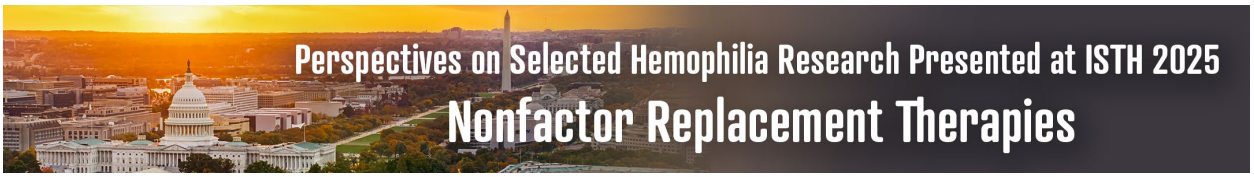

Dear Colleague:

Thank you for your recent participation in the CME/CE activity, *Perspectives on Selected Hemophilia Research Presented at ISTH 2025: Nonfactor Replacement Therapies*, developed by the Annenberg Center for Health Sciences. As you continue to advance the care you provide to these patients, here are the key concepts for you to consider:

- **Rebalancing agents** (fitusiran, concizumab, marstacimab) promote hemostasis through factor-independent pathways, offering new prophylactic options for hemophilia A and B.
    - Antithrombin percentages should range between 15% and 35% to reduce the potential of thromboembolic complications at very low antithrombin levels.
    - Concizumab is helpful as prophylaxis in patients with hemophilia B with inhibitors.
    - Weekly subcutaneous dosing of marstacimab is suitable for persons with hemophilia A or B without inhibitors.
- **Factor VIII mimetics** (emicizumab and the investigational mim8) restore thrombin generation by mimicking the cofactor function of FVIII.
    - Emicizumab prophylaxis yields low annualized bleed rates long-term, although there is still room for improvement in joint bleed rates.
    - Major surgeries are feasible for patients on emicizumab with continued hemostatic support; *a priori* factor coverage can help avoid breakthrough bleeding.
    - A seamless transition from emicizumab to mim8 prophylaxis is possible, establishing therapeutic levels quickly with flexible dosing intervals.

We hope you will be able to participate in other accredited activities we offer. You will find information at www.Annenberg.net.

Regards, The Annenberg Center Team