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## **SUPPLEMENTARY MATERIAL**

### **Pharmacokinetics of extended half-life albumin-fused factor IX and heterogeneous *F9* variants in hemophilia B: a retrospective cohort study**

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**Supplementary Table 1.** *F9* genetic components in SHL-/EHL-rFIX by NCA PK.

<b>Main observations</b>
<b><i>EHL-rIX-FP</i></b> No significant differences between distributions of null and non-null genotypes. CL in the first tertile was slower in patients with null than non-null variants / Non-null genotypes were more frequent in the third tertile. Bioinformatics analyses of missense variants may predict i) more severe disease features in the third CL tertile, ii) an appreciable intra-cluster similarity in the first and third tertiles.
<b><i>SHL-/EHL-rFIX comparison</i></b> No significant differences between distributions of null and non-null genotype groups for both products. <i>F9</i> genotype - Clearance tertile association differences between products. Overall, moderate role of <i>F9</i> variant type in inter-individual PK variability.
<b>Open issues</b>
Is NCA PK analysis suitable to detect differences in genetic components? The mechanisms underlying <i>F9</i> mutation type associations, as well as the influence of other gene components, remains to be investigated. Clinical utility definition requires studies in larger cohorts of genotyped patients.

SHL, standard half-life; EHL-rFIX, elongated half-life recombinant FIX concentrates; PK, pharmacokinetics; NCA, Non-Compartmental Analysis; FP, albumin fusion protein.