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Long-term Outcomes With Efanesoctocog Alfa Prophylaxis for Previously Treated Children With Severe Hemophilia A, an Interim Analysis of the Phase 3 XTEND-ed Study

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Disclosures for Manuela Albisetti, MD

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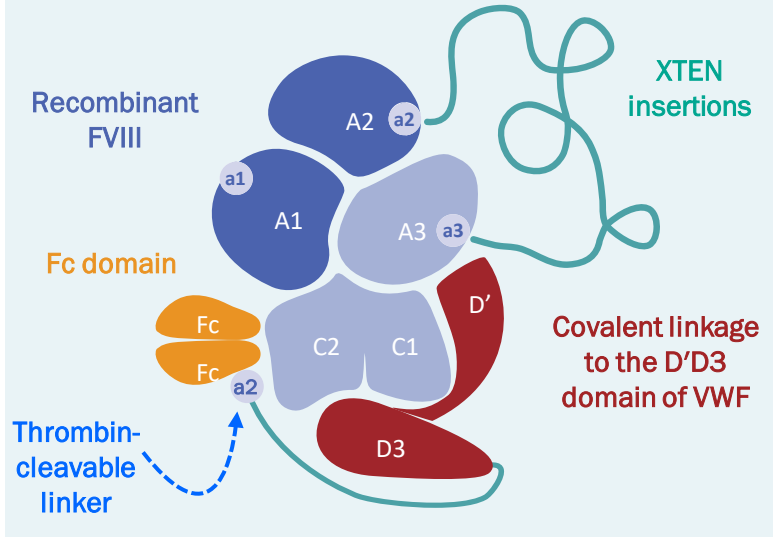
Presentation Learning Objectives

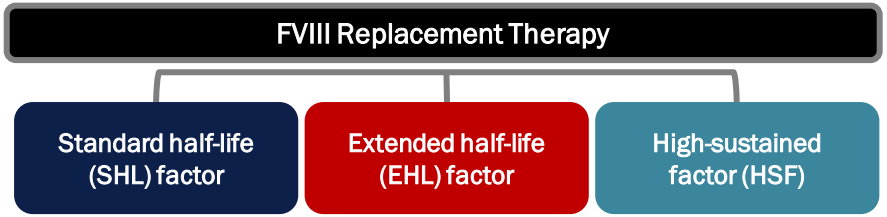
At the conclusion of this presentation, participants will be able to:

- Understand that efanesoctocog alfa continues to be **safe** and **well tolerated** and remains **highly effective for bleed protection and treatment among children** in this first interim analysis of the XTEND-ed long-term extension study
- Recognize **efanesoctocog alfa** as a first-in-class, high-sustained factor VIII (HSF) replacement therapy for the treatment of hemophilia A

Efanesoctocog Alfa is a First-in-Class High-Sustained FVIII Replacement Therapy[1,2]

Efanesoctocog alfa is a novel fusion protein that **overcomes the VWF-imposed half-life ceiling**[1,2]





Once-weekly efanesoctocog alfa **50 IU/kg** was **well tolerated** and provided **highly effective bleed protection** and factor activity within **normal to near-normal levels (>40%) for 3 days**, and of **~10% at Day 7**, in **children with severe hemophilia A** in the **XTEND-Kids study**[3]

a1, a2, and a3, acidic region 1, 2, and 3; FVIII, factor VIII; Fc, fragment crystallizable; rFVIII, recombinant factor VIII; VWF, von Willebrand factor.
1. Chhabra ES, et al. *Blood*. 2020;135(17):1484-1496. 2. Konkle BA, et al. *N Engl J Med*. 2020;383(11):1018-1027. 3. Malec L, et al. ISTH 2023 (oral presentation).

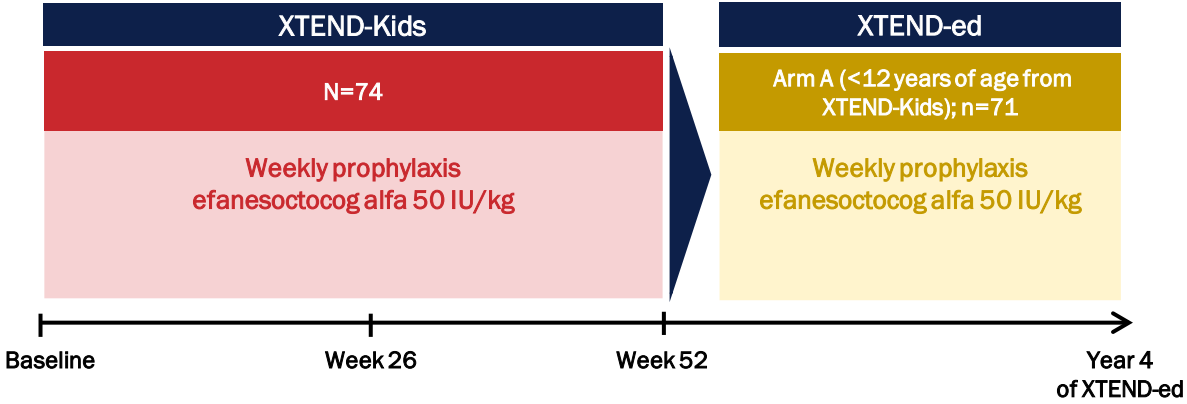
Aim

Evaluate long-term safety and efficacy of efanesoctocog alfa in children with severe hemophilia A from the Phase 3 XTEND-ed long-term extension study

First interim analysis data cut: June 8, 2023.
XTEND-ed: NCT04644575.

XTEND-ed: An Ongoing, Multicenter, Open-label Study of the Long-term Safety and Efficacy of Efanesoctocog Alfa

- Patients from the XTEND-Kids who rolled over into XTEND-ed[a]
- Severe hemophilia A (<1 IU/dL endogenous FVIII activity)[b]
- Previous treatment with any recombinant and/or plasma-derived FVIII, or cryoprecipitate[c]



Primary endpoint

- The occurrence of inhibitor development

Secondary endpoints

- Annualized bleed rates (ABRs)
- Treatment of bleeding episodes
- Safety and tolerability
- Perioperative management

This analysis: interim outcomes in children <12 years of age from XTEND-Kids (Data cut: June 8, 2023)[d]

ED, exposure days; FVIII, factor VIII.
[a]Arm A. [b]Or a documented genotype known to produce severe hemophilia A. [c]≥150 EDs for patients 6 to <12 years of age and ≥50 EDs for patients <6 years of age. [d]XTEND-ed study commenced in February 2021.

XTEND-ed: Key Patient Demographics and Disease Characteristics in Children

	<6 years (n=35)[b]	6 to <12 years (n=36)[b]	All patients (N=71)[b]
Age at enrollment in XTEND-ed, years[a]			
Median (range)	6.0 (2–8)	10.0 (7–13)	7.0 (2–13)
<12, n (%)	35 (100)	23 (63.9)	58 (81.7)
12–17, n (%)	0	13 (36.1)	13 (18.3)
Median weight, kg (range)	17.5 (11.4–25.7)	32.9 (17.2–66.5)	22.1 (11.4–66.5)
Sex, n (%)			
Male	35 (100)	36 (100)	71 (100)
Race, n (%)			
Asian	4 (11.4)	4 (11.1)	8 (11.3)
Black or African American	1 (2.9)	2 (5.6)	3 (4.2)
White	25 (71.4)	27 (75.0)	52 (73.2)
Not reported	2 (5.7)	3 (8.3)	5 (7.0)
Other	3 (8.6)	0	3 (4.2)
Completion status, n (%)			
Ongoing	34 (97.1)	36 (100)	70 (98.6)
Completed	0	0	0
Discontinued	1 (2.9)[c]	0	1 (1.4)[c]

Data cut: June 8, 2023. Percentages are based on the number of patients in the full analysis set.
[a]Age equals the year at point of informed consent for enrollment in XTEND-ed, minus the patient's year of birth.
[b]Patients were assigned to the appropriate age cohort (<6 years or 6 to <12 years of age) at baseline of the parent study (XTEND-Kids).
[c]One patient discontinued due to withdrawn consent.

No FVIII Inhibitors Developed During the XTEND-ed Study

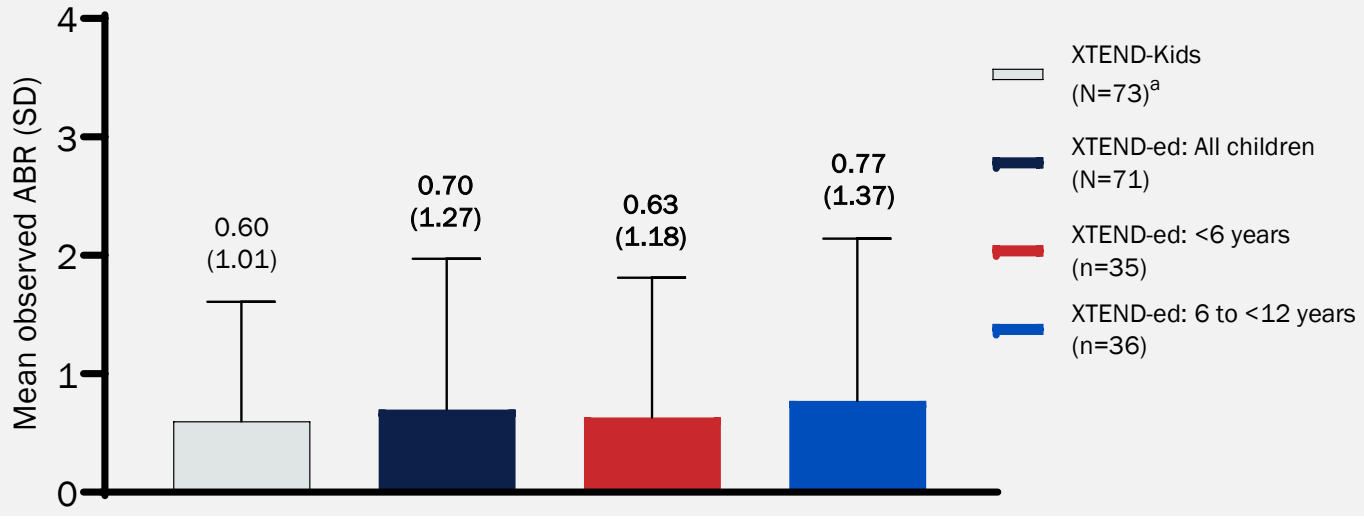
- The mean (SD) **treatment duration** during XTEND-ed was **36.2 weeks (14.3)** (median [range]: 31.6 [20.3–63.6] weeks)[a,b]
- The mean (SD) **exposure to efanesoctocog alfa** during XTEND-ed was **35.6 exposure days (14.7)** (median [range]: 31 [10–64] days)[b,c]

FVIII inhibitors **did not develop**[d,e]

- Incidence of inhibitor formation: **0.0 (95% CI: 0.0–5.1)**[f]

Data cut: June 8, 2023.
BU, Bethesda Unit; CI, confidence interval; FVIII, factor VIII.
[a]Treatment duration refers to the total duration, including periods of PK evaluations, surgery/rehabilitation (minor and major), and large injection intervals (>28 days). [b]Safety analysis set (N=71). [c]An exposure day is a 24-hour period in which one or more efanesoctocog alfa injections are given. All injections over the study course are counted. [d]Inhibitor development was evaluated using the Nijmegen-modified Bethesda assay at the central laboratory. Inhibitor development was defined as an inhibitor result of ≥0.6 BU/mL and confirmed by a second test result from a separate sample drawn 2–4 weeks following the date of the original sample. [e]All patients had previously received treatment with recombinant and/or plasma-derived FVIII, or cryoprecipitate at the start of the observation period. [f]95% CI calculated using the Clopper-Pearson exact method.

The Effective Bleed Protection Previously Shown in XTEND-Kids Was Maintained in XTEND-ed

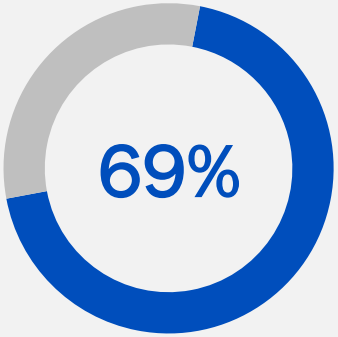


Median (IQR) ABR was 0.00 (0.00–1.07) (N=71)

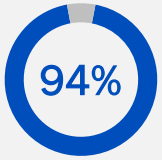
Mean (SD) efficacy period: 35.8 (14.1) weeks[c]

All bleed rates refer to treated bleeds.
Data cut: June 8, 2023. ABR, annualized bleed rate; CI, confidence interval; IQR, interquartile range; SD, standard deviation. Values are based on treated bleeds in patients with an evaluable efficacy period. [a]Based on the number of treated bleeding episodes in the sensitivity analysis set, which excluded the participant who did not receive weekly per protocol prophylaxis treatment for an extended period of time. [b]Estimated using a negative binomial model with the total number of treated bleeds during the efficacy period as the response variable and log-transformed efficacy period duration in years as an offset variable. [c]Efficacy period defined as the treatment regimen period, from the first injection of efanesoctocog alfa to the day of the last dose of efanesoctocog alfa or the data cutoff date of June 8, 2023, whichever was first. The efficacy period excluded periods of surgery/rehabilitation (minor and major) and large injection intervals (>28 days).

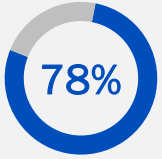
The Effective Bleed Protection Previously Shown in XTEND-Kids Was Maintained in XTEND-ed



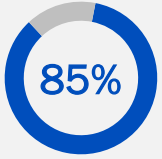
of patients **had zero bleeding episodes** (49/71)



of patients **had zero spontaneous bleeds** (67/71)



of patients **had zero traumatic bleeds** (55/71)



of patients **had zero joint bleeds** (60/71)[a]

Mean (SD) efficacy period: 35.8 (14.1) weeks[b]

All bleed rates refer to treated bleeds.
Data cut: June 8, 2023. SD, standard deviation. Values are based on treated bleeds in patients with an evaluable efficacy period. [a]Two patients experienced spontaneous joint bleeds and 9 patients had traumatic joint bleeds. [b]Efficacy period defined as the treatment regimen period, from the first injection of efanesoctocog alfa to the day of the last dose of efanesoctocog alfa or the data cutoff date of June 8, 2023, whichever was first. The efficacy period excluded periods of surgery/rehabilitation (minor and major) and large injection intervals (>28 days).

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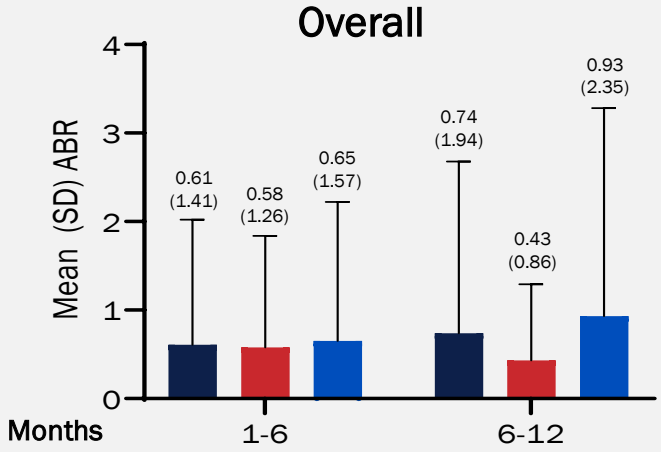
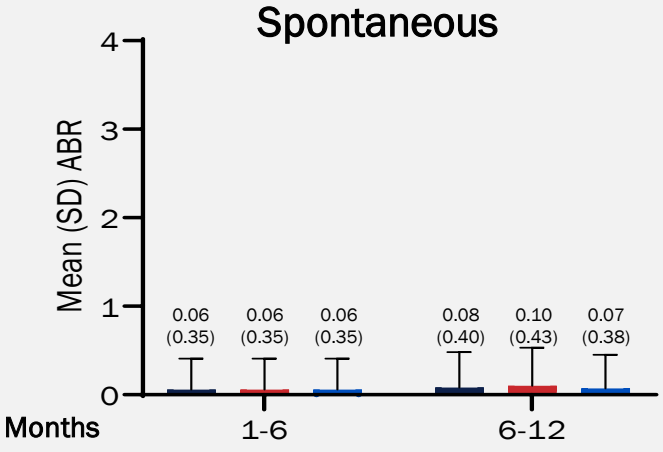
Overall and Spontaneous ABRs Remained Consistently Low Through XTEND-ed Month 12



	n	n
All patients	71	51
<6 years	35	19
6 to <12 years	36	32

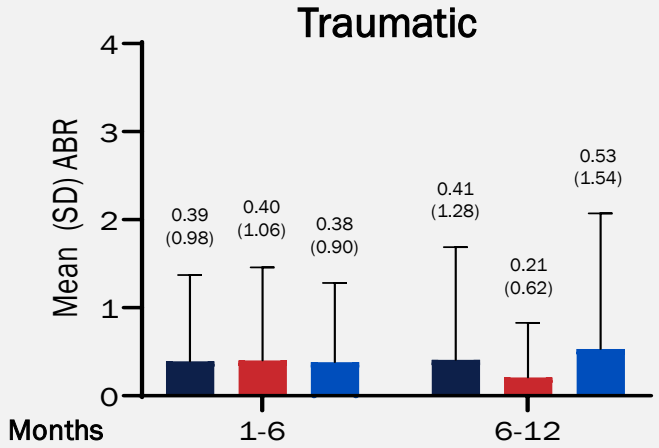


	n	n
All patients	71	51
<6 years	35	19
6 to <12 years	36	32

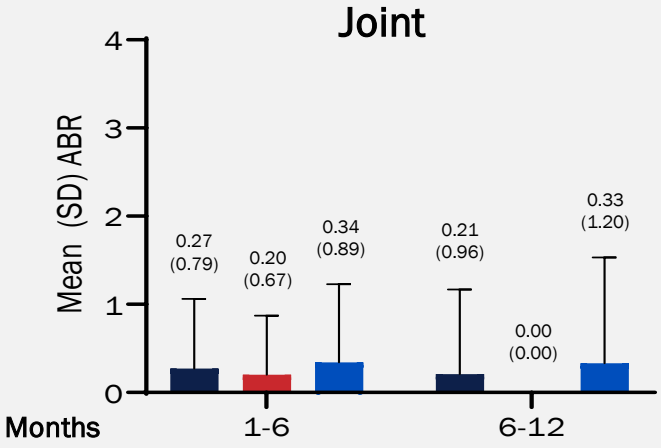
Median ABRs (IQR) were 0 (0.0–0.0) for both overall and spontaneous bleeds up to Month 12 in each age group

Data cut: June 8, 2023.
ABR, annualized bleed rate; IQR, interquartile range; SD, standard deviation. Values are based on treated bleeds in patients with an evaluable efficacy period, defined as the treatment regimen period, from the first injection of efanesoctocog alfa in XTEND-ed to the day of the last dose of efanesoctocog alfa or the data cutoff date of June 8, 2023, whichever was first. The efficacy period excluded periods of surgery/rehabilitation (minor and major) and large injection intervals (>28 days).

Traumatic and Joint ABRs Remained Consistently Low Through XTEND-ed Month 12



	n	n
All patients	71	51
<6 years	35	19
6 to <12 years	36	32

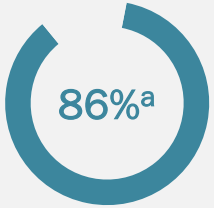


	n	n
All patients	71	51
<6 years	35	19
6 to <12 years	36	32

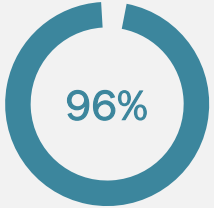
Median ABRs (IQR) were 0 (0.0–0.0) for traumatic and joint bleeds up to Month 12 in each age group

Data cut: June 8, 2023.
ABR, annualized bleed rate; IQR, interquartile range; SD, standard deviation. Values are based on treated bleeds in patients with an evaluable efficacy period, defined as the treatment regimen period, from the first injection of efanesoctocog alfa in XTEND-ed to the day of the last dose of efanesoctocog alfa or the data cutoff date of June 8, 2023, whichever was first. The efficacy period excluded periods of surgery/rehabilitation (minor and major) and large injection intervals (>28 days).

Efanesoctocog Alfa Remained Highly Effective for the Treatment of Bleeding Episodes and Perioperative Management in XTEND-ed



of bleeding episodes **resolved with one 50 IU/kg injection** of efanesoctocog alfa (30/35 bleeds)



of responses were **rated excellent/good** by patients (23/24 bleeds)[b,c]

One patient underwent **1 major surgery**[d] during the study period

The patient's **hemostatic response** to efanesoctocog alfa during the perioperative period was **deemed excellent** by the investigator or surgeon[e]

Data cut: June 8, 2023.
[a]Percentage based on the total number of treated bleeding episodes. [b]Based on the number of injections for a bleed with an evaluation. Responses were captured via electronic diaries or electronic case report form; [c]Assessed using the International Society on Thrombosis and Haemostasis (ISTH) 4-point response scale. [d]Major surgery is defined as any invasive operative procedure that requires any of the following: Opening into a major body cavity (eg, abdomen, thorax, skull), operation on a joint, removal of an organ, dental extraction of any molar teeth or ≥3 nonmolar teeth, operative alteration of normal anatomy, crossing of a mesenchymal barrier (eg, pleura, peritoneum, dura). [e]Investigators' or Surgeons' assessment of patient's hemostatic response to efanesoctocog alfa treatment on the ISTH 4-point response for surgical procedures scale.

Compliance Rates in Children Treated With Efanesoctocog Alfa in XTEND-ed Were High

The mean (SD) number of prophylactic injections per patient was **34.9 (14.5)**[a,b]

- 100% of patients were interval compliant and 96% (n=68/71) were dose compliant[c]

Data cut: June 8, 2023; SD, standard deviation.
[a]Safety analysis set (N=71). [b]Injection types are as collected in the electronic patient diary/electronic case report form. [c]For each patient, the dose compliance rate equals the number of doses taken within 80%–125% of prescribed dose divided by the total number of prophylaxis doses. For each patient, dosing interval compliance rate (based on 7-day dosing interval) equals the number of doses taken within ±36 hours of the prescribed day/time divided by the total number of intervals. Patients are considered compliant if their calculated compliance rate is ≥80%.

Efanesoctocog Alfa Was Well Tolerated

	<6 years (n=35)	6 to <12 years (n=36)	All patients (N=71)
Total number of TEAEs, n[a–c]	68	81	149
Patients with ≥1 TEAE, n (%)	19 (54.3)	24 (66.7)	43 (60.6)
Patients with ≥1 related TEAE, n (%)	1 (2.9)[d]	0	1 (1.4)[d]
Total number of TESAEs, n	1	1	2[e]
Patients with ≥1 TESAE, n (%)	1 (2.9)	1 (2.8)	2 (2.8)[e]
Patients with ≥1 related TESAE, n (%)	0	0	0
TEAEs leading to treatment discontinuation or death, n (%)	0	0	0
TEAEs occurring in >5% of patients overall, n (%)[f,g]			
Pyrexia	4 (11.4)	2 (5.6)	6 (8.5)
Arthralgia	0	5 (13.9)	5 (7.0)
Cough	1 (2.9)	4 (11.1)	5 (7.0)
Upper respiratory tract infection	2 (5.7)	2 (5.6)	4 (5.6)
Viral upper respiratory tract infection	2 (5.7)	2 (5.6)	4 (5.6)
Oropharyngeal pain	3 (8.6)	1 (2.8)	4 (5.6)

Data cut: June 8, 2023.
AE, adverse event; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.
[a]Percentages based on the number of patients in the safety analysis set. [b]AEs with missing causality assessment are included as related TEAE or related TESAE. [c]AEs that occurred during a major surgical/rehabilitation period are excluded from this table, but AEs that occurred on the day the surgical/rehabilitation period started are included. [d]Varicella (suspected chicken pox) infection of mild severity. [e]One incident of right iliopsoas hematoma and one incident of focal epilepsy secondary to a known structural abnormality. [f]Events were coded using MedDRA version 26.0. [g]Patients are counted once if they report multiple events in the same system organ class or preferred term.

Conclusions

No inhibitors developed in previously treated children (<12 years of age) treated with efanesoctocog alfa in XTEND-ed who rolled over from XTEND-Kids

ABRs remained low (<1), and **compliance** and the proportion of patients with **zero bleeding episodes** remained high, **consistent with results of the XTEND-Kids study**[1]

Efanesoctocog alfa continues to be **well tolerated**

In preliminary results from the XTEND-ed study with a mean treatment duration of 36.2 weeks, once-weekly efanesoctocog alfa prophylaxis was shown to be well tolerated and highly effective for children <12 years of age with severe hemophilia A

Data cut: June 8, 2023.
ABR, annualized bleed rate.
1. Malec L, et al. ISTH 2023 (oral presentation).

Thank you

to the study participants, their families,
and the XTEND-ed study investigators