### The Evolving Treatment Landscape of Hemophilia

#### Replacement Therapy

- **Limitations**
  - Immunogenicity
  - Treatment burden and adherence
  - Maintaining adequate factor levels

#### Non-Factor Replacement Therapies Are Evolving Rapidly

- FVIII Mimetics
- Antithrombin reduction
- Anti-TFPIs
- Anti-APC

#### The Potential of Gene Therapy

- It can achieve therapeutic factor levels in a dose-dependent fashion, achieve very low annualized bleed rates, and reduce/eliminate the need for exogenous clotting factor replacement. To date, there has been no associated inhibitors, and no therapy-associated deaths.

- There are still some remaining questions: can it be administered to those with active HIV, HBV and HCV? Is it safe for children with growing livers? Is there potential for insertional mutagenesis? Can it be re-administration?

TFPI, tissue factor pathway inhibitor; APC, activated protein C.