bluebird bio, Inc. Response to 22-month Follow-up for Evidence Regarding "Gene Therapies for Sickle Cell Disease" Report

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bluebird bio, Inc. appreciates the opportunity to submit new evidence regarding lovotibeglogene autotemcel ('lovo-cel'; LYFGENIA™) to be included as an addendum to "Gene Therapies for Sickle Cell Disease". Several data sources have continued to add evidence regarding clinical, economic, and patient reported outcomes (PROs) on health-related quality of life (HRQOL) data for lovo-cel, a one-time treatment for sickle cell disease in individuals 12 years of age and older with a history of vaso-occlusive events (VOEs). A notable update has occurred in relation to the "Final Policy Recommendations" from the assessment.

- Longer-term efficacy and safety outcomes: Outcomes up to 8 years after treatment with lovo-cel showed sustained anti-sickling HbA^{T87Q} production and elimination of VOEs and severe VOEs (sVOEs) in most participants through last follow up. 86.8% of patients achieved VOE-Complete Resolution (CR) and 94.7% achieved sVOE-CR. 50% of patients with ≥10 VOEs/year achieved VOE-CR. VOEs identified during long term follow-up were confounded by other clinical factors, such as opioid withdrawal, that may have contributed to the occurrence of a pain event. Occurrence was independent of HbA^{T87Q} levels. Patients demonstrated stable therapeutic levels of HbA^{T87Q}, increased levels of total Hb and normalization of hemolysis markers. The safety profile was consistent with underlying SCD and known effects of myeloablative conditioning.[1]
- Healthcare resource utilization (HRU): 83% of patients required 1 or 2 cycles of mobilization and apheresis. Median (min, max) duration of hospitalization from conditioning to discharge was 36.0 (26, 65) days. Median (min, max) reduction of annualized VOE-related hospital days from month 6 post gene therapy infusion through last follow-up was 100% (31.7%, 100%).[1]
- PROs on HRQOL: Clinically meaningful improvements in pain intensity, pain interference and fatigue measured by PROMIS-57 occurred early and were sustained.[2]
- Economic impact: Patients treated with lovo-cel were predicted to survive longer on average versus common care with direct costs avoided of $1,329,201 per patient. Predicted societal benefits included indirect costs avoided of $540,416 per patient. Predicted increase in earnings for patients achieving VOE-CR after lovo-cel totaled $454,483 per patient lifetime. Using a willingness-to-pay threshold of $200,000/quality-adjusted life year (QALY) and a societal perspective (including direct medical costs [lovo-cel-related and other direct costs], other societal costs, patient QALYs and caregiver QALYs lost), lovo-cel was found to be cost-effective at a value-based price of up to $4.0 million.[3]

While existing evidence is sufficient to demonstrate transformative clinical- and cost-effectiveness of lovo-cel, long term follow-up will continue for 15 years post infusion, which

will continue to add evidence of value for lovo-cel with further clinical, economic, HRU and PROs on HRQOL data.

Related to healthcare policy, the Centers for Medicare & Medicaid Services (CMS) announced bluebird bio, Inc.'s participation in the Cell and Gene Therapy Access Model,[4] which utilizes alternative payment models through outcomes-based agreements between state Medicaid agencies and the manufacturer. CMS has received applications from 35 states to join the model, representing approximately 84% of Medicaid beneficiaries with SCD, which are expected to begin participation by 2026.[5]

References

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2. Kanter, Julie, et al. "Efficacy, Safety, and Health-Related Quality of Life (HRQOL) in Patients with Sickle Cell Disease (SCD) Who Have Received Lovotibeglogene Autotemcel (Lovo-cel) Gene Therapy: Up to 60 Months of Follow-up." *Blood*, vol. 142, suppl. 1, 2023, p. 1051, https://ashpublications.org/blood/article/142/Supplement%201/1051/503860/Efficacy-Safety-and-Health-Related-Quality-of-Life.

3. Herring, William L et al. "Cost-Effectiveness of Lovotibeglogene Autotemcel (Lovo-Cel) Gene Therapy for Patients with Sickle Cell Disease and Recurrent Vaso-Occlusive Events in the United States." *PharmacoEconomics* vol. 42,6 (2024): 693-714. doi:10.1007/s40273-024-01385-9.

4. *Biden-Harris Administration Takes Next Steps to Increase Access to Sickle Cell Disease Treatments." Centers for Medicare & Medicaid Services*, 4 Dec. 2024, https://www.cms.gov/newsroom/press-releases/biden-harris-administration-takes-next-steps-increase-access-sickle-cell-disease-treatments. Accessed 3 July 2025.

5. *Cell and Gene Therapy (CGT) Access Model*. Centers for Medicare & Medicaid Services, 2025, https://www.cms.gov/priorities/innovation/innovation-models/cgt.