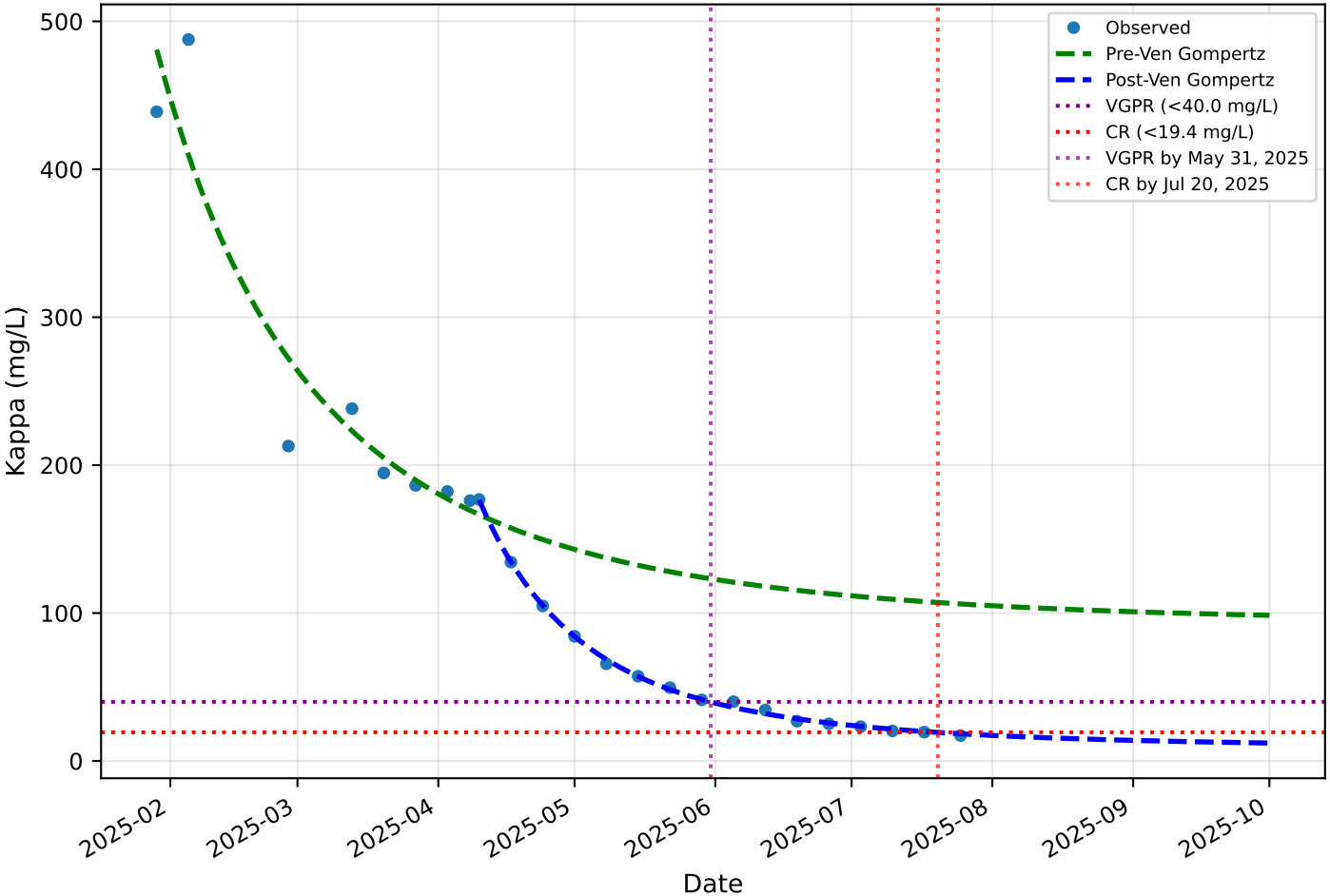
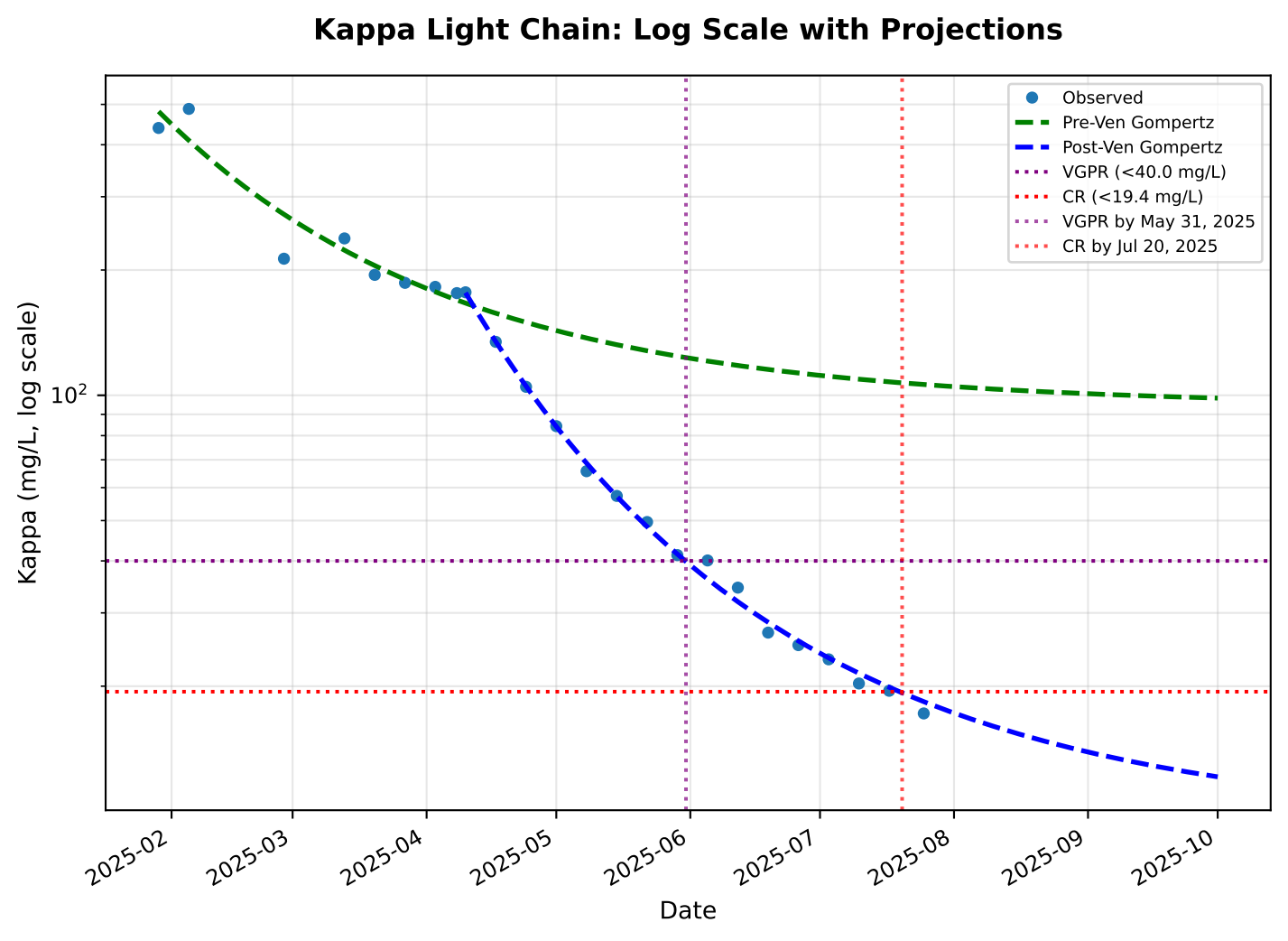

Kappa Light Chain: Linear Scale with Projections
Observed
Pre-Ven Gompertz
Post-Ven Gompertz
VGPR (<40.0 mg/L)
CR (<19.4 mg/L)
VGPR by May 31, 2025
CR by Jul 20, 2025
Kappa (mg/L)
0
100
200
300
400
500
2025-02
2025-03
2025-04
2025-05
2025-06
2025-07
2025-08
2025-09
2025-10
Date


Kappa Light Chain: Log Scale with Projections
Observed
Pre-Ven Gompertz
Post-Ven Gompertz
VGPR (<40.0 mg/L)
CR (<19.4 mg/L)
VGPR by May 31, 2025
CR by Jul 20, 2025
Kappa (mg/L, log scale)
10^2
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%
07/10	20.3	1.4	14.5	-2.9	-12.5%
07/17	19.5	1.4	13.9	-0.8	-3.9%
07/25	17.2	1.4	12.3	-2.3	-11.8%

Model Explanation & Notes

Pre-Venetoclax Phase (Dara CyBorD) – Gompertz Model
- y(t) = A·exp(-B·exp(-C·t))
  - Data shows slowing decay rate approaching asymptote at 94.3 mg/L.
  - Natural Gompertz kinetics with increasing resistance over time.
  - Asymptote above VGPR threshold - would not reach deep response.

Post-Venetoclax Phase (Dara + Ven + Dex) – Gompertz Model
- y(t) = A·exp(-B·exp(-C·t))
  - Data shows slowing decay rate approaching much lower asymptote at 9.7 mg/L.
  - Deeper displacement parameter indicating more substantial initial response.
  - Asymptote below CR threshold - achieves deep response level.
  - Projected VGPR (<40.0 mg/L) by May 31, 2025.
  - Projected CR (<19.4 mg/L) by Jul 20, 2025.

Gompertz Model Analysis - What the Data Shows
- Pre-Venetoclax Gompertz Parameters:
  - A (asymptote): 94.3 mg/L = level where decay approaches zero
  - B (displacement): -1.629 = curve shape
  - C (decay rate): 0.01483 /day = rate of decay change over time

- Post-Venetoclax Gompertz Parameters:
  - A (asymptote): 9.7 mg/L = much lower asymptotic level
  - B (displacement): -2.904 = deeper initial response
  - C (decay rate): 0.01405 /day = similar decay rate change

- Key Data Patterns:
  - Both treatments show Gompertz kinetics (natural slowing over time)
  - Pre-venetoclax trajectory heads toward 94.3 mg/L (partial response level)
  - Post-venetoclax trajectory heads toward 9.7 mg/L (deep response level)
  - 90% reduction in asymptotic target (94.3 → 9.7 mg/L)

- Clinical Interpretation:
  - Slowing decay rates are normal biological pattern, not treatment failure
  - Standard therapy would plateau above VGPR threshold
  - Venetoclax therapy approaches CR-level asymptote
  - Both show increasing resistance/slowing response over time - this is expected

Clinical Timeline Notes
- Treatment Regimen Evolution:
  - Dara CyBorD started: February 14, 2025
  - Changed to Dara Venetoclax Dex: April 10, 2025
  - Last dose of Dexamethasone: June 19, 2025
  - Dara Ven only: June 26, 2025 going forward
  - Currently considering Venetoclax monotherapy

- Treatment Optimization:
  - Venetoclax absorption optimization discovered: July 4, 2025 (40g fat intake)

IVIG Impact Assessment
- IVIG Administration:
  - First dose: May 8, 2025 (30 g)
  - Second dose: June 8, 2025 (30 g)
  - Third dose: July 11, 2025 (30 g)

- Lambda Analysis:
  - λ dropped to 1.4 mg/L on May 1 (before first IVIG)
  - Remained at 1.4 mg/L throughout = assay detection limit
  - No evidence of λ artifacts from IVIG

- Kappa Trajectory:
  - Post-venetoclax: 176.8 → 134.4 → 104.8 → 84.3... → 23.2 → 20.3 mg/L → 19.5 mg/L → 17.2 mg/L
  - Shows progressive slowing as it approaches and achieves CR threshold

- Potential IVIG Contribution Calculation:
  - 30g IVIG contains ~5.25g κ light chains
  - In 5L plasma: 1,050 mg/L total κ pool
  - Even 1% release = 10.5 mg/L artifact
  - May contribute to observed κ levels, but magnitude unclear

- Clinical Interpretation:
  - Gompertz models show natural slowing decay patterns for both treatments
  - Key difference: asymptotic targets (94.3 vs 9.7 mg/L)
  - Latest κ = 17.2 mg/L (July 25) has achieved CR
  - Venetoclax changes the fundamental response ceiling from partial to deep response