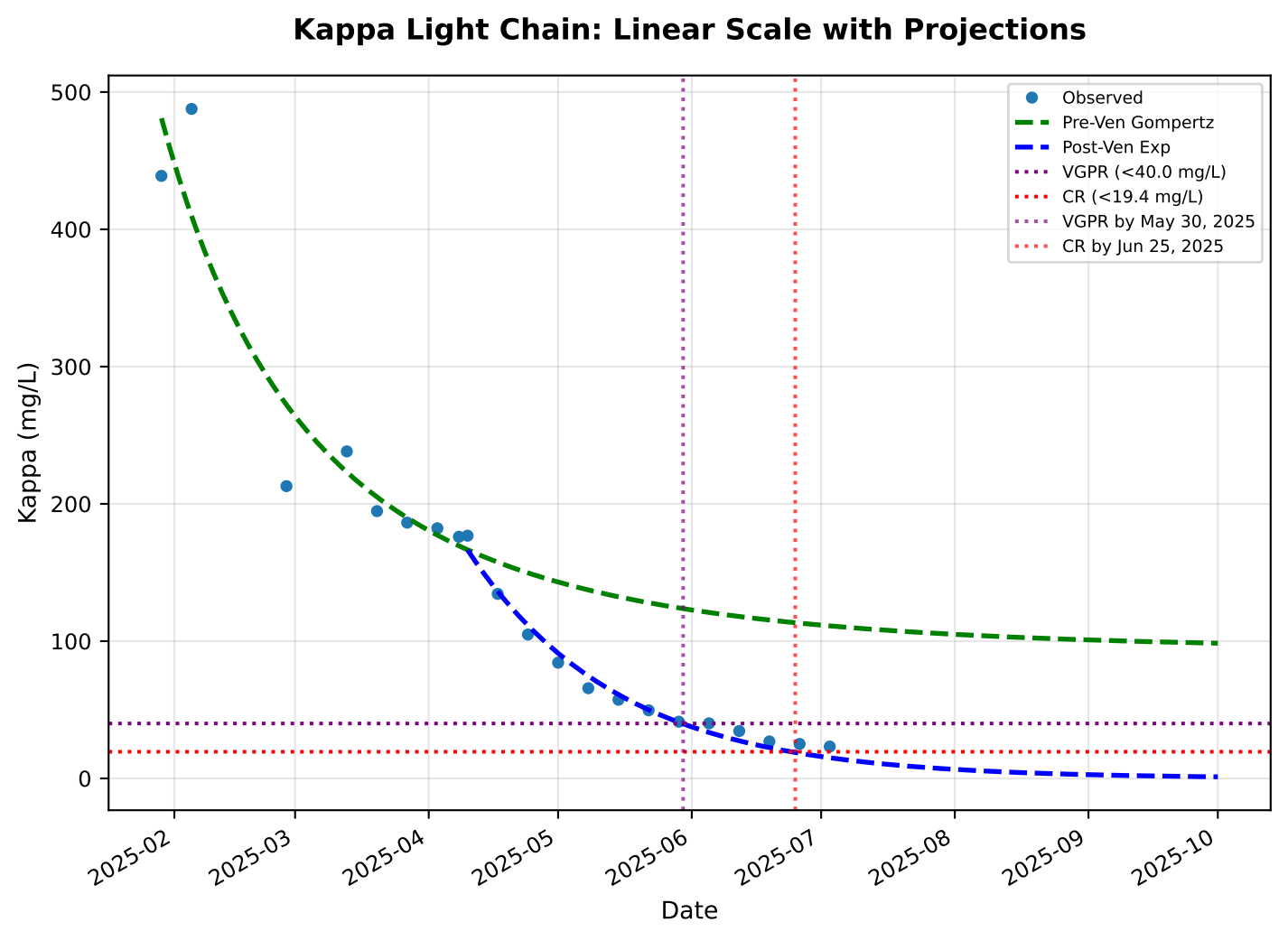
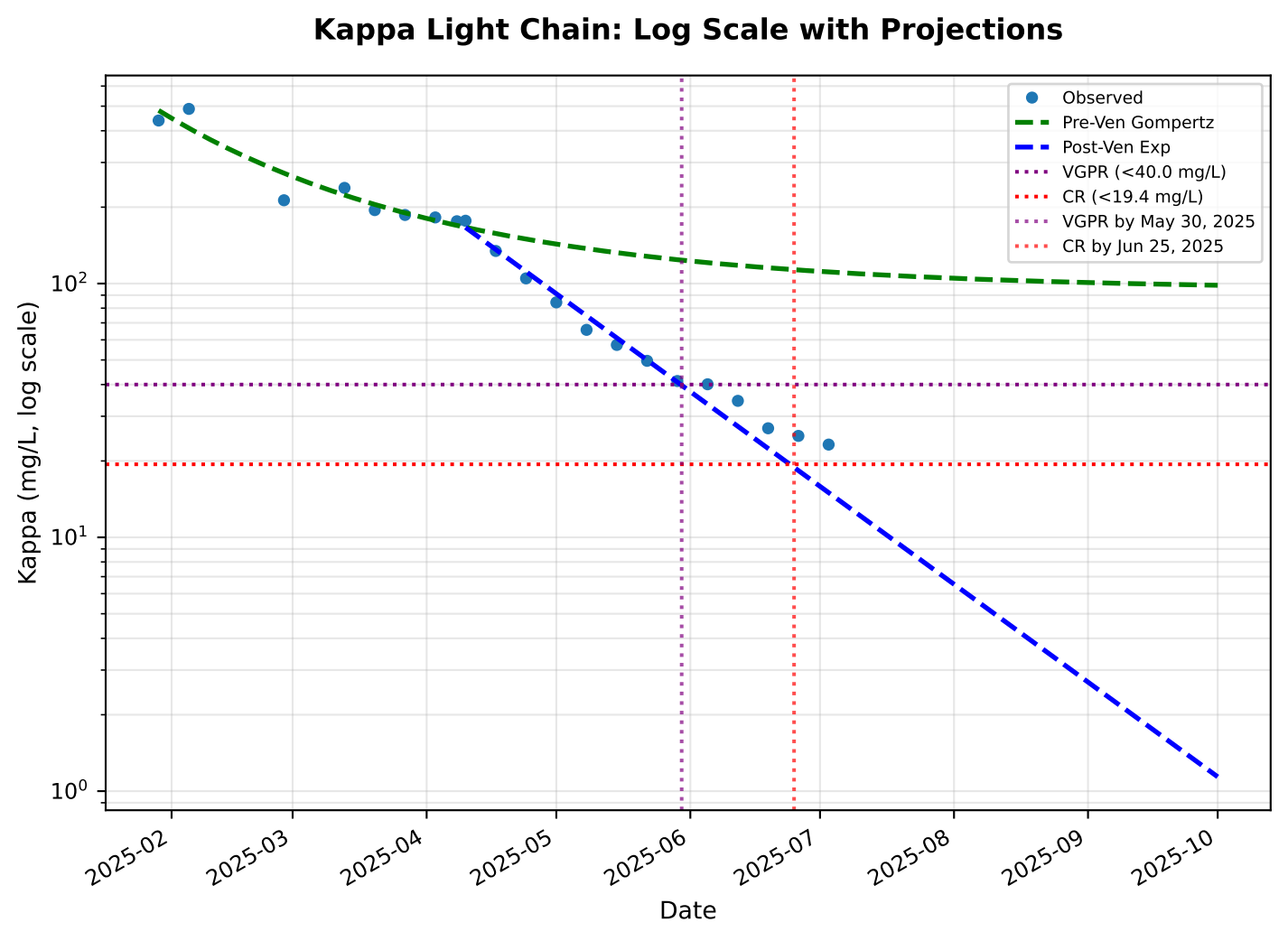

Kappa Light Chain: Linear Scale with Projections
Observed
Pre-Ven Gompertz
Post-Ven Exp
VGPR (<40.0 mg/L)
CR (<19.4 mg/L)
VGPR by May 30, 2025
CR by Jun 25, 2025
Kappa (mg/L)
500
400
300
200
100
0
2025-02
2025-03
2025-04
2025-05
2025-06
2025-07
2025-08
2025-09
2025-10
Date


Kappa Light Chain: Log Scale with Projections
Observed
Pre-Ven Gompertz
Post-Ven Exp
VGPR (<40.0 mg/L)
CR (<19.4 mg/L)
VGPR by May 30, 2025
CR by Jun 25, 2025
Kappa (mg/L, log scale)
10^2
10^1
10^0
2025-02
2025-03
2025-04
2025-05
2025-06
2025-07
2025-08
2025-09
2025-10
Date

Free Light Chain Results

Date	Kappa	Lambda	Ratio	Δ	%Δ
01/29	438.9	5.7	77.0	+0.0	0.0%
02/05	487.7	6.5	75.0	+48.8	11.1%
02/27	212.9	2.9	73.4	-274.8	-56.3%
03/13	238.2	3.0	79.4	+25.3	11.9%
03/20	194.7	2.5	77.9	-43.5	-18.3%
03/27	186.3	1.9	98.0	-8.4	-4.3%
04/03	182.2	1.8	101.2	-4.1	-2.2%
04/08	176.0	2.3	76.5	-6.2	-3.4%
04/10	176.8	2.1	84.2	+0.8	0.5%
04/17	134.4	1.8	74.7	-42.4	-24.0%
04/24	104.8	1.9	55.2	-29.6	-22.0%
05/01	84.3	1.4	60.2	-20.5	-19.6%
05/08	65.7	1.4	46.9	-18.6	-22.1%
05/15	57.3	1.4	40.9	-8.4	-12.8%
05/22	49.6	1.4	35.4	-7.7	-13.4%
05/29	41.3	1.4	29.5	-8.3	-16.7%
06/05	40.1	1.4	28.6	-1.2	-2.9%
06/12	34.5	1.4	24.6	-5.6	-14.0%
06/19	26.9	1.4	19.2	-7.6	-22.0%
06/26	25.1	1.4	17.9	-1.8	-6.7%
07/03	23.2	1.4	16.6	-1.9	-7.6%

Model Explanation & Detailed IVIG Artifact Analysis

Pre-Venetoclax Phase (CyBorD) – Gompertz Model
- y(t) = A·exp(-B·exp(-C·t))
  - Captures initial rapid kill under CyBorD and plateau as resistant subclones emerge.
  - Projected κ by Oct 1, 2025: 98.5 mg/L (no CR reached).

Post-Venetoclax Phase (Ven + Dara + Dex) – Exponential Model
- y(t) = A·exp(-k·t)
  - Reflects continuous BCL-2–dependent apoptosis enhanced by Daratumumab and Dex.
  - Projected VGPR (<40.0 mg/L) by May 30, 2025.
  - Projected CR (<19.4 mg/L) by Jun 25, 2025.

IVIG Impact Assessment & Alternative Explanations
- IVIG Administration Dates:
  - First dose: May 8, 2025 (30 g)
  - Second dose: June 8, 2025 (30 g)

- Lambda Pattern Analysis:
  - λ drops to 1.4 mg/L on May 1 (BEFORE first IVIG on May 8)
  - λ remains consistently at 1.4 mg/L throughout observation period
  - This confirms 1.4 mg/L represents assay detection/quantification limit
  - No evidence of lambda artifacts from IVIG

- Kappa Trajectory Assessment:
  - Post-venetoclax κ decline: 176.8 → 134.4 → 104.8 → 84.3... → 23.2 mg/L
  - Pattern shows progressive slowing of decline rate over time
  - Two possible explanations for this observed slowing:

- Hypothesis 1: Natural Treatment Response Kinetics
  - Classic cancer pharmacology: responses slow as resistant populations dominate
  - Initial rapid log-kill phase followed by plateau approach to minimal residual disease
  - Slower decline near CR threshold is expected biological behavior
  - No IVIG artifacts needed to explain observed pattern

- Hypothesis 2: IVIG Artifact Contribution
  - Theoretical κ artifacts from 30g IVIG degradation
  - Could contribute 5-15 mg/L to observed values during May-July period
  - Would require differential κ vs λ release rates (κ ~1.4%, λ <0.1%)
  - Less parsimonious explanation given natural response kinetics

- Clinical Assessment:
  - Current κ values (23-25 mg/L) approach CR threshold (<19.4 mg/L)
  - Trajectory consistent with natural treatment response plateau
  - λ at detection limit confirms deep response in λ-producing cells
  - IVIG impact likely minimal compared to natural response kinetics

- Recommended Interpretation:
  - Primary driver of κ pattern: natural treatment response curve
  - IVIG contribution: uncertain but likely <50% of observed levels
  - Continue monitoring for trend analysis rather than artifact correction
  - Focus on sustained decline below CR threshold for response assessment