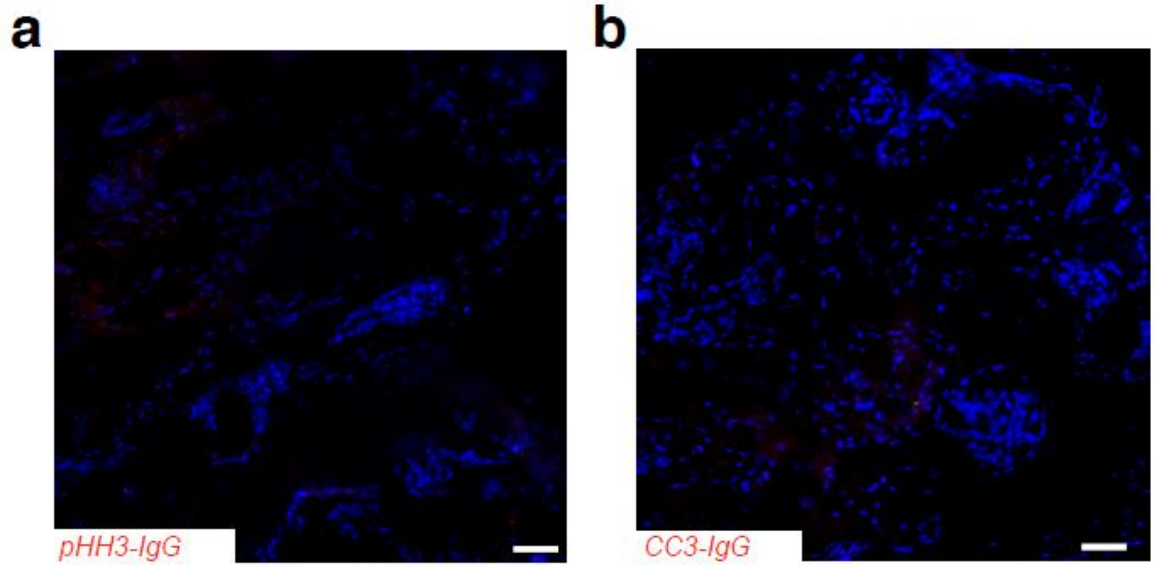

Figure S1. Representative IgG controls for phospho-histone H3 (pHH3, red, a) and cleaved caspase-3 (CC3, red, b). DAPI (blue) was used to stain nuclei. Scale bars represent 100 m.

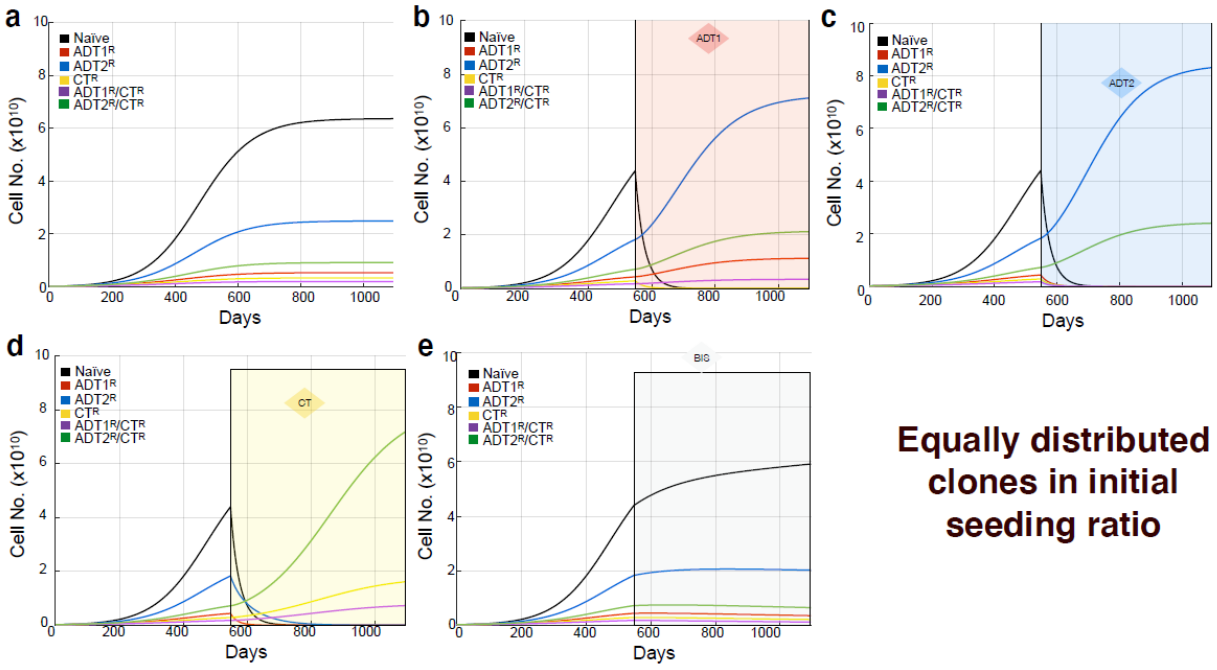

Figure S2. Evolution of equally distributed naïve and resistant phenotypes to applied treatments. The mathematical model of growth kinetics show naïve and resistant prostate cancer clones evolving differently than previously shown homogeneous initial conditions (Figure 2). These simulations are initialized with an initial 10 PSA (1.08×10^9 cells) distributed equally across the 6 clone subpopulations: naïve, ADT1R, ADT2R, CTR, ADT1R/CTR and ADT2R/CTR. **a**, Cancer grows in the absence of treatment until reaching the maximum carrying capacity (1000 PSA ~1.08×10^{11} cells), showing competition amongst cells for resources. In the absence of treatment, naïve cells have a growth advantage. **b–e**, The effects of individual treatments (continuous application) on the clonal composition of the tumor over time. Bisphosphonates can be applied continuously, but radiation and surgery can only be used once to debulk the tumor.

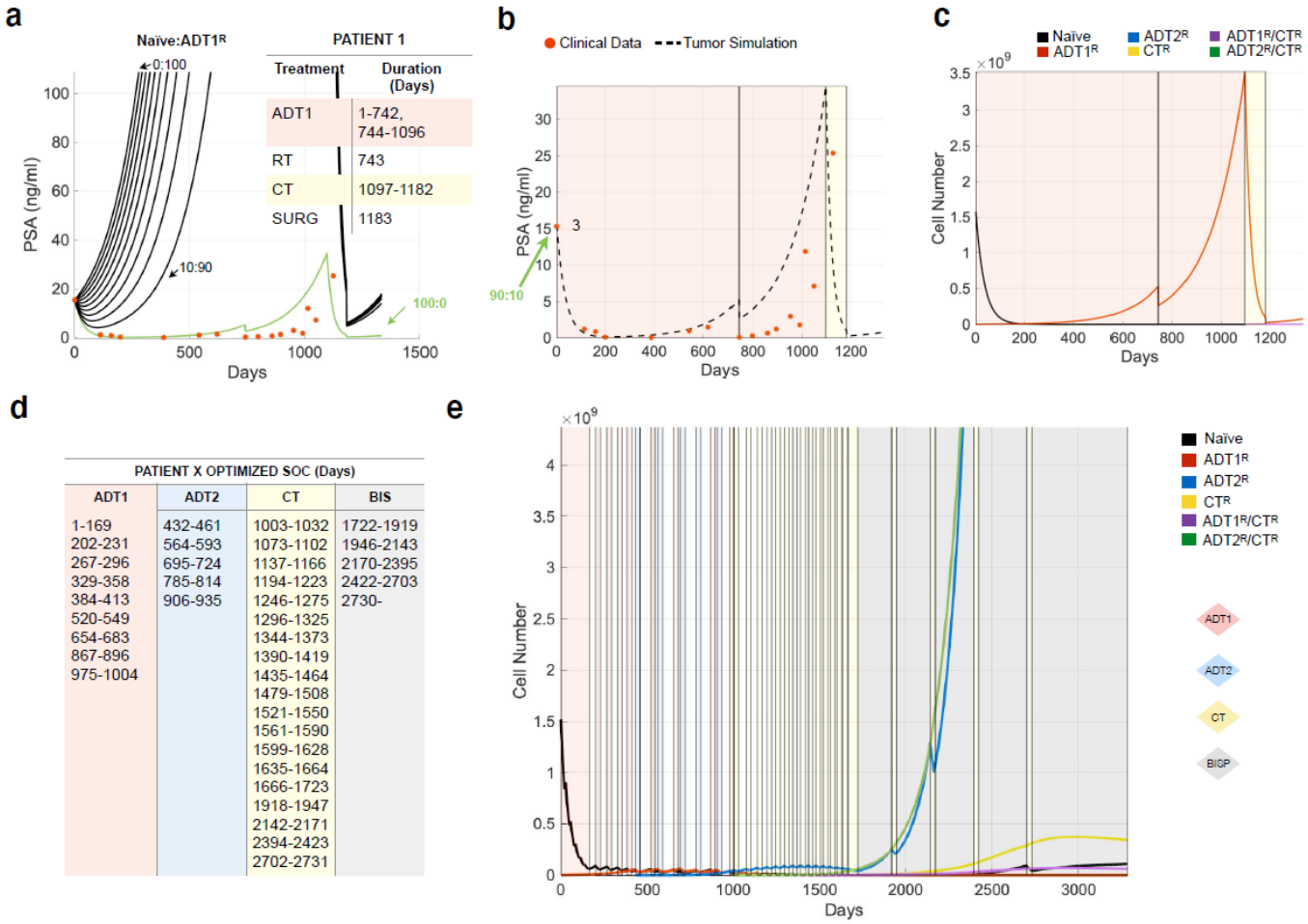

Figure S3–S25. De-identified patient simulations and patient-specific treatment optimization.

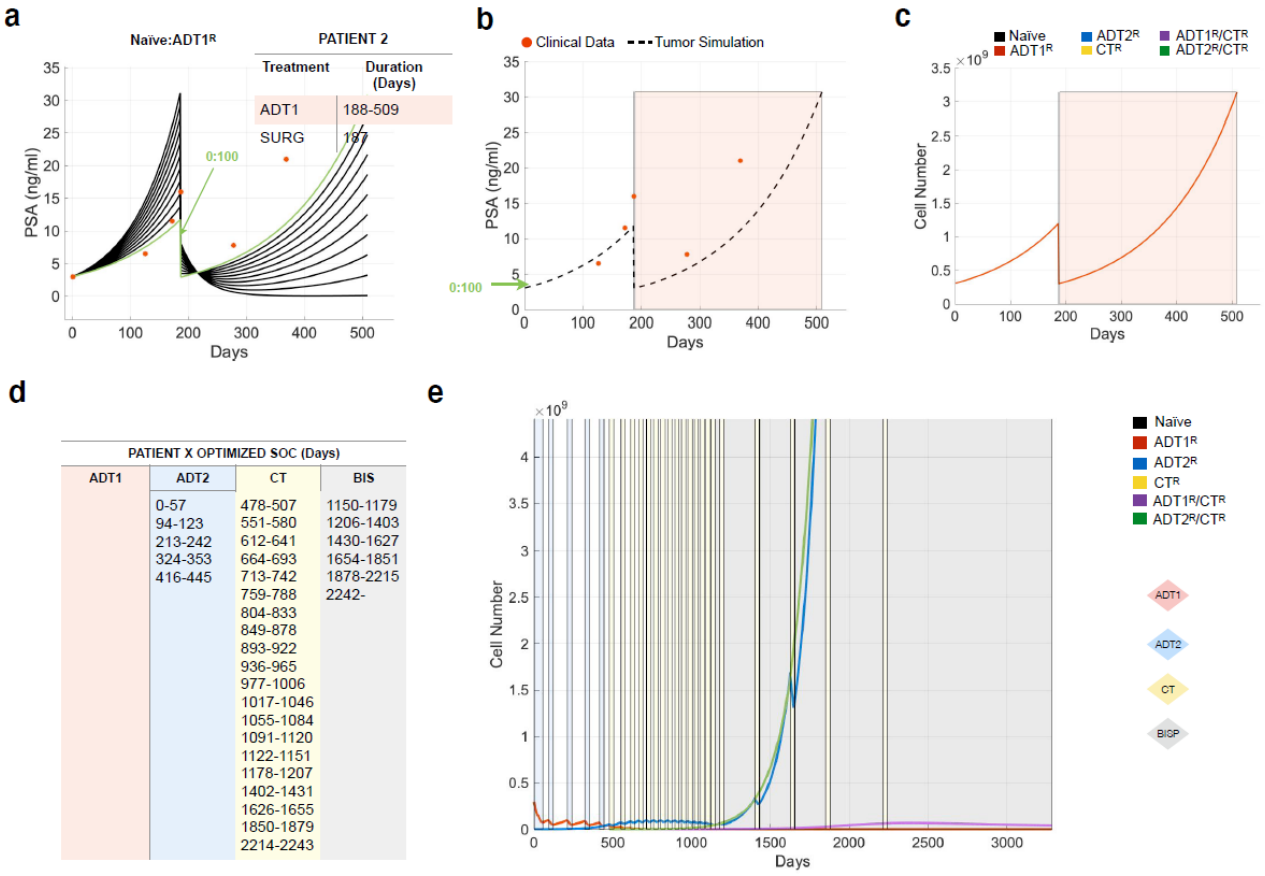

Figure S4. Araujo et al.

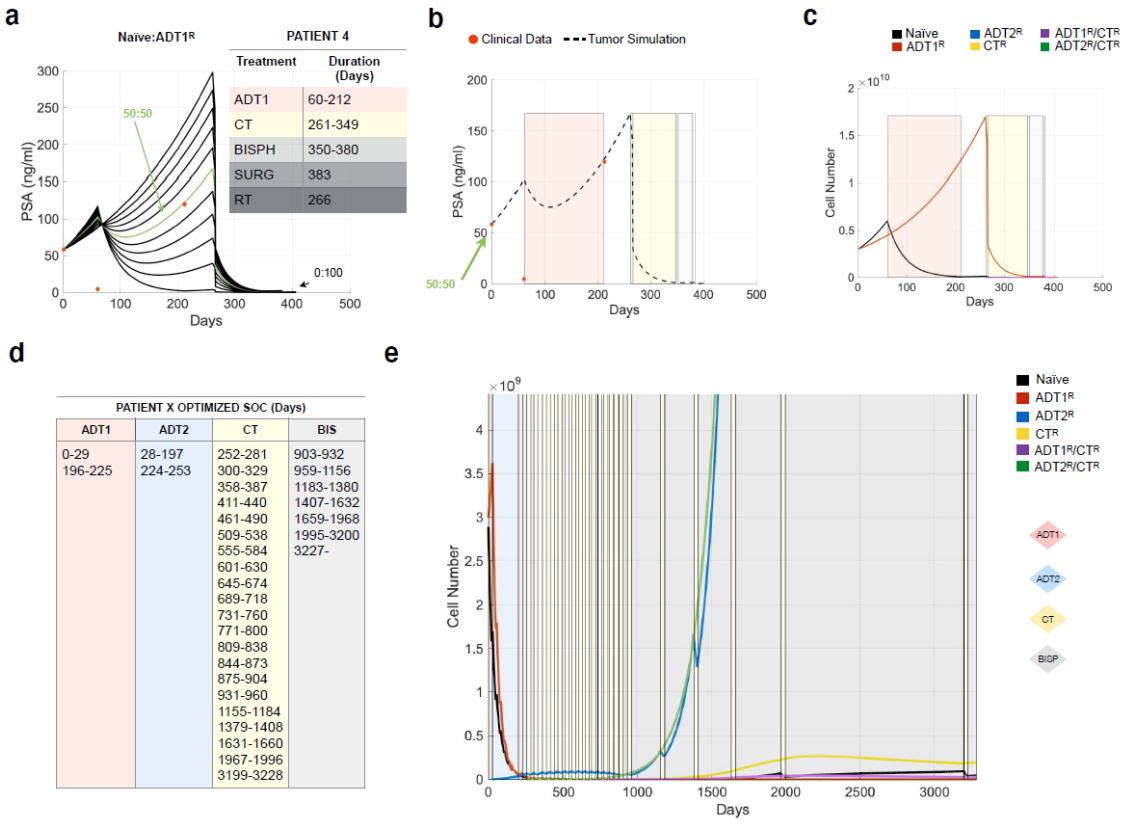

Figure S5. Araujo et al.

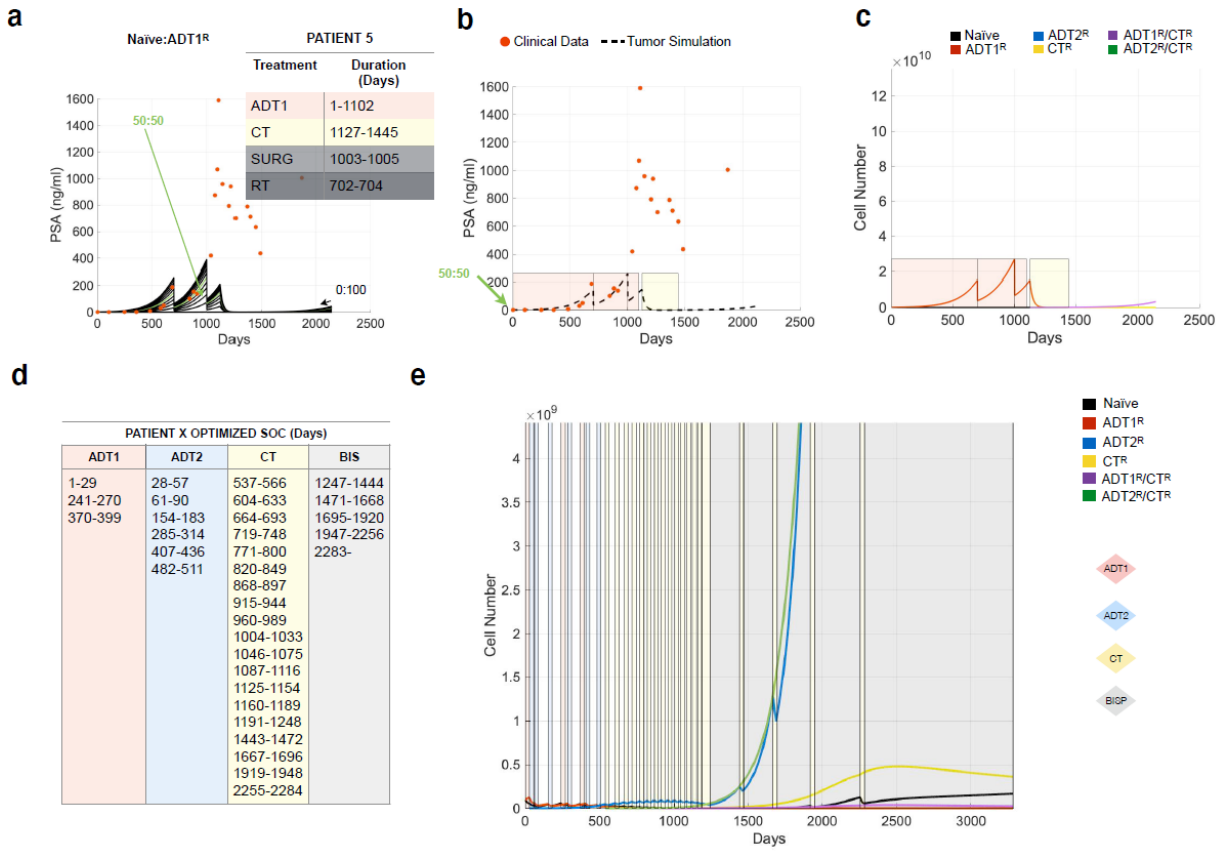

Figure S6. Araujo et al.

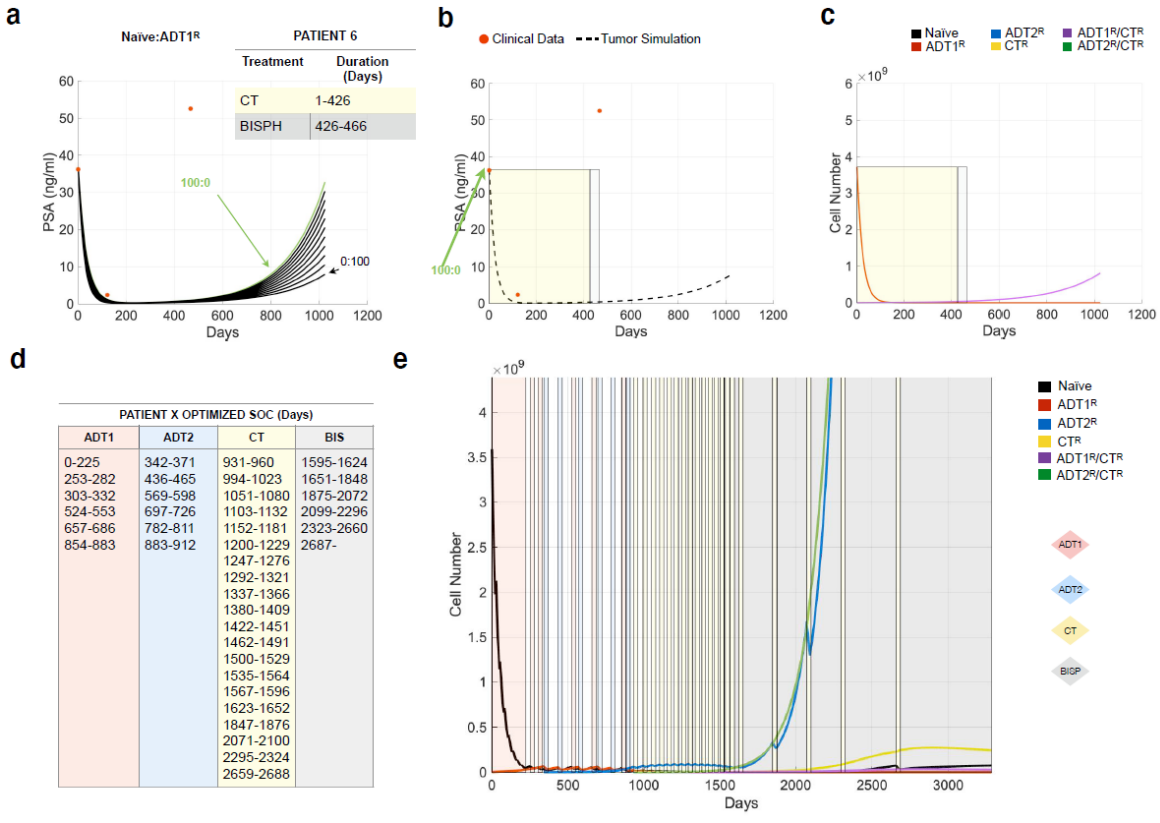

Figure S7. Araujo et al.

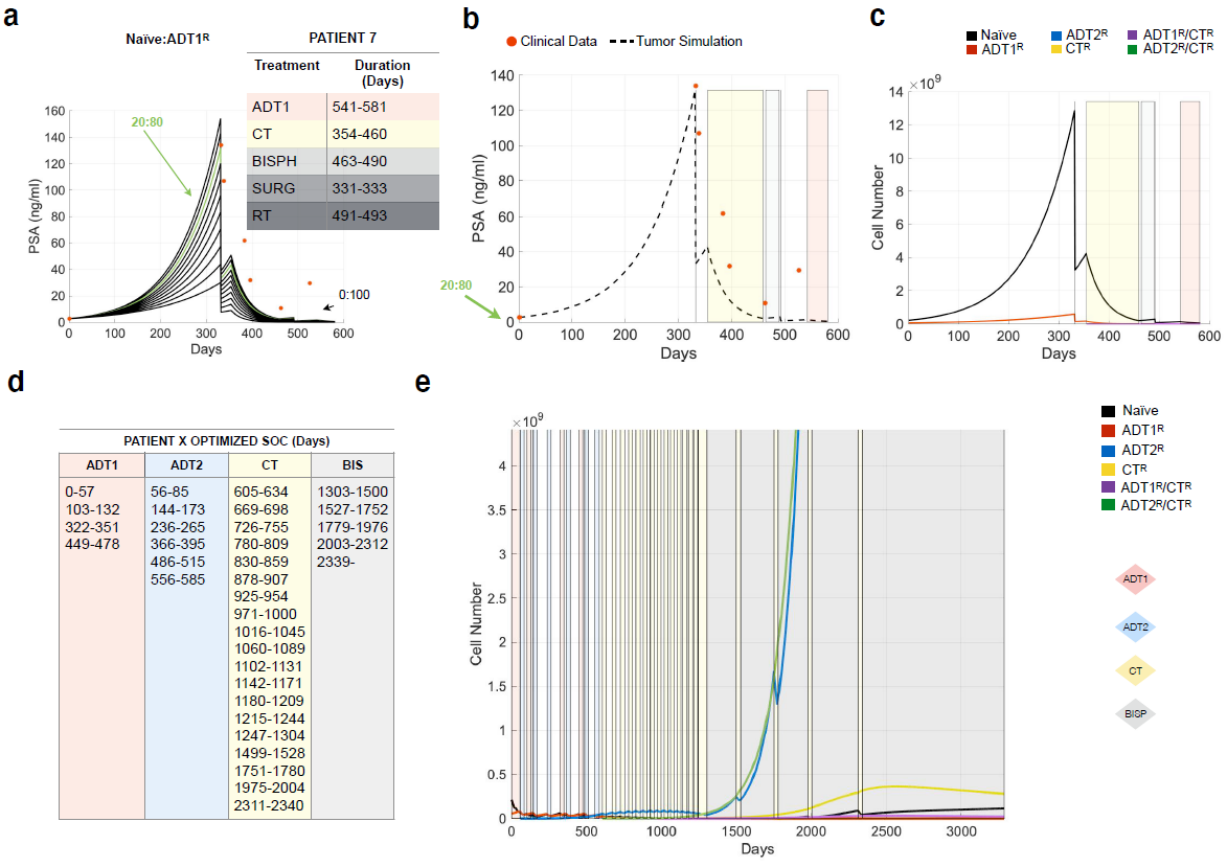

Figure S8. Araujo et al.

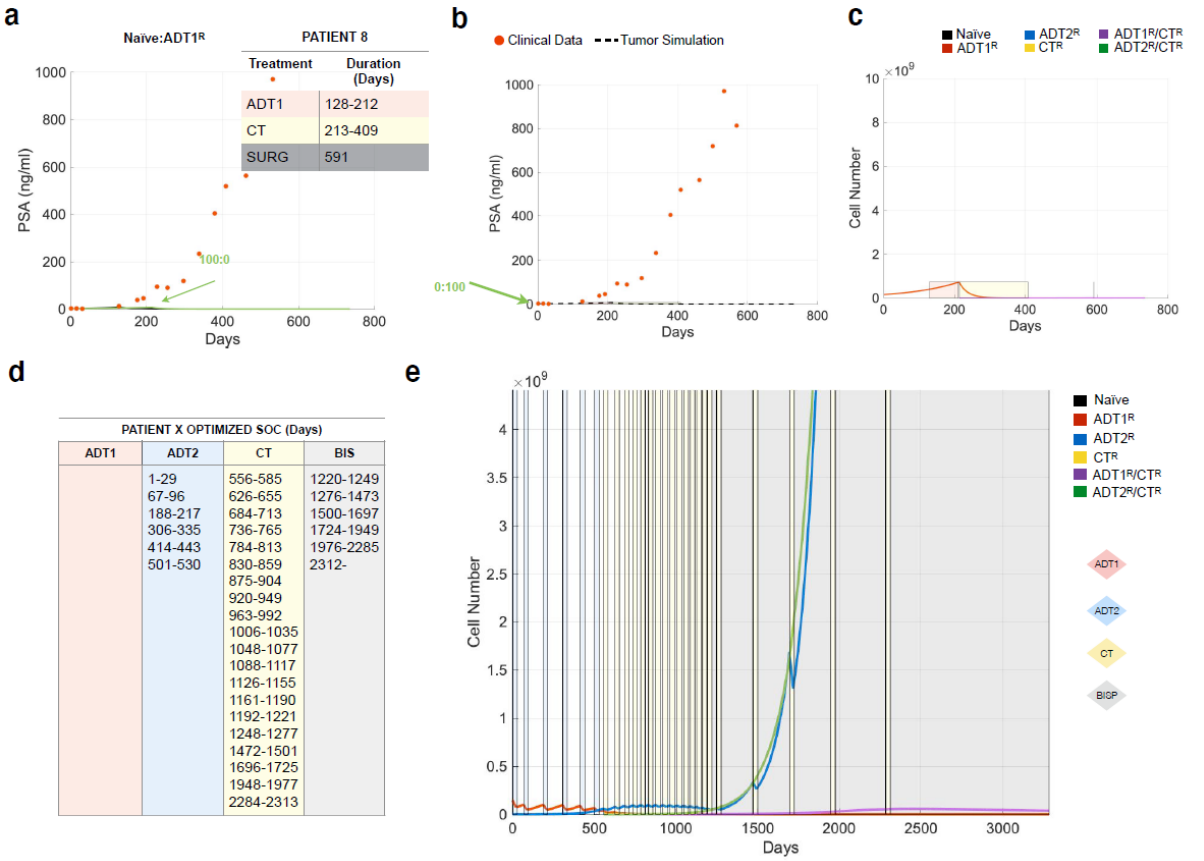

Figure S9. Araujo et al.

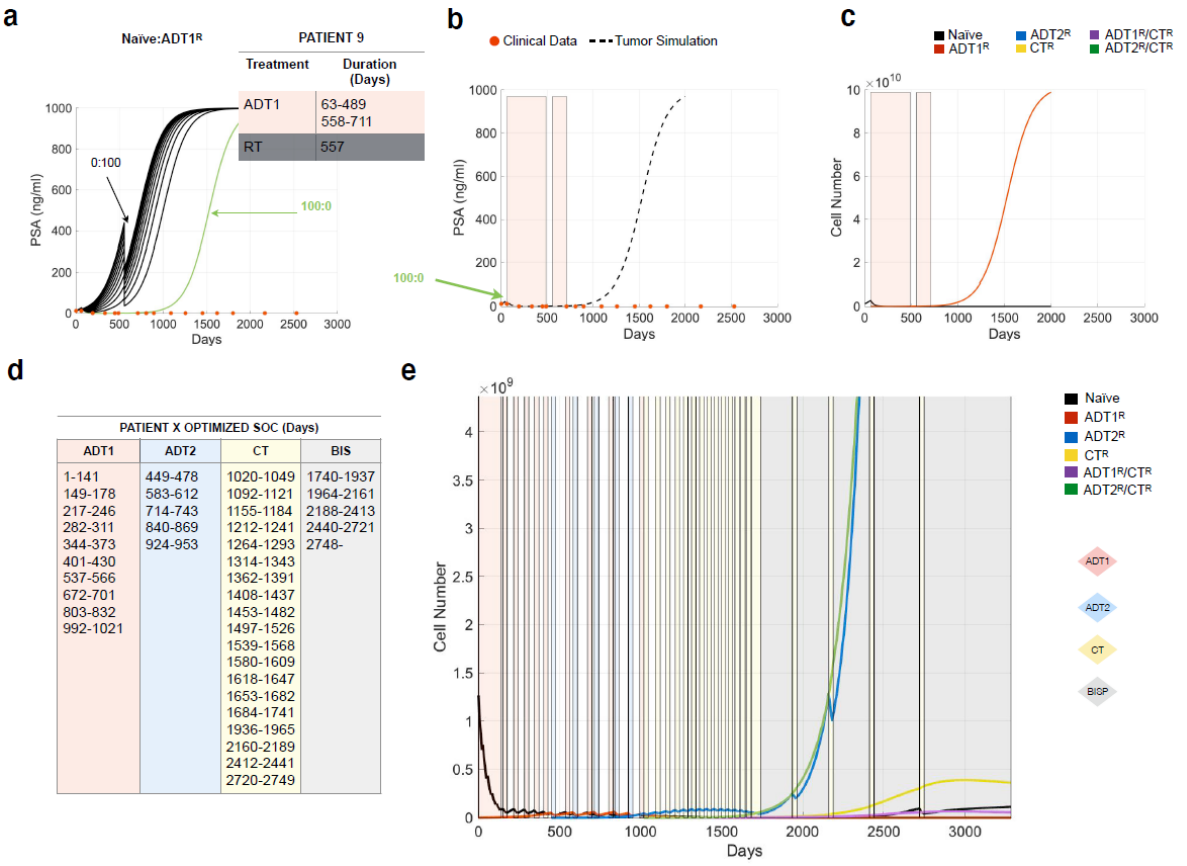

Figure S10. Araujo et al.

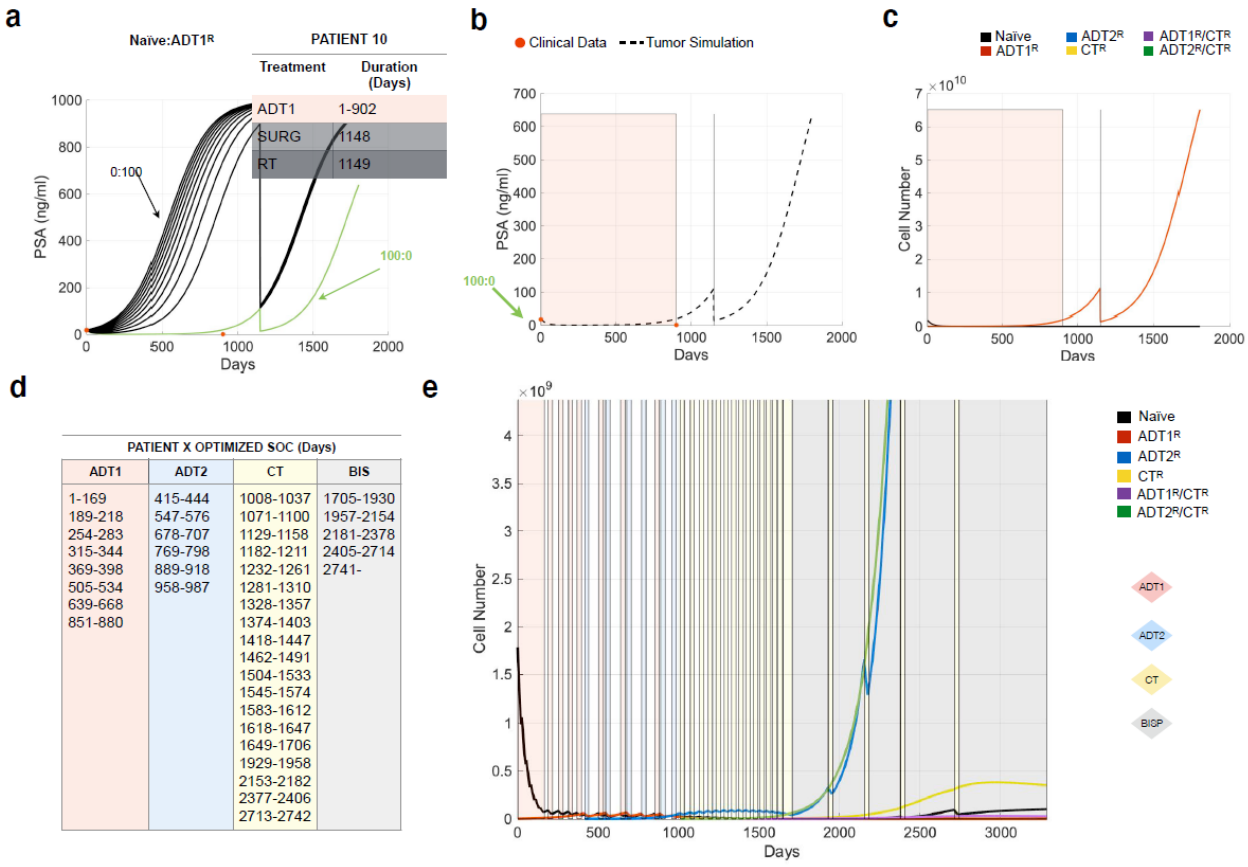

Figure S11. Araujo et al.

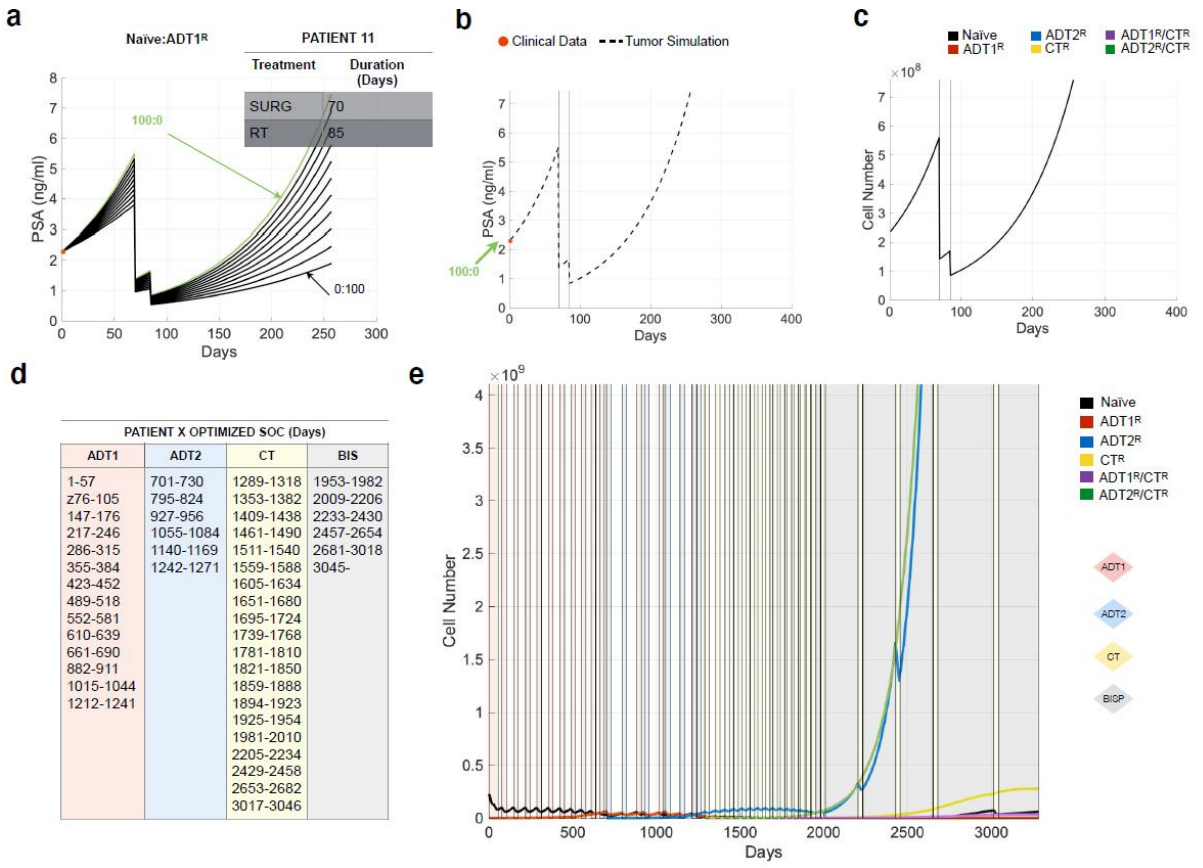

Figure S12. Araujo et al.

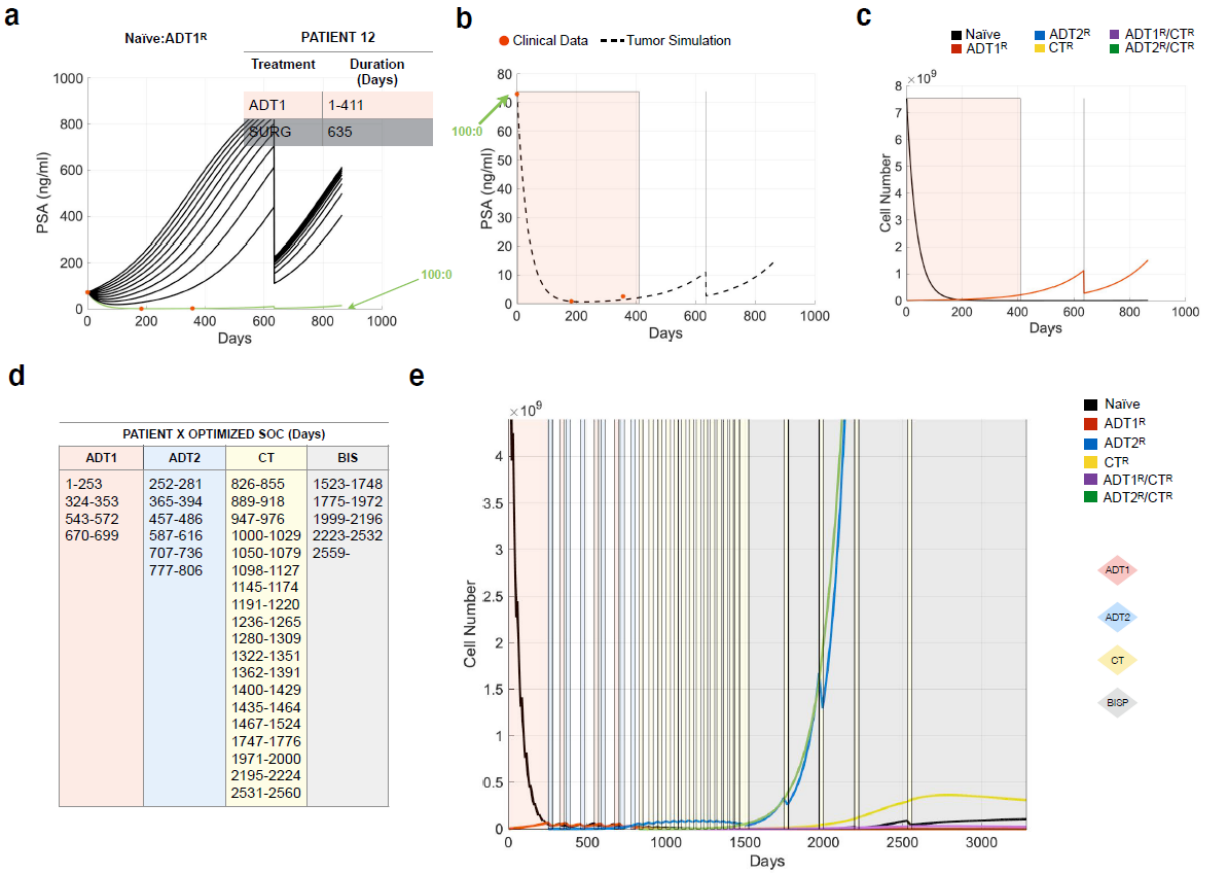

Figure S13. Araujo et al.

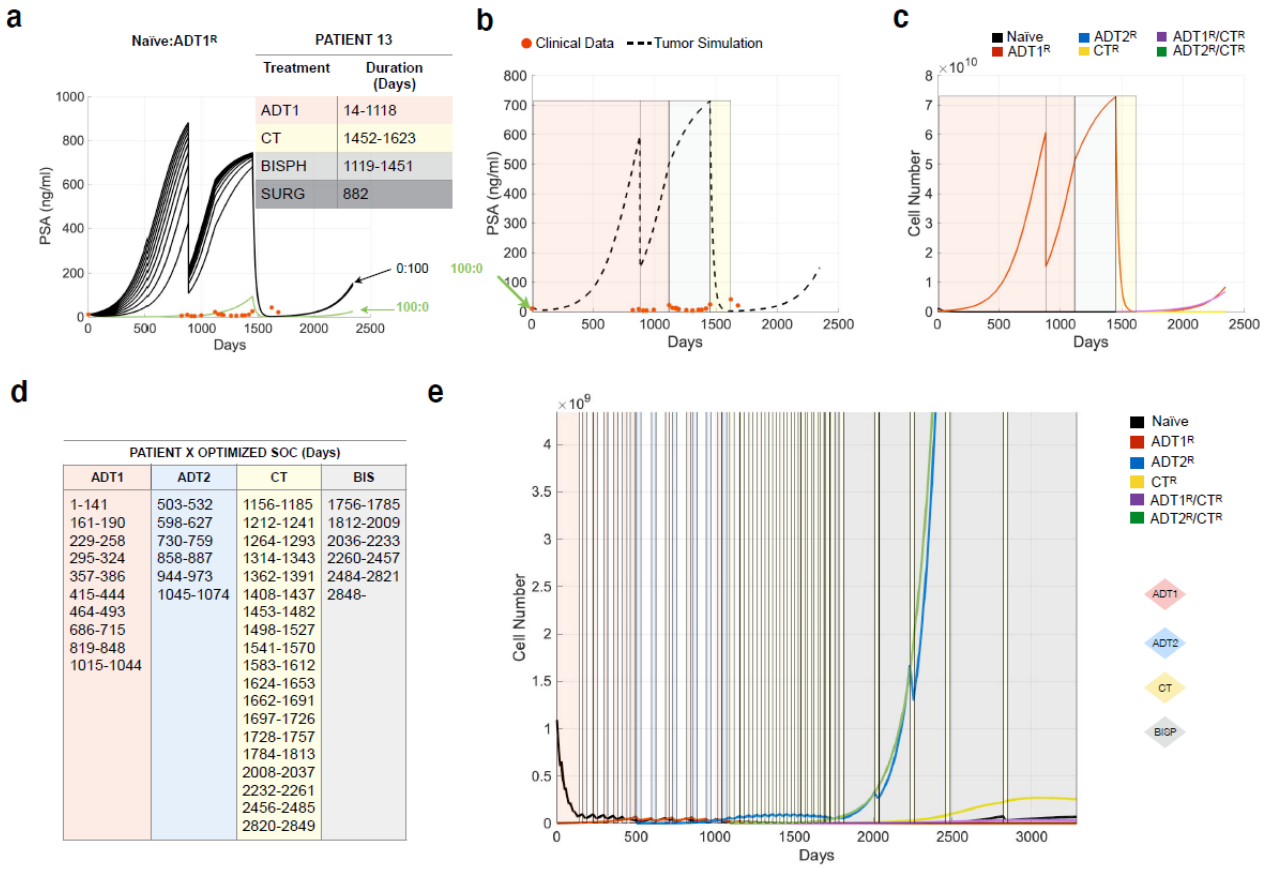

Figure S14. Araujo et al.

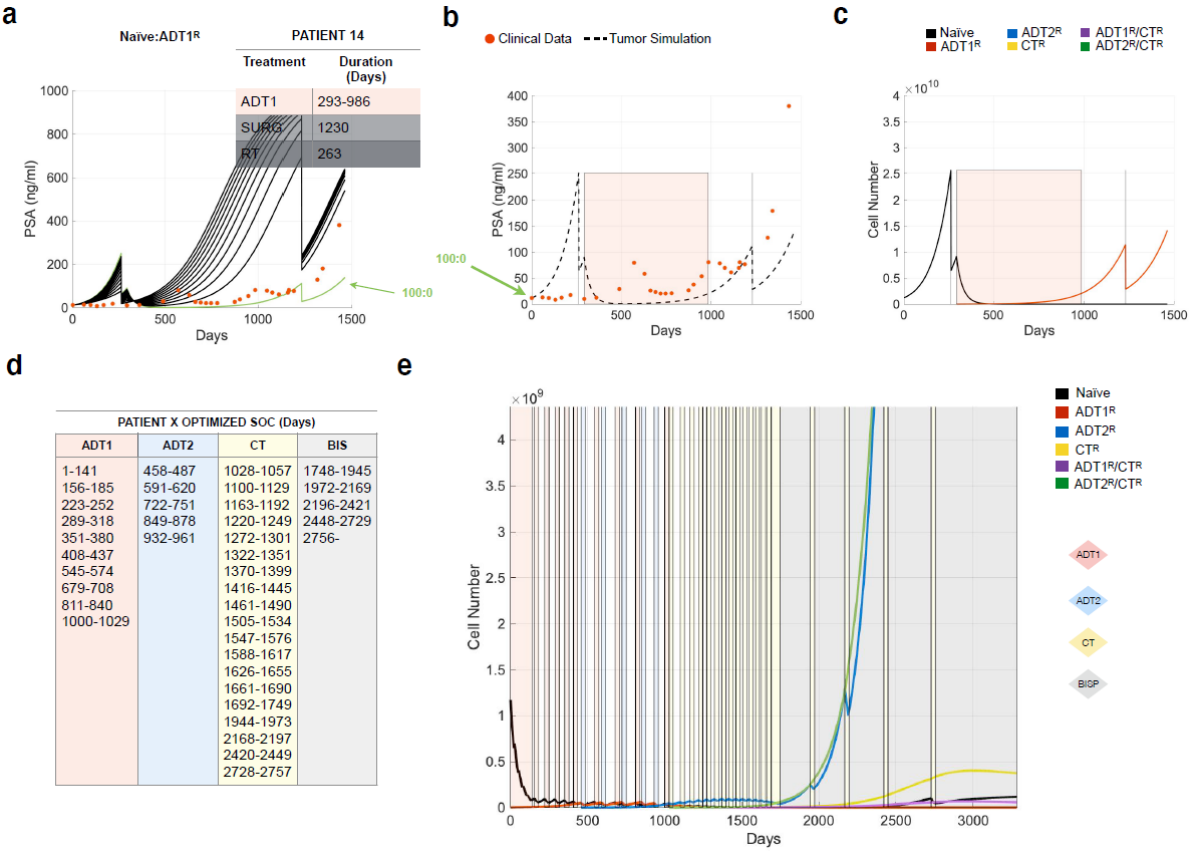

Figure S15. Araujo et al.

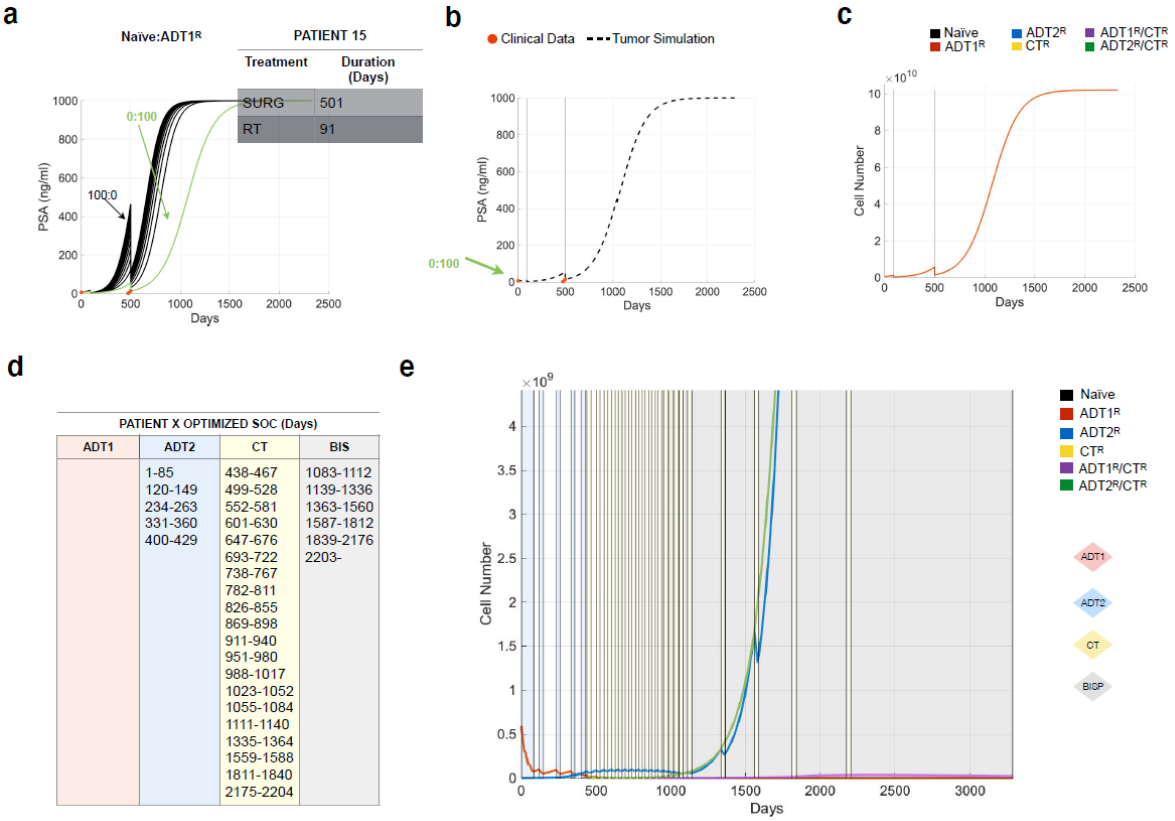

Figure S16. Araujo et al.

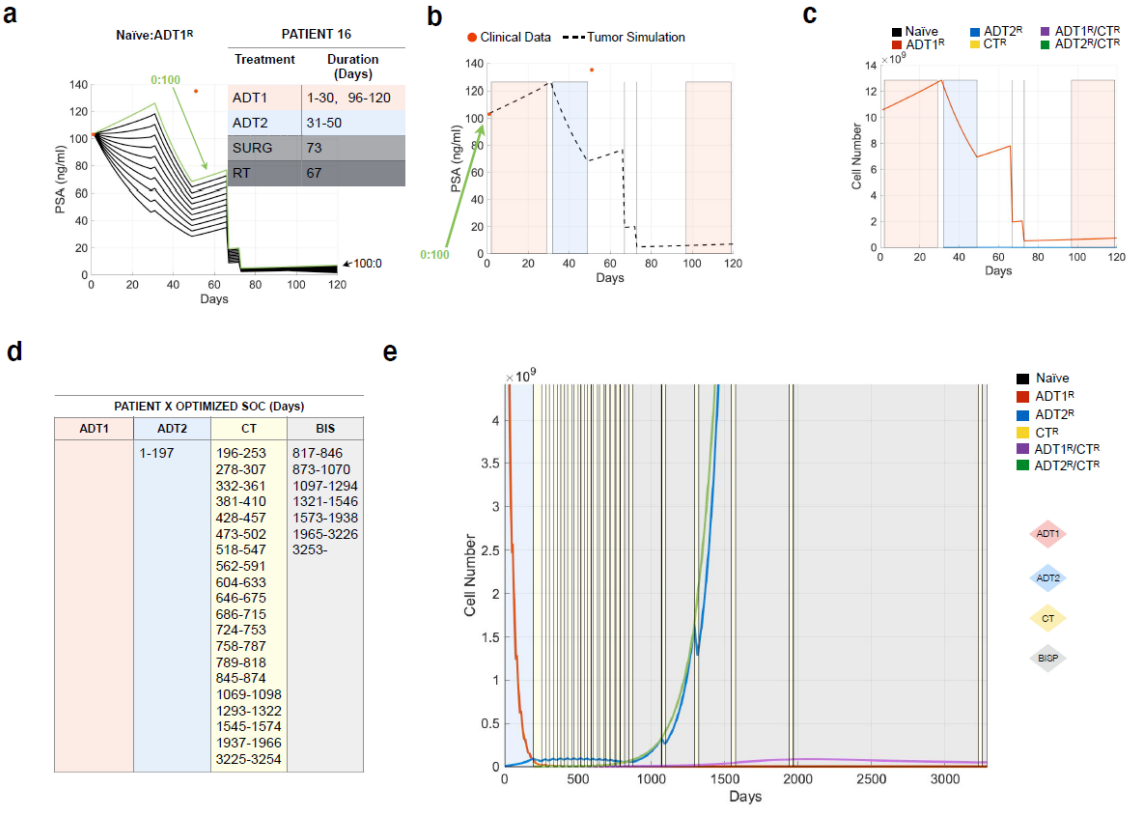

Figure S17. Araujo et al.

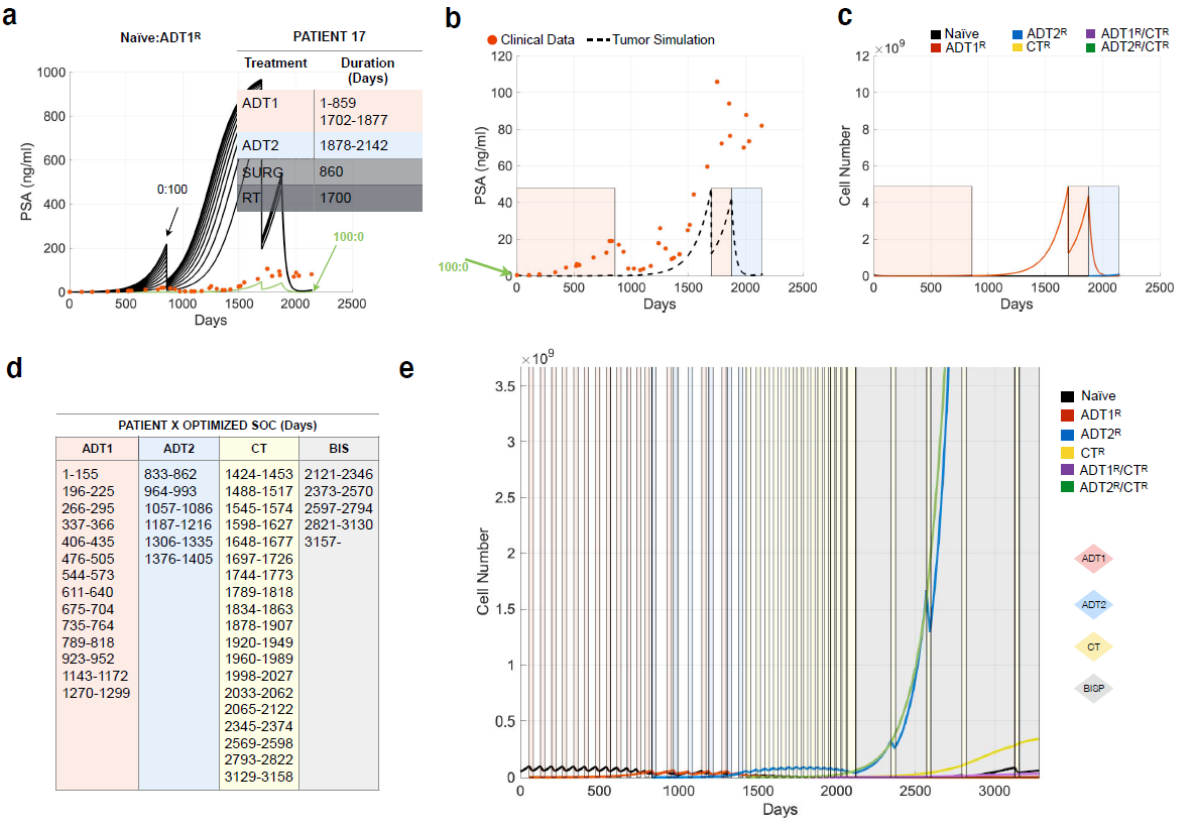

Figure S18. Araujo et al.

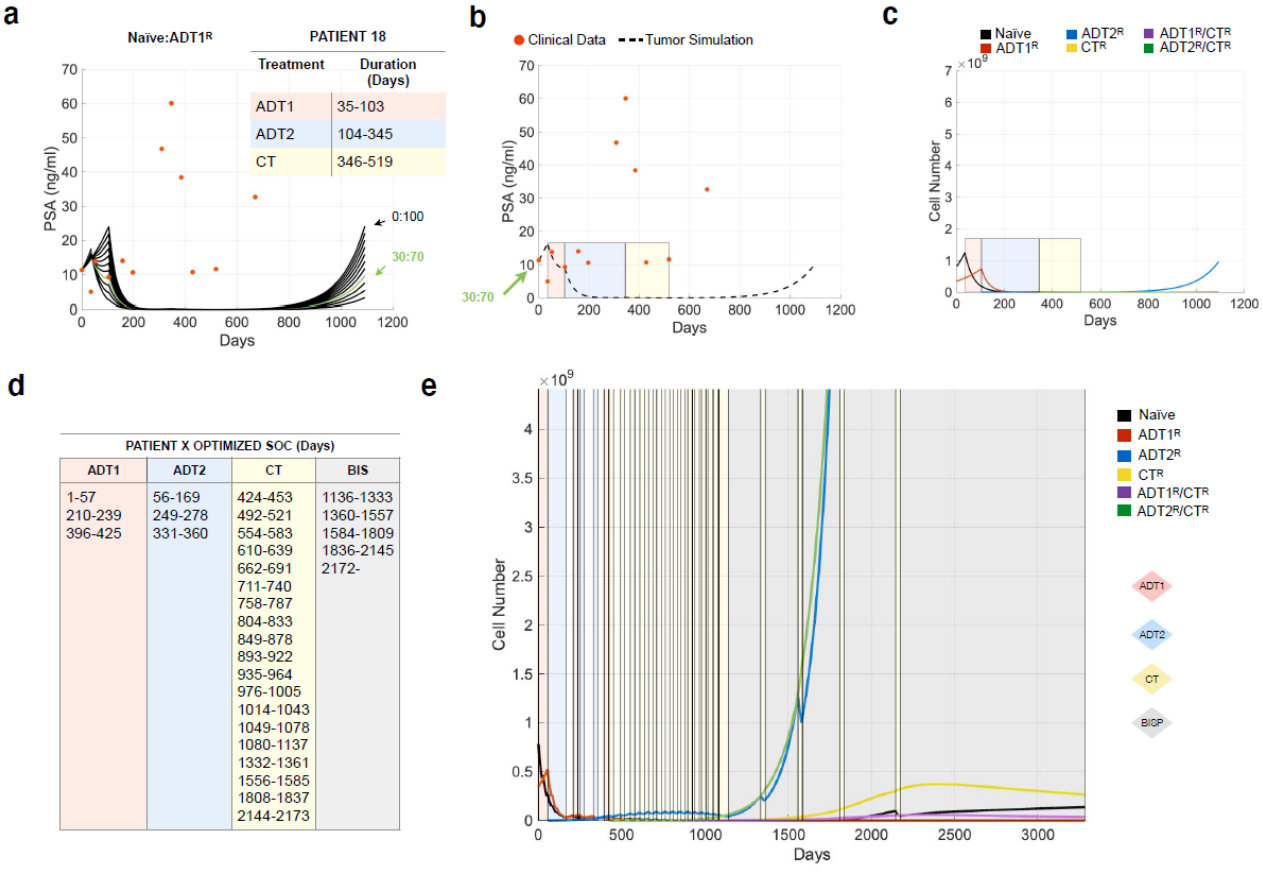

Figure S19. Araujo et al.

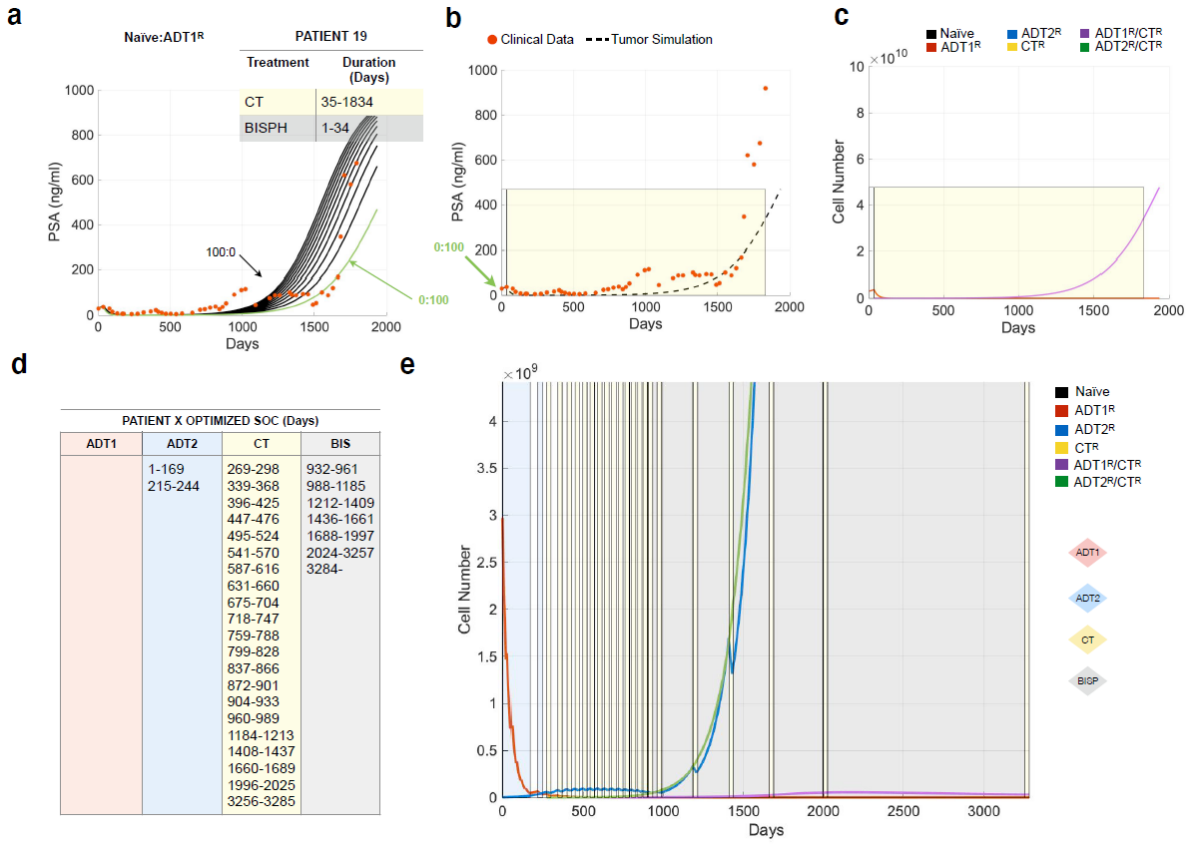

Figure S20. Araujo et al.

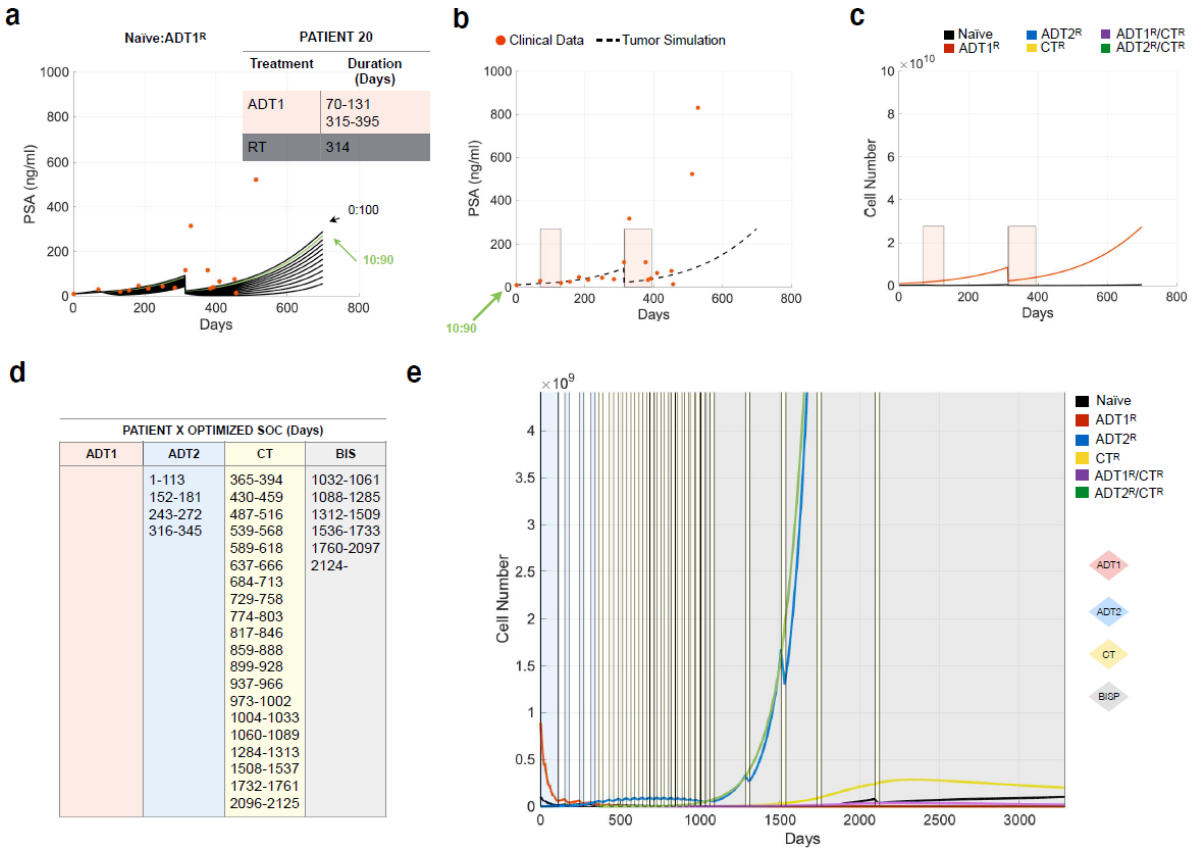

Figure S21. Araujo et al.

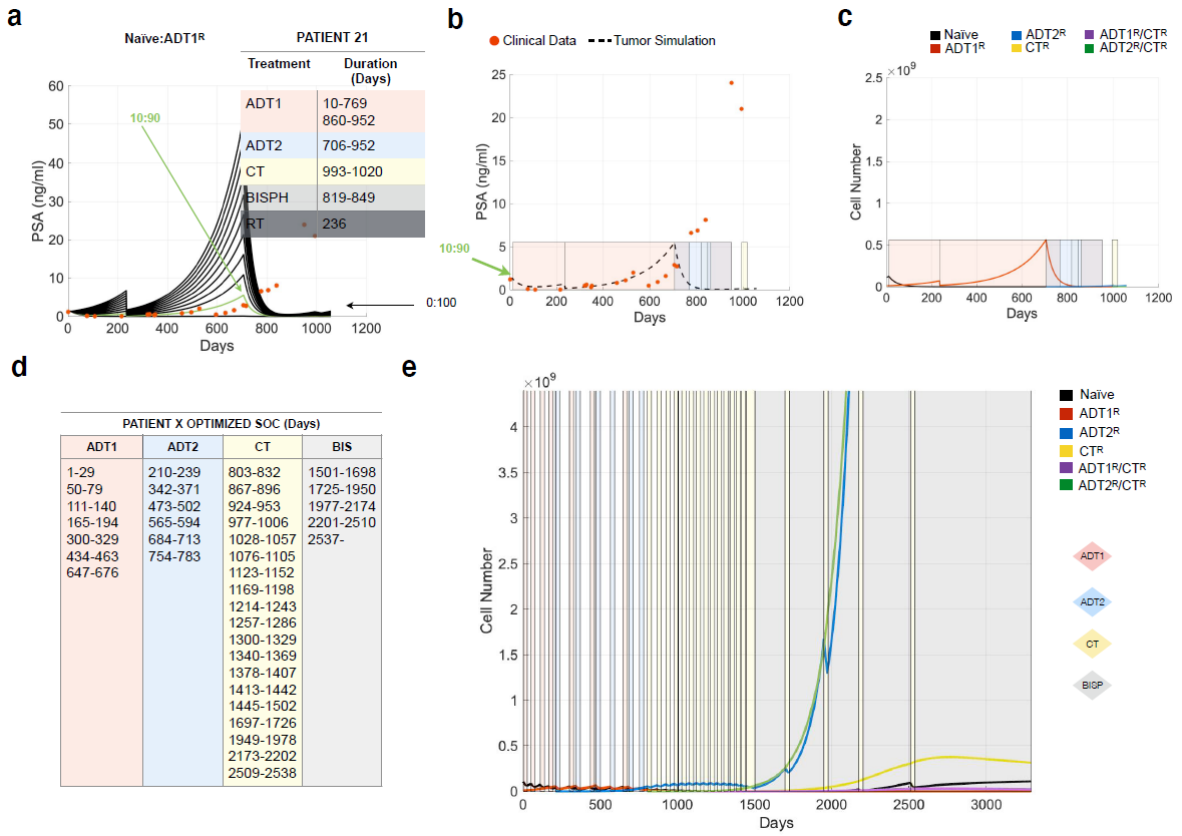

Figure S22. Araujo et al.

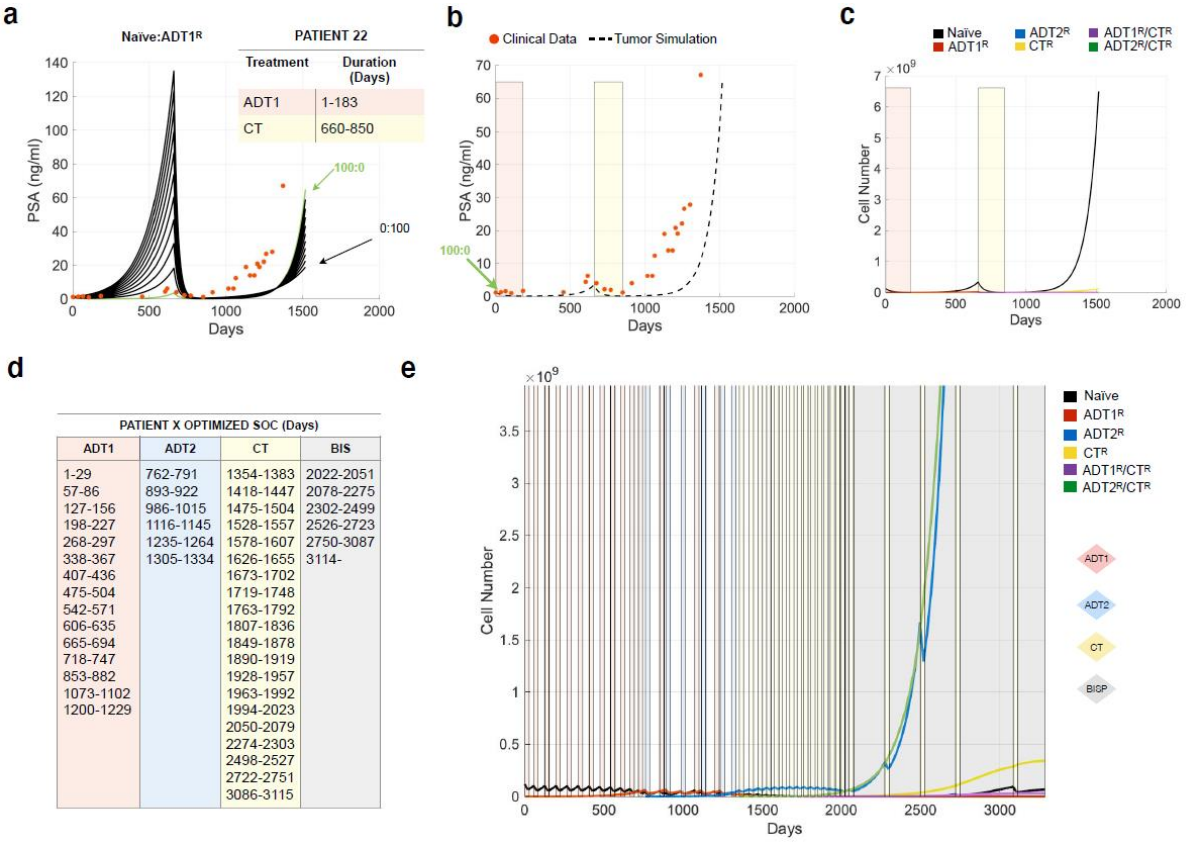

Figure S23. Araujo et al.

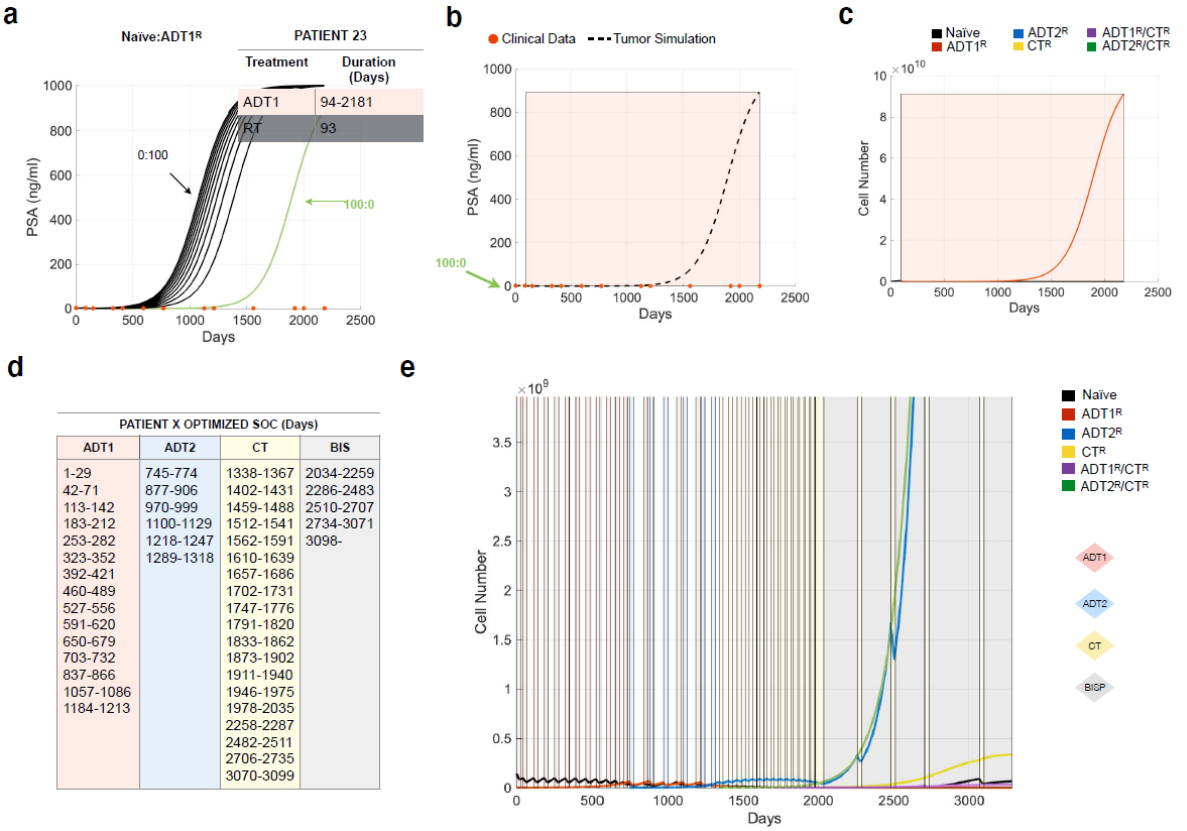

Figure S24. Araujo et al.

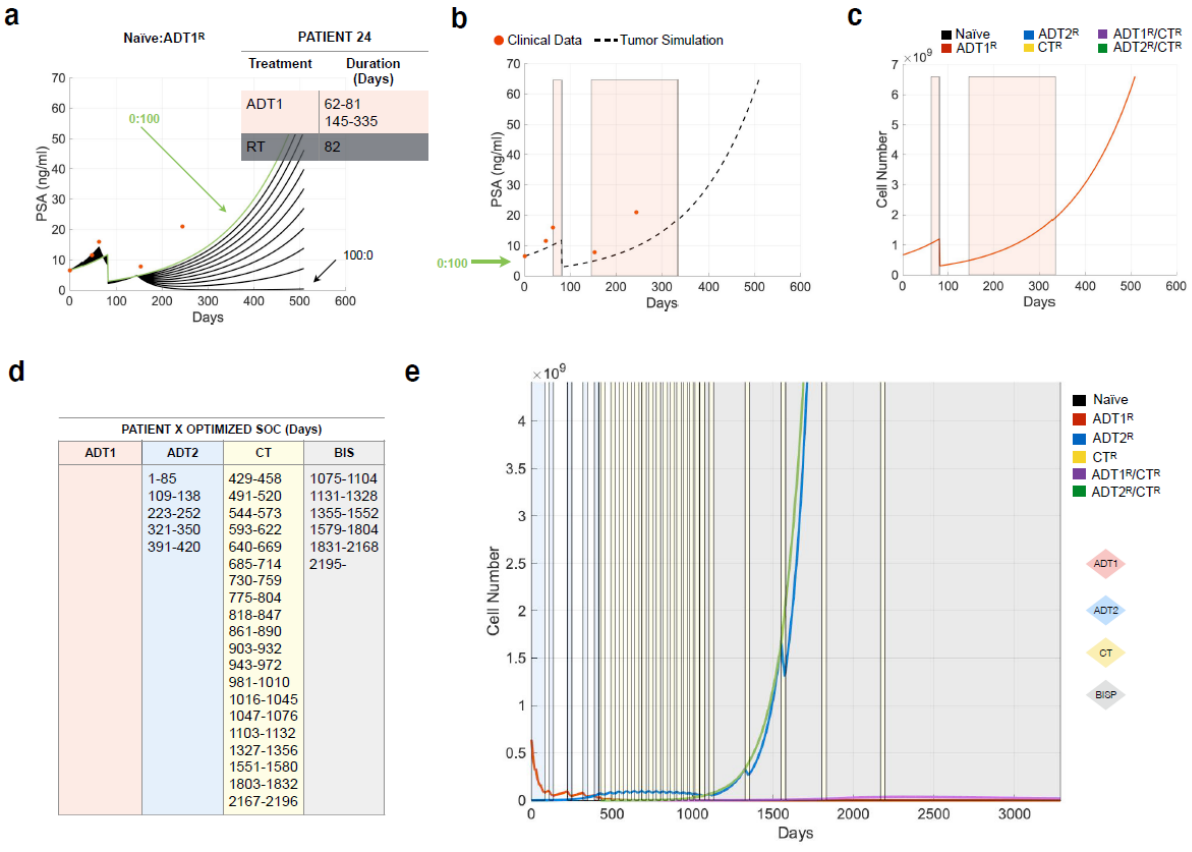

Figure S25. Araujo et al.