In an effort to understand major cost drivers and assess processing risk, Juno Therapeutics has developed a plant simulation of its global manufacturing network. With this simulation, Juno can assess the impact various control levers and sources of variability will have on key performance metrics. Juno has the ability to modify various aspects of its manufacturing operations, such as process design, staffing totals, shift schedules, facility configuration, and activity prioritization. Various sources of variability, such as time of patient specific raw material arrival at the plant, treatment rescheduling, and unit operation duration, will need to be mitigated in order to ensure robust manufacturing. In turn, with a representative simulation in place, optimization techniques can be leveraged in an effort to maximize the number of treated patients and revenue, while minimizing cost of goods and product cycle time. This work helps inform feasibility of future manufacturing paradigms and process design. An overview of Juno’s simulation and optimization methodology is presented here. Evaluations and trade-offs of point-of-care vs. centralized manufacturing and workstation vs. flexible facility configurations are presented.