A cross-sectional analysis of approved AAV gene therapy formulations linking composition, stability, and clinical administration

P0156

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Introduction

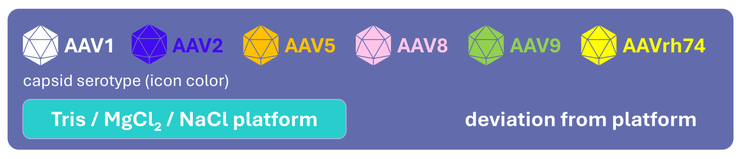
AAV gene therapies have matured into commercial medicines, yet formulation development remains largely **empirical and product-specific**.

FDA and EMA labels hold rich but fragmented information on composition, storage and administration.

We compared **twelve approved AAV products (2012–2026)**, including three that have left the market, to identify shared principles and practical benchmarks for next-generation AAV drug products.

Methods

Data extracted from current US prescribing information and EU SmPCs (status Oct 2026); molarities calculated from mg/mL where needed; titers stated as genome copies (gc) are reported as vg. Withdrawn and discontinued products are included. RT, room temperature.



Buffers

5 of 12 products share one identical platform:

20 mM Tris, 1 mM $MgCl_2$, 200 mM NaCl, pH ~8, covering every IV or intrathecal product except the three hemophilia therapies. This likely reflects platform heritage rather than stability optimization: at pH ≥ 8, **capsid deamidation** accelerates and becomes a major degradation pathway, and Tris pH rises by ~0.5 units on cooling to 2–8 °C.

The other seven use **phosphate at pH 6.9–7.8**. High ionic strength (≥ 137 mM NaCl) is universal.

Surfactants

Poloxamer 188 is the default (10 of 12, 0.001–0.2%), unlike monoclonal antibodies, where polysorbates dominate; Glybera contains no surfactant.

The only polysorbate product, **Hemgenix (0.022% polysorbate 20 + 5% sucrose)**, is also the only one with a **refrigerated liquid shelf life (24 months at 2–8 °C)**.

Label data cannot separate surfactant, sugar and capsid effects, but this questions P188 as an unchallenged default.

Stability

11 of 12 products are stored frozen, 10 of them at ≤ −60 °C, largely a historical precaution for viral vectors rather than a demonstrated need.

Glybera was stored at **−20 °C (18 months)**.
An **initial deep freeze (≤ −60 °C, ~1 week) followed by long-term storage at −20 °C** could simplify supply chains, if frozen-state behavior (Tg', NaCl eutectic at −21 °C) and real-time data support it.

In-use windows are short (4–24 h).

Opportunities

Three opportunities that need studies, not new excipients:

→ **Longer room-temperature in-use:** daily time points to day 7 (RT and 2–8 °C, final syringe or bag) plus microbial-challenge data. Today, no product allows more than 24 h.

→ **Off Tris pH 8:**
phosphate or histidine at pH ~6-7 to slow capsid deamidation.

→ **−20 °C long-term storage:**
freeze at ≤ −60 °C, then store at −20 °C, if Tg' / NaCl eutectic (−21 °C) and real-time data support it.

Approval Year / Name / Developer Serotype · Transgene · Indication	Presentation / Formulation Concentration · Vial · Composition	Stability / Route & Dose / Volume Storage · thawed · in use | route · dose | volume · prep · rate		
2026				
Fayuvi ultragenyx AAV9 *SGSH (R169Q)* Sanfilippo type A (MPS IIIA)	1E13 vg/mL 8 mL vial 2 mL fill	200 mM NaCl 20 mM Tris (pH 8.0) 1 mM $MgCl_2$ 0.001% Poloxamer 188	≤ −60 °C 12 d at 2–8 °C 24 h RT (syringe)	intravenous 3E13 vg/kg	3 mL/kg 70 kg: 210 mL undiluted ≈ 1 h
Genglycos ultragenyx AAV8 *G6PC* Glycogen storage disease type Ia	3E13 vg/mL 8 mL vial 2 mL fill	200 mM NaCl 20 mM Tris (pH 7.5–8.5) 1 mM $MgCl_2$ 0.01% Poloxamer 188	≤ −60 °C 12 d at 2–8 °C 24 h RT (diluted)	intravenous 1E13 vg/kg	0.33 mL/kg 70 kg: 24 mL ad 250 mL saline ramped, ≥ 3 h
Otarmeni REGENERON AAV1 dual vector *OTOF* OTOF-related hearing loss	3E13 vg/mL 2 mL vial 0.63 mL fill	180 mM NaCl 10 mM phosphate (pH 7.3) 5% sucrose 0.001% Poloxamer 188	≤ −60 °C 24 h at 2–8 °C 8 h RT (vial) 4 h (syringe)	intracochlear 7.2E12 vg/ear	0.24 mL/ear undiluted 0.9 mL/h, 16 min
2025				
Itvisma NOVARTIS AAV9 *SMN1* Spinal muscular atrophy	4E13 vg/mL 5 mL vial 3 mL fill	200 mM NaCl 20 mM Tris (pH 8.0) 1 mM $MgCl_2$ 0.005% Poloxamer 188	≤ −60 °C 14 d at 2–8 °C 5 h RT (syringe)	intrathecal 1.2E14 vg fixed dose	3 mL fixed undiluted bolus, 1–2 min
2024				
Beqvez Pfizer *discontinued 2025* AAVrh74var *FIX Padua* Hemophilia B	1E13 vg/mL plastic vial 1 mL fill	180 mM NaCl 10 mM phosphate (pH 7) 0.001% Poloxamer 188	≤ −60 °C 24 h at 2–8 °C 24 h RT (diluted)	intravenous 5E11 vg/kg	0.05 mL/kg 70 kg: 3.5 mL ad 200 mL saline + 0.25% albumin ≈ 60 min
2023				
Elevidys SAREPTA THERAPEUTICS AAVrh74 *micro-dystrophin* Duchenne muscular dystrophy	1.33E13 vg/mL 10 mL vial 10 mL fill	200 mM NaCl 20 mM Tris (pH 8.0) 1 mM $MgCl_2$ 0.001% Poloxamer 188	≤ −60 °C, 12 mo 14 d at 2–8 °C 24 h RT (vial)	intravenous 1.33E14 vg/kg ≥ 70 kg: fixed 9.31E15 vg	10 mL/kg 70 kg: 700 mL undiluted < 10 mL/kg/h 1–2 h
2022				
Hemgenix CSL uniQure AAV5 *FIX Padua* Hemophilia B	1E13 vg/mL 10 mL vial 10 mL fill	137 mM NaCl 10 mM phosphate (pH 7.1) 2.7 mM KCl 5% sucrose 0.022% Polysorbate 20	2–8 °C, 24 mo 24 h RT (diluted) ★ liquid at 2–8 °C	intravenous 2E13 vg/kg	2 mL/kg 70 kg: 140 mL ad 500 mL saline 500 mL/h
Roctavian BIOMARIN *withdrawal 2026* AAV5 *hFVIII-SQ* Hemophilia A	2E13 vg/mL COP vial 8 mL fill	140 mM NaCl 10 mM phosphate (pH 6.9–7.8) 2% mannitol 0.2% Poloxamer 188	≤ −60 °C, 36 mo 3 d at 2–8 °C 10 h RT (total)	intravenous 6E13 vg/kg	3 mL/kg 70 kg: 210 mL undiluted 1 → 4 mL/min
Kebilidi PTC THERAPEUTICS AAV2 *DDC* AADC deficiency	5.6E11 vg/mL 2 mL vial 0.5 mL fill	337 mM NaCl 10 mM phosphate (pH 6.9) 3 mM KCl 0.001% Poloxamer 188	≤ −65 °C, 42 mo 6 h RT after thaw	intraputaminal 1.8E11 vg total	4 × 80 µL undiluted 3 µL/min, 27 min
2019				
Zolgensma NOVARTIS AAV9 *SMN1* Spinal muscular atrophy	2E13 vg/mL 10 mL vials 5.5 or 8.3 mL fill	200 mM NaCl 20 mM Tris (pH 8.0) 1 mM $MgCl_2$ 0.005% Poloxamer 188	≤ −60 °C, 24 mo 14 d at 2–8 °C 8 h RT (syringe)	intravenous 1.1E14 vg/kg	5.5 mL/kg 21 kg: 116 mL undiluted 60 min
2017				
Luxturna NOVARTIS AAV2 *RPE65* RPE65 retinal dystrophy	5E12 vg/mL 2 mL vial 0.5 mL fill + diluent	180 mM NaCl 10 mM phosphate (pH 7.3) 0.001% Poloxamer 188	≤ −65 °C, 36 mo 4 h RT (diluted)	subretinal 1.5E11 vg/eye	0.3 mL/eye diluted 1:10
2012				
Glybera uniQure *withdrawn 2017* AAV1 *LPL S447X* LPL deficiency	3E12 vg/mL 2 mL vial 1 mL fill	137 mM NaCl 10 mM phosphate (pH 7.4) 2.7 mM KCl 5% sucrose *no surfactant*	−20 °C, 18 mo 8 h at 2–8 °C 8 h RT (syringe)	intramuscular 1E12 vg/kg	0.5 mL/site 70 kg: 47 sites undiluted one session

Summary

5 / 12
share one platform:
Tris / $MgCl_2$ / NaCl, pH ~8

10 / 12
use Poloxamer 188; only Hemgenix uses polysorbate 20

11 / 12
are stored frozen; only Hemgenix is a 2–8 °C liquid

4–24 h
typical in-use window after thaw or dilution

0 / 12
freeze-dried formulations

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