INNOVATION PARTNERSHIPS
UNIVERSITY OF MICHIGAN

Spiroazetidinyl 1,3-Dioxanes as LSD1 Inhibitors for Treatment of Sickle Cell Disease and B-Thalassemia

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OVERVIEW

A new class of small molecule drugs—spiroazetidinyl 1,3-dioxanes—offer a groundbreaking, non-gene therapy approach for treating sickle cell disease and β-thalassemia by activating fetal hemoglobin production.

- Non-invasive pharmacologic solution for two major inherited blood disorders, accessible globally and scalable.
- Novel LSD1 inhibitors profoundly boost therapeutic fetal hemoglobin levels in patients, addressing unmet medical needs where gene therapy and transplant solutions are limited or impractical.

BACKGROUND

Inherited blood disorders, notably sickle cell disease (SCD) and β-thalassemia, impose a severe global health burden; existing treatments are costly, complex, and inaccessible for most affected individuals worldwide. Bone marrow transplants and gene therapies require specialized facilities, carry significant risks, and are available to less than 10% of SCD patients. Current pharmacological options provide only modest and temporary benefit for many patients. Both diseases can be substantially alleviated if the body produces more fetal hemoglobin (HbF), known to promote longer blood cell survival and less severe disease. There is pressing demand

for a broadly accessible, effective therapy that is easy to administer, offers lasting results, and does not require advanced medical infrastructure—a need highlighted by global prevalence, regulatory approvals of limited alternatives, and continuing investment in LSD1 inhibitor research for various diseases.

INNOVATION

This technology centers on a new set of highly specialized molecules—spiroazetidinyl 1,3-dioxanes—that safely block a key enzyme (LSD1) responsible for repressing fetal hemoglobin production. Rather than genetically modifying cells or performing risky transplants, these small molecules are taken as medicines and shift hemoglobin balance in the body, encouraging production of protective fetal hemoglobin that can compensate for faulty adult hemoglobin underlying SCD and β-thalassemia. Unlike current gene editing or transplant-dependent interventions, these drugs can be mass produced, distributed globally, and simply administered as daily pills—expanding life-changing treatment to millions. Early testing shows these compounds outperform previous LSD1 inhibitors, offering stronger and more specific results with fewer side effects. This approach also opens new opportunities in other conditions linked to LSD1, including certain cancers and metabolic diseases, potentially multiplying its market reach.