

Factor IX Gene Therapy Phase 1 /2 Trial Update*

- BAX 335 is a novel liver-directed scAAV8 vector from Baxalta that delivers a codon optimized hyperactive F9 transgene (FIXR338Lopt)¹
- First-in-human safety and single ascending dose-finding trial ongoing in adults with severe hemophilia B

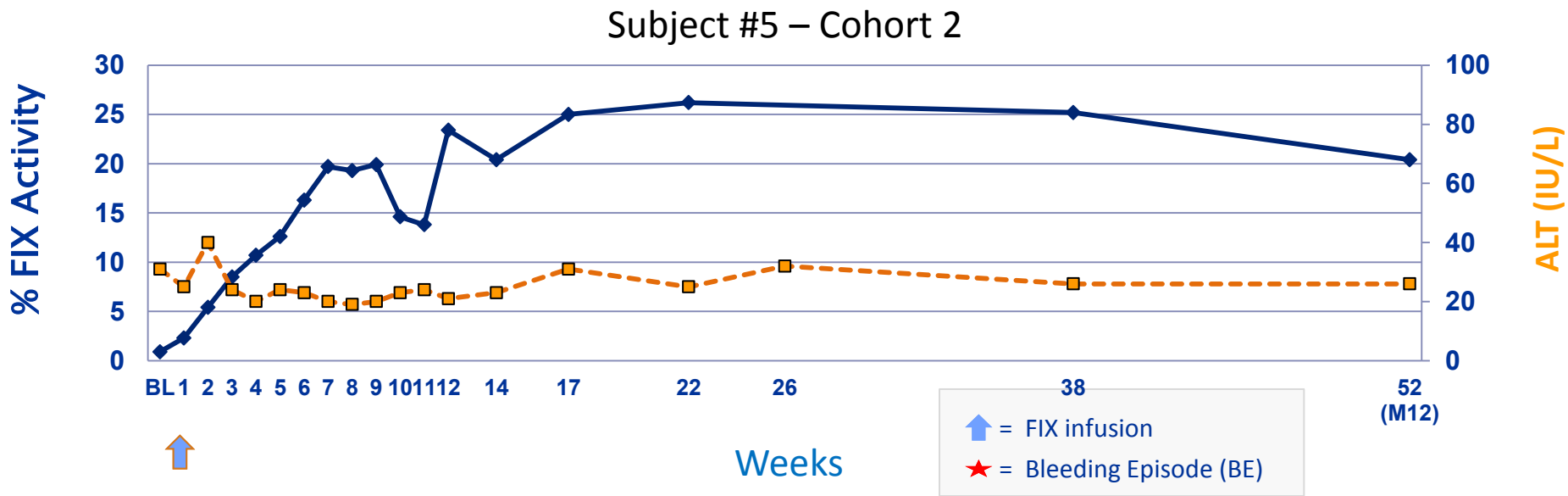
Cohort	Dose (vector genomes [vg]/kg)	# subjects dosed
1	2.0×10^{11}	2
2	1.0×10^{12}	3
3	3.0×10^{12}	2

* *Preliminary data*

¹Monahan PE, et al *Hum Gene Ther* 2015

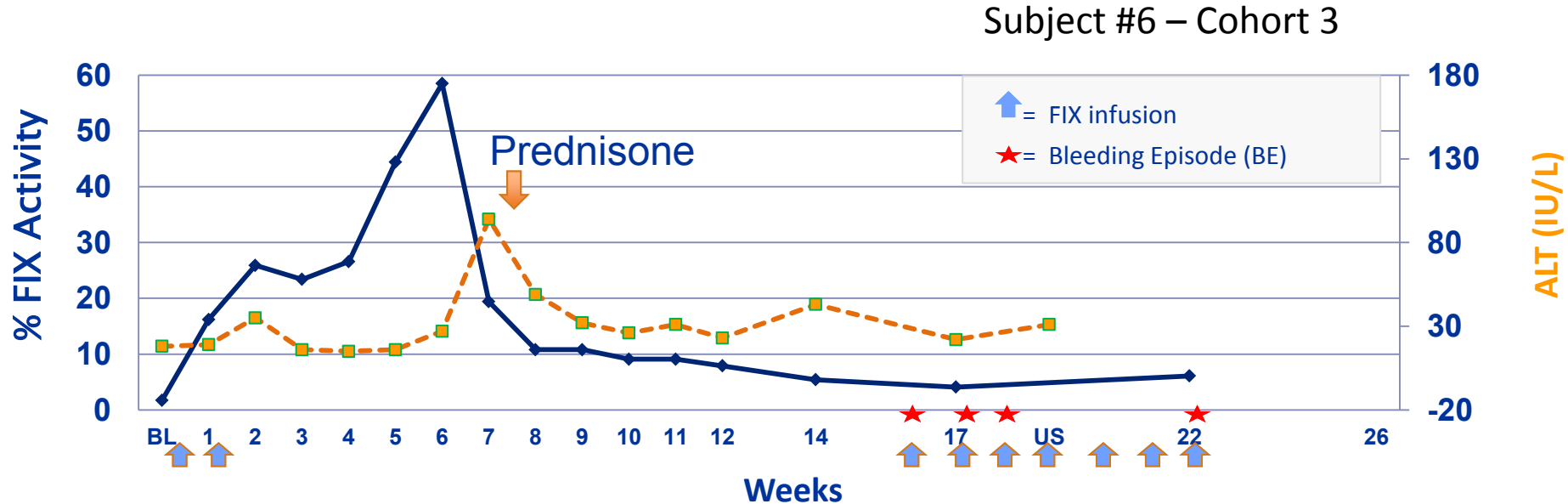
BAX335 Phase 1 / 2 Study: 1st and 2nd dose cohorts

- Dose-dependent FIX expression in both cohorts
- Sustained FIX expression of 20–25% in one subject in Cohort 2 with no bleeding and no exogenous FIX infusions



BAX335 Phase 1/2 Study: 3rd dose cohort – enrollment ongoing

- Dose-dependent FIX expression observed with peak levels >50% in 3rd dose cohort
- T-cell mediated immune response and liver enzyme elevations observed in two patients, with declining FIX expression triggering immunosuppression with corticosteroids



Summary

- The ongoing BAX 335 Phase 1 /2 study has escalated to 3rd dose cohort. An additional 5 patients will be dosed
- Sustained expression of 20–25% for 1 year was observed in cohort 2
- Peak FIX activity level >50 % achieved in Cohort 3 but persistent, stable expression was not achieved in the first two patients in this cohort
- Dose-dependent immune responses were observed in two patients in cohort 3 and treated with corticosteroid. FIX expression has subsequently declined in both subjects, likely due to delayed start of corticosteroid
- No inhibitors observed in any of the subjects treated to date
- **Conclusion:** Hemostatically effective plasma FIX activity levels were achieved in cohort 2 and 3 with sustained high level expression in one patient (20–25%)