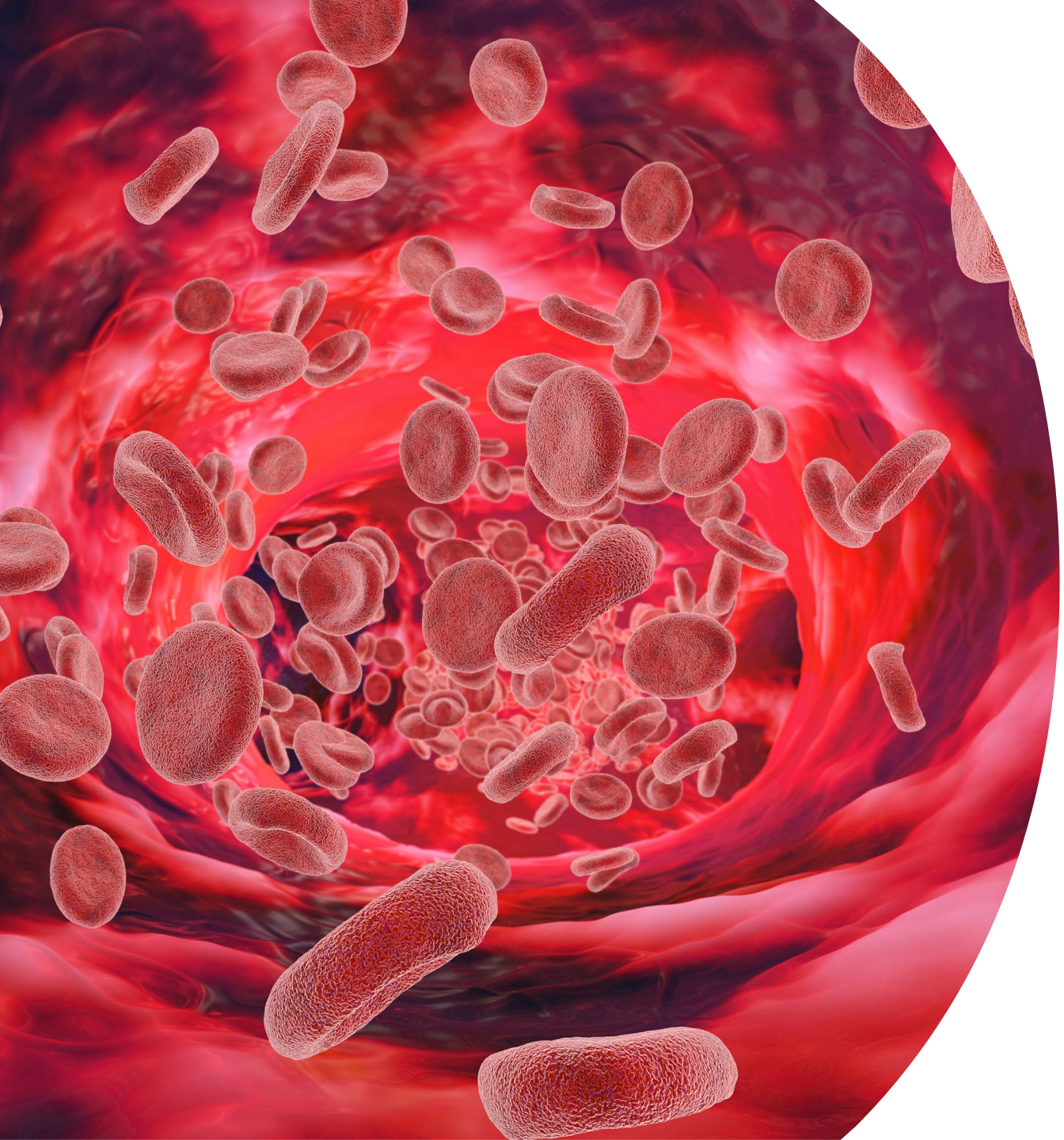

sanofi



Hemophilia Investor Event

London, UK

July 13, 2022

Forward-looking statements

This document contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans" and similar expressions. Although Sanofi's management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates, the fact that product candidates if approved may not be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities, to complete related transactions and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic and market conditions, cost containment initiatives and subsequent changes thereto, and the impact that COVID-19 will have on us, our customers, suppliers, vendors, and other business partners, and the financial condition of any one of them, as well as on our employees and on the global economy as a whole. Any material effect of COVID-19 on any of the foregoing could also adversely impact us. This situation is changing rapidly, and additional impacts may arise of which we are not currently aware and may exacerbate other previously identified risks. The risks and uncertainties also include the uncertainties discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in Sanofi's annual report on Form 20-F for the year ended December 31, 2021. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

Agenda

Hemophilia Investor Event

01 • Sanofi’s ambition in Rare Blood Disorders

Dietmar Berger
Global Head of Development, CMO

02 • Clinical experience with fitusiran

Guy Young, MD
Director, Hemostasis and Thrombosis Center at Children's Hospital Los Angeles

03 • Clinical experience with efanesoctocog alfa

Angela Weyand, MD
Assistant Professor at Michigan Medicine

04 • Advancing hemophilia treatment standards

Bill Sibold
GBU Head Specialty Care

05 • Close and Q&A

Sanofi’s ambition in Rare Blood Disorders

Dietmar Berger

Global Head of Development,
CMO

Transforming the lives of people with rare blood disorders

Sanofi RBD portfolio

Marketed products

Hemophilia

ELOCTATE® [Antihemophilic Factor (Recombinant), Fc Fusion Protein]

ALPROLIX® [Coagulation Factor IX (Recombinant), Fc Fusion Protein]

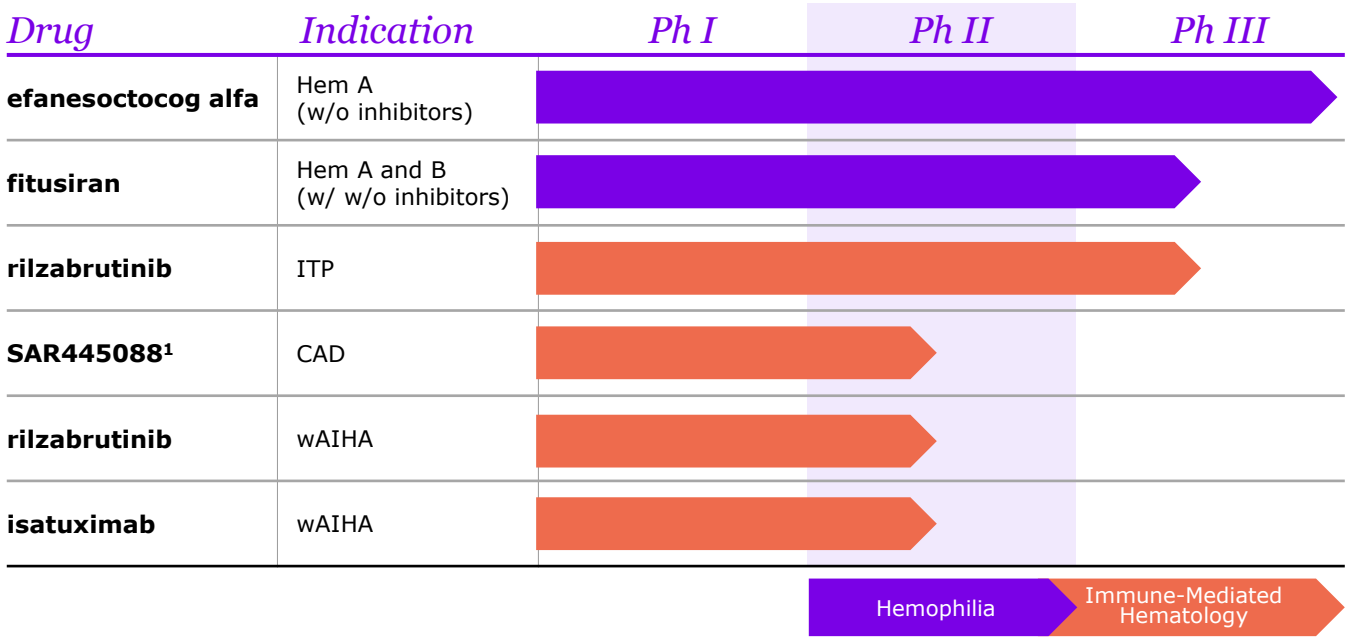
CAD

Enjaymo™ sutimlimab-jome Injection for intravenous use

aTTP

Cablivi® caplacizumab-yhdp

Molecules under investigation



aTTP: acquired Thrombotic Thrombocytopenic Purpura. CAD: Cold Agglutinin Disease. ITP: Immune Thrombocytopenia. Hem: Hemophilia. wAIHA: warm Autoimmune Hemolytic Anemia.
1. Formerly known as BIVV020.

Broad set of *innovative* pipeline assets addressing unmet needs

Drug	*Target Indication*	*Description*	*Modality*	*Unmet need*
efanesoctocog alfa	Hem A (w/o inhibitors)	Factor VIII replacement	Biologic	• Breakthrough bleeds and joint deterioration • Treatment burden • Access to treatment
fitusiran	Hem A and B (w/ w/o inhibitors)	siRNA antithrombin	siRNA	
rilzabrutinib	ITP	BTKi	Small Molecule	• Fatigue • Quality of life
SAR445088[1]	CAD	mAb to Activated C1S	Biologic	• Address C1s mediated hemolysis
rilzabrutinib	wAIHA	BTKi	Small Molecule	• Acute disease with **no approved treatments**
isatuximab	wAIHA	Anti-CD38	Biologic	

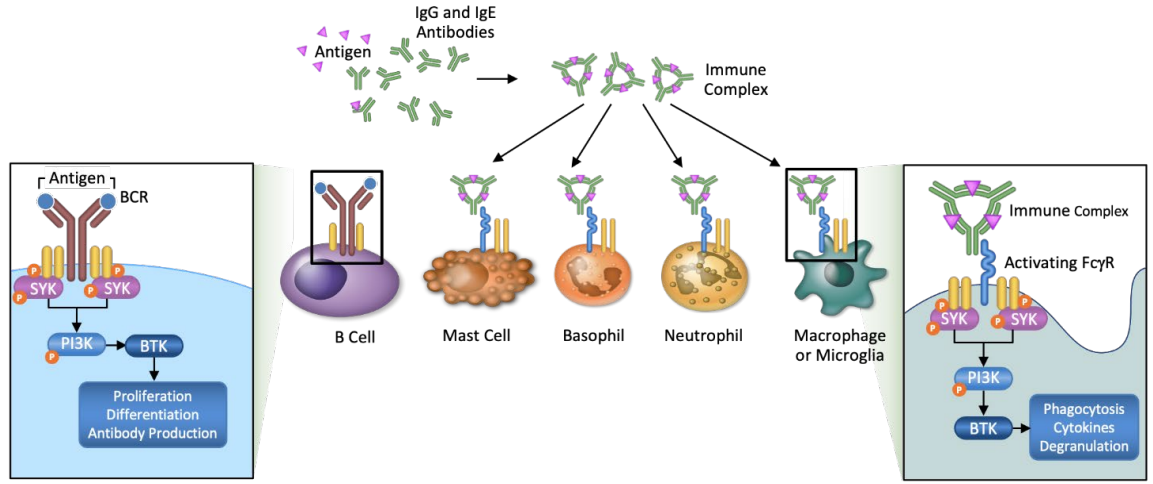
1. Formerly known as BIVV020.

Rilzabrutinib is a potential first in class *oral, reversible BTK inhibitor* in ITP

High unmet need

- Patients needs extend *beyond platelet counts* to fatigue and quality of life
- *Inflammatory process* plays an important role in the ITP pathophysiology and drives symptoms
- Consequences of inflammation (ex. microbleeds) could potentially lead to *irreversible damage* if not addressed
- *~25k+ chronic ITP adults in the US* are eligible for 2L+ treatment after steroids

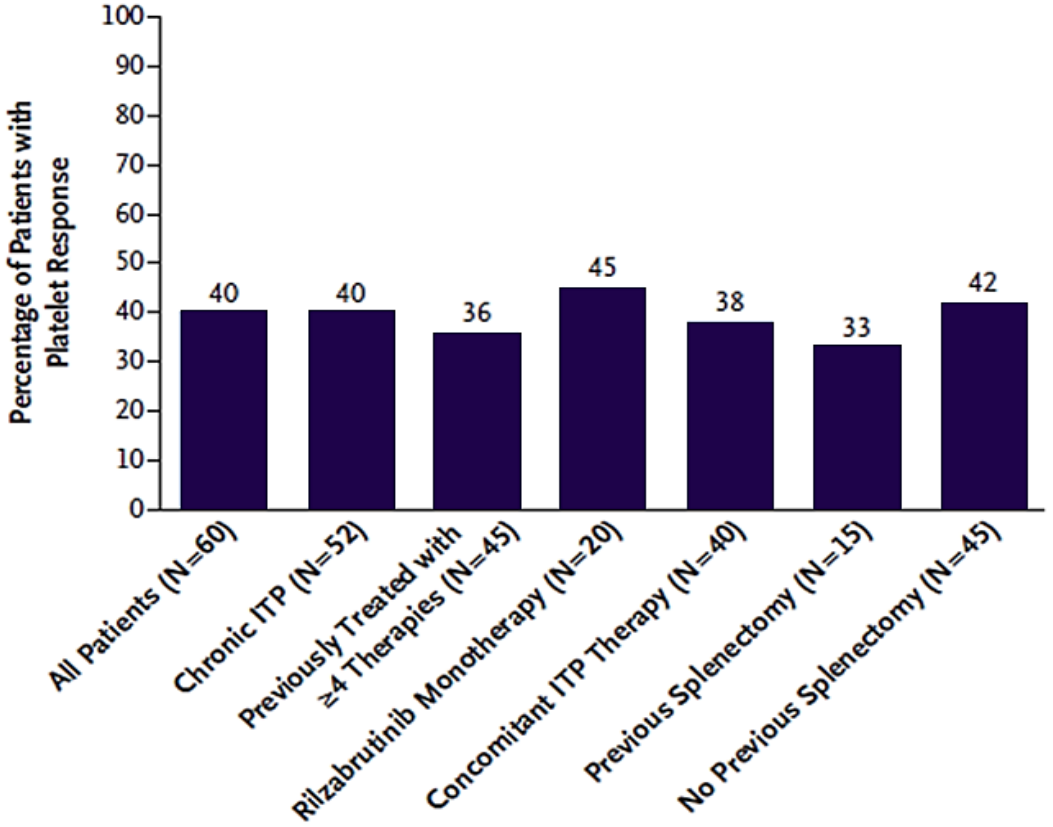
Rilzabrutinib has the potential to target *the underlying cause of the disease*



- BTK inhibition has the potential to *reduce* both Fcγ receptor-mediated macrophage function and autoantibody production[1,2]
- BTK targets *multiple cell types*, potentially allowing patients to achieve more than platelet count improvements through *anti-inflammatory effect*

1. Bradshaw JM, et al. Nat Chem Biol. 2015;11:525-31. 2. Langrish C, et al. J immunol. 2021;206:1454-1468.

Positive Phase I/II published in NEJM, *strong effect* across all analyzed subgroups



The New England Journal of Medicine, April 14, 2022

Rilzabrutinib, an Oral BTK Inhibitor, in Immune Thrombocytopenia.
David J. Kuter, M.D, et al.

N Engl J Med 2022; 386:1421-1431
DOI: 10.1056/NEJMoa2110297

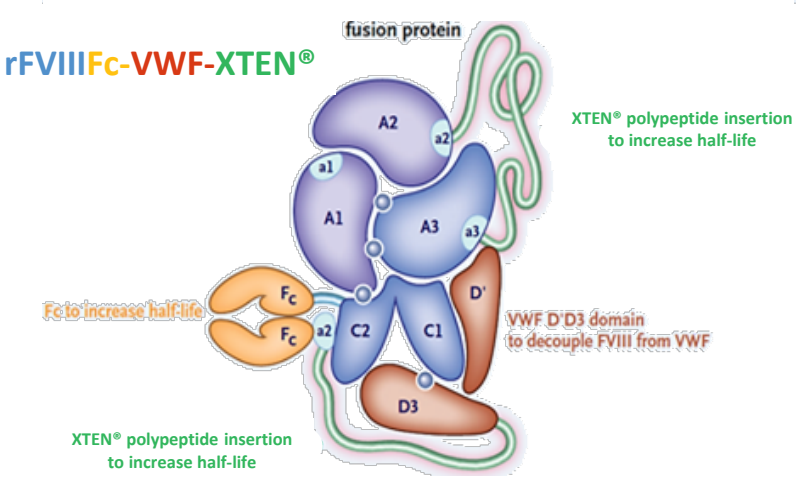
In highly refractory patients, rilzabrutinib was *well-tolerated* and had *durable*, *clinically* significant platelet responses that were *maintained* with extended treatment in long-term extension

Platelet response defined as at least two consecutive platelet counts of ≥50×103 per cubic millimeter and an increase from baseline of ≥20×103 per cubic millimeter without the use of rescue medication.

Sanofi is well positioned to *define new standards* in hemophilia with these two novel molecules

Hemophilia A without inhibitors:

efanesoctocog alfa

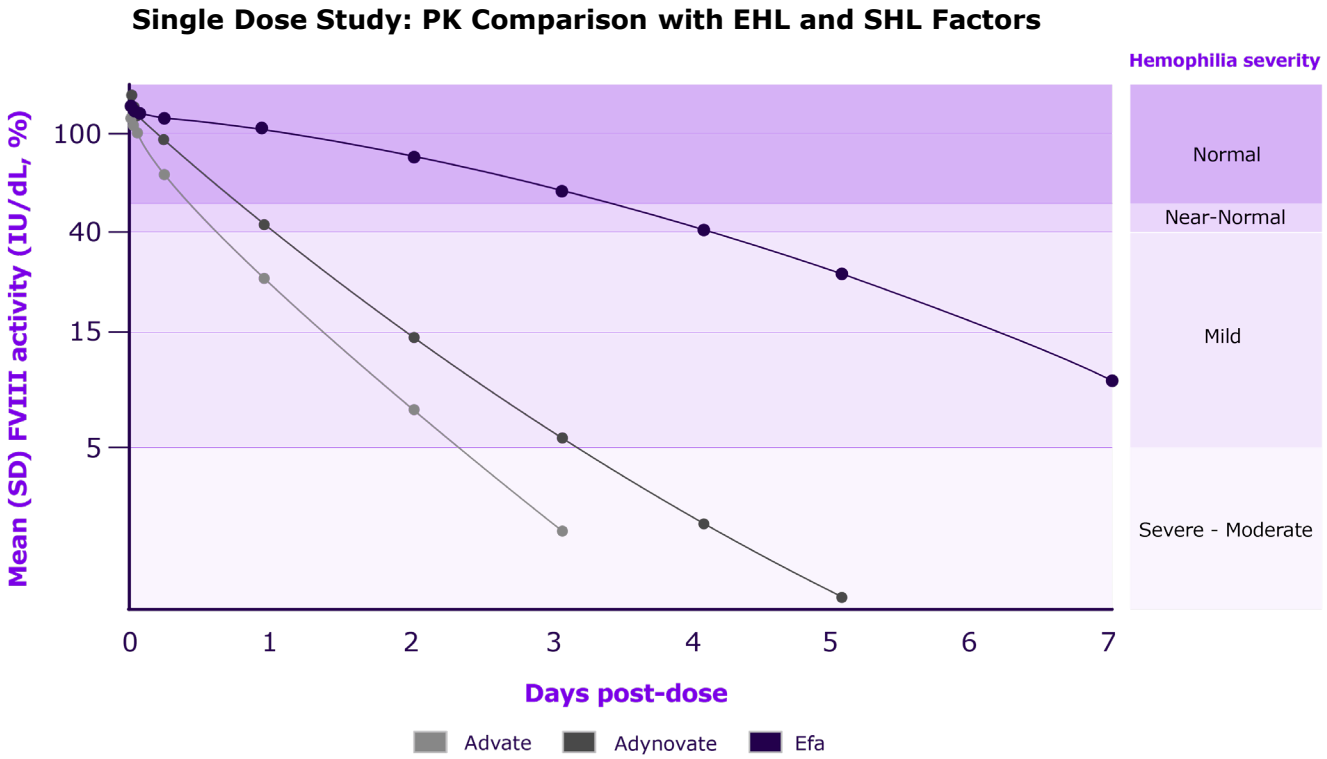


Hemophilia A or B, with or without inhibitors:

fitusiran

First-in-class siRNA targeting anti-thrombin

Efanesoctocog alfa has the potential to *revolutionize* hemophilia A treatment by providing close to normal factor activity levels

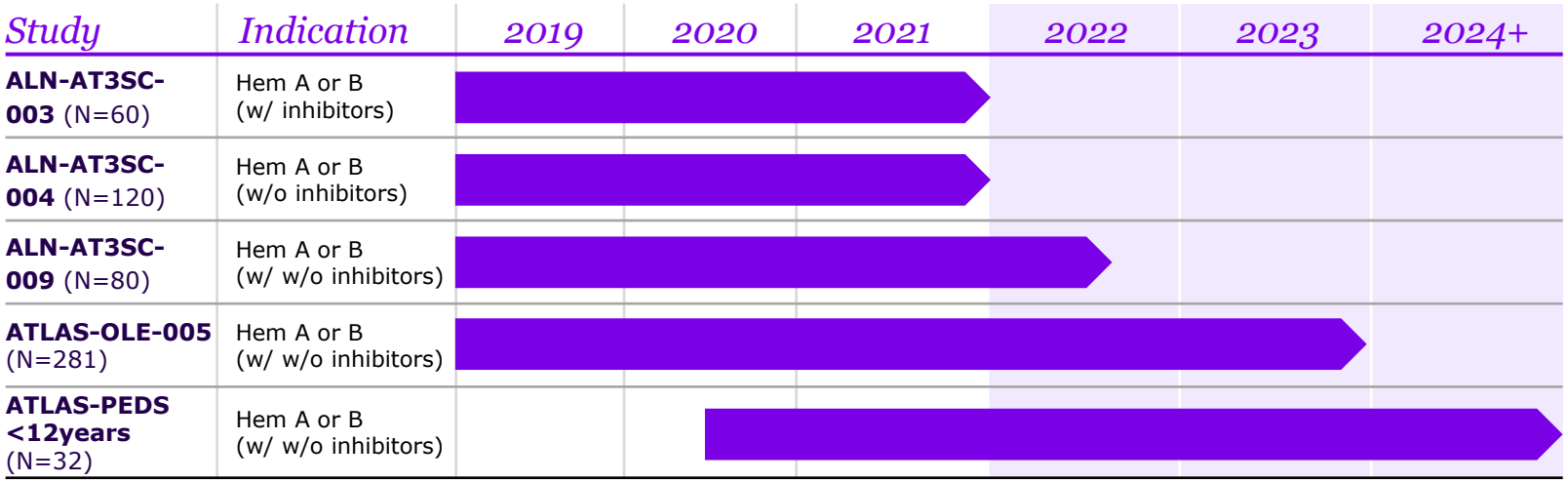


efanesoctocog alfa

- **Positive Phase 3 data** : primary and key secondary endpoints met
- FDA **BLA submitted; Breakthrough** Designation and **Fast Track** Designation granted
- **Japan** filing H2 2022

Note: Data for Efa, Adynovate, and Advate from the sequential pharmacokinetic study (PKM17085).

Fitusiran has a robust clinical program designed for all patients with hemophilia A or B, with or without inhibitors



- **Completed** three Phase 3 studies in adults and adolescents (>12years) with 80 mg monthly dose
- Program **continuing** with **amended protocol** with 2 lower doses to optimize benefit/risk profile
- Data with **lower doses expected in H2 2023**
- First filling planned for **2024**
- **Pediatric (age 1-11) study ongoing**, first filing planned in 2026

a. The fitusiran onset period is estimated to take approximately 28 days to reach target pharmacodynamic effect of AT lowering in the majority of participants. b. Based on current fitusiran TPP with 50 mg and 20 mg doses; ~80% patients will dose 6 times per year and ~20% patients will dose 12 times per year.

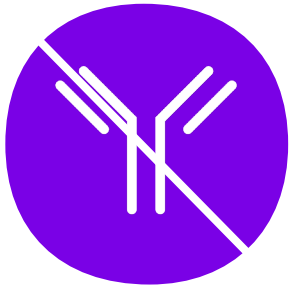
1. Pasi KJ, et al. J Thromb Haemost 2021;19:1436–46. 2. Pipe S, et al. Presented at ISTH 2022.

Clinical experience with fitusiran

Guy Young, MD

Director, Hemostasis and Thrombosis Center at Children's Hospital Los Angeles

What are the *unmet needs*?



Non-inhibitor patients

- We need equally safe and efficacious treatments which *reduce* treatment burden

Inhibitor patients

- We need (much) better agents to *prevent* bleeding in inhibitor patients

Necessary to reduce mortality, morbidity and improve quality of life

Curing hemophilia

the ultimate unmet need

Nogami K and Shima M. Blood. 2019;133(5):399–406.
Presented at ASH December 2021.

Fitusiran has *completed three phase 3 studies* in adults and adolescents ≥ 12 years

ALN-AT3SC-003 (N=54)

- Patients with Hem A or B aged ≥12 years
- *With* inhibitors
- Fitusiran 80mg QM
- Bleed managed by BPA on-demand

Plenary presentation

ALN-AT3SC-004 (N=120)

- Patients with Hem A or B aged ≥12 years
- *Without* inhibitors
- Fitusiran 80mg QM
- Bleed managed by factor on-demand

Late breaker

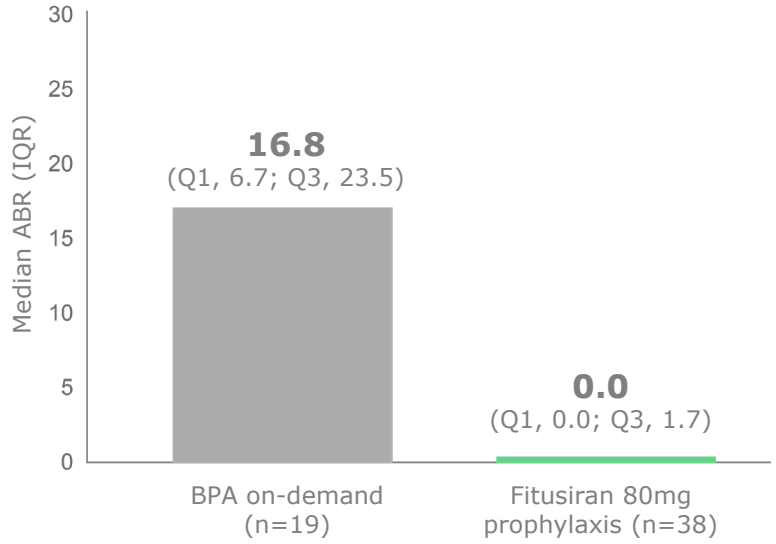
ALN-AT3SC-009 (N=80)

- Patients with Hem A or B aged ≥12 years
- *With or without* inhibitors
- Fitusiran 80mg QM
- Compared with factor / BPA prophylaxis

Late breaker

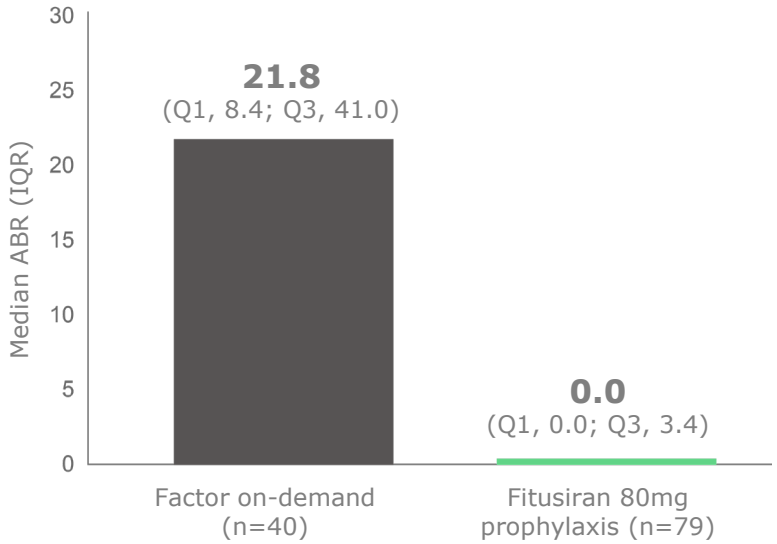
Phase 3 studies demonstrate statistically significant *reduction* in bleeding and a *median ABR of zero* across on-demand patient populations

Estimated ABR reduction: *89.2%*
(95%CI; 79.3; 94.4) (p<0.0001)



ATLAS-INH: fitusiran vs on-demand bypassing agents: hem A or B **with** inhibitors[1]

Estimated ABR reduction: *89.9%*
(95% CI; 84.1; 93.6) (p<0.0001)

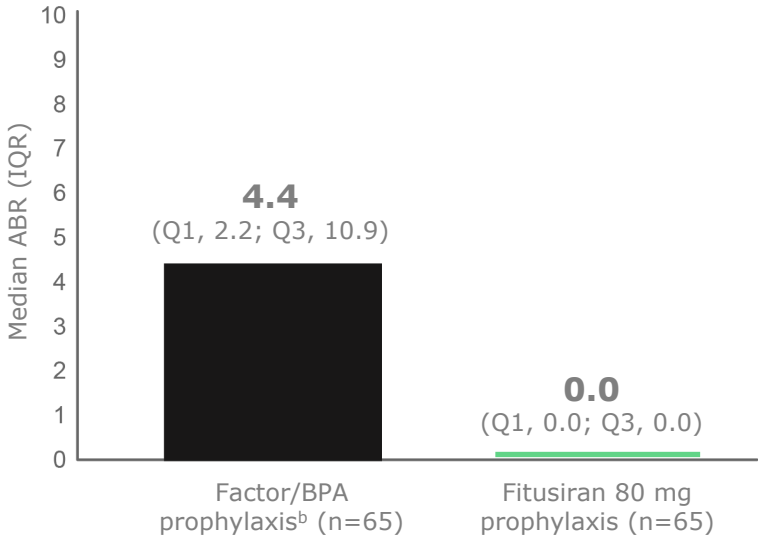


ATLAS-A/B: fitusiran vs on demand factor: hem A or B **without** inhibitors[2]

1. Young G, et al. Blood 2021;138(Supplement 1):4. 2. Srivastava A, et al. Blood 2021;138(Supplement 2):LBA-3.

Phase 3 studies demonstrate statistically significant *reduction* in bleeding and a *median ABR of zero* when compared with prior prophylaxis

Estimated ABR reduction: *61.1%*
(95% CI; 32; 77.6) (p=0.0008)

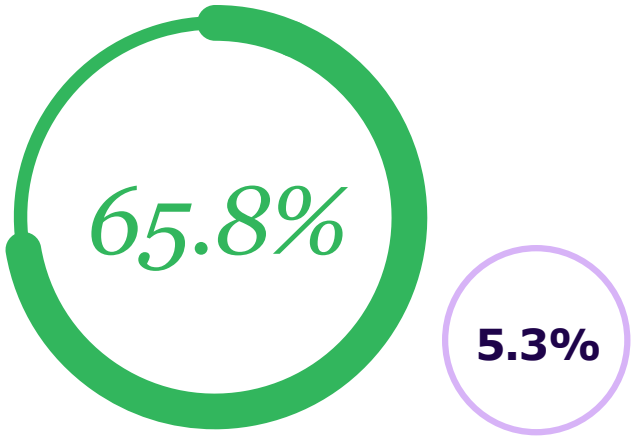


ATLAS-PPX: fitusiran vs prior factor/BPA prophylaxis: hem A or B, **with or without** inhibitors[1]

1. Kenet G, et al. presented at ISTH 2022.

Phase 3 studies consistently demonstrated majority of people with hemophilia experienced *zero treated bleeds*

Percentage of participants with zero bleeds in the efficacy period



Fitusiran prophylaxis 80mg (n=38)

On-demand BPA (n=19)

ATLAS-INH: fitusiran vs on-demand bypassing agents: hem A or B **with** inhibitors[1]

Fitusiran prophylaxis 80mg (n=80)

On-demand factor (n=40)

ATLAS-A/B: fitusiran vs on demand factor: hem A or B **without** inhibitors[2]

Fitusiran prophylaxis 80mg (n=65)

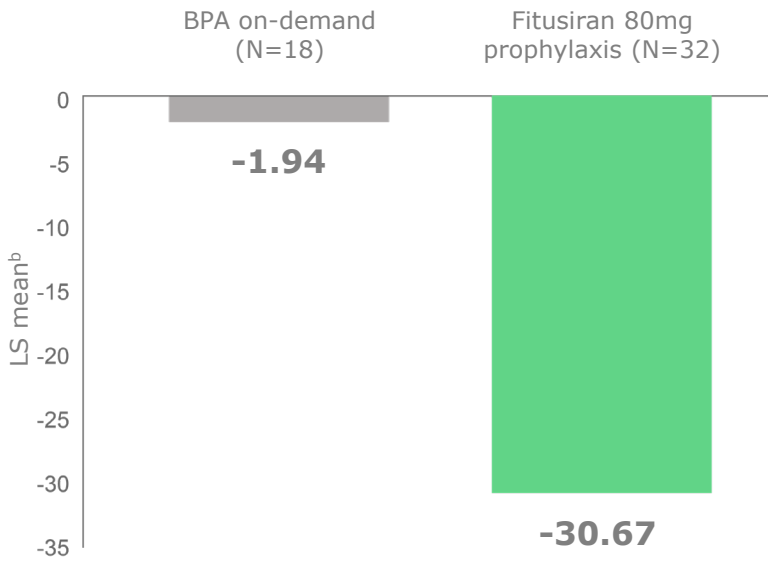
Factor/BPA prophylaxis (n=65)

ATLAS-PPX: Fitusiran vs prior factor/BPA prophylaxis: with hem A or B, **with or without** inhibitors[3]

1. Young G, et al. Blood 2021;138(Supplement 1):4. 2. Srivastava A, et al. Blood 2021;138(Supplement 2):LBA-3. 3. Kenet G, et al. presented at ISTH 2022.

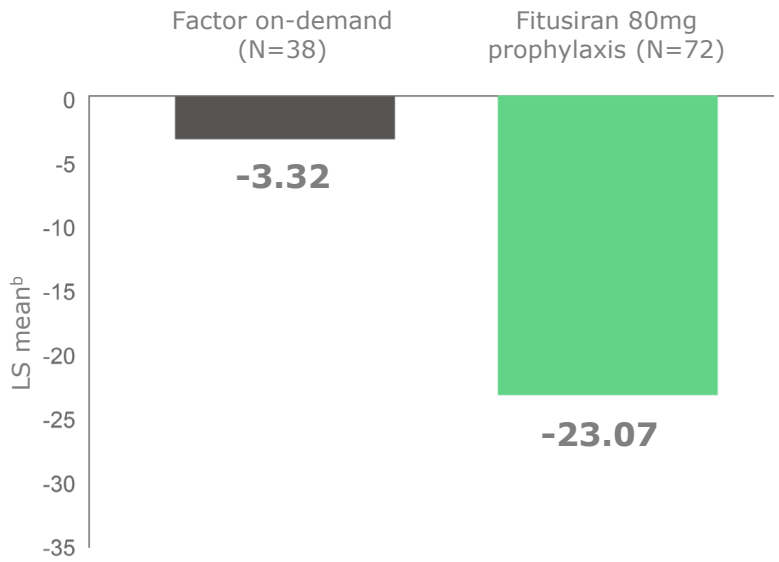
Fitusiran prophylaxis *improved* health-related quality of life as measured by Haem-A-QoL *physical health domain*

Measured by Reduction from Baseline to End of Study



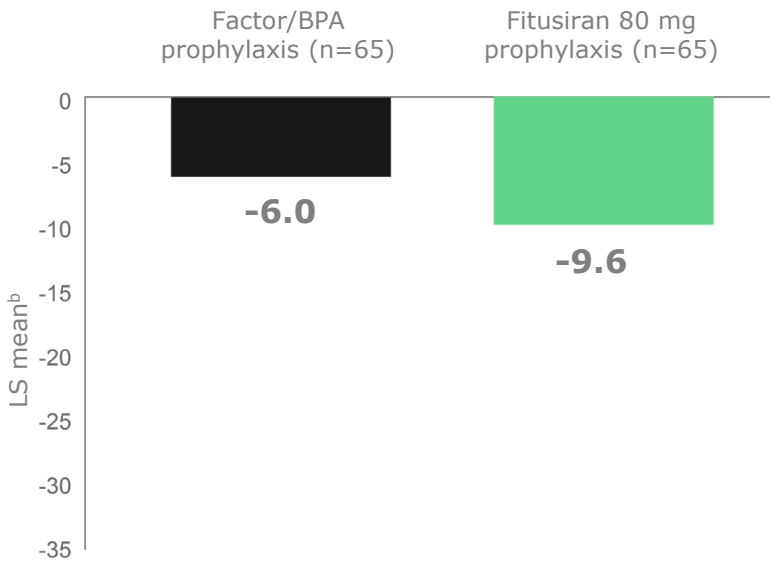
Mean difference of *-28.72*, p<0.0001

ATLAS-INH: fitusiran vs on-demand bypassing agents: hem A or B **with** inhibitors[1]



Mean difference of *-19.75*, p<0.0001

ATLAS-A/B: fitusiran vs on demand factor: hem A or B **without** inhibitors[2]



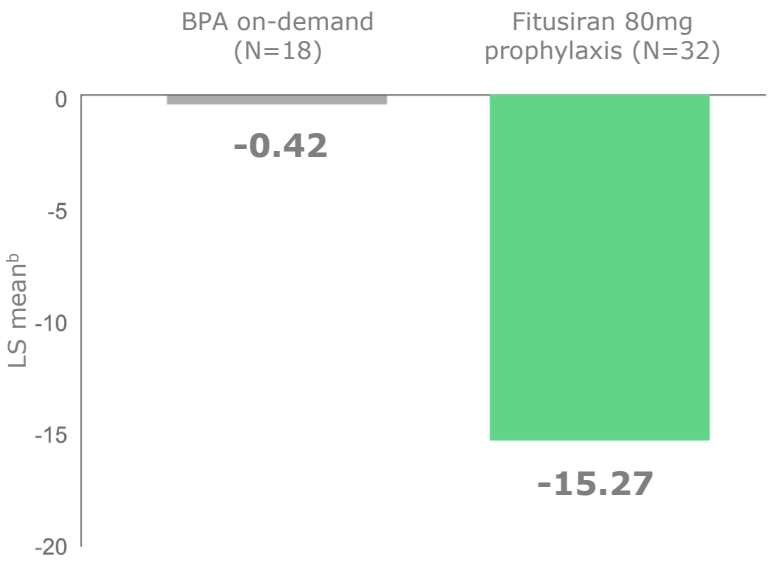
Mean difference of *-3.60*, p<0.3008

ATLAS-PPX: fitusiran vs prior factor/BPA prophylaxis: hem A or B, **with or without** inhibitors[3]

1. Young G, et al. Blood 2021;138(Supplement 1):4. 2. Srivastava A, et al. Blood 2021;138(Supplement 2):LBA-3. 3. Kenet G, et al. presented at ISTH 2022.

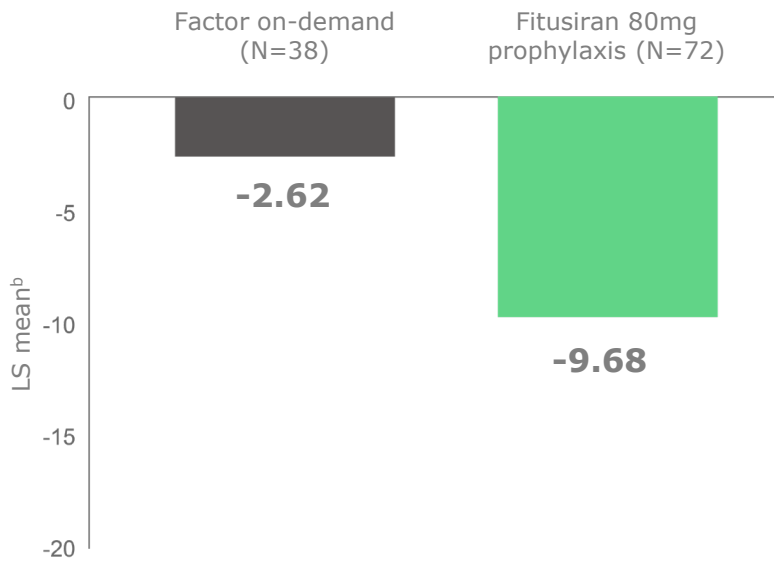
Fitusiran prophylaxis *improved* health-related quality of life as in Haem-A-QoL *total score*

Measured by Reduction from Baseline to End of Study



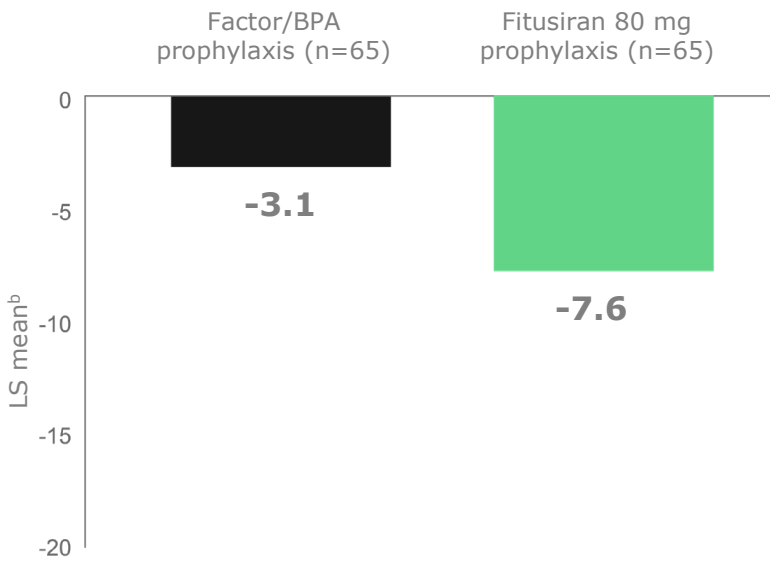
Mean difference of *-14.85*, <0.0001

ATLAS-INH: fitusiran vs on-demand bypassing agents: hem A or B **with** inhibitors[1]



Mean difference of *-7.07*, <0.0011

ATLAS-A/B: fitusiran vs on demand factor: hem A or B **without** inhibitors[2]



Mean difference of *-4.55*, p<0.01

ATLAS-PPX: fitusiran vs prior factor/BPA prophylaxis: hem A or B, **with or without** inhibitors[3]

1. Young G, et al. Blood 2021;138(Supplement 1):4. 2. Srivastava A, et al. Blood 2021;138(Supplement 2):LBA-3. 3. Kenet G, et al. presented at ISTH 2022.

ATLAS-INH: Fitusiran vs on-demand bypassing agents, hem A or B **with** inhibitors: *Safety* and *Tolerability*[1]

Overview of Treatment Emergent Adverse Events (TEAEs) Category, n (%)	BPA On-demand (N=19)	Fitusiran 80 mg Prophylaxis (N=41)
Any TEAE	11 (57.9%)	38 (92.7%)
Any TESAE (Treatment-Emergent Serious Adverse Event)	5 (26.3%)	7 (17.1%)
Any TEAE leading to treatment discontinuation[a]	0 (0%)	1 (2.4%)
Any TEAE leading to death	0 (0%)	0 (0%)
Any TEAESI	0 (0%)	11 (26.8%)
Treatment Emergent Adverse Events of Special Interest (TEAESI) CategoryPreferred Term, n (%)	**BPA On-demand** (N=19)	**Fitusiran 80 mg Prophylaxis** (N=41)
ALT or AST elevations >3 x ULN		
Increased transaminases	0 (0%)	5 (12.2%)
Increased alanine aminotransferase	0 (0%)	4 (9.8%)
Increased hepatic enzyme	0 (0%)	1 (2.4%)
Cholestasis	0 (0%)	1 (2.4%)
Suspected or confirmed thromboembolic events		
Deep vein thrombosis[b]	0 (0%)	1 (2.4%)
Subclavian vein thrombosis[b]	0 (0%)	1 (2.4%)
Thrombophlebitis superficial[b]	0 (0%)	1 (2.4%)
Thrombosis[c]	0 (0%)	1 (2.4%)

Same patient

a. One patient in the fitusiran arm experienced TEAEs that resulted in treatment discontinuation (spinal vascular disorder [verbatim: vascular myelopathy] and thrombosis [verbatim: suspected spinal vessel thrombosis]). b. TEAESIs occurred in a single subject in the setting of central venous access and infectious complications. All assessed by the Investigator as unlikely related to fitusiran. c. Verbatim: suspected spinal vessel thrombosis. Assessed by the Investigator as possibly related to fitusiran and resulted in treatment discontinuation. For additional details on thrombotic events in the fitusiran clinical development program, please refer to the following presentations: Andersson S, et al. Oral Presentation at the European Association for Haemophilia and Allied Disorders (EAHAD) Congress, 2021; Negrier C, et al. Oral Presentation at the Society of Thrombosis and Haemostasis Research (GTH) Congress, 2021.

1. Young G, et al. Blood 2021;138(Supplement 1):4.

ATLAS-A/B: Fitusiran vs on demand factor, hem A or B **without** inhibitors: *Safety* and *Tolerability*[1]

TEAE Category, n (%)	**On-demand Factor Concentrates** (N=40)	**Fitusiran 80 mg Prophlyaxis** (N=79)
Any TEAE	18 (45.0)	62 (78.5)
Any TESAE	5 (12.5)	5 (6.3)
Any TEAE leading to treatment discontinuation[a]	-	2 (2.5)
Any TEAE leading to death	0 (0.0)	0 (0.0)
Any TEAESI	1 (2.5)	15 (19.0)
ALT increased	0 (0.0)	12 (15.2)
AST increased	1 (2.5)	3 (3.8)
Hepatic enzyme increased	0 (0.0)	1 (1.3)
Transaminases increased	0 (0.0)	1 (1.3)

a. In the fitusiran arm, 2 participants (2.5%) experienced TEAEs that resulted in fitusiran discontinuation (cholecystitis and increased ALT, in 1 participant each).
1. Srivastava A, et al. Blood 2021;138(Supplement 2):LBA-3.

ATLAS-PPX: Fitusiran vs prior factor/BPA prophylaxis, hem A or B, **with or without** inhibitors: *Safety* and *Tolerability*[1]

Event, n (%)	Factor/BPA prophylaxis (N=65[a])	Fitusiran 80 mg prophylaxis (N=67[a,b])
Participants with any AE (Adverse Event)	22 (33.8)	48 (71.6)
Participants with any SAE (Serious Adverse Event)	5 (7.7)	9 (13.4)
Most common SAEs[c]		
Haemophilic arthropathy	2 (3.1)	2 (3.0)
Participants with AEs leading to fitusiran discontinuation[d]	-	2 (3.0)
Participants with any AE leading to death	0	0
Adverse Events of Special Interest (AESI)		
Participants with any AESI	2 (3.1)	22 (32.8)
Suspected or confirmed thromboembolic events[e]	0	2 (3.0)
ALT or AST elevations >3 x ULN[f]	2 (3.1)	17 (25.4)
Cholecystitis	0	5 (7.5)
Cholelithiasis	0	5 (7.5)

a. Includes all participants who enrolled and then received at least one dose of fitusiran before dose resumption (after the Sponsor initiated pause in dosing). b. Includes two participants from the cohort A subgroup who started directly with fitusiran 80 mg QM. c. In the factor/BPA prophylaxis period, additional SAEs included gastroenteritis, haemarthrosis, and muscle haemorrhage (1 [1.5%] participant each). In the fitusiran prophylaxis period, additional SAEs included vascular device infection, biliary neoplasm, cerebrovascular accident, asthma late onset, pancreatitis acute, cholelithiasis, stevens-johnson syndrome, C-reactive protein increased, fall, femur fracture, and central venous catheter removal (1 [1.5%] participant each). d. Includes AEs of cerebrovascular accident and abdominal discomfort. e. Includes AEs of cerebrovascular accident and thrombosis (suspected thrombosis on papilla of left eye). The participant with cerebrovascular accident had a history of right lower extremity deep vein thrombosis not known by the Investigator at the time of enrolment (exclusion criterion); f. Laboratory abnormalities consistent with Hy's Law were identified in 1 of these participants at the end of study visit. Additional doses of fitusiran were not administered and all abnormalities resolved.

1 Kenet G, et al. presented at ISTH 2022.

Rationale for *revised* dose and dosing regimen

Vascular thrombotic event[b]	Patient characteristics		Medical history/comments	AT category
	Age range (years)	Hem subtype and inhibitor status		
Cerebrovascular accident	30–40	Hem A patient w/o inhibitor	Deep vein thrombosis (not identified at enrollment; a study exclusion criterion), diabetes, obesity, HCV and tobacco use	**<10%**
Cerebral infarct	>60	Hem A patient w/o inhibitor	Well-controlled HIV, HCV, and prostate cancer status-post radical prostatectomy with recent prostate-specific antigen within normal limits	**<10%**
Spinal vascular disorder	20–30	Hem A patient w/ inhibitor	Suspected thrombosis involving a spinal injury	**<10%**
Atrial thrombosis	20–30	Hem B patient w/ inhibitor	Concomitant use of BPA (rFVIIa) in excess of the current bleed management guidelines in fitusiran clinical studies	**10–20%**
Cerebral venous sinus thrombosis	20–30	Hem A patient w/o inhibitor	Concomitant use of factor concentrate in excess of the current bleed management guidelines in fitusiran clinical studies. Event initially diagnosed and treated as a subarachnoid hemorrhage and resulted in a fatal outcome.	**10–20%**

*As of 5 November 2020, **259 participants** have received at least 1 dose of fitusiran in the clinical development program[a] with an estimated total of **293 patient-years of exposure**.*

- Data suggest that the risk of vascular thrombotic events may be **greater with Anti-thrombin (AT) levels <10%**
- Based on intra-individual variability in AT levels
  - A lower AT threshold of **15%** was selected to minimize the occurrence of AT levels <10% in patients exposed to fitusiran
  - An upper AT threshold of **35%** was chosen as a **target** based on blinded fitusiran efficacy data

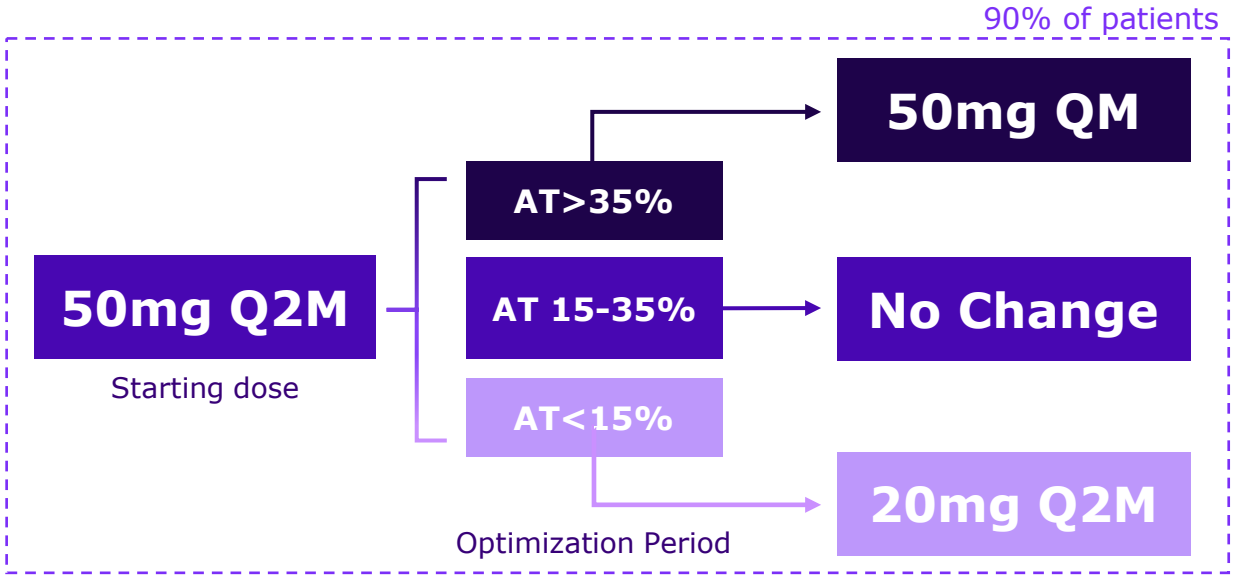
A simulation based on PK/PD modeling was conducted to identify a **dose and regimen** that would **target AT levels between 15% and 35%.**

a. Excluding the data in phase 1 and paediatric studies. b. Adverse event data as of 20 October 2020.

Fitusiran revised dose and *dose regimen* is designed to enhance the benefit risk balance

In all ongoing Phase 3 trials, all patients start on **50mg, 6 injections per year**

~90% of all patients require **zero** or **one** dose **change**



~80% of patients **remain on 6 injections per year schedule**

Individualized dosing based on AT levels

- Target range: AT level ≥15% to ≤35%
- De-escalation if >2 AT level <15%
- Escalation if >2 SS AT level >35%

Conclusions

Based on three completed Phase 3 studies with 80 mg dose, *monthly fitusiran prophylaxis* resulted in a *sustained* lowering of antithrombin and *increased* thrombin generation[1]

The present findings and low ABR in the 80 mg monthly dose suggest that fitusiran *rebalances* hemostasis, provides *continuous* and *sustained* steady-state bleed protection[1]

The potential for *risk-optimization* of fitusiran therapy based on an individual's response is currently under investigation

1. Based on 80mg monthly dosing.

Clinical experience with efanesoctocog alfa

Angela Weyand, MD

Assistant Professor at Michigan Medicine

Efanesoctocog alfa has a *comprehensive clinical* development program

Phase 1/2 PK Studies

Complete

Adult PTPs (18–65 years)

- Phase 1 Single-Dose Study[1]
- Phase 1 Repeat Dose Study[2]
- Sequential PK study[3]

XTEND-1 *Phase 3 Studies*

Complete

Adult and adolescent PTPs (≥12 years)

- XTEND-1 Phase 3 Pivotal Study[4]

Ongoing

Pediatric PTPs (<12 years)

- XTEND-Kids Phase 3 Pivotal Study[5]

Adult and adolescent PTPs (≥12 years)

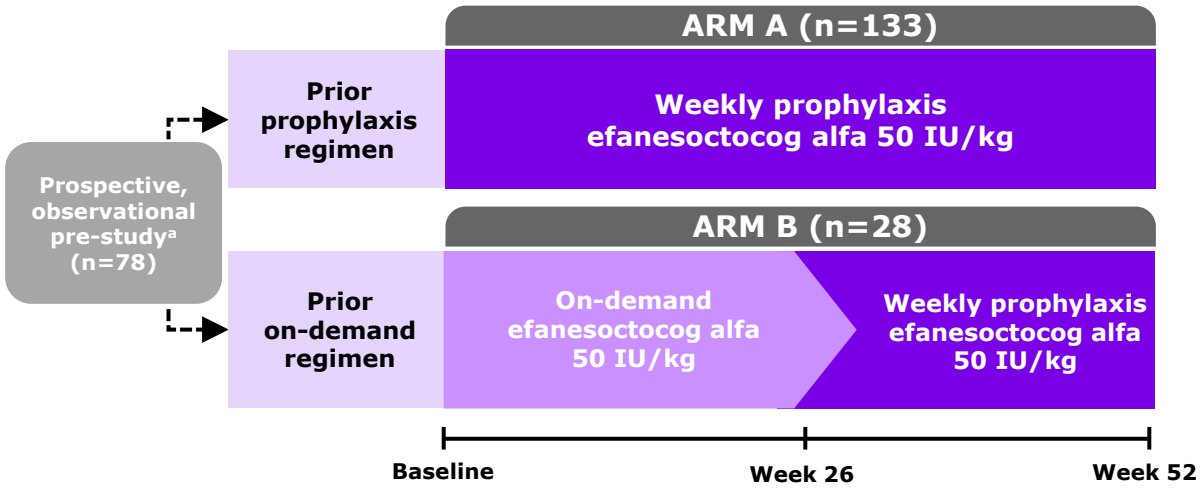
- XTEND-ed Phase 3 Long Term Extension Study XTEND-1[6]

PTP: Previously Treated Patients.
1. Konkle B, et al. N Engl J Med. 2020;383:1018-1027. 2. Lissitchkov T, et al. Blood Adv. 2022;6(4):1089-1094. 3. Clinicaltrials.gov. NCT05042440. 4. Clinical trials.gov. NCT04161495. 5. Clinical trials.gov. NCT04759131. 6. Clinical trials.gov. NCT04644575.

XTEND-1 was an open-label, multicenter, phase 3 study of efa in previously treated patients[1]

Key eligibility criteria

- Adult and adolescent patients (≥12 years) with severe hemophilia A
- Previous treatment with any recombinant and/or plasma-derived FVIII, or cryoprecipitate for ≥150 EDs



Primary endpoint

ABR in the prophylaxis treatment arm (ARM A)

Secondary and exploratory endpoints

Intra-subject ABR comparison (key secondary endpoint)[b]

- Joint health outcomes (HJHS, target joint, joint US imaging[c])
- QoL (PROs, physical activity tracking[c])
- PK
- Efanesoctocog alfa consumption
- Treatment of bleeds
- Perioperative management
- Safety and tolerability

EDs: Exposure Days. HJHS: Hemophilia Joint Health Score. PRO: Patient-Reported Outcome. US: Ultrasound.
a. Prospective pre-study is Study 242HA201/OBS16221. b. ABR during the efanesoctocog alfa weekly prophylaxis treatment period vs ABR during pre-study prophylaxis from the prior perspective study (Study 242HA201/OBS16221). c. Exploratory endpoint.
1. ClinicalTrials.gov NCT04161495.

Efanesoctocog alfa prophylaxis provided *highly effective* protection against bleeds, *superior* to Prior FVIII Therapy

Primary Endpoint Met

Clinically meaningful bleed control

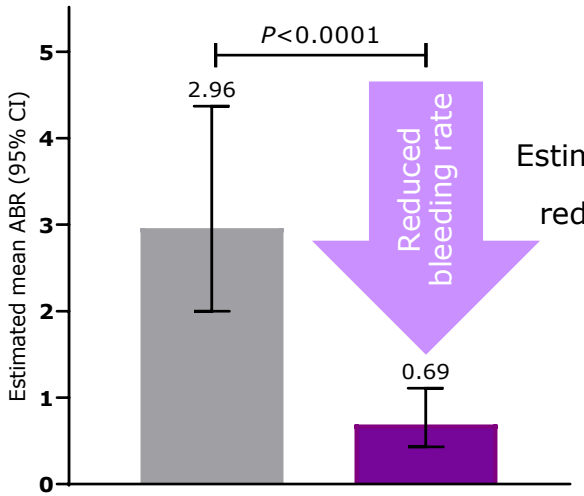
	Arm A (n=133)
ABR, median (IQR)	0.00 (0.00–1.04)
ABR, model based[a] mean (95% CI)	0.71 (0.52–0.97)

The primary endpoint was met, demonstrating that efanesoctocog alfa provides *effective* bleed protection with an upper limit of the ABR one-sided 97.5% CI was ≤6.

Key Secondary Endpoint Met

Superior bleed control versus prior FVIII prophylaxis

Intra-patient ABR comparison (n=78)[b,c]



Estimated mean ABR reduction: *77%*

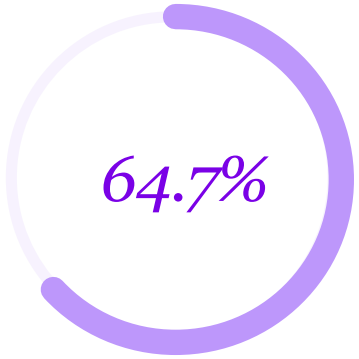
	Pre-study FVIII prophylaxis	Efanesoctocog alfa weekly prophylaxis
Median (IQR) ABR:	**1.06 (0.00–3.74)**	**0.00 (0.00–1.04)**

a. The CI of the mean ABR was estimated using a negative-binomial model with the total number of treated bleeding episodes during the efficacy period as the response variable and log-transformed efficacy period duration (in years) as an offset variable. b. Estimated using a negative binomial regression model with treatment (efanesoctocog alfa prophylaxis vs pre-study FVIII prophylaxis) as covariate. c. P-value relates to the null hypothesis that the rate ratio of efanesoctocog alfa prophylaxis/pre-study prophylaxis is equal to 1.

The majority of patients receiving efanesoctocog alfa prophylaxis had *zero bleeds*

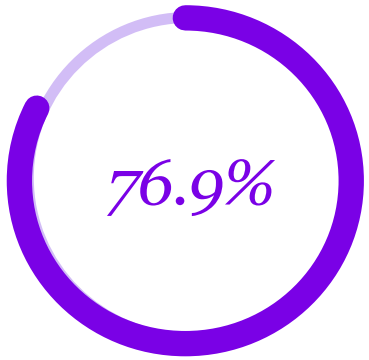
Percentage of Patients with Zero Bleeds

Switched to efanesoctocog prophylaxis from prior prophylaxis (Arm-A)



N=86/133 of patients in Arm A

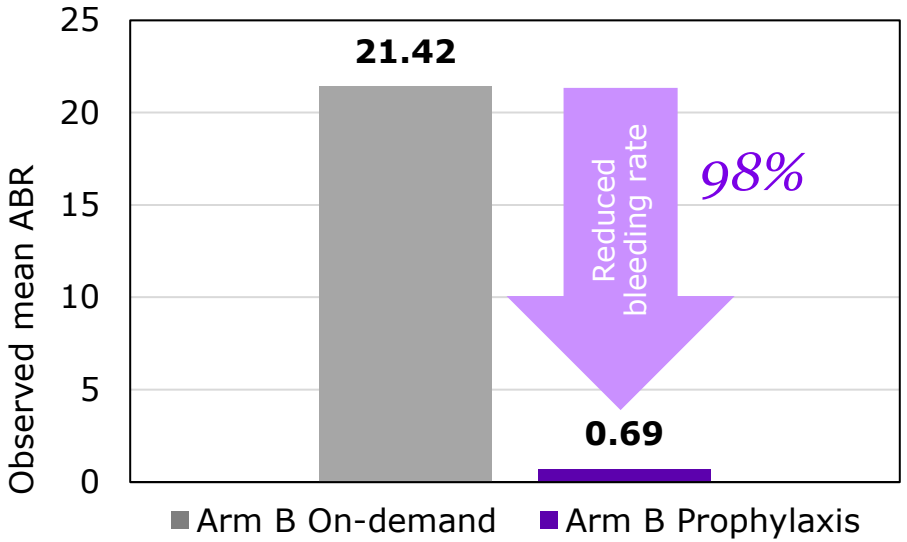
Switched to efanesoctocog prophylaxis from on-demand (Arm-B)



N=20/26 of patients in Arm B

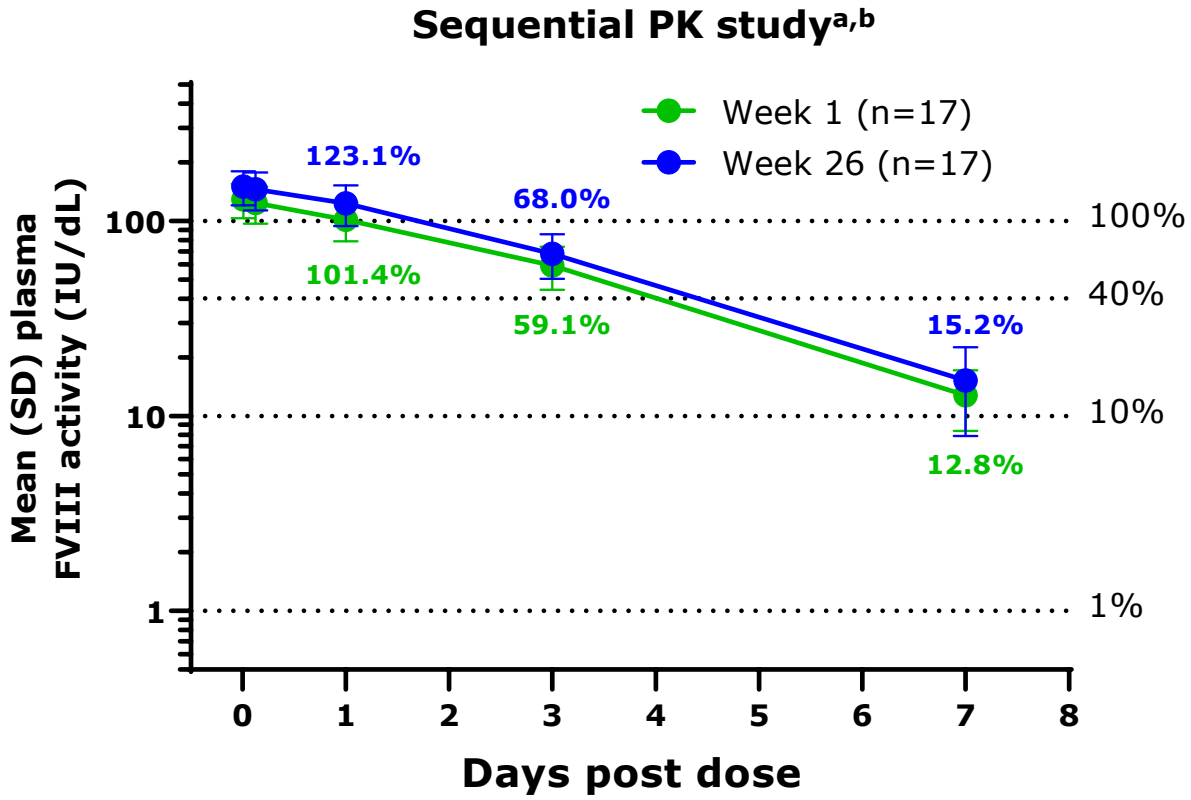
Key Secondary Endpoint On-demand vs Prophylaxis

Superior bleed control versus prior FVIII on-demand (Arm B)



Mean (SD) estimated number of bleeds in the 12 months prior to the study was 35.7 (22.2)

Efanesoctocog alfa *sustained* FVIII levels in the normal to near-normal range for most of the week



FVIII activity was measured with an aPTT-based one-stage clotting assay. b. Samples were continued out to 14 days for the sequential pharmacokinetics group. The first 7 days are depicted to correspond to the once-weekly dosing regimen used for prophylaxis in XTEND-1.
A total of 17 patients underwent a sequential PK study at baseline and Week 26a.

At Week 26, patients had a geometric mean (95% CI) half-life of *47.0 (42.3–52.3) hours*[a]

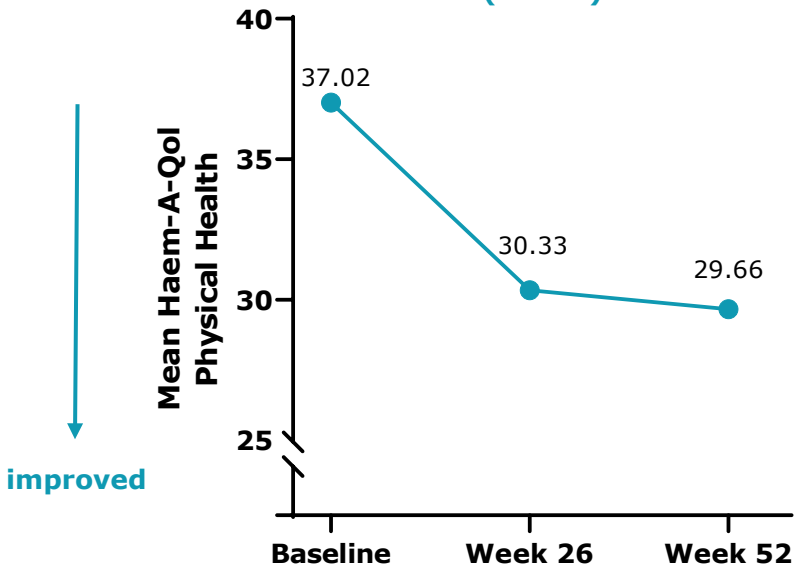
Mean FVIII levels remained in the *normal to near-normal range (>40 IU/dL) for ~4 days* post dose, and at 15 IU/dL at Day 7

Minimal accumulation and *low variability* in clearance

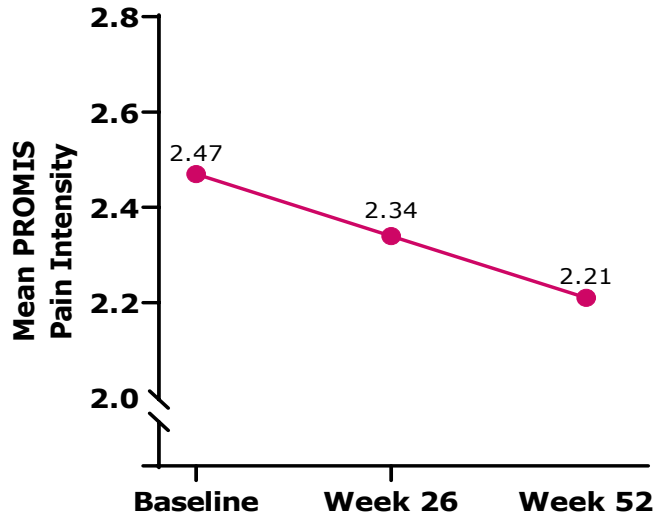
Efanesoctocog alfa prophylaxis led to clinically *meaningful improvements* in physical health and pain

In participants who completed exit interviews, *100%* (29/29) selected efanesoctocog alfa as their *preferred* hemophilia A treatment over their pre-study treatment

Haem-A-QoL Physical Health Score[a,b] (Arm A)



PROMIS Pain Intensity[a,c] (Arm A)



Baseline to Week 52 (Arm A), n	**98**	**119**
Estimated mean change (95% CI)	-6.74 (-10.13 to -3.36)	-0.21 (-0.41 to -0.02)
P-value	0.0001	0.0276
Observed mean change (SD)	-6.79 (18.59)	-0.21 (1.20)

PROMIS: Patient-Reported Outcomes Measurement Information System.
a. The adjusted mean change in each of the 2 endpoints from baseline to Week 52 in Arm A, along with its 95% CI, was estimated by the mixed-effect model repeated measures model. b. Physical health was assessed in participants aged ≥17 years old with the Haem-A-QoL Physical Health score. c. Pain was assessed in participants of all ages using the PROMIS Pain Intensity 3a, which evaluates the intensity of pain at its worst score in the last 7 days (PAINQU6).

Significant improvement in joint health with efanesoctocog alfa prophylaxis

72%

of patients in Arm A did not experience *any joint bleeds*

All 45 target joints[a] *resolved* in the 14 patients that had at least 12 months of continuous prophylaxis

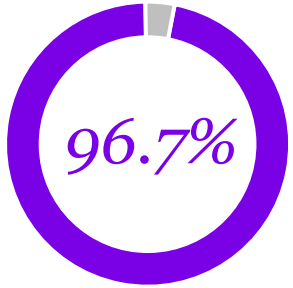
96%

reduction in target joint bleeds was observed in Arm B following the switch from on-demand to prophylaxis

Improved joint outcomes as measured by the mean HJHS decrease (P=0.01)[b]

HJHS: Hemophilia Joint Health Score.
a. A target joint resolved is defined as ≤2 bleeds (regardless of type) into that joint during 12 months of continuous exposure. b. The adjusted mean change in HJHS from baseline to Week 52 in Arm A, along with its 95% CI, was estimated by the mixed-effect model repeated measures model.

Efanesoctocog Alfa was *highly effective* in treatment of bleeding episodes and perioperative management



of bleeding episodes were *resolved with a single 50 IU/kg injection* of efanesoctocog alfa (350/362 bleeds)[a]

All patients' *hemostatic response (100%)* to efanesoctocog alfa use during the perioperative period was *deemed excellent* by the investigator or surgeon[b]

Bleed treatment assessed during the efficacy period. The efficacy period reflects the sum of all intervals of time during which patients are treated with efanesoctocog alfa, according to the study arms and treatment regimens, excluding periods of PK evaluations, surgery/rehabilitation (minor and major), and large injection intervals (>28 days). Patients are included in each study arm and treatment regimen they participated in for the duration of time on that regimen and, as such, may appear in more than one treatment regimen.
a. Substantial majority of bleeding events in XTEND-1 (74%, 268/362) occurred within the first 6 months whilst patients were receiving on-demand treatment prior to switching to 6 months of prophylaxis. b. Eighteen patients underwent 21 major surgeries during the study period.

Efanesoctocog alfa was *well tolerated*

Safety Results from XTEND-1

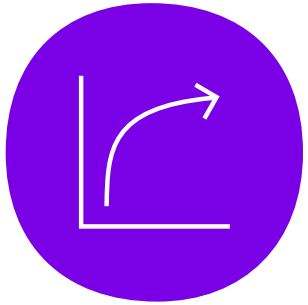
n (%)[a]	Overall (N=159)
Patients with ≥1 TEAE	123 (77%)
Patients with ≥1 TESAE	15 (9%)[b]
TEAEs leading to death	1 (1%)[c]
TEAEs leading to treatment discontinuation	2 (1%)[d]
Most common TEAE[e]	
Headache	32 (20%)
Arthralgia	26 (16%)
Fall	10 (6%)
Back pain	9 (6%)

Inhibitor development to FVIII was *not detected*

No reports of serious allergic reactions, anaphylaxis, or vascular thrombotic events

a. Percentages are based on the number of patients in the Safety Analysis Set. b. The most common TESAE was hemophilic arthropathy (2 patients [1%]). All other TESAEs were reported in 1 patient (<1%) each. c. Metastatic pancreatic carcinoma assessed by the investigator as unrelated to efanesoctocog alfa. d. Decreased CD4 lymphocyte count in a patient with a history of HIV infection, and combined tibia-fibula fracture in a patient who received treatment with another FVIII product which was prohibited during the study. e. Reported in >5% of patients overall.

Once-weekly efanesoctocog alfa prophylaxis provided *superior* bleed protection with *clinically meaningful improvements* in patient outcomes



High sustained factor activity

within normal to **near-normal levels (>40%)** for most of the week and at 15% on Day 7

Superior bleed protection

to prior SOC FVIII prophylaxis provided by **once-weekly** efanesoctocog alfa prophylaxis

Clinically meaningful improvements

in physical health, pain, and joint health **experienced by patients** receiving efanesoctocog alfa prophylaxis

Well tolerated

Reported treatment emergent adverse events were generally **consistent** with what is anticipated in an adult and adolescent population with severe hemophilia A

SOC: Standard Of Care.

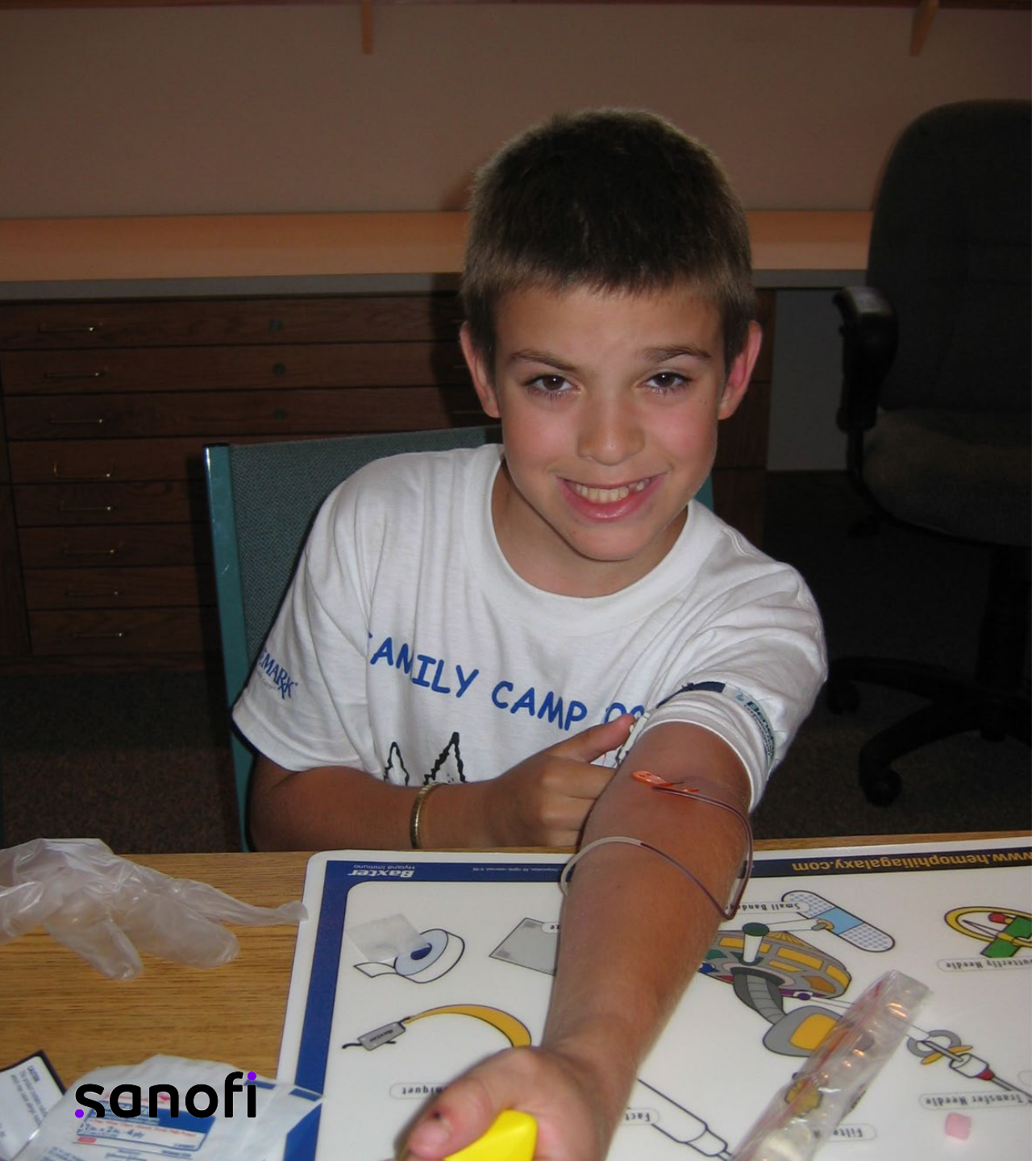
Raising the bar: creating new possibilities for people with hemophilia

"I think there has been a *switch in my mind, of can do, rather than can't do.* I used to shy away from doing stuff before, in case I had a problem, to a certain extent. Whereas now, I think you know, I'll…I feel like I can push myself that little bit more"

- **XTEND-1 Participant from UK**

"…[I was] with my dad and we were just kind of hiking through the woods and he stopped and said the way I was walking was different, like *I was more confident instead of kind of second guessing every step* and hoping I don't hurt myself… I think that's one of the differences that's kind of hard to define but it is critical where I felt so much more confident in not having bleeds that *I wasn't even thinking or worrying about injuring myself anymore*."

- XTEND-1 Participant from US



Advancing hemophilia treatment standards

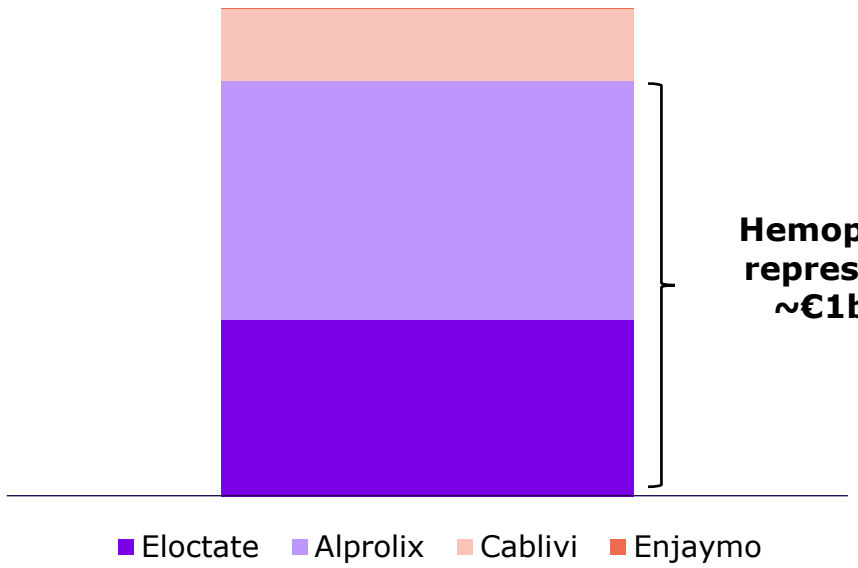
Bill Sibold

GBU Head Specialty Care

Hemophilia is the *key driver* of the >€1.2B Sanofi RBD franchise

Global revenue by product (Q2 2021 – Q1 2022)

€ 1.2bn



Enjaymo®
First treatment for CAD, recently launched

Cablivi®
First treatment for aTTP

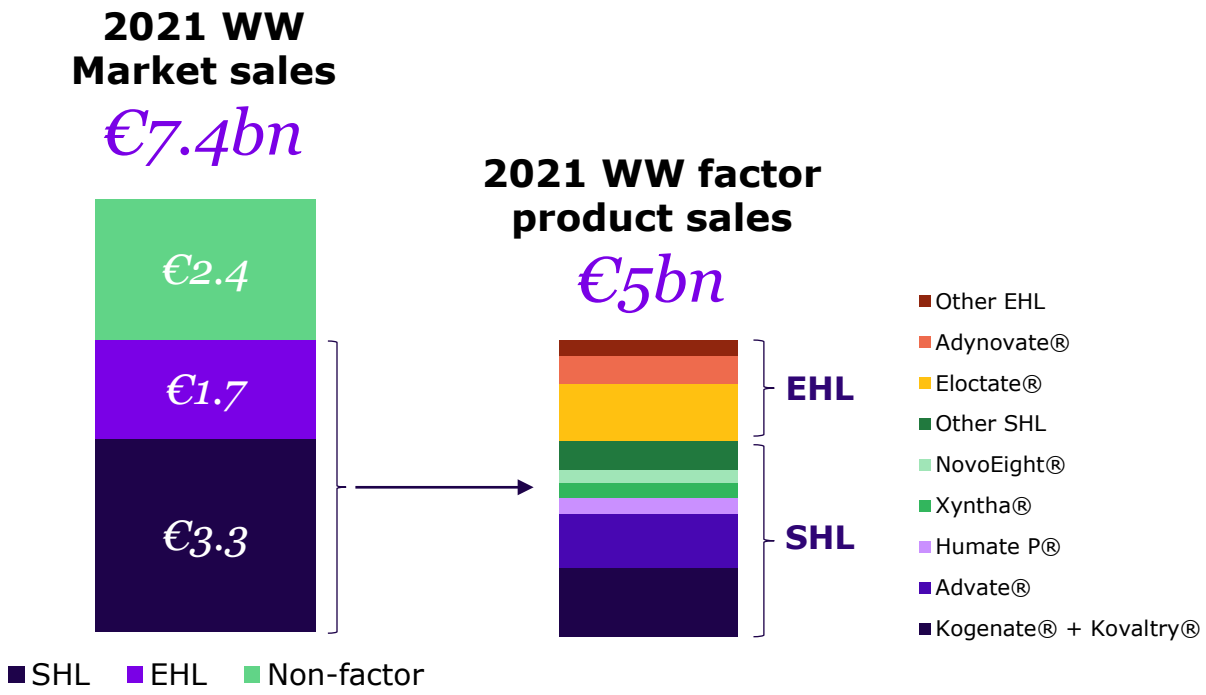
Alprolix®
First EHL launched for hem B

Eloctate®
First EHL launched for hem A, #1 EHL FVIII in US

EHL: Extended-Half Life.
1. in Sanofi territories only.

Factor remains a cornerstone of hemophilia A treatment

Hemophilia A non-inhibitor: global revenues

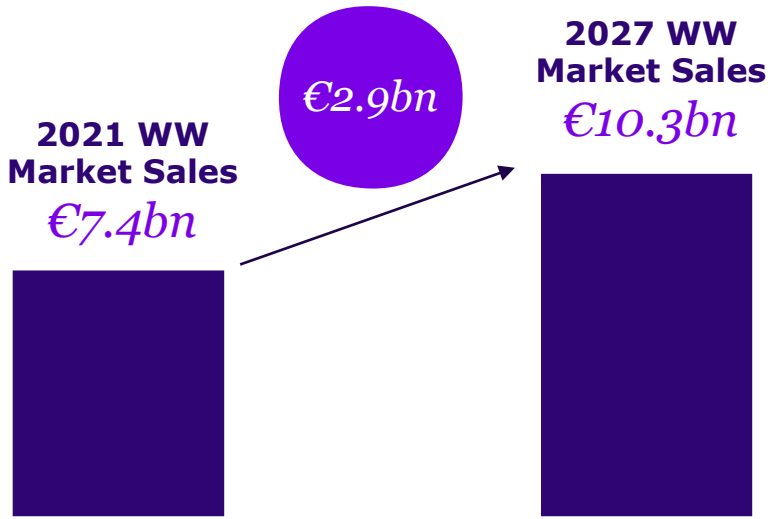


- Of the €7.4bn hemophilia A non-inhibitor market today, *70% is factor*
- The €5bn factor market today is highly *fragmented* and relatively *undifferentiated*

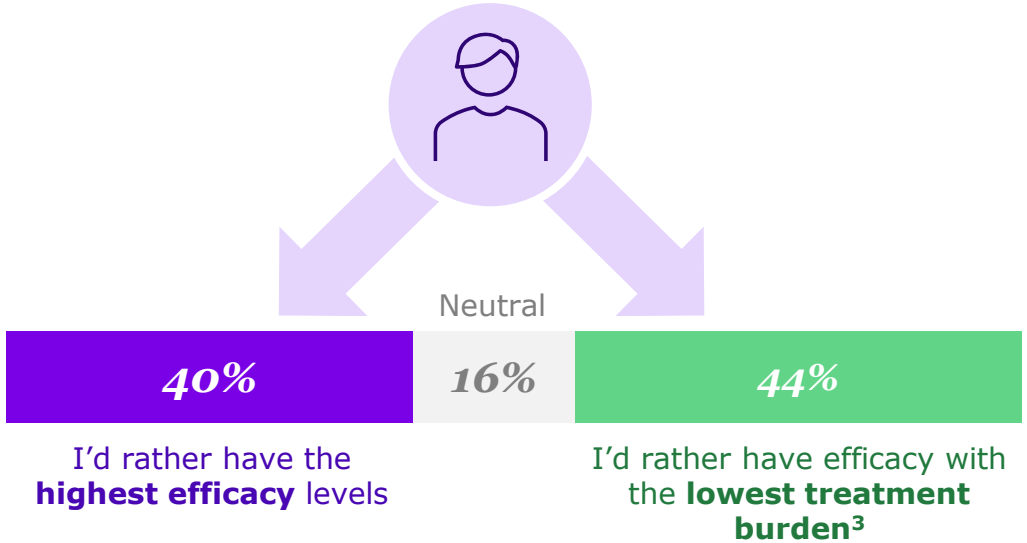
EHL: Extended Half-Life. SHL: Standard Half-Life.
The trademarks referenced are the property of their respective owners.
Sources: Evaluate pharma WW sales actuals, Jun 2022 and Data Monitor 2021 Report.
Hemlibra sales split b/w inh and non/inh based on BoFA analyst report July 30, 2021.

Patient preference will determine how the growing hemophilia market evolves

Hemophilia A non-inhibitor global revenues



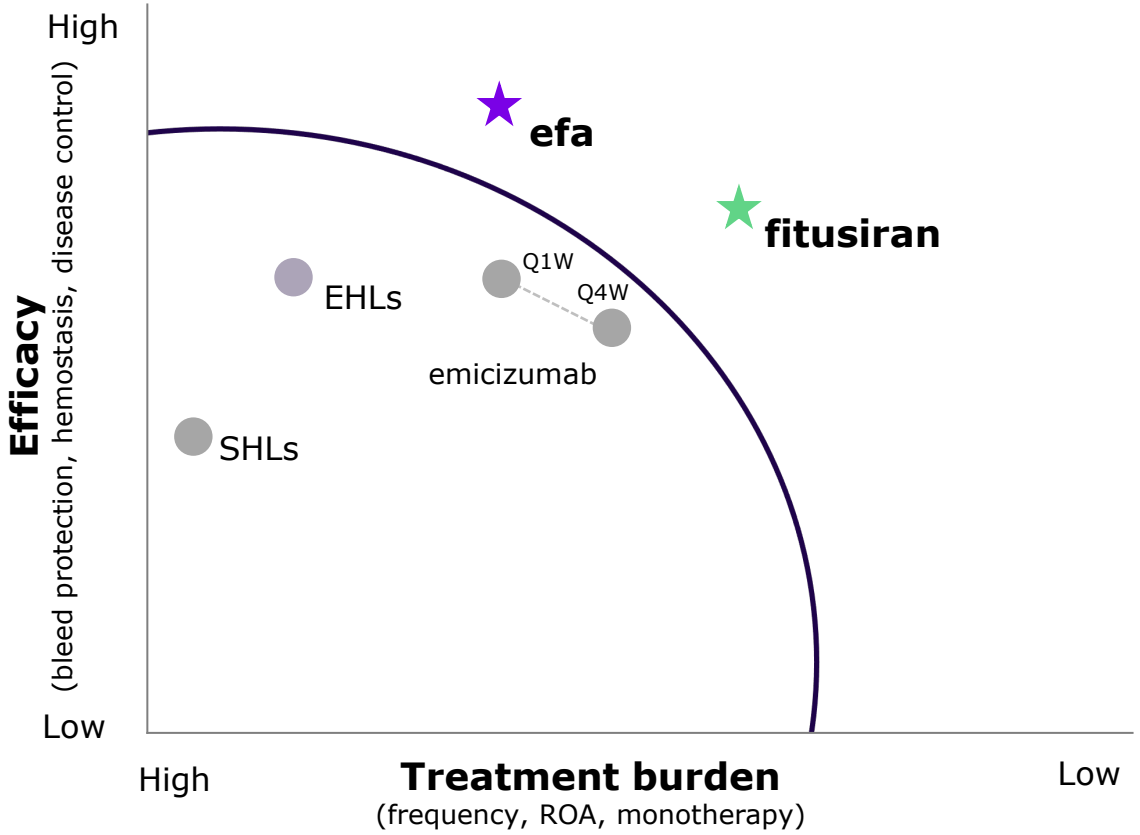
Treatment Attitudes[1]



6 out of 10 hemophilia A patients are open or likely to *switch treatments* within 2 years[2]

Source: VOP Hem A Perceptions Micro-Survey.
1. Among Total Respondents, % Rating on 7-Point Scale, n=85. 2. Among Total Respondents, % Top-Two Box Rating on 7-Point Scale, n=85. 3. efficacy that lasts 1 to 2 months.

Sanofi is advancing hemophilia A treatment by setting *new standards*



High efficacy class

efanesoctocog alfa

potential *gold-standard* in protection with *weekly* dosing

Extended efficacy class

fitusiran

potential for *consistent* protection with *as few as 6 subcutaneous injections per year*[1]

Q1W: Once Weekly. Q4W: Once Every 4 Weeks.
Comparison based on Target Product Profiles. Compared to emicizumab monthly dose
1. Based on current fitusiran TPP with 50 mg and 20 mg doses; ~80% patients will dose 6 times per year and ~20% patients will dose 12 times per year.

Close

Dietmar Berger

Global Head of Development, CMO

Key takeaways

Sanofi is committed to bringing innovative *first-in-class* therapies in Rare Blood Disorders

The growing hemophilia A market will evolve based on patient preference for *high efficacy or extended efficacy*

Sanofi is well positioned to *set new standards* and transform the lives of people with hemophilia with *efanesoctocog alfa* and *fitusiran*

Q&A session

Dietmar Berger, MD PhD
Global Head of Development,
CMO

Bill Sibold
GBU Head Specialty Care

Guy Young, MD
Director, Hemostasis and Thrombosis
Center at Children's Hospital Los Angeles

Angela Weyand, MD
Assistant Professor at Michigan
Medicine

Abbreviations (1/2)

AE	Adverse Event
AESI	Adverse Event of Special Interest
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
AT	Antithrombin
aTTP	acquired Thrombotic Thrombocytopenic Purpura
ABR	Annualized Bleeding Rate
BCR	B-Cell Receptor
BLA	Biologics License Applications.
BPA	Bypassing Agent
BTK	Bruton's Tyrosine Kinase
CAD	Cold Agglutin Disease
CD	Cluster of Differentiation
CI	Confidence Interval
C1s	Complement component 1s
EDs	Exposure Days
EHL	Extended Half-Life
FcγR	Fcγ Receptor
GalNAc	N-Acetylgalactosamine
Haem-A-QoL	Haemophilia A Quality-of-Life Questionnaire for Adults
HCV	Hepatitis C
Hem	Hemophilia

HIV	Human Immunodeficiency Virus
HJHS	Hemophilia Joint Health Score
IQR	Interquartile Range
Ig	Immunoglobulin
ITP	Immune Thrombocytopenia
LS	Least Squares
LTE	Long Term Efficacy
mAb	monoclonal Antibody
PI3K	Phosphatidylinositol 3-Kinase
PK	Pharmacokinetics
PRO	Patient-Reported Outcome
PROMIS	Patient-Reported Outcomes Measurement Information System
PTP	Previously Treated Patients
QoL	Quality of Life
QM	Once Monthly
Q1W	Once Weekly
Q2M	Once Every 2 Months
Q4W	Once Every 4 Weeks
rFVIIIFc	recombinant coagulation Factor VIII Fc
rFIXFc	recombinant coagulation Factor IX Fc
rFVIIIFc-vWF-XTEN	recombinant coagulation Factor VIII Fc – von Willebrand Factor – XTEN Fusion protein

Abbreviations (2/2)

ROA	Route Of Administration
SAE	Serious Adverse Event
siRNA	small interfering RNA
SD	Standard Deviation
SHL	Standard Half-Life
SOC	Standard Of Care
SS	Steady State
SYK	Spleen Tyrosine Kinase
TEAE	Treatment-Emergent Adverse Event
TEAESI	Treatment Emergent Adverse Events of Special Interest
TESAE	Treatment-Emergent Serious Adverse Event
ULN	Upper Limit Of Normal
US	Ultrasound
wAIHA	warm Autoimmune Hemolytic Anemia
2L	Second Line