FORENSIC SHORT REPORT

Capricor Therapeutics

How HOPE-3 failed under its original statistical framework, passed under later analyses, and financed a $250 million equity raise

CENTRAL FINDING

FDA staff reconstructed HOPE-3 under the analysis framework used to design the trial and obtained negative results for upper-limb function (p=.24) and cardiac function (p=.97). Capricor reported success after later endpoint, missing-data, covariate, population, and model choices produced p=.029 and p=.041. The company then raised approximately $250 million gross into the re-rating. We expect another Complete Response Letter, assign zero value to deramiocel and the exosome pipeline, and estimate $1.72 per share of recoverable equity in our base run-off case.

Research date	Catalyst state	Reference price	Valuation conclusion
27 July 2026	Before 29 July FDA advisory committee	$6.995 after a 64.5% one-day decline	$1.72 base; $1.28-$2.82 range

Position disclosure. This report presents an adversarial short thesis. The author may hold short exposure to CAPR and may trade at any time. The analysis states opinions derived from public records available through 27 July 2026, 8:00 p.m. ET. It does not provide investment, legal, accounting, or medical advice.

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SHORT THESIS

HOPE-3 failed before Capricor declared it a success

Capricor Therapeutics entered December 2025 as a small biotechnology company with a rejected biologics application and a single late-stage asset. It left the month with a stock price almost five times higher, approximately $250 million of new gross equity capital, and an investor narrative built around a supposedly definitive Phase 3 success. FDA's 27 July 2026 briefing document dismantled that narrative at its statistical foundation.

HOPE-3 enrolled 106 patients with Duchenne muscular dystrophy and was designed around two clinically intelligible measurements: the change in a patient's Performance of the Upper Limb 2.0 total score, measured in points, and the change in left-ventricular ejection fraction, measured in percentage points. FDA staff reconstructed those analyses from the trial's original framework. The upper-limb comparison favored deramiocel by only 0.66 point, with a 95% confidence interval from -0.45 to 1.77 and p=.24. The cardiac comparison was effectively zero: -0.041 percentage point, p=.97. The pivotal endpoint missed, and the key secondary endpoint produced no evidence of benefit.[1]

The company reported a different pair of results on 3 December 2025. Its preferred upper-limb analysis divided each patient's change by the patient's baseline score and expressed the result as a percentage. It also applied revised rules to two placebo observations and retained a slow-progressor term that FDA says should have been removed under the sponsor's own minimum-cell rule. The resulting estimate was 4.55 percentage points, p=.029. Its preferred cardiac analysis converted raw LVEF changes into ranks, required both baseline and month-12 scans, excluded 23 of 106 randomized patients, imputed certain missing outcomes, and added an age-by-baseline interaction in the clinical study report. That route produced p=.041.[1][2]

The chronology supplies the central evidentiary problem. HOPE-3's randomized, double-blind follow-up ended on 18 June 2025. SAP 2.0 was dated 26 September. SAP 3.0 was dated 24 November, one day before database lock and formal unblinding. The clinical study report was dated 3 February 2026 and contained terms beyond SAP 3.0. Formal treatment codes remained concealed until the lock, according to the company. The scientific vulnerability survives that defense because all primary observations already existed, blinded pooled data revealed distributional features and dropout patterns, infusion reactions created a substantial risk of functional unblinding, and the analyses that crossed .05 appeared at the end of the sequence.[1][2]

Capricor described the December evidence as "strong and definitive" and said the totality of the data should support approval. The release omitted the failed original analyses and the post-completion chronology. CAPR closed at $29.96 on 3 December after closing at $6.36 the previous day. Two days later, Capricor priced 6.9 million shares at $25, raising $172.5 million gross. Its September-December at-the-market program sold another 2.682 million shares at an average $28.89 for $77.5 million gross. The financing converted the disputed clinical interpretation into approximately $250 million of corporate cash.[3][7][9]

FDA staff concluded that HOPE-3 does not provide substantial evidence of effectiveness and that the benefit-risk balance is unfavorable without demonstrated efficacy. Capricor disputes the staff's reconstruction and argues that its later methods were scientifically justified, planned while blinded, and consistent with regulatory dialogue. Those arguments create an approval tail and event risk for a short position. They do not restore a stable result across reasonable analyses. We expect a negative advisory-committee outcome followed by another Complete Response Letter.[1][5]

Our valuation removes all product and platform value. Estimated July liquidity of $215-$235 million provides real balance-sheet support, although it cannot be distributed without first funding existing obligations, program termination, legal and partner disputes, severance, facilities, and corporate closure. Using approximately 61.1 million diluted shares, the base run-off bridge leaves $105 million, or $1.72 per share. A disciplined high-recovery case yields $2.82; a delayed and costly run-off yields $1.28. Continued development, another trial, or a low-price financing can consume the remaining equity value.

The investment case rests on a narrow proposition: the trial's success disappears when the analysis returns to the framework used to design it. The balance sheet delays the terminal outcome; management's use of that balance sheet determines whether shareholders recover it.

Contents

I. COMPANY AND PRODUCT

Capricor, Duchenne muscular dystrophy, and deramiocel

Capricor is a clinical-stage biotechnology company whose valuation depends overwhelmingly on deramiocel, an experimental cell therapy for Duchenne muscular dystrophy. The underlying disease is genetically simple and biologically devastating: mutations in the DMD gene prevent normal production of dystrophin, a structural protein that helps muscle fibers survive repeated contraction. The resulting injury accumulates across skeletal muscle, respiratory muscle, and the heart.

Duchenne progressively destroys skeletal and cardiac muscle

Duchenne muscular dystrophy occurs primarily in boys because the DMD gene lies on the X chromosome. Early childhood often brings delayed motor milestones, difficulty rising from the floor, and a characteristic waddling gait. Progressive weakness eventually impairs ambulation and upper-limb function. Improvements in corticosteroid treatment, ventilation, cardiac surveillance, and mutation-specific therapies have extended survival, increasing the clinical importance of cardiomyopathy. Patients can preserve substantial upper-limb ability after losing ambulation, which makes an upper-limb endpoint meaningful in older and non-ambulatory populations.

The disease mechanism also sets a demanding standard for any therapy that does not replace dystrophin. Every dose must influence tissue that remains subject to the same genetic injury. A therapy can create value by slowing inflammation, fibrosis, or cell death even if it never repairs the mutation. The effect must be durable enough, reproducible enough, and large enough to exceed the natural variability of a heterogeneous rare-disease population.

Deramiocel is an intravenously delivered allogeneic cell product

Each deramiocel dose contains roughly 150 million donor-derived cardiosphere-derived cells, described in current company materials as cardiac stromal cells. The cells are manufactured from donor heart tissue and administered intravenously every three months. They are not gene-editing cells, and Capricor does not expect them to permanently repopulate the patient's heart or skeletal muscle. The proposed mechanism is paracrine: the administered cells release proteins, lipids, extracellular vesicles, and other molecular cargo that may reduce inflammation and fibrosis and promote tissue repair.[1][2]

That mechanism has biological plausibility. It also creates a long causal chain between infusion and clinical benefit. The product must be consistent across donors and manufacturing lots; its secreted factors must remain active; systemic delivery must expose relevant tissues; repeated dosing must sustain the effect; and the resulting physiological change must preserve function. FDA staff reports cardiac retention below 1% after intravenous delivery; the proposed cardiac mechanism therefore depends predominantly on indirect signaling.[1][15]

HOPE-3 measured arm function and cardiac function

The Performance of the Upper Limb 2.0 instrument, or PUL 2.0, is a clinician-administered assessment of shoulder, elbow, wrist, and hand tasks. Its total score is expressed in points, with higher scores reflecting greater retained function. A treatment for progressive DMD should reduce the number of points lost over time. HOPE-3 was powered around an expected 1.5-point treatment difference at 12 months. A percent-change version answers a related statistical question, although the clinical meaning of a percentage depends heavily on a patient's starting score.

Left-ventricular ejection fraction, or LVEF, measures the percentage of blood ejected from the left ventricle with each contraction. It is familiar, clinically relevant, and noisy. MRI acquisition, reader interpretation, missing scans, baseline values, and disease stage can materially affect small differences. Late gadolinium enhancement, or LGE, detects fibrotic scar on MRI and can add biological context. In HOPE-3, evaluable LGE data existed for only a minority of randomized patients, limiting its ability to rescue an uncertain LVEF result.

Measure	Clinical quantity	Original HOPE-3 role	Central interpretive problem
PUL 2.0	Upper-limb function in points	Primary endpoint at month 12	FDA reconstructed a +0.66-point difference, p=.24; Capricor reported percent change, p=.029.
LVEF	Ventricular pump function in percentage points	Key secondary endpoint	Original change analysis was p=.97; final rank analysis was p=.041.

Measure	Clinical quantity	Original HOPE-3 role	Central interpretive problem
LGE	MRI evidence of myocardial fibrosis	Supportive cardiac measure	Sparse evaluable data and no persuasive confirmatory pattern.
Infusion reactions	Hypersensitivity and related treatment-emergent events	Safety and blinding context	41.5% on deramiocel versus 15.4% on placebo in HOPE-3.

The statutory question is evidentiary reliability

A Biologics License Application asks FDA to authorize commercial marketing. Clinical efficacy, safety, manufacturing controls, potency, and product consistency all enter the review. Priority Review, orphan-drug designation, and Regenerative Medicine Advanced Therapy status can accelerate meetings or the review clock; none supplies the missing evidence of effectiveness. FDA ordinarily seeks at least two adequate and well-controlled studies, while allowing one exceptionally persuasive study with independent confirmation in appropriate cases. Rare disease can justify flexibility in trial size and evidence assembly. The result still has to withstand prospective rules, missing-data assumptions, multiplicity control, and sensitivity analysis.

The statistical analysis plan, or SAP, specifies the rulebook before treatment outcomes are available. It defines the endpoint scale, analysis population, model, covariates, handling of missing observations, intercurrent events, and the order in which hypotheses are tested. A p-value assumes that the question and analytical procedure were fixed independently of the observed result. Repeatedly changing the question or procedure after data accumulate can make chance findings easier to discover. Formal blinding reduces that risk, while pooled outcome distributions, dropout timing, adverse-event patterns, and operational knowledge can still disclose consequential information.

Regulatory term	Operational meaning in this case
BLA	The marketing application for deramiocel. FDA previously issued a Complete Response Letter in July 2025 and accepted a resubmission in March 2026.
SAP	The instructions for converting HOPE-3 observations into efficacy estimates. SAP 2.0 and SAP 3.0 post-dated completion of randomized follow-up.
Database lock	The cleaned database was frozen and formally unblinded on 25 November 2025, one day after SAP 3.0.
Advisory committee	Outside experts advise FDA in public. Their vote is influential and legally nonbinding.
Complete Response Letter	FDA has completed review and cannot approve the application in its current form. The letter can require new clinical or manufacturing work.
PDUFA date	The current target date for FDA action is 22 August 2026; the date does not imply approval.

II. PROMOTION AND CHRONOLOGY

The December 2025 declaration converted disputed efficacy into cash

Capricor's December announcement matters because it did more than summarize a statistical table. It closed the evidentiary gap created by the July 2025 Complete Response Letter in the minds of investors, repriced the company, and established the market into which Capricor issued approximately one quarter-billion dollars of equity.

The first BLA had already failed on substantial evidence

Capricor's original application relied heavily on HOPE-2 and its open-label extension. On 11 July 2025, the company disclosed that FDA had issued a Complete Response Letter. FDA had not accepted HOPE-2 and its extension as substantial evidence of effectiveness. The randomized trial was very small, prespecified analyses did not establish the claimed effects, later cardiac analyses followed unblinding, and the extension lacked a concurrent randomized control. HOPE-3 therefore carried a precise regulatory burden: it had to provide a prospectively interpretable pivotal result and convert earlier suggestive findings into independent confirmation.[1][2][32]

The randomized HOPE-3 period ended on 18 June 2025. At that point all 12-month observations relevant to the primary analysis existed. The initial SAP framework dated to July 2022. A December 2023 version introduced an adverse-event discontinuation worst-score rule and a slow-progressor term before trial completion. SAP 2.0, dated 26 September 2025, changed the PUL endpoint scale and other analysis features after follow-up had ended. SAP 3.0, dated 24 November, added the final ranked LVEF framework and prohibited-medication handling one day before lock and formal unblinding. The February 2026 clinical study report included additional modeling terms.[1]

CAPR price and regulatory disclosure timeline

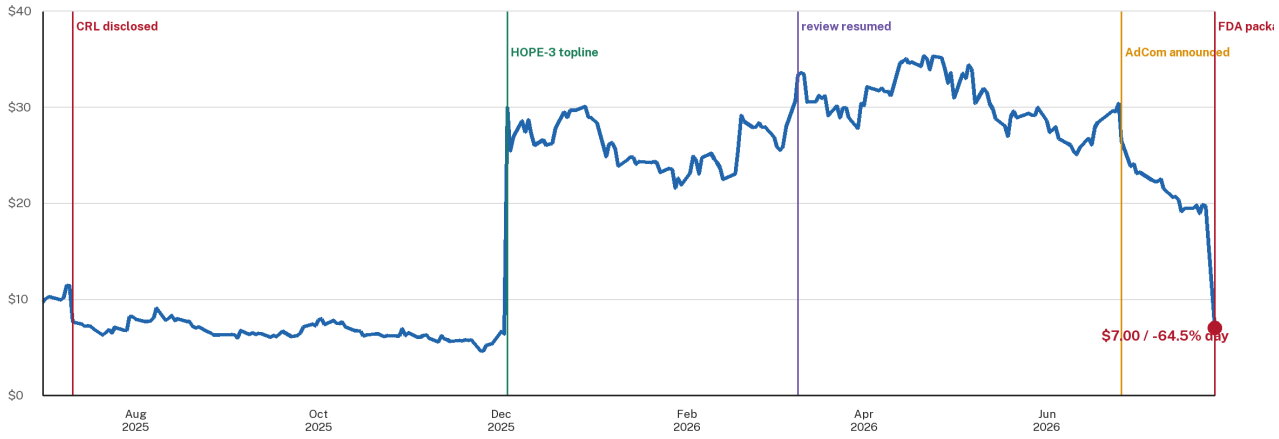


Figure 1. CAPR closing prices and principal regulatory disclosures. The 3 December 2025 release produced the valuation used for the subsequent offering; the 27 July 2026 FDA briefing produced the collapse. Source: Nasdaq historical data, Capricor filings, and FDA meeting materials.

Date	Event	Effect on the evidentiary record
19 Jul 2022	SAP 1.1 dated	Original absolute-change PUL and LVEF framework used to design and power the study.
6 Dec 2023	SAP 1.7 dated	Slow-progressor term and adverse-event discontinuation worst-score rule appeared before completion.
11 Jul 2025	First deramiocel CRL disclosed	FDA had not accepted HOPE-2/OLE as substantial evidence.
18 Jun 2025	Randomized double-blind follow-up completed	All month-12 efficacy observations had been collected.
26 Sep 2025	SAP 2.0 dated	PUL changed from absolute points to percent change; analysis rules changed after follow-up.
24 Nov 2025	SAP 3.0 dated	Ranked LVEF and prohibited-medication handling added one day before lock.

Date	Event	Effect on the evidentiary record
25 Nov 2025	Database lock and formal unblinding	Company states treatment assignments remained concealed until this date.
3 Dec 2025	Positive topline release	Capricor declared both principal endpoints significant and called the evidence definitive.
5 Dec 2025	6.9 million-share offering at $25	$172.5 million gross raised into the clinical re-rating.
3 Feb 2026	Clinical study report dated	Final implementation retained or added terms beyond the final SAP.
27 Jul 2026	FDA briefing released	Original p=.24 and p=.97 results and the full analysis ladder became public.

Capricor's release described an unqualified Phase 3 success

The 3 December release said HOPE-3 met its primary endpoint and key secondary endpoint. It stated that all prespecified, Type I-error-controlled primary and secondary endpoints were statistically significant. Linda Marbán characterized the results as "strong and definitive," and the company said the evidence was consistent with prior FDA guidance that the study should support approval. The release emphasized a 54% slowing in PUL decline and a 91% slowing in LVEF decline.[3][4]

Those percentages were rhetorically powerful. The 54% figure divides the modeled 4.55-percentage-point treatment difference by the placebo group's modeled 8.41% decline. It does not mean patients recovered 54% of lost arm function. The 91% cardiac figure similarly expresses a relative reduction under the preferred model. Both presentations depend on the same analytical choices that FDA later challenged.

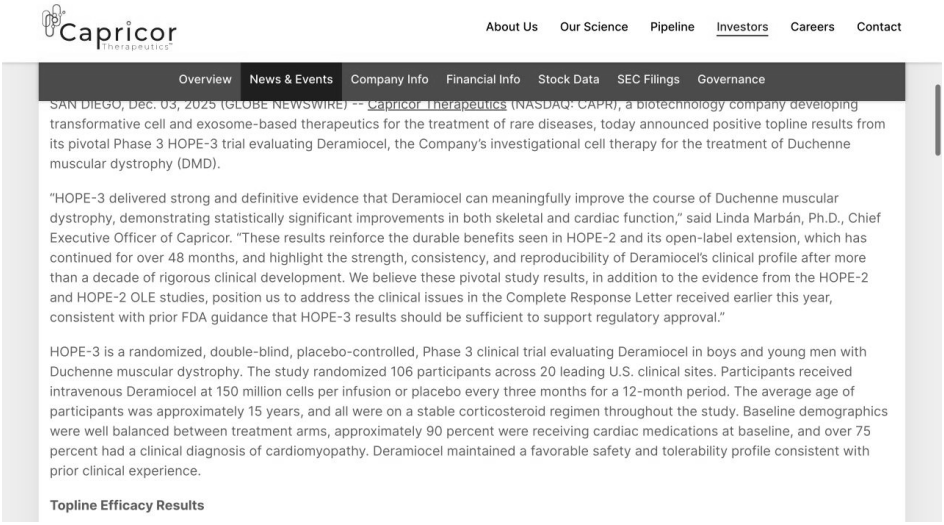


Figure 2. Capricor's 3 December 2025 release described the HOPE-3 evidence as strong and definitive and linked it to regulatory approval. Source: Capricor press release and SEC-filed Exhibit 99.1.

The release disclosed the results generated by the final preferred analyses. Investors were not shown the negative original PUL and LVEF results, the post-completion SAP chronology, the dependence of the PUL result on two placebo observations, the exclusions embedded in the ranked LVEF analysis, or the terms added in the clinical study report. Those omissions deprived the market of the facts needed to distinguish a robust confirmatory result from an analysis-dependent one.

The stock re-rating supplied the financing window

CAPR closed at $6.36 on 2 December. It opened at $30.00 on 3 December, traded as high as $40.37, and closed at $29.96. On 5 December, Capricor priced 6.9 million shares, including the underwriters' full over-allotment, at $25 per share. Gross proceeds were $172.5 million and estimated net proceeds were approximately $161.9 million. The offering price was almost four times the pre-release close.[9]

Capricor also sold 2.682 million shares through an at-the-market program for $77.5 million gross at an average price of $28.89. The program began before 3 December, and the company has not disclosed daily allocations. The realized average nevertheless shows that the program captured the post-topline price regime. Together, the ATM and follow-on produced approximately $250.0 million gross and $237.1 million after disclosed fees.[7][9]

The disputed analysis created the valuation, and the valuation created the cash. FDA's later criticism therefore reaches beyond approval odds. It changes the economic interpretation of the financing that now supports the company.

III. STATISTICAL RECONSTRUCTION

HOPE-3 failed under the analysis FDA reconstructed from the original plan

The decisive evidence appears in FDA's side-by-side reconstructions. The same randomized patients produce a negative pivotal study under the original absolute-change framework and nominally positive results under the sponsor's final implementation. The path between those outcomes comprises changes to endpoint scale, intercurrent-event rules, analysis population, covariates, and the cardiac model.

The original framework asked clinically direct questions

SAP 1.1 analyzed change from baseline in PUL 2.0 total points through a mixed model for repeated measures, commonly abbreviated MMRM. The model used all available post-baseline observations under a missing-at-random assumption and adjusted for prespecified variables. FDA identifies the month-12 treatment contrast as the primary comparison. The trial's sample-size calculation assumed a 1.5-point difference between groups, an effect expressed in the same units as the clinical instrument.[1]

The original cardiac analysis likewise used a longitudinal repeated-measures model for change in LVEF. Raw percentage-point change preserves clinical magnitude: a two-point treatment contrast means two additional points of ejection fraction under the model. The longitudinal method can incorporate partial follow-up without requiring every patient to have both a baseline and month-12 MRI.

FDA's reconstruction produced a PUL difference of +0.66 point, 95% confidence interval -0.45 to +1.77, p=.24. The interval includes no treatment effect and falls well short of establishing the 1.5-point difference used for power. For LVEF, the reconstructed treatment difference was -0.041 percentage point, 95% confidence interval -2.58 to +2.49, p=.97. The estimated cardiac difference was essentially zero.[1]

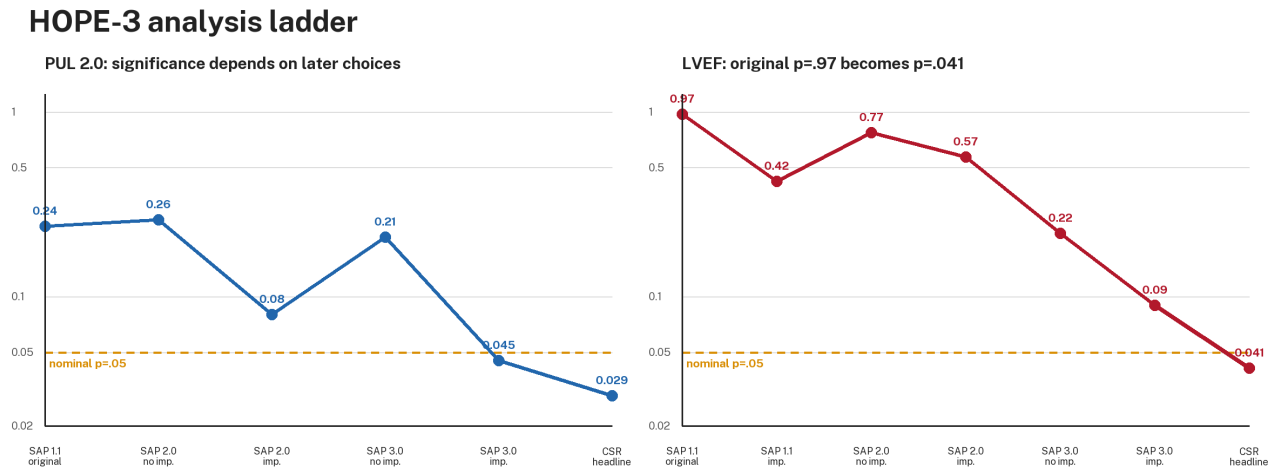


Figure 3. FDA-reported p-values across the HOPE-3 analytical sequence. The orange line marks nominal p=.05. Each point represents a different endpoint definition, missing-data rule, model, or final-report implementation. Source: FDA briefing Tables 7 and 9.

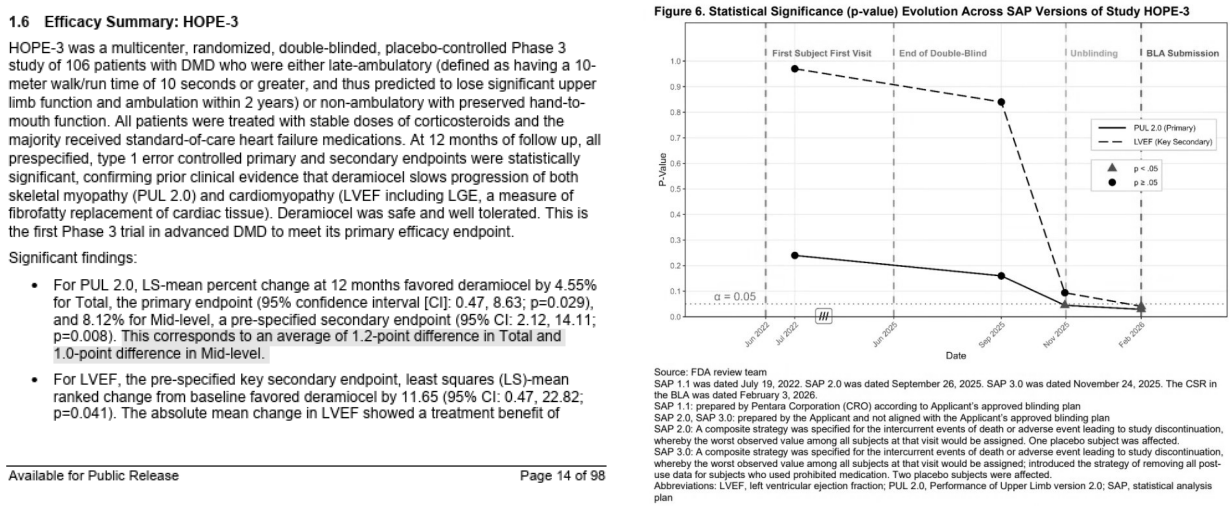
Endpoint	Original result	Intermediate results	Final applicant result
PUL 2.0	+0.66 point; p=.24	Percent models range from p=.26 to p=.045 depending on imputation and SAP version	+4.55 percentage points; p=.029
LVEF	-0.041 percentage point; p=.97	Absolute models p=.42-.77; rank models p=.22 and p=.09 before final interaction	+11.65 mean-rank units; p=.041

A conventional p-value measures how incompatible the observed data are with a no-effect model under a specified analytical procedure. It does not measure the probability that the drug works. The nominal .05 threshold also presumes that the procedure was selected independently of the observed data. HOPE-3's problem is therefore larger than two unfavorable

original numbers: significance appears only after the endpoint scale, intercurrent-event rules, analysis population, covariates, and cardiac model changed.

The sponsor's efficacy summary omitted the original failures

Capricor's BLA efficacy summary states that all prespecified, Type I-error-controlled primary and secondary endpoints were significant. It reports 4.55 percentage points for PUL and a mean-rank difference of 11.65 for LVEF. The summary does not disclose the +0.66-point, p=.24 PUL analysis or the -0.041-point, p=.97 LVEF analysis that FDA reconstructed from SAP 1.1. A reader relying on the sponsor's summary would have no reason to understand that ordinary versions of both endpoints had failed.[1][2]



1.6 Efficacy Summary: HOPE-3

HOPE-3 was a multicenter, randomized, double-blinded, placebo-controlled Phase 3 study of 106 patients with DMD who were either late-ambulatory (defined as having a 10-meter walk/run time of 10 seconds or greater, and thus predicted to lose significant upper limb function and ambulation within 2 years) or non-ambulatory with preserved hand-to-mouth function. All patients were treated with stable doses of corticosteroids and the majority received standard-of-care heart failure medications. At 12 months of follow up, all prespecified, type 1 error controlled primary and secondary endpoints were statistically significant, confirming prior clinical evidence that deramiocel slows progression of both skeletal myopathy (PUL 2.0) and cardiomyopathy (LVEF including LGE, a measure of fibrofatty replacement of cardiac tissue). Deramiocel was safe and well tolerated. This is the first Phase 3 trial in advanced DMD to meet its primary efficacy endpoint.

Significant findings:

- For PUL 2.0, LS-mean percent change at 12 months favored deramiocel by 4.55% for Total, the primary endpoint (95% confidence interval [CI]: 0.47, 8.63; p=0.029), and 8.12% for Mid-level, a pre-specified secondary endpoint (95% CI: 2.12, 14.11; p=0.008). This corresponds to an average of 1.2-point difference in Total and 1.0-point difference in Mid-level.
- For LVEF, the pre-specified key secondary endpoint, least squares (LS)-mean ranked change from baseline favored deramiocel by 11.65 (95% CI: 0.47, 22.82; p=0.041). The absolute mean change in LVEF showed a treatment benefit of

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Figure 6. Statistical Significance (p-value) Evolution Across SAP Versions of Study HOPE-3

Source: FDA review team
SAP 1.1 was dated July 19, 2022. SAP 2.0 was dated September 26, 2025. SAP 3.0 was dated November 24, 2025. The CSR in the BLA was dated February 3, 2026.
SAP 1.1: prepared by Pentara Corporation (CRO) according to Applicant's approved blinding plan
SAP 2.0, SAP 3.0: prepared by the Applicant and not aligned with the Applicant's approved blinding plan
SAP 2.0: A composite strategy was specified for the intercurrent events of death or adverse event leading to study discontinuation, whereby the worst observed value among all subjects at that visit would be assigned. One placebo subject was affected.
SAP 3.0: A composite strategy was specified for the intercurrent events of death or adverse event leading to study discontinuation, whereby the worst observed value among all subjects at that visit would be assigned; introduced the strategy of removing all post-use data for subjects who used prohibited medication. Two placebo subjects were affected.
Abbreviations: LVEF, left ventricular ejection fraction; PUL 2.0, Performance of Upper Limb version 2.0; SAP, statistical analysis plan

Figure 4. Capricor's BLA efficacy summary and FDA's chronology of statistical significance across SAP versions. The sponsor presents a uniformly positive package; FDA shows the primary and key secondary p-values declining only after study completion. Sources: Capricor BLA summary and FDA review Figure 6.

The two documents are describing the same trial from different positions in the analytical chronology. Capricor treats the final analyses as the operative prespecified tests because SAP 3.0 preceded formal unblinding. FDA treats analyses defined after the double-blind period as post hoc for confirmatory purposes. The observed p-value progression gives the regulatory disagreement practical force: the methods selected later are also the methods that produce success.

III. STATISTICAL RECONSTRUCTION

Percent change altered the primary endpoint and the weight assigned to each patient

Changing PUL from point change to percent change did more than relabel the vertical axis. It changed the estimand, the clinical unit, and the influence of patients with different baseline scores.

Absolute points and percentages answer different questions

Under absolute change, a two-point decline contributes two points regardless of baseline. Under percent change, the same two-point decline equals 20% for a patient beginning at 10 and 5% for a patient beginning at 40. Patients with lower starting scores can therefore exert greater leverage on the percentage endpoint. Baseline adjustment within an absolute-change model can account for prognostic differences without redefining the outcome itself.

Capricor says pooled blinded data showed heteroscedasticity, meaning the variance of change differed across baseline levels. Percent scaling can be a legitimate response to proportional variability. FDA replies that baseline heterogeneity was known when the study was designed, baseline score was already included as a covariate, the trial was powered in PUL points, and percent PUL lacks an established clinical interpretation. FDA also found no persuasive blinded analysis plan contemporaneously demonstrating that percent change solved the alleged problem without introducing new weighting.[1][2]

The numerical consequence was immediate. FDA's SAP-1.1 reconstruction was +0.66 point, p=.24. The sponsor's later absolute-change sensitivity analysis was +1.08 points, p=.0503. The preferred percent-change model was +4.55 percentage points, p=.029. Rounding 1.08 to 1.1 explains one apparent discrepancy in public slides; an approximate 1.2-point clinical

translation and the 4.55-percentage-point model estimate refer to different calculations. Rounding, translation, and endpoint scale account for the inconsistent public figures.

Capricor, Inc. Cellular, Tissue, and Gene Therapy Advisory Committee

Table 9: Performance of the Upper Limb 2.0 Total Score — Month 12 Treatment Difference by SAP Version

MMRM; ITT population (N=54 deramiocel, N=52 placebo); deramiocel minus placebo.

Analysis metric	Estimate, D − P	95% CI	P value
Prespecified primary — CSR / SAP v3.0			
Percent change (PCHG)	4.55	0.47 to 8.63	0.0290
Prespecified sensitivity — SAP v3.0			
Absolute change (CHG)	1.08	0.00 to 2.16	0.0503
Supportive — earlier SAP versions			
PCHG (v2.0)	4.85	0.72 to 8.99	0.0219
CHG (v2.0)	1.14	0.04 to 2.23	0.0416
CHG (v1.7)	1.12	−0.01 to 2.25	0.0522

v1.7 reports change from baseline (CHG): Kenward-Roger denominator df, slow-progressor interaction terms, baseline-by-visit, least-squares means evaluated at slowprgn=0. **This was last SAP version that was based directly on FDA feedback on v1.6.**
v2.0 reports percentage change from baseline (PCHG, primary) and CHG (sensitivity): ARH(1) covariance, slow-progressor interaction terms, least-squares means at slowprgn=0.
v3.0 reports PCHG (prespecified primary) and CHG (sensitivity): ARH(1) covariance, slow-progressor as main effect only, unconditioned; covariance fallback per attempt primary — CSH — CS.
SITEGR1 and SLOWPRGN use the locked ADaM (v3.0) derivations; v1.7 and v2.0 rows differ only in model structure. Locked ADaM 20260129_Final_DB; ANL01FL=Y; APHASE=BLINDED TREATMENT.
Abbreviations: ARH(1), heterogeneous first-order autoregressive covariance; CHG, change from baseline; CI, confidence interval; CS/CSH, compound symmetry/heterogeneous compound symmetry; D − P, deramiocel minus placebo; MMRM, mixed model for repeated measures; PCHG, percentage change from baseline; PUL 2.0, Performance of the Upper Limb module 2.0; SAP, statistical analysis plan.

Figure 5. Public comparison of Capricor's 1.08, 1.1, approximately 1.2, and 4.55 figures alongside the sponsor's exact SAP table. The figures arise from rounding, translation, and different endpoint scales. The exact absolute-change sensitivity result is p=.0503. Sources: Capricor advisory materials and FDA-released BLA excerpts.

The sharper disclosure issue concerns prominence. The December materials led with the scale that crossed the threshold and framed the relative difference as 54% slowing. The original point-scale analysis and the exact p=.0503 sensitivity result were not supplied to investors. The presentation conveyed convergence across methods when the underlying table showed threshold sensitivity.

Interim trajectories weakened the visual impression of a stable effect

FDA's absolute-score trajectory shows little separation at month 3, similar decline at month 6, a placebo advantage at month 9, and a deramiocel advantage at month 12. Capricor's investor figure presents percent change at baseline, month 6, and month 12, with the month-12 separation visually dominant. A 12-month primary endpoint does not require every interim visit to appear in a topline chart. The omitted visits nevertheless bear on consistency, because a disease-modifying effect that appears mainly at the final visit is more vulnerable to missing-data and model assumptions than a persistent separation across time.

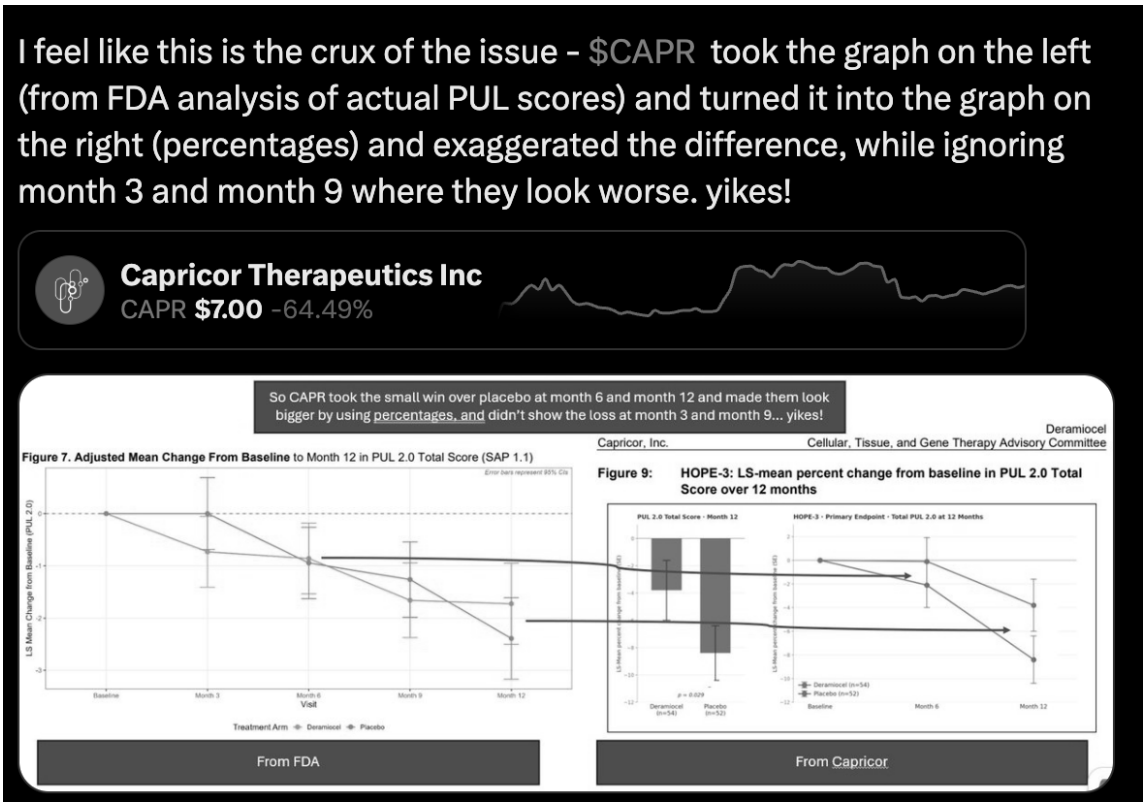


Figure 6. Composite comparison of FDA's adjusted mean absolute PUL trajectory and Capricor's percent-change presentation. The underlying panels come from the FDA review and Capricor advisory materials. Month 12 was the prespecified decision point; the fuller trajectory shows that separation was not sustained across interim visits.

The visual comparison also illustrates why relative and absolute scales should remain separate in investor communication. The percentage graph makes a modest absolute difference appear wider because each patient's change is divided by baseline and the y-axis is expressed in percent. Capricor selected the formulation under which the treatment comparison looks strongest.

III. STATISTICAL RECONSTRUCTION

Two placebo observations moved the PUL result across .05

The cleanest robustness test in the FDA package holds the percent-change model largely constant and changes the treatment of two placebo patients. The result moves from p=.21 to p=.045.

The adverse-event discontinuation rule assigned the worst observed outcome

One placebo patient discontinued after an adverse event. Under the original missing-at-random approach, the repeated-measures model used observed data without assigning a deterministic worst outcome at every later visit. The composite strategy adopted in later SAPs assigned the worst PUL value observed among all subjects at the affected visits. Such a strategy can address the possibility that discontinuation reflects poor outcome. It also applies a severe assumption to a single observation in a 106-person trial.[1]

Observed improvement after prohibited medication was removed

A second placebo patient used a prohibited medication and subsequently improved. SAP 3.0's composite strategy removed post-use observations and assigned the worst observed value. The rule affected two placebo patients and no deramiocel patient in that category. Three deramiocel consent withdrawals were handled as missing at random. The asymmetry follows the chosen intercurrent-event categories; statistical impact depends on those categories and requires direct sensitivity analysis.[1]

PUL analysis	Treatment difference	p-value	Incremental choice
SAP 3.0 structure without new imputation	+2.53 percentage points	.21	Observed-data style treatment retained
SAP 3.0 with composite handling	+4.16 percentage points	.045	Two placebo observations assigned or removed under new rules
CSR applicant analysis	+4.55 percentage points	.029	Slow-progressor term retained in final model

The inference does not depend on guessing intent. With the later percent endpoint held in place, the result fails comfortably when the two placebo observations remain under the prior approach and crosses nominal significance when the composite rules are applied. The final covariate moves it further below .05. A confirmatory result intended to support approval should remain persuasive under reasonable treatments of two observations; HOPE-3 does not.

The slow-progressor term survived a removal rule triggered by its smallest cell

The slow-progressor term first appeared in SAP 1.7 dated 6 December 2023, before the randomized period ended. That chronology matters because the term itself was not invented after follow-up. The final implementation presents a different problem. Five placebo patients and one deramiocel patient met the category. FDA says the sponsor's own minimum-cell rule required removal when a cell contained fewer than two patients. The treated slow-progressor cell contained one patient, yet the clinical study report retained the term.[1]

A prognostic covariate can improve precision when prespecified, stable, and supported by adequate data. An interaction or subgroup term built on a one-patient cell is structurally fragile. Retaining it after the stated removal rule is triggered makes the final p=.029 result depend on a model term whose implementation conflicts with the sponsor's own written criterion.

The combined sequence is dispositive for the primary endpoint. Percent change alone did not create significance. Percent change plus composite handling produced a marginal p=.045. The clinical study report then retained the slow-progressor term and reported p=.029. The company's phrase "met regardless of analysis" compresses materially different answers into a single claim.

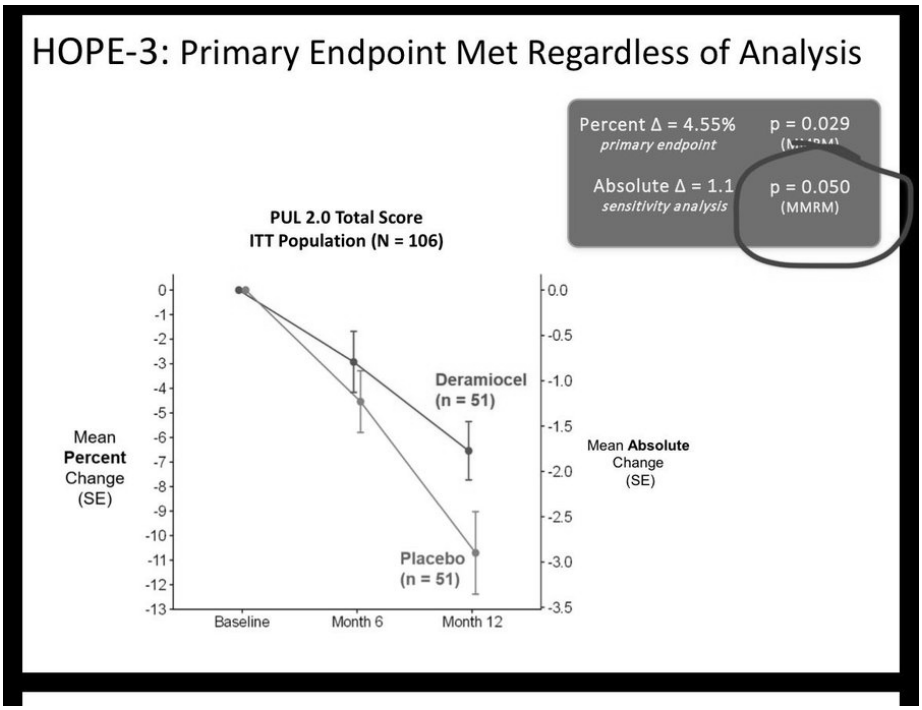


Figure 7. Capricor's advisory slide states that the primary endpoint was met regardless of analysis and rounds the absolute sensitivity result to p=.050. The underlying table reports p=.0503, while FDA's original reconstruction reports p=.24. Source: Capricor advisory-committee presentation.

III. STATISTICAL RECONSTRUCTION

The cardiac endpoint became positive only after it became a rank

The LVEF result travels farther from the original clinical question than the PUL result. Raw change showed no signal. The final claim emerged after converting LVEF changes to ranks, narrowing the analysis to complete baseline and month-12 scans, adding imputation, and adding a model interaction in the clinical study report.

Absolute-change models remained negative

FDA's original repeated-measures analysis estimated -0.041 percentage point, p=.97. An imputed version was p=.42. Later absolute-change variants were p=.77 and p=.57. None approached nominal significance. The absence of a raw-scale result means the sponsor cannot point to a stable two- or three-percentage-point effect that survives ordinary modeling choices.[1]

SAP 3.0 replaced the raw endpoint with a rank of month-12 change. Ranking orders patients from worse to better and tests whether treated patients tend to occupy more favorable positions. It can reduce sensitivity to extreme values and non-normal distributions. It also discards the original unit of clinical magnitude. A difference of 11.65 mean-rank units is not an 11.65-percentage-point improvement in ejection fraction.

The rank analysis excluded 23 randomized patients

The longitudinal original analysis used available repeated measurements. The ranked month-12 analysis required both baseline and month-12 LVEF, leaving 39 deramiocel and 44 placebo patients. Twenty-three of 106 randomized patients, or 21.7%, were absent. Missingness at that scale enters the treatment estimate materially.

FDA compared the ranked population with the original repeated-measures population and identified six additional exclusions with directional consequences. One excluded placebo patient had improved by 9.93 LVEF points at month 6. Five excluded deramiocel patients included three with declines of approximately 5, 5, and 15 points. Requiring a month-12 scan removed favorable placebo experience and unfavorable treated experience described by FDA, mechanically improving the comparative rank distribution.[1]

LVEF analysis	Population / method	p-value	Interpretation
SAP 1.1 original	Longitudinal absolute change	.97	No original cardiac signal
SAP 1.1 with imputation	Absolute change	.42	Negative
SAP 2.0 variants	Absolute change	.77 / .57	Negative
SAP 3.0 without imputation	Month-12 ranks	.22	Negative after endpoint transformation
SAP 3.0 with imputation	Month-12 ranks	.09	Closer to threshold
CSR applicant analysis	Ranks plus age-by-baseline interaction	.041	Only nominally significant implementation

The final interaction was absent from SAP 3.0

SAP 3.0's ranked analysis with imputation produced p=.09. The clinical study report added an age-by-baseline-LVEF interaction and reported p=.041. Interactions can model genuine effect modification or baseline-dependent trajectories. In a small dataset, they can also fit idiosyncratic imbalances and reduce residual variance. A term added after formal unblinding cannot carry the same evidentiary status as a prospectively specified factor.

The treatment group began with lower mean LVEF: 55.3% versus 59.3% on placebo. Five treated patients and no placebo patients had baseline LVEF below 45%. Lower baselines create more room for apparent improvement and regression toward the mean. A stable prespecified adjustment can address that imbalance. The late interaction made the result dependent on the relationship among age, baseline, and outcome after the data were available.

Table 5. Baseline Population Characteristics, Study HOPE-3

Characteristic	Placebo (N=52)	Deramiocel (N=54)
Baseline PUL 2.0 entry item score, n (%)	-	-
2	2 (3.8)	2 (3.7)
3	26 (50.0)	24 (44.4)
4	8 (15.4)	7 (13.0)
5	15 (28.8)	18 (33.3)
6	1 (1.9)	3 (5.6)
Baseline PUL 2.0 entry item score group, n (%)	-	-
2, 3	28 (53.8)	26 (48.1)
4, 5, 6	24 (46.2)	28 (51.9)
Baseline PUL 2.0 Total Score	-	-
Mean (SD)	26.5 (6.70)	27.6 (7.36)
Median (min, max)	25.3 (15.7, 39.7)	27.5 (12.7, 39.0)
DMD mutation type, n (%)	-	-
Deletion	33 (63.5)	34 (63.0)
Non-deletion[a]	19 (36.5)	20 (37.0)
"Slow progressor" indicator for PUL outcomes, n (%)[b]	-	-
Not "slow progressor"	47 (90.4)	53 (98.1)
"Slow progressor"	5 (9.6)	1 (1.9)
Baseline LVEF (%)	-	-
n	46	45
Mean (SD)	59.3 (6.11)	55.3 (7.74)
Median (min, max)	59.3 (47.4, 74.0)	55.9 (36.5, 71.1)
Baseline LVEF Group, n (%)	-	-
<45%	0 (0)	5 (9.3)
≥45%	46 (88.5)	40 (74.1)
Missing	6 (11.5)	9 (16.7)

Figure 8. FDA baseline table. The deramiocel group began with lower mean LVEF, contained all five patients below 45%, and had one slow progressor versus five on placebo. Source: FDA review Table 5.

III. STATISTICAL RECONSTRUCTION

Cardiac measurement variability exceeded the translated treatment effect

The analysis dispute sits on top of an imaging process that could not execute its planned two-reader design. The resulting measurement uncertainty is large relative to the effect Capricor asks investors and FDA to accept.

The planned two-reader-plus-adjudication process was not followed

The MRI charter contemplated two independent central readers and a third-reader adjudication process for specified disagreements. Reader B's data were unavailable for 20 of 82 subjects in the efficacy dataset because of a data-transfer problem. The final efficacy analysis used Reader A. For the 62 patients with paired reads, FDA reported mean absolute Reader A/Reader B differences of 2.99 LVEF percentage points at screening and 3.20 points at month 12.[1][2]

Capricor translated its 11.65 mean-rank difference to approximately 2.37 LVEF percentage points. The average absolute disagreement between the two intended readers at month 12 was therefore larger than the claimed translated effect. Centralized reading can improve consistency, and the disagreement may be nondifferential across treatment arms. A measurement discrepancy larger than the claimed effect nevertheless limits confidence in a physiological interpretation.

The proposed cardiomyopathy population was broader than the ordinary clinical label

Capricor described more than three quarters of HOPE-3 patients as having DMD cardiomyopathy. FDA examined the definition and found that it could be satisfied through selected medical-history terms, screening LVEF at or below 55%, or any positive LGE segment. Medical-history diagnoses could not be uniformly verified, LVEF from 45% to 55% can fall within normal or near-normal ranges depending on age and method, and evaluable LGE existed for only 27 of 106 randomized patients.[1]

Mean baseline LVEF was normal in both groups, and only five patients had LVEF below 45%, all in the deramiocel arm. The trial may contain patients at genuine early cardiac risk, and DMD cardiomyopathy can precede severe LVEF decline. The broad label nevertheless overstates the amount of independent evidence generated in a population with established systolic impairment.

The sponsor's defenses explain preferences without establishing robustness

Capricor offers a coherent account of its decisions. SAP 1.1 was unsigned and incomplete; subsequent versions incorporated regulatory discussion, advances from HOPE-2, and blinded assessment of pooled data; percent change addressed baseline-dependent variance; ranks protected against outliers; SAP 3.0 preceded formal unblinding; the MRI readers were independent; and multiple estimates favored treatment. Severe unmet need and the consistency of direction across skeletal and cardiac measures, the company argues, should allow FDA to consider the totality.[2][5]

The defense does not produce FDA concurrence for the final plan. Submission of a document or the absence of immediate objection is different from affirmative agreement on a pivotal estimand. The defense also leaves the numerical ladder intact. Percent PUL remained negative without the new placebo handling. Ranked LVEF remained negative without imputation and the later interaction. The final clinical study report departed from SAP 3.0. Imaging variability exceeded the translated cardiac effect. Directionally favorable point estimates cannot convert this dependence into substantial evidence.

FDA's reconstruction shows statistical significance emerging only under the final analytical implementation.

IV. BIOLOGY AND CLINICAL CONTEXT

Mechanism and prior studies do not independently confirm HOPE-3

Deramiocel has a plausible paracrine hypothesis, published preclinical work, and suggestive earlier clinical observations. None supplies the independent confirmation required to overcome an analysis-dependent pivotal trial.

Systemic delivery relies on indirect signaling

Cardiosphere-derived cells secrete extracellular vesicles and other factors that may modulate inflammation, fibrosis, and repair. DMD provides a rational biological target for such effects because chronic injury and fibrotic replacement contribute to functional decline beyond the primary dystrophin defect. Paracrine signaling does not permanently repair the genome, so any benefit would require repeated dosing.

Intravenous administration distributes cells predominantly outside the heart, and FDA cites cardiac retention below 1%. The treatment thesis therefore depends on circulating or tissue-mediated signals reaching skeletal and cardiac muscle at effective concentrations. That dependence raises potency questions: a release assay must measure a product attribute connected to clinical activity, donor and lot variability must remain controlled, and animal dose-response must support the human regimen.[1][15]

The pivotal animal evidence used a high single dose under limited conditions

FDA's review of the mdx mouse work notes that the key study used analogous murine cardiosphere-derived cells at a single dose corresponding to approximately 5.83 times the human-equivalent exposure. The study was non-GLP, used saline without a full procedural control, and did not establish an adequate dose-response relationship. Such experiments can support biological plausibility; they cannot determine whether repeated 150-million-cell human infusions produce a clinically meaningful effect.[1][13]

Later animal and extracellular-vesicle studies extend the mechanistic literature, while donor-dependent variability in cell potency remains documented. The exosome program may eventually produce a more defined product. It remains early, unapproved, and dependent on many of the same assumptions about cargo, potency, biodistribution, and human translation. We assign it no value.[14][15]

HOPE-Duchenne generated hypotheses in 25 patients

HOPE-Duchenne randomized approximately 25 patients and delivered cells by an intracoronary route, which differs from HOPE-3's systemic infusion. The study reported exploratory cardiac MRI and scar findings. Its size, route, multiple measures, and exploratory nature prevent it from serving as a confirmatory efficacy study for the current regimen.[31]

HOPE-2 was too small and analytically disputed to confirm HOPE-3

HOPE-2 enrolled roughly 20 patients in its randomized phase. Capricor emphasizes upper-limb and cardiac signals, including rank-based and later analyses, followed by persistence in an open-label extension. FDA concluded that the prespecified randomized analyses did not establish effectiveness and that post-unblinding cardiac work could not supply confirmation. That conclusion produced the July 2025 CRL.[1][2][32]

The open-label extension follows treated participants without a concurrent randomized control. Attrition, survivor selection, changes in standard care, and natural-history matching complicate causal inference. Long follow-up can support durability after a credible randomized effect has been established; it cannot manufacture the missing randomized comparison.

ALLSTAR supplies only remote platform context

The ALLSTAR trial tested cardiosphere-derived cells in patients with recent myocardial infarction through an intracoronary route and failed its primary scar-size endpoint. The disease, route, dose context, and clinical objective differ substantially from DMD. It is weak contextual evidence that platform biology has not translated consistently across indications, and it should not be treated as a direct deramiocel efficacy test.[33]

Program	Design and setting	Result relevant to this report	Evidentiary weight
HOPE-Duchenne	About 25 DMD patients; intracoronary cells	Exploratory MRI and scar signals	Hypothesis-generating
HOPE-2	About 20 randomized DMD patients; IV dosing	Sponsor cites PUL/cardiac signals; FDA rejected prespecified package as substantial evidence	Insufficient independent confirmation
HOPE-2 OLE	Open-label extension	Long-term persistence claims without concurrent randomized control	Supportive only
HOPE-3	106 randomized DMD patients; IV dosing	Original PUL and LVEF analyses negative; final analyses positive	Decisive disputed dataset
ALLSTAR	Post-MI cardiac disease; intracoronary route	Primary scar-size endpoint failed	Remote platform context

Safety creates a recurring burden that requires proven benefit

HOPE-3 does not reveal a catastrophic organ-toxicity or malignancy pattern. Six serious adverse events occurred during the blinded period, five on placebo and one on deramiocel. The integrated sponsor database describes most infusion and hypersensitivity events as transient and manageable with premedication, monitoring, and treatment.[1][2]

The burden is still material. Hypersensitivity occurred in 22 of 53 deramiocel recipients with post-baseline exposure, or 41.5%, compared with 8 of 52 placebo recipients, or 15.4%. Across the broader treated database, the sponsor reports grouped infusion or hypersensitivity events in 48 of 125 patients, or 38.4%. Repeated quarterly infusions impose cumulative clinic time, premedication, monitoring, reaction management, and the possibility that adverse events reveal assignment.

A recurring manageable risk can support approval when benefit is demonstrated. The original HOPE-3 framework failed to establish that benefit, leaving the safety burden without an offsetting efficacy case and contributing to FDA staff's unfavorable benefit-risk conclusion.

V. REGULATORY DISPOSITION

The current application lacks the evidence required for approval

FDA staff framed the deramiocel dispute as a failure of substantial evidence. That formulation matters. A manufacturing deficiency can sometimes be corrected with a new assay, inspection, or validation package. A failed efficacy case ordinarily requires new clinical evidence. The difference determines both time and capital.

FDA staff rejected the inferential chain supporting both endpoints

The review team concluded that HOPE-3 did not demonstrate a statistically significant or clinically meaningful improvement on the prespecified primary PUL endpoint or the prespecified key secondary LVEF endpoint. It treated the later analyses as post hoc because they were specified after study completion, found the results sensitive to endpoint and missing-data choices, and declined to use HOPE-2 as independent confirmation. In the staff's assessment, the absence of established benefit left the recurring infusion and hypersensitivity burden without a favorable clinical counterweight.[1]

Staff briefing documents precede the committee vote and do not constitute FDA's final action. Review divisions can modify positions after advisory discussion, internal review, sponsor submissions, or senior-level deliberation. The strength of this memorandum lies in its specificity. FDA supplied the original estimates, reconstructed each analytical step, identified the observations that changed under the later rules, and explained how the clinical study report departed from the final SAP. A favorable decision would require the Agency to accept a package its own reviewers have described as analysis-dependent and insufficient.

Capricor's formal-blinding defense does not cure post-completion analysis

Capricor says the operative changes were developed from blinded pooled data and scientific considerations, SAP 3.0 preceded formal unblinding, and FDA dialogue informed the program. Its 27 July response calls SAP 1.1 incomplete and says the final analyses were prospectively specified before the database was unlocked. The company further argues that percent change accommodates heterogeneity and that ranks protect the cardiac analysis from non-normality.[2][5]

Formal concealment of treatment codes lowers the risk of direct outcome selection. It cannot make an analysis prospective after every 12-month observation has been collected. Blinded pooled data can expose variance, ceiling effects, dropout timing, medication use, and the distributional consequences of a candidate endpoint. Operational personnel can also infer assignment imperfectly from adverse events. Hypersensitivity occurred in 41.5% of deramiocel patients and 15.4% of placebo patients in HOPE-3. FDA also notes that programming and biostatistical work moved in-house during the trial outside the approved blinding plan. The public record does not establish treatment-code access; it establishes conditions under which analytical discretion remained consequential despite formal blinding.[1]

The advisory committee influences FDA without binding it

The Cellular, Tissue, and Gene Therapies Advisory Committee will consider whether the application supplies substantial evidence. Its vote is public, influential, and nonbinding. A study of human-drug advisory meetings from 2010 through 2021 found that FDA's one-year action aligned with committee recommendations in roughly 88% of reviewed cases. Following negative votes, 58 of 66 products were not approved within one year. The historical rate cannot decide an individual BLA, although it shows how unusual a prompt approval becomes after a decisively adverse vote.[6][25]

We expect the committee to reject the proposition that HOPE-3 supplies substantial evidence and expect FDA to issue another Complete Response Letter by or around the 22 August target date. A favorable committee vote would increase approval odds and squeeze risk. A favorable FDA decision would restore commercial optionality.

A second CRL points toward another randomized study

The staff memorandum attacks the pivotal evidence itself. A durable remedy would require a new protocol agreed with FDA, a final SAP completed before informative outcome data accumulate, independent statistical execution, reliable cardiac imaging, and enough patients to preserve power under realistic dropout and missing-data assumptions. The treatment period alone is 12 months. Protocol negotiation, site activation, enrollment in a rare disease, follow-up, database cleaning, analysis, BLA preparation, and a new review imply a multi-year path.

The cost extends beyond the trial invoice. Capricor would have to manufacture repeated doses, maintain quality systems and staff, support existing long-term follow-up, defend litigation, manage the Nippon dispute, and preserve corporate infrastructure until another readout. Management's 2026 program-spending guide of $100-$125 million for deramiocel plus $7-$10 million for exosomes was issued before an explicit new pivotal program. A re-trial would therefore convert today's cash support into future dilution or a shrinking liquidation value.[7]

Relevant precedents required credible new evidence after analytical failure

Product	Regulatory record	Read-through for deramiocel
NurOwn / BrainStorm	ALS Phase 3 missed primary and secondary endpoints. The 2023 committee voted 17-1-1 against substantial evidence; the sponsor withdrew the BLA and pursued another study.	Closest process analogue among cell therapies: severe disease and post hoc arguments did not overcome a failed randomized package.
Ryoncil / Mesoblast	FDA approved remestemcel-L in 2024 after prior CRLs and additional work on clinical evidence, potency, and manufacturing.	A CRL can be cured. The precedent requires further evidence and product work; it does not validate the present HOPE-3 package.
Exondys 51 / Sarepta	Accelerated approval relied on increased dystrophin, a surrogate reasonably likely to predict benefit, with confirmatory obligations.	Demonstrates DMD flexibility under a distinct statutory route and molecular surrogate.
Elevidys / Sarepta	Accelerated gene-therapy approval relied on micro-dystrophin expression; indication and safety treatment later changed after postmarket events.	Shows both rare-disease flexibility and the continuing importance of benefit-risk after approval.
Deramiocel 2025 BLA	FDA issued a CRL after HOPE-2 and its extension failed to supply substantial evidence.	Same product, sponsor, review organization, and disagreement over later cardiac analyses. HOPE-3 was intended to cure this defect.

The precedent set cuts both ways. Ryoncil demonstrates that a cell therapy can survive repeated regulatory setbacks. Exondys and Elevidys demonstrate FDA's willingness to exercise flexibility in DMD. Their relevance ends where the evidentiary route diverges. Deramiocel seeks a direct clinical-effect claim from endpoints whose significance FDA says depends on post-completion methods. The closest internal precedent is Capricor's own 2025 CRL.

Competition lowers the value of a delayed salvage program

Competition determines the salvage value and commercial position remaining after the expected rejection. DMD treatment is moving through approved steroids and epigenetic therapy, mutation-specific exon skipping, and systemic gene therapy. Several investigational programs are entering or completing prospective pivotal studies. A multi-year deramiocel retrial would mature this landscape before Capricor could return to FDA.

Company / product	Status as of July 2026	Competitive relevance
Sarepta / ELEVIDYS	Approved for ambulatory patients age four and older under a revised indication with boxed safety warnings.	Major gene-therapy benchmark; limited direct overlap with older non-ambulatory HOPE-3 patients.
Sarepta / EXONDYS 51, VYONDYS 53, AMONDYS 45	Accelerated approvals for mutation-defined populations.	Mutation-specific competitors. AMONDYS 45 belongs to Sarepta, not Amgen.
NS Pharma / VILTEPSO	Approved exon-53 therapy.	Commercially relevant because NS Pharma is Capricor's disputed U.S. distributor.
Santhera / AGAMREE; Italfarmaco / DUVYZAT	Approved broad DMD therapies.	Raise the standard-of-care and reimbursement bar.
Dyne / z-rostudirsen	Phase 3 FORZETTO initiated May 2026.	Prospective targeted oligonucleotide competitor.
Solid Biosciences / SGT-003	Randomized blinded Phase 3 initiated May 2026.	Prospective micro-dystrophin program with an evidentiary design contrasting with HOPE-3's analysis dispute.
REGENXBIO / RGX-202	Company reported pivotal AFFINITY DUCHENNE data in May 2026.	Potential gene-therapy entrant; approval status remains distinct from company-reported results.
Amgen	No active DMD therapeutic program identified in current pipeline disclosures.	Search results commonly confuse Sarepta's AMONDYS 45 with Amgen.

VI. MANAGEMENT AND GOVERNANCE

Scientific credentials coexist with an unproven approval record

Linda Marbán's biography supplies relevant scientific training. The governance concern arises from the decisions made under her leadership: a definitive investor narrative built around fragile analyses, financing and compensation linked to the resulting share price, a commercial-scale operating posture before approval, and limited evidence of independent challenge at the point when statistical discretion mattered most.

Linda Marbán is a cardiac physiologist and biotechnology executive

The 2026 proxy states that Marbán earned a Ph.D. in cardiac physiology from Case Western Reserve University, completed postdoctoral work at Johns Hopkins, advanced to Research Assistant Professor in Pediatrics, worked at the Cleveland Clinic, and held senior operations and business-development roles at Excigen. She joined Capricor in 2005, became chief executive in 2010, and has served as a director since 2013. The company does not present her as a physician, and no M.D. is disclosed.[10]

Her training is directly relevant to cardiovascular biology. The public biography does not show prior leadership of an FDA-approved product or a commercial launch. Capricor's senior operating group combines a scientist-business developer, a finance executive, and a senior lawyer. The record therefore places unusual weight on the independence and authority of outside clinicians, statisticians, regulatory specialists, and directors. FDA's account of post-completion analysis changes and in-house programming raises the question of whether those controls constrained management's preferred interpretation.

Excigen provides a record of credible science without clinical translation

Before Capricor, Marbán spent 2003-2009 at Excigen, a gene-therapy venture associated with a biological pacemaker program. The underlying scientific work was real. Eduardo Marbán and colleagues published a 2002 Nature paper showing pacemaker-like activity after gene transfer in a research model, and contemporaneous reporting described a collaboration between Excigen and Genzyme Biosurgery. A 2008 scientific review still characterized biological pacing as proof of concept requiring additional work to become stable and reliable; a 2014 study reported activity in pigs.[18][19][20]

No FDA-approved product, marketed therapy, or attributable human ClinicalTrials.gov program emerged from the Excigen materials reviewed. Excigen left a record of promising cardiac biology without a validated human product. The same translational distance remains central to Capricor.

The technology originated in the laboratory of the CEO's spouse

Capricor was founded to commercialize cardiosphere-derived-cell work developed by Eduardo Marbán, M.D., Ph.D., Linda Marbán's spouse. The company licenses cell and exosome intellectual property from Cedars-Sinai Medical Center and holds negotiation rights for future work arising under Eduardo Marbán's direction. The licenses require institutional royalties and sublicense consideration. Current filings do not disclose direct royalty payments from Capricor to Eduardo Marbán.[8][10][21]

Founder-family relationships are common in academic biotechnology. They increase the importance of independent board review when scientific claims, licensing strategy, executive compensation, and capital allocation turn on a platform associated with the family. Executive Chairman Frank Litvack also receives $10,000 per month under a consulting agreement; Capricor paid $120,000 in 2025 and $30,000 in the first quarter of 2026.[7][8]

Compensation rewarded regulatory progress, financing, and the share price

Capricor's 2025 bonus framework included deramiocel regulatory and clinical progress, stock-price performance, and completion of a successful financing. The compensation committee awarded bonuses ranging from 25% to 90% of base salary and cited significant regulatory and clinical achievements, financing execution, and strong share-price performance. Marbán's reported 2025 compensation was $3.522 million, including $300,000 salary, $270,000 bonus, and $2.941 million of option grant-date value. CFO Anthony Bergmann received $1.671 million, and General Counsel Karen Krasney received $1.270 million.[10]

Stock-based compensation creates normal alignment in development-stage biotechnology. Tying rewards simultaneously to regulatory progress, financing, and market price also concentrates incentives around the communication of clinical success. The December release satisfied each category at once: it established a Phase 3 victory, multiplied the share price, and enabled the largest financing in the company's history.

On 24 March 2025, the company increased qualifying severance for Marbán, Bergmann, and Krasney from six to 12 months of salary. The grants and protections do not establish misconduct. They describe the incentives and downside protection surrounding the decisions at issue.[8][10]

Figure 12. Linda Marbán holding a Martin Shkreli cutout at a company gathering. Date and original publication context are unverified.

The image captures management's public posture toward short sellers. That posture is relevant because Capricor's FDA response emphasizes critics' reliance on old or incomplete plans while the regulator's tables focus on the numerical dependence of the final results.

VII. CAPITAL FORMATION AND INSIDER TRANSACTIONS

Capricor monetized the rerating before FDA accepted the evidence

The December financing is central to the short case because it transformed a contested clinical interpretation into lasting corporate resources. Shareholders purchased stock at $25 after being told that HOPE-3 had produced definitive evidence. The regulator later disclosed that the original analyses had failed and that the successful results depended on later analytical choices.

Liquidity is real; so is the burn

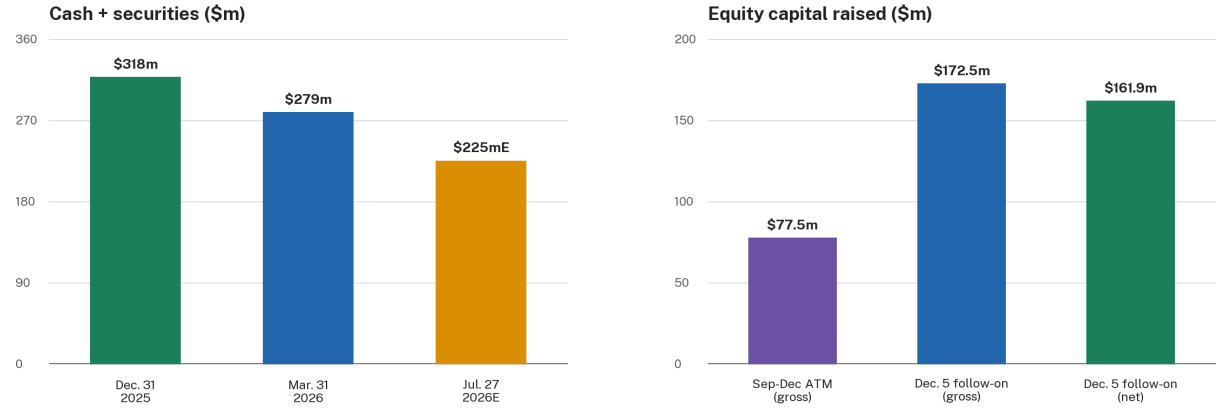


Figure 13. Reported cash and securities and the two principal late-2025 equity financings. July liquidity is estimated. Source: Capricor Form 10-Q, prospectus supplement, and analyst calculations.

Transaction	Shares	Average / offer price	Gross proceeds	Disclosed net or fees
Sep-Dec 2025 ATM	2.682m	$28.89	$77.5m	Approximately $2.4m aggregate fees
5 Dec 2025 follow-on	6.900m	$25.00	$172.5m	Approximately $161.9m net

Transaction	Shares	Average / offer price	Gross proceeds	Disclosed net or fees
Combined	9.582m	Mixed	$250.0m	Approximately $237.1m after disclosed fees

The ATM authorization preceded the topline announcement, and daily sale allocation is unavailable. Its $28.89 realized average places most of its economics in the post-release price regime. The follow-on presents no allocation ambiguity: Capricor priced it two days after the announcement and sold the full over-allotment at nearly four times the prior $6.36 close.[7][9]

Insider plans were adopted after the release and financing

Marbán, Bergmann, and Krasney adopted Rule 10b5-1 plans on 30 December 2025 for up to 250,000, 150,000, and 100,000 shares, respectively. Director Karimah Es Sabar adopted a plan on 27 December for 122,529 shares. The earliest reported sales occurred on 31 March 2026, after the applicable 90-day period and after the annual report was filed. A properly adopted and operated plan can provide an affirmative defense under Rule 10b5-1; a plan label in a Form 4 does not establish every legal condition.[8][10][11][42]

Bergmann and Krasney each sold 75,000 shares from March through June for calculated gross proceeds of approximately $2.305 million. Es Sabar sold 122,529 shares for approximately $3.756 million, exhausting the stated maximum of her plan. The aggregate for those three sellers was approximately $8.366 million. Capricor's proxy says the company inadvertently omitted Es Sabar's plan from the 2025 Form 10-K and corrected the disclosure in the first-quarter Form 10-Q.[10][11]

Common stock purchase or sale:

Transaction Date	Reported DateTime	Company	Symbol	Insider Relationship	Shares Traded	Average Price	Total Amount	Shares Owned	Filing
2026-06-25 Sale	2026-06-29 9:30 pm	CAPRICOR THERAPEUTICS INC.	CAPR	Krasney Karen EVP, GENERAL COUNSEL	24,100	$30.38	$732,158	61,808 (Direct)	View
2026-06-25 Sale	2026-06-29 9:30 pm	CAPRICOR THERAPEUTICS INC.	CAPR	Bergmann Anthony CHIEF FINANCIAL OFFICER	24,100	$30.38	$732,158	103,203 (Direct)	View
2026-06-22 Sale	2026-06-24 8:00 pm	CAPRICOR THERAPEUTICS INC.	CAPR	Krasney Karen EVP, GENERAL COUNSEL	900	$30	$27,000	141,669 (Direct)	View
2026-06-22 Sale	2026-06-24 8:00 pm	CAPRICOR THERAPEUTICS INC.	CAPR	Bergmann Anthony CHIEF FINANCIAL OFFICER	900	$30	$27,000	243,783 (Direct)	View
2026-05-01 Sale	2026-05-04 4:30 pm	CAPRICOR THERAPEUTICS INC.	CAPR	Krasney Karen EVP, GENERAL COUNSEL	25,000	$31.7	$792,548	86,808 (Direct)	View
2026-05-01 Sale	2026-05-04 4:30 pm	CAPRICOR THERAPEUTICS INC.	CAPR	Bergmann Anthony CHIEF FINANCIAL OFFICER	25,000	$31.7	$792,540	125,203 (Direct)	View
2026-04-02 Sale	2026-04-03 5:00 pm	CAPRICOR THERAPEUTICS INC.	CAPR	Sabar Karimah Es Director	7,529	$32	$240,928	161 (Direct)	View
2026-03-31 Sale	2026-04-01 8:00 pm	CAPRICOR THERAPEUTICS INC.	CAPR	Krasney Karen EVP, GENERAL COUNSEL	25,000	$30.12	$752,935	188,820 (Direct)	View
2026-03-31 Sale	2026-04-01 8:00 pm	CAPRICOR THERAPEUTICS INC.	CAPR	Sabar Karimah Es Director	115,000	$30.57	$3,515,468	53,735 (Direct)	View
2026-03-31 Sale	2026-04-01 8:00 pm	CAPRICOR THERAPEUTICS INC.	CAPR	Bergmann Anthony CHIEF FINANCIAL OFFICER	25,000	$30.13	$753,153	150,203 (Direct)	View

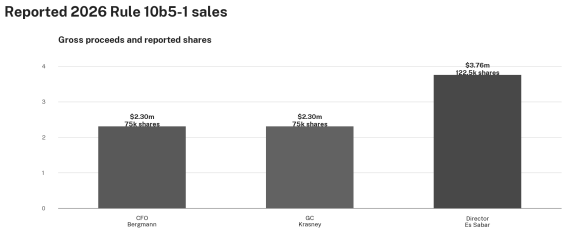


Figure 14. Third-party transaction aggregation and the reconciled Form 4 totals. The filings identify December 2025 Rule 10b5-1 plans; gross proceeds are calculated from reported shares and weighted-average prices.

The timing does not support a claim that sellers reacted to the July briefing document. The relevant date is plan adoption in late December, after the topline release and capital raise. Public filings do not disclose the plan instructions, the information available to each participant at adoption, subsequent modifications, or the internal understanding of the statistical package. The plans therefore narrow the inference available from execution while leaving the adoption-date disclosure question unresolved.

The cash balance is substantial and already declining

At 31 March 2026, Capricor reported $105.421 million of cash and equivalents and $173.188 million of marketable securities, for total liquidity of $278.864 million. It reported $249.452 million of working capital and $47.6 million of liabilities. Those liabilities included approximately $14.8 million of lease obligations, $14.5 million of accounts payable and accrued expenses, $12.0 million of deferred revenue, and a $6.3 million California Institute for Regenerative Medicine repayment obligation.[7]

First-quarter operating cash use was $29.255 million, compared with $6.434 million in the prior-year quarter. Property, equipment, leasehold-improvement, and construction spending added approximately $10.8 million. R&D; expense reached $27.377 million and G&A; expense reached $9.396 million. Professional services increased by approximately $2.49 million, or 741%, driven largely by legal, regulatory, and pre-commercial work. For full-year 2025, Capricor used $69.811 million of operating cash and reported a $105.044 million net loss.[7][8]

We estimate 27 July cash and marketable securities at $215-$235 million, with a $225 million midpoint. The bridge begins with the March balance and deducts second-quarter and July program spending plus the disclosed CIRM repayment. The estimate remains unaudited and will be replaced by the June-quarter filing. The range is sufficient for valuation analysis because management's future spending policy creates more uncertainty than a few million dollars of quarter-end timing.

A 171,000-square-foot facility expresses management's approval posture

On 9 July 2026, 18 days before the FDA briefing became public, Capricor signed a lease for approximately 171,000 rentable square feet in San Diego for headquarters, manufacturing cleanrooms, laboratories, and offices. Initial base rent is approximately $958,000 per month, rises 3% annually, and excludes taxes, insurance, maintenance, and operating expenses. Rent begins after a delayed commencement and abatement structure.[12]

The lease contains a decisive contingency. Either party may terminate within five business days after 31 December 2026 if deramiocel has not received FDA approval. Applying the disclosed rent, abatements, term, and escalator yields approximately $136.2 million of nominal base rent if the lease proceeds. That amount is not a current balance-sheet liability. The agreement nevertheless shows that management prepared for commercial-scale operations before the resubmitted BLA had survived FDA's efficacy review.

A timely termination after a CRL would protect much of the future rent. A waiver, missed deadline, negotiated exit, or approval followed by a failed launch would expose shareholders to a much larger fixed-cost structure. The existing 34,348-square-foot facility already carried approximately $14.8 million of lease liabilities at 31 March.

VIII. COMMERCIAL AND LITIGATION LIABILITIES

The approval case already contains a distribution dispute

Even an unexpected FDA approval would arrive into a commercial structure that Capricor itself describes as economically unworkable. The U.S. distributor is also the company's largest strategic shareholder, and the relationship is now the subject of rescission litigation.

Nippon Shinyaku is partner, distributor, shareholder, and defendant

Under the 2022 U.S. distribution agreement, Nippon Shinyaku and NS Pharma received exclusive U.S. distribution rights while Capricor retained development and manufacturing responsibility. Capricor received $30 million upfront and two $10 million milestones. The agreement provides for a potential $80 million approval milestone, additional sales milestones, and a 30%-50% share of product revenue. Japan rights produced a separate $12 million upfront payment and potential future economics.[7][10]

Nippon is also an approximately 11.9% beneficial owner. The proxy attributes 4.944 million common shares and 2.146 million warrant shares exercisable within 60 days to the shareholder. That ownership makes the breakdown more consequential than an ordinary vendor dispute: Capricor is litigating against the strategic counterparty that financed, owns, and was expected to commercialize the asset.[10]

Capricor filed its New Jersey complaint in May 2026 seeking rescission, declaratory relief authorizing alternative distribution, preliminary injunctive relief, restitution or disgorgement, and fees. It alleges that the pricing formula contains a fatal flaw under Medicare Part B average-sales-price reimbursement and that Nippon and NS Pharma failed to prepare adequately for launch. Key pricing terms are redacted. The public complaint records Capricor's allegations; the court has not adjudicated them.[16][17]

The economic consequence extends beyond legal fees. If Capricor prevails, it must replace or build the U.S. distribution, reimbursement, and commercial apparatus it had outsourced. If it loses, it remains bound to a channel it says cannot launch the product on viable terms. A CRL reduces the near-term launch problem while preserving defense costs, counterclaim risk, and damage to the strategic relationship. We therefore assign no value to the $80 million approval milestone or future sales milestones in the cash-only valuation.

Existing securities and derivative litigation predates the July briefing

The first-quarter Form 10-Q disclosed a putative securities class action filed on 17 July 2025 against Capricor and Linda Marbán, two derivative actions filed in August and November 2025 against directors, a Section 220 books-and-records demand, and former-employee claims raised in April 2026. The suits seek unspecified relief, and the company had not recorded a material loss contingency.[7]

The July briefing creates a plausible new pleading theory. Purchasers can argue that the December release and offering materials conveyed a clean pivotal success while omitting the failed original analyses and the late analytical dependence. A Rule 10b-5 claim would require proof of a material misstatement or omission, scienter, reliance, loss causation, and damages. A Securities Act claim traceable to the December offering can proceed under a different liability framework. Public records cannot establish knowledge or intent, although they supply a concrete basis for materiality analysis.[29][30]

Potential litigation cost is large enough to matter and too uncertain for false precision

A mechanical comparison between the $25 offering price and a $7 market price across 6.9 million shares equals $124.2 million. That arithmetic is not a damages forecast. Statutory offsets, tracing, sales before suit, loss causation, dismissal, insurance, indemnity, and settlement negotiation can reduce or eliminate issuer cash exposure. The figure demonstrates the size of the offering cohort relative to Capricor's remaining capital.

Published settlement data supply a scale reference and do not predict Capricor's outcome. Cornerstone reported a $17.3 million median securities-class-action settlement for 2025 and a $32.5 million median for Securities Act-only cases. NERA reported an $18 million median and $54 million average for the first half of 2026. Capricor's D&O; insurance limits, retentions, coverage positions, and indemnification cash flows are undisclosed.[26][27]

Case posture	Illustrative gross range	Economic condition
Early dismissal or insured defense	$2m-$8m	Claims fail early or consolidate; insurance absorbs much of defense.
Pleading survives and settlement follows	$10m-$35m	Materiality and causation remain live; negotiated resolution tracks small and mid-sized historical cases.
High-severity offering / Rule 10b-5 tail	$40m-$125m+	Traceable offering claims and market-loss claims survive with limited insurance recovery.
Nippon dispute	$3m-$10m fees plus commercial cost	Multi-year litigation, counterclaims, or replacement-channel build; revenue delay can exceed legal fees.

The valuation bridge reserves $8-$27 million for legal and partner costs depending on the scenario. That range reflects expected cash friction within an overall run-off estimate; it does not state an accounting liability or probable settlement.

IX. VALUATION

Deramiocel and the exosome pipeline receive zero value

The clinical conclusion determines the valuation method. Revenue forecasts, peak-sales multiples, approval milestones, and platform option value all depend on a reliable efficacy package. We remove them. The remaining question is how much corporate cash can reach shareholders after the company stops behaving like an operating biotechnology platform.

The diluted denominator is approximately 61.1 million shares at $7

Capricor reported 57.912 million basic shares outstanding on 11 May 2026. At 31 March, it had approximately 13.904 million options outstanding at a weighted-average exercise price of $8.90, of which 8.628 million were exercisable at an average $4.90. It also had approximately 3.346 million warrants at an average $5.70 and 15,000 restricted stock units. A simplified treasury-stock calculation at $7 produces approximately 61.1 million diluted shares.[7][10]

The calculation is approximate because public tables do not disclose the full strike distribution, vesting schedule, or the overlap between March awards and the May basic-share count. At the reference price, it avoids treating out-of-the-money instruments as current dilution and avoids adding every security at face value.

Gross cash overstates distributable value

Cash frame	Equity value	Per diluted share	Interpretation
Reported 31 Mar liquidity	$278.9m	$4.56	Historical cash, equivalents, and marketable securities before subsequent spending.
Estimated 27 Jul gross liquidity	$215m-$235m	$3.52-$3.85	Midpoint $225m; derived from March cash, program spend, capital expenditure, and CIRM repayment.
Static zero-asset recovery	$150m-$195m	$2.45-$3.19	Assumes rapid preservation after ordinary liabilities and modest closure friction.
Selected post-run-off range	$78m-$172m	$1.28-$2.82	Reflects obligations, continued operations, legal/partner costs, severance, and closure.
Base post-run-off value	$105m	$1.72	Our selected target using $225m liquidity and $120m total deductions.

The March balance sheet reported $47.6 million of liabilities: $14.5 million of payables and accruals, $14.8 million of lease liabilities, $12.0 million of deferred revenue, and $6.3 million owed to CIRM. The July liquidity estimate already deducts the expected CIRM repayment. Our $30 million base obligation line approximates payables, accruals, and existing lease liabilities. Deferred revenue is not assumed to create a dollar-for-dollar refund; related contract risk sits in the legal and partner reserve.

Zero-asset valuation: cash is consumed before it is recoverable

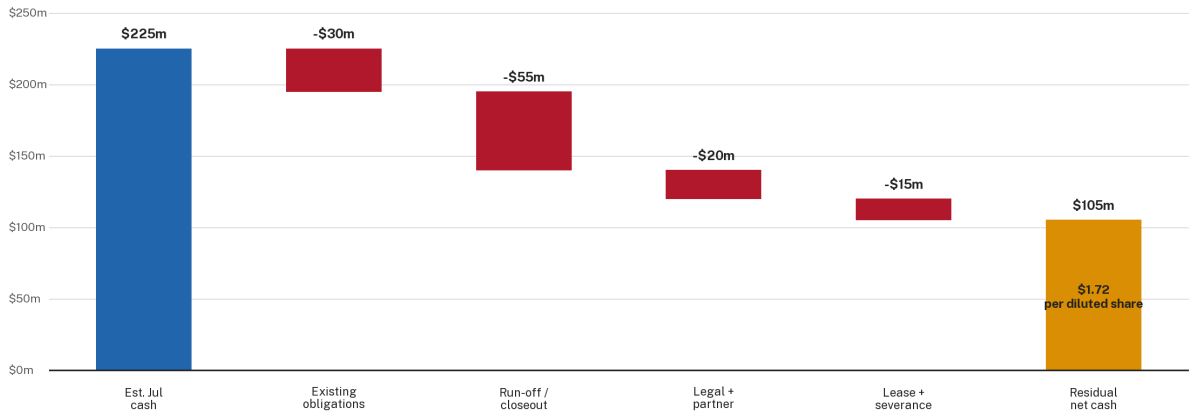


Figure 15. Base cash-only bridge. Deductions shown are analytical estimates. Source: Capricor filings and report calculations.

Bridge	Gross liquidity	Existing obligations	Run-off operations	Legal / partner	Closure	Residual	Per share
Delayed / low	$215m	$35m	$60m	$27m	$15m	$78m	$1.28
Base	$225m	$30m	$55m	$20m	$15m	$105m	$1.72
Disciplined / high	$235m	$25m	$25m	$8m	$5m	$172m	$2.82

The low case assumes management spends through a prolonged regulatory response, carries more operational infrastructure, and incurs substantial legal and partner cost before closing. The base case allows roughly $55 million for program and corporate run-off and $35 million for new legal, commercial, severance, and closure friction in addition to existing obligations. The high case requires immediate discipline, aggressive cost reduction, use of the new-lease termination right, and limited litigation leakage.

Continued development can drive cash-supported equity toward zero

Capricor's disclosed course is continued operation: a $100-$125 million deramiocel spending guide, $7-$10 million for exosomes, manufacturing expansion, inventory build, a 171,000-square-foot lease, and active litigation over commercialization rights. No liquidation, return-of-capital, or wind-down plan has been announced. A board pursuing another pivotal trial would preserve the corporate mission while consuming the principal asset supporting today's equity.

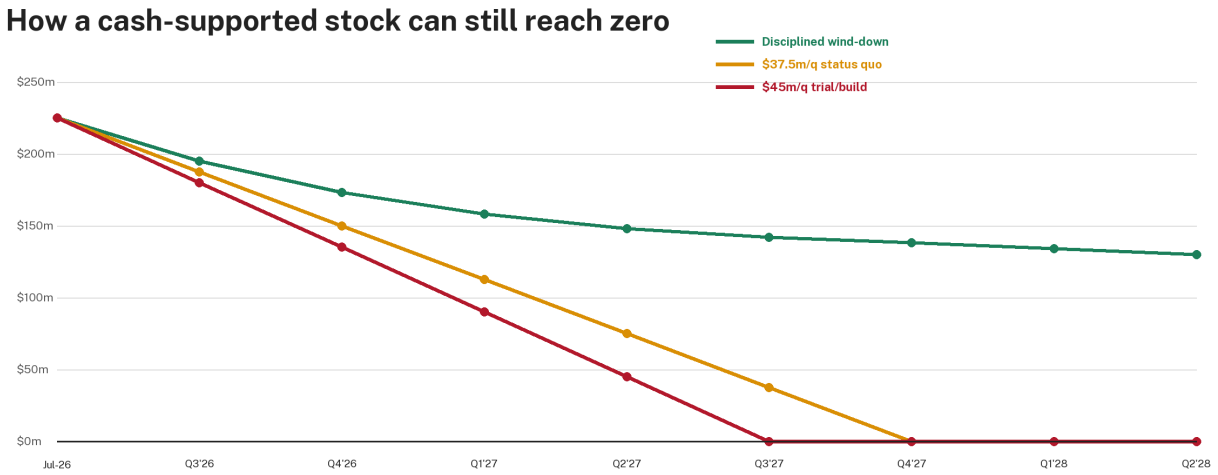


Figure 16. Illustrative liquidity paths beginning at $225 million under report assumptions.

At $37.5 million of quarterly cash use, gross liquidity reaches zero during 2027. A $45 million quarterly path reaches zero sooner. Management can extend the runway through layoffs, lease termination, program cuts, partnering, or financing. Equity financing preserves cash at the corporate level by transferring value through dilution. A $150 million raise at $4 requires 37.5 million new shares before fees, increasing the share count by more than 60% relative to the current diluted estimate. The same raise at $3 requires 50 million shares.

The selected target is $1.72 per share

At the $6.995 reference price, CAPR's basic market capitalization is approximately $405 million and diluted value is approximately $427 million. Estimated gross liquidity of $225 million leaves roughly $180-$200 million of market value attributable to future development, approval, platform value, or excess recovery above the base run-off. We assign zero to those claims and deduct the cost of reaching a distributable state.

Our $1.72 base target represents approximately 75% downside from the reference price. The $1.28-$2.82 range spans delayed consumption and disciplined preservation. Terminal equity reaches zero if management continues operating until the cash is exhausted, assumes new fixed commitments, loses material litigation, or finances at successively lower prices without producing an approvable asset.

A surprise approval would restore commercial optionality

A favorable 2026 FDA decision would restore commercial optionality, activate the $80 million U.S. approval milestone, accelerate manufacturing scale-up, and create immediate squeeze risk. Advisory votes, sponsor press releases, and partnership announcements can also move the stock sharply before final action. FDA's decision will establish whether the present evidence is sufficient.

The trade also carries path risk independent of fundamental value. Approximately 14.739 million shares were reported short at 30 June, roughly one quarter of the May basic count. Float definitions vary, borrow terms were not independently verified, and event-driven option positioning can dominate short-term price formation. A binary approval tail can produce losses exceeding the apparent downside even when the clinical criticism remains well founded.[28]

CONCLUSION

Capricor financed a success that FDA's analysis does not support

HOPE-3 was supposed to answer the deficiency that produced Capricor's first Complete Response Letter. Under the framework FDA reconstructed from the trial's design, it failed both principal questions. Upper-limb function produced p=.24, and cardiac function produced p=.97. The trial's apparent success emerged under later methods adopted after randomized follow-up had ended.

The statistical evolution was cumulative. PUL moved from points to percent change; later rules assigned or removed placebo outcomes; the final report retained a slow-progressor term despite the sponsor's minimum-cell rule. LVEF moved from raw change in a repeated-measures model to a rank analysis that excluded 23 randomized patients, then acquired imputation and an interaction beyond the final SAP. The MRI process lost the planned second-reader dataset, and the documented reader disagreement exceeded the sponsor's translated treatment effect. Each choice can be defended in isolation. Their joint product is a result that crosses .05 only under the preferred final implementation.

Capricor did not disclose that dependence when it told investors the evidence was strong and definitive. The stock rose from $6.36 to a $29.96 close, and the company raised approximately $250 million gross through a high-priced ATM and a $25 follow-on. Directors and executives adopted sale plans later in December; the CFO, general counsel, and one director subsequently sold approximately $8.366 million of stock. Management expanded manufacturing, signed a major facility lease, and paid compensation tied partly to regulatory progress, financing, and share performance before FDA accepted the pivotal evidence.

The cash raised in December now supplies the only value we recognize. It also finances the path that can destroy that value. Another trial would require years of operations, repeated-dose manufacturing, clinical execution, and new capital. The U.S. commercial partner is in court, existing securities litigation can expand, and the new facility creates a contingent fixed-cost tail. Capricor has announced no plan to distribute cash or discontinue development.

We expect another Complete Response Letter. Deramiocel receives zero value, and the exosome pipeline receives zero value. Estimated July gross liquidity is $215-$235 million. After existing obligations and the cost of run-off, our selected equity value is $105 million, or $1.72 per diluted share, with a $1.28-$2.82 range. Continued spending can carry the terminal value to zero. A surprise approval is the principal near-term squeeze risk.

VALUATION

Reference price: $6.995. Deramiocel value: $0. Exosome pipeline value: $0. Base post-run-off value: $1.72 per share. Selected range: $1.28-$2.82. Terminal value under continued cash consumption: $0.

APPENDIX A

Statistical reconciliation

PUL estimates refer to different scales and models

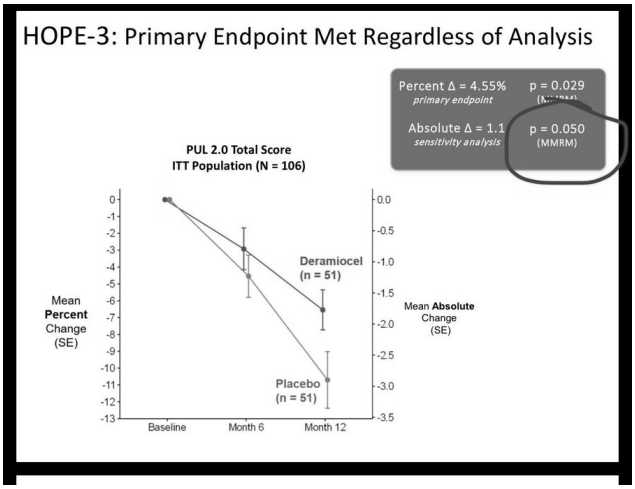
Reported figure	Analysis	Interpretation
0.66 point; p=.24	FDA SAP 1.1-style absolute-change MMRM	Original design and power framework; 95% CI -0.45 to 1.77.
1.08 points; p=.0503	SAP 3.0 absolute-change sensitivity	Later model and handling; lower confidence bound printed 0.00.
1.1 points	Rounded presentation of 1.08	Rounded form of the same estimate.
Approximately 1.2 points	Sponsor translation of preferred percent result	Approximate clinical translation that is not transparently reconciled to 1.08.
4.55 percentage points; p=.029	Preferred CSR percent-change analysis	Difference between modeled -3.86% active and -8.41% placebo decline.
54% slowing	4.55 divided by placebo decline of 8.41	Relative expression; it does not describe restoration of 54% of arm function.

LVEF estimates use raw units, ranks, and relative framing

Reported figure	Analysis	Interpretation
-0.041 percentage point; p=.97	Original SAP 1.1-style absolute-change MMRM	No treatment advantage under the original model.
11.65; p=.041	Difference in mean ranks under the CSR model	Mean-rank units; no direct LVEF-percentage-point magnitude.
Approximately 2.4 percentage points	Sponsor translation to the raw LVEF scale	Smaller than the 3.20-point mean absolute reader disagreement at month 12.
91% slowing	Relative comparison under preferred analysis	Sensitive to a small denominator and the selected analysis.

The clean PUL tipping sequence

The SAP-3-style percent model produced p=.21 using observed data. Applying the composite handling of two placebo observations moved the result to p=.045. Retaining the slow-progressor term in the final clinical study report moved the result to p=.029. The sequence isolates the analytical dependence without requiring an allegation that any underlying patient measurement was altered.



Capricor, Inc. Cellular, Tissue, and Gene Therapy Advisory Committee

Table 9: Performance of the Upper Limb 2.0 Total Score — Month 12 Treatment Difference by SAP Version

MMRM; ITT population (N=54 deramiocel, N=52 placebo); deramiocel minus placebo.

Analysis metric	Estimate, D − P	95% CI	P value
Prespecified primary — CSR / SAP v3.0			
Percent change (PCHG)	4.55	0.47 to 8.63	0.0290
Prespecified sensitivity — SAP v3.0			
Absolute change (CHG)	1.08	0.00 to 2.16	0.0503
Supportive — earlier SAP versions			
PCHG (v2.0)	4.85	0.72 to 8.99	0.0219
CHG (v2.0)	1.14	0.04 to 2.23	0.0416
CHG (v1.7)	1.12	−0.01 to 2.25	0.0522

v1.7 reports change from baseline (CHG): Kenward-Roger denominator df, slow-progressor interaction terms, baseline-by-visit, least-squares means evaluated at slowprgn=0. **This was last SAP version that was based directly on FDA feedback on v1.6.**
v2.0 reports percentage change from baseline (PCHG, primary) and CHG (sensitivity): ARH(1) covariance, slow-progressor interaction terms, least-squares means at slowprgn=0.
v3.0 reports PCHG (prespecified primary) and CHG (sensitivity): ARH(1) covariance, slow-progressor as main effect only, unconditioned; covariance fallback per attempt primary — CSH — CS.
SITEGR1 and SLOWPRGN use the locked ADaM (v3.0) derivations; v1.7 and v2.0 rows differ only in model structure. Locked ADaM 20260129_Final_DB; ANL01FL=Y; APHASE=BLINDED TREATMENT.
Abbreviations: ARH(1), heterogeneous first-order autoregressive covariance; CHG, change from baseline; CI, confidence interval; CS/CSH, compound symmetry/heterogeneous compound symmetry; D − P, deramiocel minus placebo; MMRM, mixed model for repeated measures; PCHG, percentage change from baseline; PUL 2.0, Performance of the Upper Limb module 2.0; SAP, statistical analysis plan.

Figure A1. Capricor presented the absolute-change sensitivity result as p=.050, while the underlying table reports p=.0503. The discrepancy reflects rounding and presentation; the exact result sits above .05. Source: Capricor advisory-committee materials.

APPENDIX B

Complete chronology

Date	Event	Consequence
19 Jul 2022	SAP 1.1 dated; first visit 22 Jun 2022	Original absolute PUL/LVEF framework.
Oct 2023	Programming/biostatistics moved from vendor to Capricor	FDA says the departure from the approved blinding plan increased process risk.
6 Dec 2023	SAP 1.7 dated	Slow-progressor and adverse-event discontinuation rules appeared before completion.
18 Jun 2025	Randomized double-blind period completed	All month-12 efficacy observations collected.
11 Jul 2025	First deramiocel CRL disclosed	FDA had not accepted HOPE-2/OLE as substantial evidence.
26 Sep 2025	SAP 2.0 dated	Percent PUL and new handling.
10 Nov 2025	FDA call without immediately submitted SAP	Formal status recorded; no FDA concurrence disclosed.
24 Nov 2025	SAP 3.0 dated	Ranked LVEF and prohibited-medication censoring.
25 Nov 2025	Database lock and formal unblinding	Company's stated end of treatment-code concealment.
3 Dec 2025	Positive topline release and investor deck	Stock closed $29.96 versus $6.36 on 2 Dec.
5 Dec 2025	6.9m-share offering priced at $25	$172.5m gross raised.
27/30 Dec 2025	Director and officer Rule 10b5-1 plans	Plans adopted after release and financing.
3 Feb 2026	Clinical study report dated	Final analysis included terms beyond SAP 3.0.
10 Mar 2026	FDA resumed review; Class 2 resubmission	22 Aug target date announced.
May 2026	Capricor sued Nippon / NS Pharma	Commercial channel disputed.
26 Jun 2026	Advisory committee announced	Unresolved efficacy dispute moved to public review.
9 Jul 2026	171,000-square-foot lease disclosed	Approval-contingent fixed-cost expansion.
27 Jul 2026	FDA and sponsor briefing packages released	FDA's p=.24/.97 reconstruction became public; stock fell 64.5% to approximately $7.
29 Jul 2026	Scheduled advisory committee	Expected public vote on substantial evidence.
22 Aug 2026	PDUFA target date	Expected Complete Response Letter under this thesis.

APPENDIX C

Valuation assumptions

Input	Base	Source / formula	Limit
Reference price	$6.995	27 Jul market quote	Extreme event volatility.
Basic shares	57.912m	11 May 2026 disclosure	Later exercises can change count.
Estimated diluted shares	61.1m	Treasury-stock estimate at $7 using March awards	Strike distribution and vesting are incomplete; March/May timing can overlap.
31 Mar liquidity	$278.864m	Q1 10-Q	Reported historical balance.
27 Jul liquidity	$225m midpoint	Estimated from March cash, Q2/July burn, and CIRM repayment	Unaudited; range $215m-$235m.
Existing obligations	$30m base	Payables/accruals plus existing lease liabilities	CIRM already deducted from July estimate.
Run-off operations	$55m base	Program termination, corporate operations, inventory, facilities	Board behavior dominates.
Legal / partner	$20m base	Securities, derivative, employment, Nippon, advisers	No company reserve or insurance limits disclosed.
Closure	$15m base	New-site exit, severance, and closure	Excludes existing lease liabilities counted above.
Residual equity	$105m / $1.72	$225m less $120m; divided by 61.1m	Selected short target.
Clinical and platform value	$0	Cash-only bear convention	A favorable FDA decision would restore commercial optionality.

Base arithmetic

$225 million estimated liquidity less $30 million of existing obligations, $55 million of run-off operations, $20 million of legal and partner costs, and $15 million of new-site exit, severance, and closure expense leaves $105 million. Dividing by 61.1 million estimated diluted shares produces $1.72 per share.

No value is assigned to deramiocel, the exosome platform, contingent milestones, tax attributes, or an asset sale. Public cash can remain trapped or consumed if the board continues development and declines to pursue a wind-down.

APPENDIX D

Primary source record

The numbered citations refer to the following public records. FDA, SEC, court, company, and peer-reviewed sources supply the evidentiary base.

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11. Capricor insider transaction Forms 4, SEC EDGAR filing data, Mar-Jun 2026. Open source

12. Capricor, 9 Jul 2026 Form 8-K reporting San Diego lease. Open source

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33. ALLSTAR randomized clinical publication. Open source

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41. Edgewise Therapeutics quarterly pipeline update covering DMD studies LYNX and FOX. Open source

42. SEC, Rule 10b5-1 insider-trading arrangements compliance guide. Open source

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Publication terms

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