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Takeda announces results from Phase IIIb/IV clinical trial for ADYNOVATE

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The PROPEL study is a PROspective, randomized, multi-center study comparing the safety and efficacy of ADYNOVATE following PK-guided prophylaxis targeting two different Factor Eight (FVIII) through activity Levels in subjects with severe hemophilia A.

Takeda, an R&D-driven, global biopharmaceutical company with a leadership position in rare diseases has announced updated results from its phase IIIb/IV clinical trial for ADYNOVATE [Antihemophilic Factor (Recombinant), PEGylated] at the 27th Annual International Society on Thrombosis and Haemostasis Congress (ISTH), in Melbourne, Australia. The PROPEL study is a PROspective, randomized, multi-center study comparing the safety and efficacy of ADYNOVATE following**P**K-guided prophylaxis targeting two different Factor **E**ight (FVIII) through activity **L**evels in subjects with severe hemophilia A.

The latest results of the landmark PROPEL study show that ADYNOVATE prophylaxis in severe hemophilia A patients may enhance a patient's PK profile - by targeting FVIII trough levels of 8–12% (elevated prophylaxis arm, ELE) as compared with 1–3% (reference prophylaxis arm, REF). This represents a clinically meaningful trend towards more patients experiencing zero bleeds [62% ELE versus 42% REF, respectively; p=0.0545].1 Patients randomized to the 8-12% target group also saw a:

Reduced mean total annualized bleed rate (ABR); (1.6 ELE versus 3.6 REF, respectively).
Reduced mean spontaneous joint ABR (0.5 ELE versus 2.0 REF)
The data supports the view that patients may benefit from PK-driven dosing that targets FVIII trough levels of 8–12%. The safety findings from this latest update were also comparable and consistent with previous ADYNOVATE trials.1,2 Ongoing analyses will further characterize the relationship between PK-tailored dosing of ADYNOVATE FVIII levels and bleeding events.

Adapting the dosing regimen for an individual patient, guided by that patient's individual PK characteristics, has great potential – for managing patients with hemophilia A, particularly those desiring greater bleed protection.1

"These results, for the first time, provide proof of concept that targeting higher FVIII troughs can benefit severe hemophilia A patients with no adverse event profile change. The next step will be to characterize the relationships between

pharmacokinetic profiles, FVIII activity levels and bleeding events, so that we can understand more about the optimal approach for personalized prophylaxis in hemophilia A and help more patients reach zero bleeds," said PD Dr. med. Robert Klamroth, Head of the Department of Internal Medicine Angiology and Coagulation Disorders and Director of the Comprehensive Care Haemophilia Treatment Center and the Haemostasis and Thrombosis Unit at the Vivantes Klinikum in Berlin, Germany.

"The PROPEL data confirm the critical role of FVIII replacement therapy and demonstrate that with PK-guided prophylaxis with ADYNOVATE individualized FVIII levels of 8–12% can be reliably achieved to improve the outcomes for some patients. Hence, the study reinforces Takeda's leadership in advancing treatment for hemophilia A, which also includes a comprehensive gene therapy clinical trial program," said Dr. med. Wolfhard Erdlenbruch, Vice President Head of Global Medical Hematology, Takeda. "ISTH provides a great opportunity for us to demonstrate our ongoing commitment to the hemophilia community and we are excited to be sharing several important updates from our R&D portfolio this week."

In addition to PROPEL, Takeda are presenting 47 other data updates across the hematology portfolio. Most notably, 14 presentations will unveil some of the foundational work being carried out within the Takeda Hematology gene therapy pipeline, looking at ways to help hemophilia patients naturally produce factor VIII or IX, in order to eliminate or experience fewer bleeding episodes.