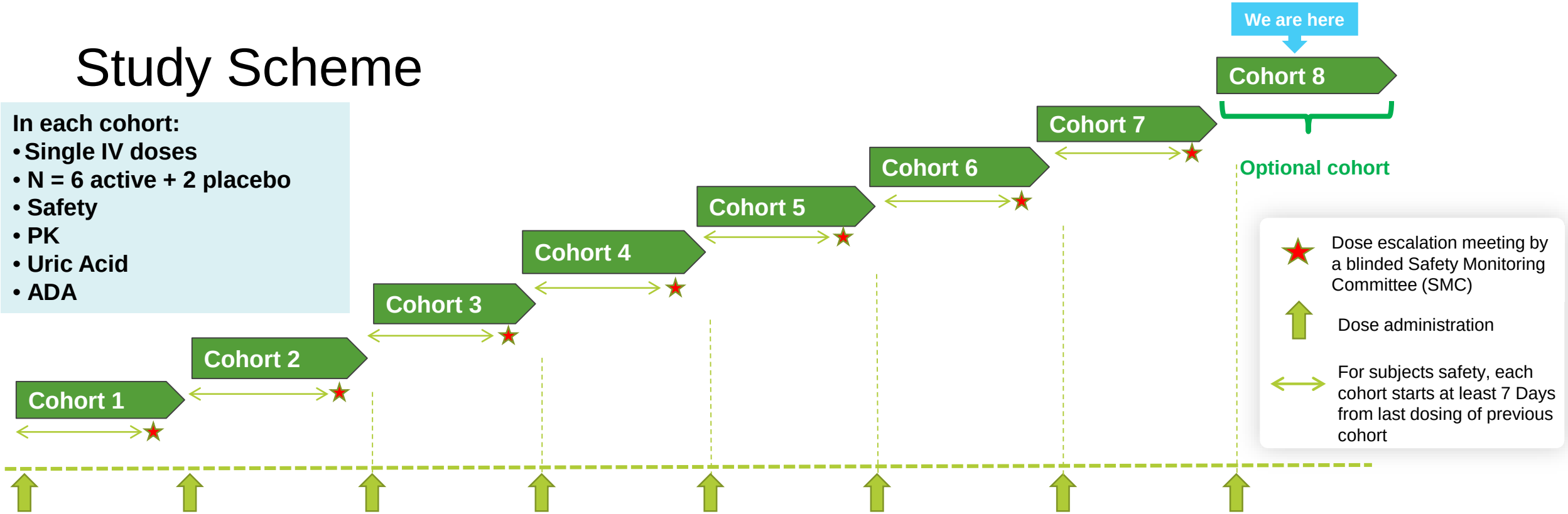
To evaluate the safety and tolerability of PRX-115 after a single ascending intravenous (IV) infusion dose in adult male and female participants with elevated uric acid levels.

Secondary Objectives:

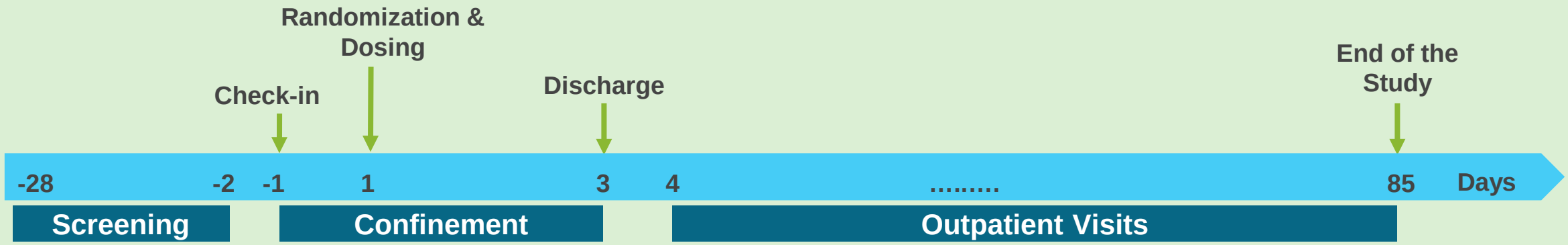
To evaluate the pharmacokinetics (PK), pharmacodynamics (PD), and immunogenicity of PRX-115 after a single ascending IV infusion dose in adult male and female participants with elevated uric acid levels.

Study Scheme

In each cohort:
- **Single IV doses**
- **N = 6 active + 2 placebo**
- **Safety**
- **PK**
- **Uric Acid**
- **ADA**



Study schedule per patient



Study Population

- Males or females 18 to 65 years of age, inclusive
- Serum uric acid 6.0 mg/dL → reduced to ≥ 4.7* mg/dL, at Screening
- Body mass index within the range 18.5 to 40 kg/m^2, inclusive, at the Screening visit
- Had no gout flare in the last year prior to either Screening or Day -1
- Had no clinical evidence of subcutaneous tophi at either Screening or Day -1

* Only 5 patients in the active treatment groups had baseline UA below 6.0mg/dL

Statistical Aspects

Sample Size Determination and Rationale:

- As this is a first-in-human trial, no formal sample size determination is appropriate. Eight (8) participants at each dose level are considered to be adequate to detect adverse effects and safety signals of PRX-115.

Summary of Demographics and Baseline Characteristics

Parameter	Statistic	PRX-115 Overall	Pooled Placebo	Overall
	n	42	14	56
Age (years)	Mean	36.8	34.3	36.2
	SD	12.5	11.2	12.2
Sex n(%)	Female	13 (31.0%)	3 (21.4%)	16 (28.6%)
	Male	29 (69.0%)	11 (78.6%)	40 (71.4%)
Race n (%)	American Indian or Alaska Native	0	0	0
	Asian	5 (11.9%)	5 (35.7%)	10 (17.9%)
	Black or African American	1 (2.4%)	0	1 (1.8%)
	Native Hawaiian or Other Pacific Islander	6 (14.3%)	2 (14.3%)	8 (14.3%)
	White	31 (73.8%)	7 (50.0%)	38 (67.9%)
	Other	1 (2.4%)	1 (7.1%)	2 (3.6%)
Weight (kg)	Mean	89.36	87.02	88.77
	SD	17.76	19.45	18.04
Body Mass Index(kg/m^2)	Mean	29.57	27.95	29.16
	SD	5.15	5.74	5.30

Overall Summary of Adverse Events: PRX-115 was Well-Tolerated

Number of Participants Reporting at Least 1 AE

	PRX-115								
	Cohort 1 n(%)	Cohort 2 n(%)	Cohort 3 n(%)	Cohort 4 n(%)	Cohort 5 n(%)	Cohort 6 n(%)	Cohort 7 n(%)	PRX-115 Overall n(%)	Pooled Placebo n(%)
N	6	6	6	6	6	6	6	42	14
Adverse Event	5(83.3)	6(100.0)	5(83.3)	3(50.0)	6(100.0)	5(83.3)	3(50.0)	33(78.6)	11(78.6)
Related TEAE	1(16.7)	5(83.3)	3(50.0)	1(16.7)	1(16.7)	0	0	11(26.2)	1(7.1)
Serious Related TEAE	0	1(16.7)	0	0	0	0	0	1(2.4)	0
TEAE Leading to Study Drug Discontinuation	0	1(16.7)	0	0	0	0	0	1(2.4)	0
TEAE Leading to Study Discontinuation	0	0	0	0	0	0	0	0	0

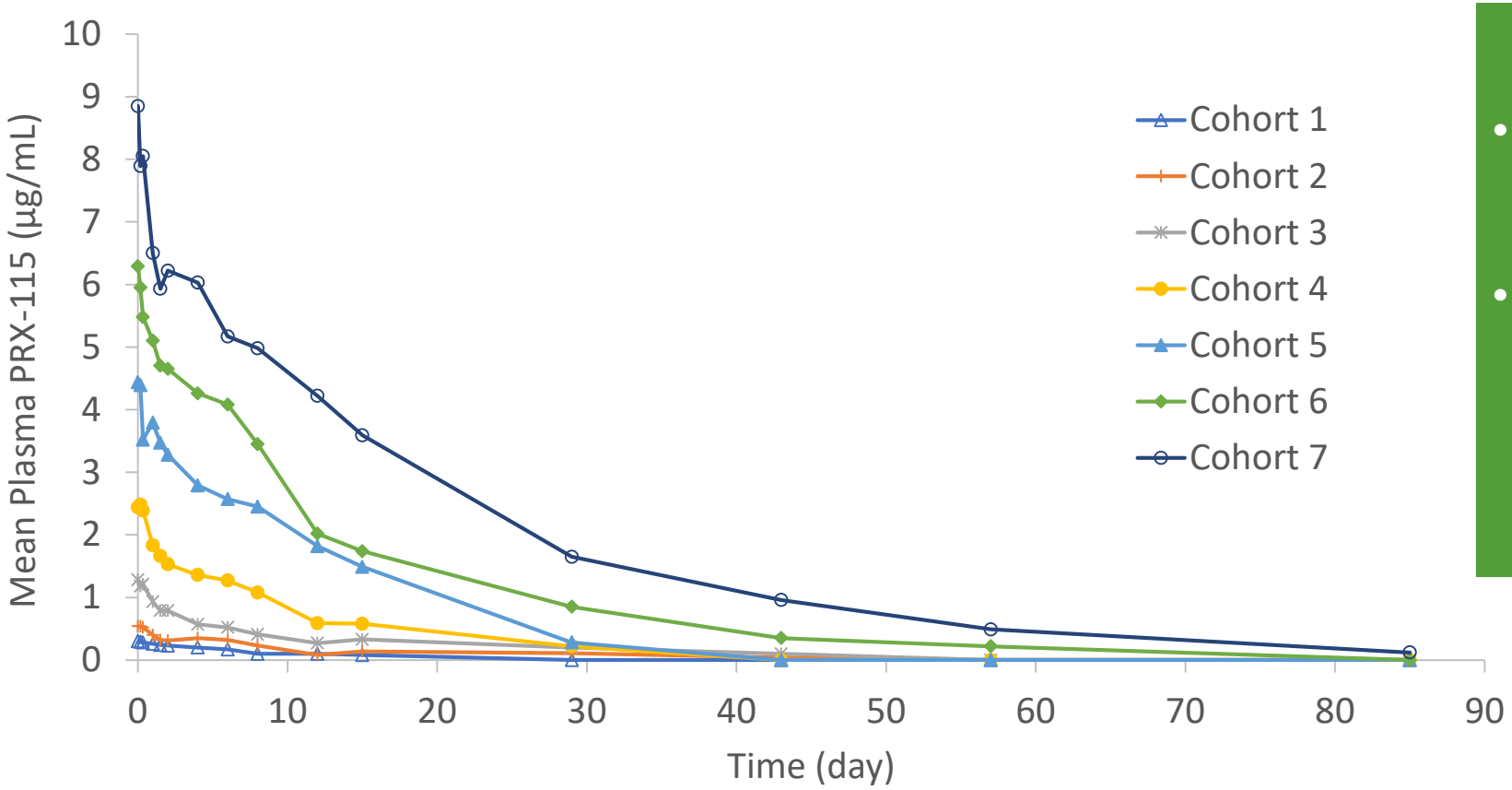
- All randomized patients completed the study
- One patient experienced an anaphylactic reaction immediately (6 min) following the commencement of the infusion.
  - The reaction was fully resolved
  - Patient continued in the study for FU safety assessments
- No other serious adverse events (SAEs) were reported during the study.
- No related AEs were reported for participants treated in cohorts 6 and 7

TEAE= Treatment Emergent Adverse Event

Immunogenicity Evaluation: Preliminary Results

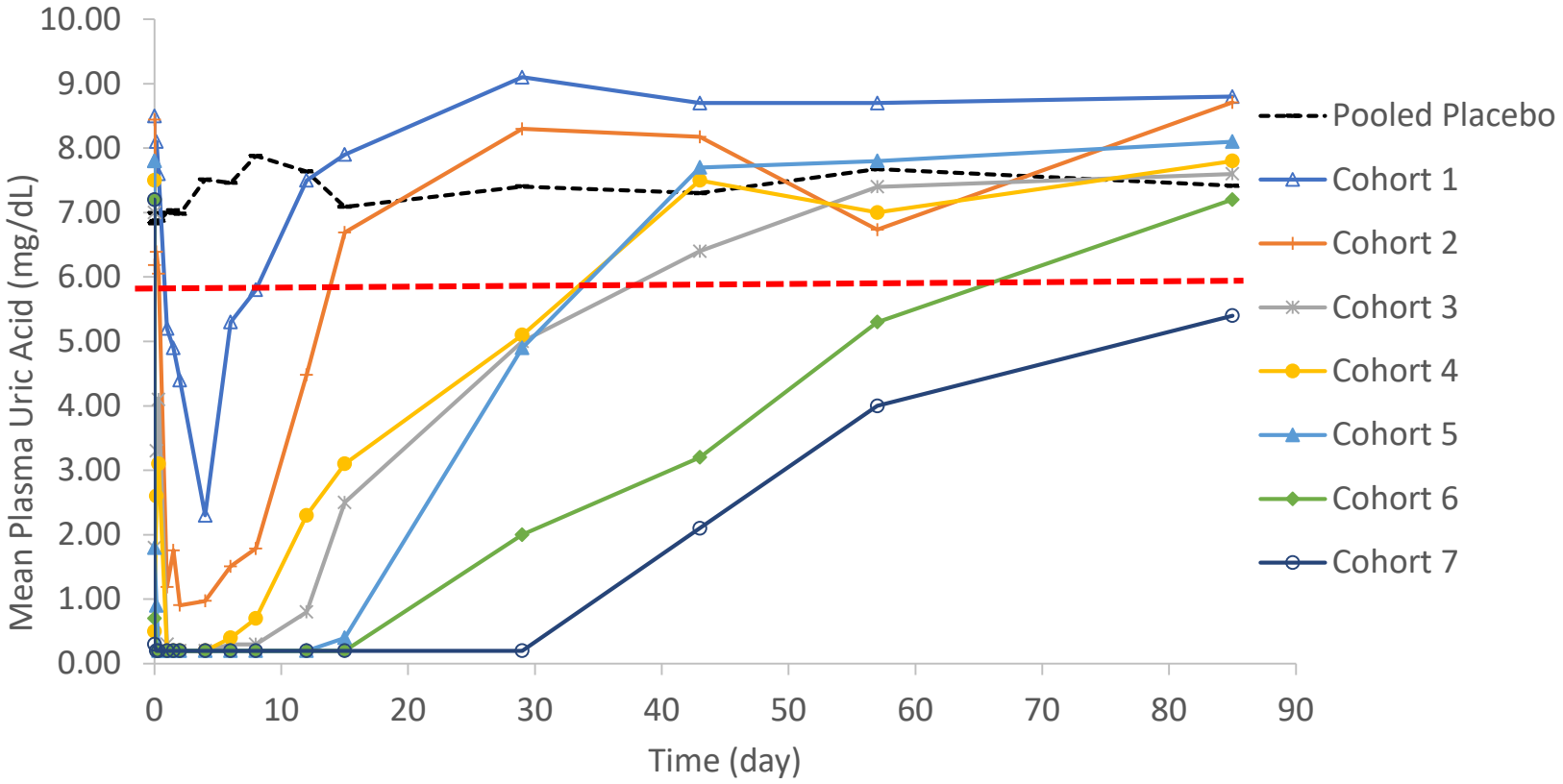
- Preliminary antidrug IgG antibody assessment revealed that many subjects developed a positive, low-titer IgG response following a single administration of PRX-115.
  - PRX-115 immunogenicity is still under evaluation including correlation to PK, PD (uric acid) and safety.
  - Taking under consideration that this is a single dose study, it would be valuable to evaluate PRX-115 immunogenicity following repeated dose studies.

Mean PRX-115 Plasma Concentrations (µg/mL)



- **Exposure of PRX-115 increased with the increase of dose**
- **Detectable exposures beyond day 56 was observed in plasma of treated patients in cohorts 6 and 7**

Mean Uric Acid Concentrations (mg/dL)



Cohort 2 excludes one patient who received 5% of the full dose

- **Administration of PRX-115 leads to a rapid reduction of plasma uric acid**
- **Effect of PRX-115 on plasma uric acid levels and duration of response is dose dependent and lasted beyond 4 weeks**

Summary

SAFETY

- All randomized patients completed the study
- PRX-115 was found to be well tolerated in the study
- Only 11/42 (26%) patients reported study drug related AE, most mild to moderate in severity, with the exception of one patient that experienced a severe AE of an anaphylactic reaction immediately following the commencement of the infusion. The reaction was fully resolved and the patient continued in the study for safety assessments
- No other serious adverse events (SAEs) were reported during the study.
- No related AEs were reported in cohorts 6 and 7

PK

- Increased exposure with increasing dose
- PRX-115 was detected beyond day 56 (8 weeks) in cohorts 6 and 7

PD

- Administration of PRX-115 leads to a rapid reduction of plasma uric acid
- Effect of PRX-115 on plasma uric acid levels and duration of response is dose dependent and lasted beyond 4 weeks

Cohort 8 completed recruitment, and follow-up is ongoing


THANK YOU