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Zetyra Executive Brief

18 Validated Statistical Calculators for Efficient Clinical Trial Design

For: VPs of R&D, CMOs, Clinical Development Leaders **Reading Time:** 5-7 min

FDA BAYESIAN GUIDANCE (January 12, 2026)

FDA released draft guidance extending Bayesian methodology to drugs and biologics (PDUFA VII commitment). Zetyra's Bayesian Toolkit is purpose-built for this regulatory shift. This guidance is not yet final and is not for implementation.

THE CLINICAL TRIAL EFFICIENCY PROBLEM

Trials Are Too Expensive and Too Slow

Phase III clinical trials cost $50-100 million and require 4-6 years. Most use conservative designs that inflate costs:

Inefficiency	Impact	Cost to Industry
Ignoring baseline covariates	15-35% sample size inflation	$7-35M per Phase III
No interim monitoring	Continuing futile trials	6-18 months wasted
No adaptive re-estimation	Wrong assumptions → underpowered	Failed trials, $50-100M lost
Binary go/no-go decisions	$50-100M on doomed Phase III	50-60% failure rate

Why Efficient Designs Aren't Used

- Software is expensive: $5,000-$15,000 annual licenses (East, PASS, ADDPLAN)
- IT barriers: Desktop installation requires IT department involvement
- Fragmented tools: Separate software for each methodology, no integration
- No public validation: Commercial vendors publish zero accuracy data

THE OPPORTUNITY: 18 CALCULATORS, ONE PLATFORM

Zetyra integrates frequentist, Bayesian, adaptive, and master protocol methods in a single web-based platform:

Covariate Adjustment (15-35% reduction) | Group Sequential Design (20-40%) | Bayesian Predictive Power | Survival Power Analysis | Sample Size Re-estimation (blinded, unblinded, single-arm) | Response-Adaptive Randomization | Master Protocols (basket, umbrella, platform) | Full Bayesian Toolkit (6 modules)

All validated against **896 automated tests**. All publicly auditable. From $0/month (Free Tier).

Beyond Cost Savings: Strategic Benefits

- Faster time to market: Accelerated BLA submissions mean earlier revenue and patient access
- Reduced investor risk: Quantitative go/no-go decisions with Bayesian probability statements
- Regulatory alignment: FDA Jan 2026 draft guidance + ICH E9(R1) increasingly support modern methods
- Adaptive flexibility: Blinded, unblinded, and single-arm SSR protect against planning assumptions

THE ZETYRA PLATFORM

18 Calculators: Evidence Pro + Bayesian Toolkit Add-On

FREE TIER	EVIDENCE PRO
$0/month	**$99/mo ($29 .edu)**
Sample Size (continuous, binary, survival, CRT, longitudinal) Chi-Square (independence, power, sample size, McNemar)	CUPED | GSD | Bayesian PPoS Survival Power | Blinded SSR Unblinded SSR | Single-Arm SSR RAR | Basket | Umbrella | Platform CSV Upload | API
BAYESIAN TOOLKIT (ADD-ON)	**ENTERPRISE**
+$149/mo ($49 .edu)	**Custom pricing**
Prior Elicitation | Bayesian Borrowing Single-Arm Design | Two-Arm Design Sequential Monitoring | Predictive Power	All calculators + Team features FDA compliance documentation Priority support | Custom integrations

Evidence Pro Highlights

Calculator	What It Does	Typical Savings
CUPED	Sample size reduction from baseline-outcome correlations	**15-35% fewer patients**
Group Sequential	Stopping boundaries with Type I error control (incl. survival)	**15-30% expected N reduction**
Bayesian PPoS	Probability of success given interim data (binary/continuous/survival)	**Quantitative go/no-go**
Survival Power	Event-driven sample size (Schoenfeld/Freedman)	**Optimized event targets**
SSR (3 modes)	Blinded, unblinded, and single-arm re-estimation	**Preserves power adaptively**
RAR	Response-adaptive randomization (DBCD, Thompson, Neyman)	**More patients on better arm**
Master Protocols	Basket (BHM/EXNEX), umbrella, platform (MAMS)	**Shared infrastructure savings**

Validation Excellence: 896 Tests, 100% Pass Rate

Module	Tests	Benchmark	Max Deviation
Group Sequential	103	gsDesign, rpact, HPTN 083, PACIFIC	**0.034 z-score**
CUPED	55	Analytical formula, Walters 2019	**Exact match**
Bayesian (Pro + Toolkit)	248	Conjugate priors, Zhou & Ji 2024	**Exact match**
Free + Survival + SSR + RAR	374	Cohen, Schoenfeld, Mehta-Pocock, rpact, Lee & Liu	**< 0.01**
Master Protocols + Cross-checks	116	I-SPY 2, STAMPEDE, REMAP-CAP, offline formulas	**Exact match**

All validation code is public: github.com/evidenceinthewild/zetyra-validation | 42 validation scripts, MIT license

Competitive Positioning (as of May 2026)

Feature	Zetyra	East	PASS	ADDPLAN	nQuery
Calculators	**18**	GSD focus	Power focus	Adaptive	Power focus
Public validation	**896 tests**	No	No	No	No
Bayesian Toolkit	**6 modules**	Limited	No	Limited	No
Master Protocols	**3 types**	No	No	Limited	No
Web-based	**Yes**	No	No	No	No
Annual cost	**From $0**	$15,000	$8,000	$12,000	$6,000

BUSINESS IMPACT

Quantified Case Studies

Note: Case studies are illustrative scenarios based on typical trial parameters. Actual savings depend on correlation strength, interim timing, and program-specific factors.

Case Study 1: Oncology Phase II — CUPED (30% Sample Size Reduction)

HER2+ metastatic breast cancer, single-arm Phase II evaluating ORR

$3.6M Saved | **30%** Reduction | **3.6mo** Faster

Standard: 240 pts, $12.0M
CUPED: 168 pts, $8.4M
Correlation: rho=0.55 (baseline tumor burden)

Case Study 2: Cardiovascular Phase III — GSD ($18M Saved, Early Stop)

PCSK9 inhibitor for MACE; 4-look O'Brien-Fleming with non-binding futility

$18.1M Saved | **24%** Cost Cut | **12mo** Faster

Stopped at Interim 2 (Month 36)
HR=0.68, Z=2.89 > boundary 2.754
BLA submission 12 months earlier

Case Study 3: Rare Disease — Bayesian Decision Framework

DMD gene therapy, 6-minute walk distance endpoint

Traditional: p=0.08 → "Not significant" → No-go	**Bayesian: 78% probability of benefit → Go***
Potentially wrong decision	**FDA granted Breakthrough Therapy Designation**

**Decision incorporated clinical relevance, unmet need, and regulatory feedback—not a single probability threshold.*

Case Study 5: Immuno-Oncology — Survival Power + GSD Integration

PD-L1 combination therapy, event-driven Phase III, OS primary endpoint

$8.4M Saved | **22%** Cost Cut | **8mo** Faster

Schoenfeld event calculation + GSD
Target HR=0.75, 396 events
3-look OF stops at Interim 2

Case Study 4: Full Program — CUPED + GSD + Bayesian + SSR

NSCLC immunotherapy, Phase II → Phase III development

Element	Traditional	Zetyra-Optimized	Savings
Phase II	80 pts, 12 mo, $4.0M	53 pts, 8 mo, $2.4M	**$1.6M (40%)**
Phase III	500 pts, 54 mo, $100M	425 exp, 42 mo, $87.5M	**$12.5M (13%)**
Total	66 months, $104M	50 months, $89.9M	**$14.1M (14%)**
BLA	Month 72	Month 56	**16mo earlier**

Revenue Upside: For successful programs with $2B peak sales, 16-month acceleration yields ~$2.1B NPV gain. Revenue acceleration can dominate cost savings; magnitude depends on commercial assumptions.

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WHY ZETYRA

Competitive Advantages

1 Transparent Validation

896 automated tests, 42 scripts, 100% pass rate. Public GitHub repo. No commercial tool offers this transparency.

2 18 Integrated Calculators

Frequentist + Bayesian + Adaptive + Master Protocol in one platform. No juggling East, PASS, ADDPLAN, and custom R scripts.

3 Regulatory-Ready

FDA/EMA guidance citations in outputs. Pre-written SAP language. Aligned with Jan 2026 Bayesian draft guidance.

4 Zero IT Friction

Web-based, any device. Free Tier with no credit card. Time to first calculation: minutes, not weeks.

Regulatory Support

- CUPED: May 2023 FDA guidance calls covariate adjustment "low-hanging fruit"
- Group Sequential: Nov 2019 FDA guidance: "simplest and most established" adaptive designs
- Bayesian: Jan 12, 2026 draft guidance extends Bayesian methods to drugs and biologics
- SSR: ICH E9(R1) estimands framework supports pre-planned adaptive re-estimation

Pricing

Free	Evidence Pro	Bayesian Toolkit (add-on)	Evidence Collective	Enterprise
$0/mo	$99/mo ($29 .edu)	+$149/mo ($49 .edu)	$349/mo (5 seats)	Custom
2 calculators (9 modes)	11 calculators + API	6 Bayesian modules	Team + projects	All + compliance

Free trial available. No credit card required. Equivalent functionality from East + PASS + ADDPLAN: $35K+/year.

GETTING STARTED

1. Free trial: zetyra.com (no credit card required) — first calculation in minutes
2. Schedule demo: maggie@zetyra.com (30-minute walkthrough)
3. White paper: zetyra.com/whitepaper (132-page technical whitepaper)
4. Validation: github.com/evidenceinthewild/zetyra-validation (896 tests, MIT license)

What Makes Zetyra Different?

The only platform integrating frequentist, Bayesian, adaptive, and master protocol methods with 18 calculators and 896 publicly validated tests. From free to enterprise. Web-based, no IT required. Purpose-built for the FDA's evolving guidance on modern statistical methods.

Zetyra supports trial planning and design decisions; sponsors retain responsibility for final regulatory strategy.

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The future of clinical trial design is transparent, validated, accessible, and efficient.