SCE 0901 Public Evidence Appendix

The translational pathway

Literature review date: September 13, 2026

Controlling principle. Each translational stage answers a different evidentiary question. Evidence should not be promoted from one stage to another without the data required for that stage, and conclusions remain specific to the exact product, indication, dose, route, population, comparator, endpoint, manufacturing process, and follow-up.

Point-by-point framework

Stage	Primary question	Key interpretive boundary
Discovery	Is there a plausible biological target, product, or mechanism?	Plausibility is not evidence of patient benefit.
Proof of concept	Can the proposed intervention produce the intended effect under defined conditions?	A simplified experimental effect may not survive clinical complexity or manufacturing scale-up.
Animal studies	How does the intervention behave in an intact organism?	Species and disease-model differences limit direct prediction of human efficacy.
Toxicology	What harms may occur at the intended product, dose, route, and schedule?	Safety data are product- and context-specific and do not transfer automatically across platforms.
Phase 1	Can the product be administered to humans with an acceptable initial safety/tolerability profile?	Exploratory efficacy signals are not confirmatory evidence.
Phase 2	Which dose, population, and endpoints warrant further testing, and is there a credible efficacy signal?	Primary endpoints, effect size, multiplicity, missing data, and clinical importance remain critical.
Phase 3	Do larger confirmatory trials support the proposed clinical use?	Reaching Phase 3 does not guarantee success or authorization.
Regulatory review	Does the total product-specific evidence support the proposed indication and benefit-risk balance?	Authorization, evidence level, development stage, guideline position, and manufacturing quality remain separate labels.
Postmarketing surveillance	What benefits, risks, and use patterns emerge in broader real-world practice?	Authorization does not end evidence generation; uncommon and delayed effects may emerge later.

Evidence-handling rules

Positive, negative, mixed, null, and inconclusive findings are retained according to study design, directness, exact product identity, manufacturing consistency, comparator, endpoint, and duration of follow-up.

Mechanistic evidence, preclinical evidence, clinical efficacy, safety, development stage, regulatory status, guideline position, manufacturing quality, and postauthorization evidence remain distinct analytical dimensions.

Principal references

1. 1. U.S. Food and Drug Administration. Frequently Asked Questions — Developing Potential Cellular and Gene Therapy Products. Guidance for Industry. August 2026.

2. 2. International Council for Harmonisation. E6(R3) Good Clinical Practice and related efficacy and safety guidance.

3. 3. Welsh JA, Goberdhan DCI, O'Driscoll L, Théry C, Witwer KW. Minimal information for studies of extracellular vesicles (MISEV2023): From basic to advanced approaches. J Extracell Vesicles. 2024;13:e12404.

4. 4. U.S. Food and Drug Administration. Human Gene Therapy Products Incorporating Human Genome Editing. Guidance for Industry. January 2024.

5. 5. U.S. Food and Drug Administration. Chemistry, Manufacturing, and Controls Flexibilities for Developing Human Cellular and Gene Therapy Products for a Biologics License Application. Guidance for Industry. May 2026.

6. 6. U.S. Food and Drug Administration. Innovative Designs for Clinical Trials of Cellular and Gene Therapy Products in Small Populations. Draft Guidance for Industry. September 2025.

7. 7. U.S. Food and Drug Administration. Long Term Follow-up After Administration of Human Gene Therapy Products. Guidance for Industry. January 2020.

8. 8. U.S. Food and Drug Administration. Postapproval Methods to Capture Safety and Efficacy Data for Cell and Gene Therapy Products. Draft Guidance for Industry. September 2025.