SunAct

Volume 02
Issue 02

OncoVantage

Insights into global breakthroughs in cell-based therapies

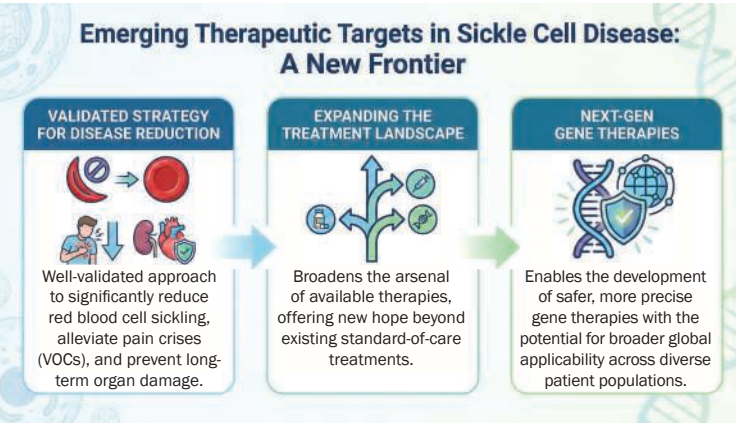
Novel Genetic Target for SCD | Low-Cost Detection of SCD and β-Thalassemia | New FDA Approval

Joining Announcement | SunAct

SunAct is pleased to welcome **Dr. Mamta Manglani** as Director, Pediatric Hematology - Oncology & Bone Marrow Transplant. Dr. Manglani brings extensive expertise in pediatric cancers and hematological disorders, with special focus on hemoglobinopathies and a keen interest in pediatric bone marrow transplantation.

Landmark GWAS Reports a Novel Genetic Target for Sickle Cell Disease

A landmark 2025 genome-wide association study (GWAS) published in *Nature Communications* has identified **14 novel candidate loci**—most notably **FLT1**—that regulate fetal hemoglobin (HbF) levels in patients of African ancestry with Sickle Cell Disease (SCD). By analyzing a combined cohort of **3,751 individuals** from Cameroon, Tanzania, and the USA, researchers demonstrated that these markers explain a staggering **94% of HbF heritability** in African populations, a massive leap from the previously understood 10–24%.



Clinical Implications

- Potential therapeutic target for SCD.
- Increasing fetal hemoglobin levels is a well-validated strategy to reduce red blood cell sickling, pain crises, and organ damage.
- Expands treatment options.
- Findings support the development of next-generation gene therapies that could be safer or more broadly applicable, especially in resource-limited settings.

This discovery adds to the growing pipeline of genetic strategies aimed at providing **durable and curative treatments** for SCD, which affects approximately **300,000 newborns worldwide each year.**

Why it Matters?

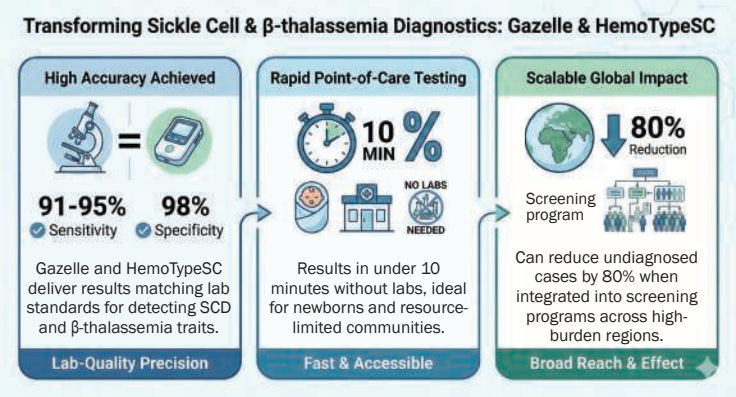
- FLT1 is a newly identified regulator of fetal hemoglobin, reinforcing HbF induction as a key therapeutic strategy in SCD.
- Provides an alternative or complementary gene-editing target to BCL11A, potentially improving safety and expanding treatment options.
- Supports development of next-generation, more accessible curative therapies, especially relevant for high-burden, resource-limited settings.

Source: Wonkam, A., Esoh, K., Levine, R.M. *et al. FLT1* and other candidate fetal haemoglobin modifying loci in sickle cell disease in African ancestries. *Nat Commun* 2025;**16:**2092.

Breakthrough in Low-Cost Detection of SCD and β-Thalassemia

A landmark 2025 study published in *The Lancet Regional Health – Southeast Asia* evaluated affordable point-of-care devices for **diagnosing sickle cell disease (SCD) and β-thalassemia** trait across 12 international sites in Africa, Asia, and the Middle East. In this open-label, multicentre trial involving over 4,500 participants, tools like the Gazelle Hb Variant Test, HemoTypeSC, and automated sickling tests were evaluated against gold-standard HPLC methods. These innovations detect key hemoglobin variants (HbS, HbF, HbA) rapidly without needing labs, delivering results in under 10 minutes.

Devices **achieved impressive metrics:** Gazelle and HemoTypeSC offered **91–95% sensitivity and 98% specificity for SCD and carrier states,** while sickling tests hit **89% accuracy** overall. They performed reliably across diverse populations, though elevated fetal hemoglobin (HbF) occasionally caused interference. **The trial highlights their potential for newborn and community screening in high-burden, resource-limited areas.**



Clinical Implications

- The high sensitivity (91–95%) and specificity (98%) of devices like Gazelle and HemoTypeSC enable rapid, lab-independent detection of SCD and β-thalassemia traits in newborns.
- Supports early intervention in resource-limited African, Asian, and Middle Eastern settings.
- Furthermore, the devices reduce diagnostic delays, lower healthcare burdens from advanced disease, and support epidemiological surveillance to track hemoglobinopathy prevalence in real-time.

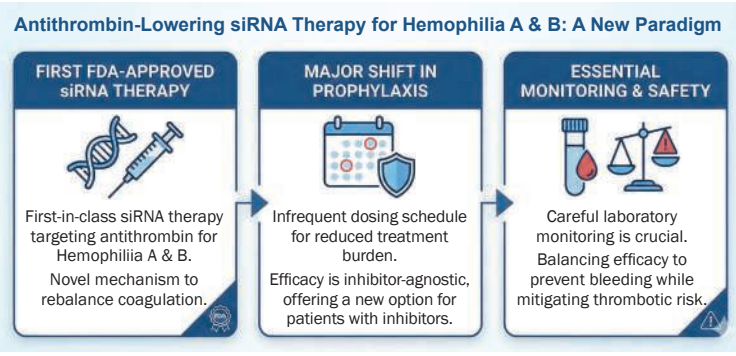
Why it Matters?

- **High Accuracy Achieved**: Gazelle and HemoTypeSC deliver 91–95% sensitivity and 98% specificity for detecting SCD and β-thalassemia traits, matching lab standards.
- **Rapid Point-of-Care Testing:** Results in under 10 minutes without labs, ideal for newborns and resource-limited regions.
- **Scalable Global Impact**: Can reduce undiagnosed cases by 80% when integrated into screening programs across Africa, Asia, and Middle East.

Source: Shrestha P, Lohse H, Bhatla C, *et al*. Evaluation of low-cost techniques to detect sickle cell disease and β-thalassemia: an open-label, international, multicentre study. *Lancet Reg Health Southeast Asia*. 2025;**35:**100571.

FDA Approves Qfitlia (Fitusiran): A First-in-Class Prophylaxis for Hemophilia A and B

Fitusiran (Qfitlia) is a novel **siRNA-based, non–factor rebalancing therapy** approved by the USFDA in March 2025 **for routine prophylaxis of bleeding in patients aged ≥12 years with hemophilia A or B, with or without inhibitors**. Unlike factor replacement therapies, Fitusiran **targets hepatic antithrombin (AT) mRNA**, leading to reduced antithrombin levels and enhanced thrombin generation, thereby restoring hemostatic balance. It is administered as a **subcutaneous injection once every 4–8 months**, with individualized dose adjustment guided by antithrombin activity. Data from the ATLAS **phase 3 clinical program** demonstrated **marked reductions in annualized bleeding rates** across both inhibitor and non-inhibitor populations, highlighting its broad applicability. Safety monitoring is critical, as the therapy carries a **boxed warning for thrombotic events and gallbladder disease**, along with the need for regular liver function and antithrombin level assessments.



Clinical Implications

- Fitusiran offers transformative prophylaxis for hemophilia A/B patients ≥12 years, with or without inhibitors, by reducing annualized bleeding rates (ABR) via monthly-to-quarterly SC dosing.
- Broad Applicability Across Subtypes: ATLAS phase 3 data show >50% ABR reduction in inhibitor/non-inhibitor cohorts, enabling unified therapy for diverse hemophilia populations and simplifying management over factor concentrates.
- Patient-Centric Dosing Flexibility: 50–80 mg every 4–8 weeks (AT-guided titration to 35–75% activity) minimizes clinic visits, improving adherence and quality of life, especially in adolescents with infrequent injections.

Why it Matters?

- First FDA-approved antithrombin-lowering siRNA therapy for hemophilia A and B.
- Infrequent dosing and inhibitor-agnostic efficacy represent a major shift in hemophilia prophylaxis.
- Careful laboratory monitoring is essential to balance efficacy with thrombotic risk.

Source: U.S. Food and Drug Administration. *FDA Approves Novel Treatment for Hemophilia A or B, with or without Factor Inhibitors (Qfitlia (fitusiran))*; March 28, 2025. https://www.fda.gov/news-events/press-announcements/fda-approves-novel-treatment-hemophilia-or-b-or-without-factor-inhibitors)

At SunAct, we remain dedicated to tracking and sharing global advances that continue to redefine the landscape of cellular therapy and oncology. Stay tuned for our next edition as we uncover more breakthroughs and emerging trends shaping the future of cancer research.

Disclaimer: This newsletter is intended for healthcare professionals and researchers. Information is for educational purposes only.