GNQ INSILICO

Silicon-to-Patient™ | Q-BRM – The Power behind GNQ Precision Medicine Platforms

PHARMA & BIOTECH EDITION

WHITE PAPER

Q-BRM for Drug Development

Improving Probability of Success, Go/No-Go Precision, and Combination Therapy Design

Confidential | For Authorized Use Only | **April 2026**
Sudhir Saxena | C.T.O | gnq.ai

Executive Summary

Late-stage clinical trial failure costs the pharmaceutical industry billions annually and delays life-saving therapies by years. The root cause is not insufficient data — it is insufficient **mechanistic understanding** of why a drug works, which patient it works for, and how resistance emerges. Conventional AI cannot solve this problem because it describes what has been observed, not what will happen under a specific intervention in a specific patient.[3,4]

GNQ Insilico's **Q-BRM — Quantum Biomedical Reasoning Model** — addresses drug development at the causal level. Q-BRM powers GNQ's Drug Assessment Platform (DAP) and Drug Simulation Platform (DSP) to deliver mechanistic insight across the full drug development lifecycle: target validation, patient stratification, combination design, resistance prediction, and go/no-go decision support. All insights are generated from first principles — quantum physics, systems biology, and formal causal inference — with real-world evidence from datasets such as the MMRF CoMMpass cohort serving as **validation**, not as primary source.

> **Value Proposition for Pharma/Biotech CFOs and CMOs**
> Q-BRM improves the three input parameters that govern every rNPV calculation: probability of clinical success (PoS), go/no-go decision timing, and compound rescue potential. For programs where mechanism-based failure prediction is possible before Phase II enrollment, the cost avoidance can be as much as $100M–$500M per program.

1. The Core Challenge in Drug Development

The pharmaceutical industry faces three structural problems that current AI platforms cannot address:

1.1 Late-Stage Failure from Population Heterogeneity

Clinical trials fail predominantly because the enrolled population contains non-responders who dilute efficacy signals and responders with emerging resistance who confound durability endpoints. Standard genomic stratification identifies correlates of response, not causal drivers. A biomarker correlated with response in one trial may reflect a bystander pathway, not the mechanism of action — and the correlation may not replicate.

Q-BRM's **Integral Variant Scoring (IVS)** identifies responder subpopulations through causal pathway analysis. Instead of asking 'which patients have this variant?' Q-BRM asks 'which patients' causal pathway state will be mechanistically altered by this intervention?' — a fundamentally different and more predictive question.

1.2 Resistance as an Emergent Biological Process

Resistance to targeted therapy is not a static property — it is an emergent process in which pathway rewiring, clonal selection, and compensatory signaling progressively undermine drug efficacy. Current platforms model resistance as a flag or a probability estimate. Q-BRM models it as a dynamic causal trajectory.

Q-BRM's **Drug Simulation Platform (DSP)** deploys Neural Stochastic Differential Equations (Neural SDEs) over patient-specific Relational Dynamic Graphs, simulating the continuous evolution of pathway states under treatment pressure. The time at which resistance pathways cross clinical significance thresholds becomes a predictable output — enabling proactive therapy sequencing before progression, not reactive switching after it.[6]

1.3 Combination Therapy Design Without Clinical Data

Rational combination therapy design is constrained by the combinatorial explosion of drug pairings and the absence of clinical data for most combinations. Empirical synergy testing is slow, expensive, and cannot scale. Q-BRM solves this through quantum-informed causal graph simulation.

Using DMET+SQD quantum simulation, Q-BRM computes binding free energies (ΔG) for each drug-target pair at quantum accuracy.[2] Graph Neural ODEs then propagate the joint effect of multiple interventions through the patient's causal pathway network — generating combination synergy predictions that account for pathway complementarity, pharmacokinetic interactions, and resistance escape route coverage. Smaller clinical data sets are sufficient for effective insights, and validation.[6]

2. How Q-BRM Powers Drug Development

2.1 Drug Assessment Platform (DAP): Target Validation and Patient Stratification

The DAP implements Q-BRM's **Integral Variant Scoring (IVS)** framework — a causal pathway scoring methodology that quantifies how a patient's specific genomic variant profile activates or suppresses key biological pathways relevant to a drug's mechanism of action. IVS scores are directional: pathways requiring maximization (e.g., apoptosis induction) are scored differently from those requiring minimization (e.g., BCL2-dependent survival signaling).

The DAP delivers drug development intelligence at three levels:

- **Feasibility Assessment:** Mechanistic go/no-go signals for new compounds based on pathway causal analysis before clinical investment.
- **Responder Population Definition:** Causal pathway-defined patient subpopulations for trial enrollment criteria — derived from biology, not from prior trial observations.

- **Combination Hypothesis Generation:** Pathway complementarity analysis identifying rational combination partners that address resistance escape routes in the target indication.

2.2 Drug Simulation Platform (DSP): Resistance Prediction and Trial Simulation

The DSP is powered by Q-BRM's dynamic causal simulation engine — the platform layer that converts static pathway knowledge into temporal predictions of drug response and resistance.

Key DSP capabilities for drug development:

- **Resistance Trajectory Simulation:** Neural SDEs model continuous pathway rewiring under treatment pressure. The specific resistance mechanisms most likely to emerge — and the timeline for their emergence — are predictable outputs, not post-hoc observations.
- **Zero-Shot Combination Prediction:** For drug combinations with no existing clinical data, Q-BRM computes quantum binding affinities for each agent, propagates joint pathway effects through the causal graph, and generates response predictions with uncertainty quantification.
- **Counterfactual Arm Simulation:** For ongoing or planned trials, Q-BRM simulates alternative treatment arm outcomes using patient-specific causal states — enabling prospective power analysis based on mechanism rather than historical precedent.
- **Biomarker Discovery:** Novel predictive signatures emerge from Q-BRM's latent causal graph representation — surfacing enrollment biomarkers that go beyond standard genomic markers to capture causal pathway state.

2.3 rNPV Impact: Translating Causal Intelligence to Financial Value

Every drug development investment decision is ultimately expressed in **rNPV terms**. Q-BRM improves rNPV by directly shifting the input parameters that govern it:

rNPV Input Parameter	Traditional Approach	With Q-BRM
rNPV Input	Traditional Approach	With Q-BRM
PoS (Phase II)	Historical indication average ~40%	Mechanism-defined responder PoS: targeted upward signal
PoS (Phase III)	Historical indication average ~60%	Resistance-adjusted durability prediction
Go/No-Go Timing	Post-Phase II readout	Pre-Phase II resistance foresight — 18–24 months earlier
Compound Rescue Value	Near-zero for shelved compounds	Causal subpopulation discovery reactivates optionality
Trial Efficiency	Broad enrollment, post-hoc analysis	Causal stratification — smaller, faster, higher PoS trials

3. Real-World Evidence: Validation Layer, Not Data Source

A critical architectural distinction of Q-BRM is the epistemic role assigned to real-world clinical data. Most drug development AI platforms are fundamentally data-driven: they learn from historical trial outcomes and extrapolate patterns to new compounds. **Q-BRM inverts this.**

Q-BRM generates mechanistic predictions from three first-principles sources:

- **Quantum-computed molecular interaction energies (DMET+SQD)** — physics, not statistics
- **Curated biological pathway knowledge encoded in the RDG** — established mechanistic biology, not trial associations
- **Causal inference propagated through the Quantum RCM** — mathematical causal reasoning, not pattern matching

Real-world evidence — such as the MMRF CoMMpass dataset (1,100+ multiple myeloma patients with longitudinal genomic and clinical data) — then **validates** these predictions. When Q-BRM predicts that PSMB5 A49T mutation confers bortezomib resistance via proteasome pathway causal analysis, CoMMpass outcomes confirm it. This is the strongest possible evidence structure: mechanistic prediction confirmed by empirical observation, rather than empirical correlation without mechanistic grounding.

> **Why This Matters for Novel Programs**
> For first-in-class compounds, rare disease indications, and novel combination partners, there is no historical data to learn from. Q-BRM's first-principles approach generates reliable mechanistic predictions precisely in the scenarios where data-driven platforms produce noise — which is exactly when pharma needs guidance most.

4. Competitive Differentiation for Drug Development

Capability	Conventional AI (Most)	SCM / Causal AI (Emerging)	GNQ Q-BRM
PoS Estimation	⚠ Historical trial averages	⚠ Partial causal signal	✅ Mechanism-first causal PoS
Go/No-Go Timing	✗ Late-stage failure	⚠ Limited prediction	✅ Pre-Phase II resistance foresight

Capability	Conventional AI (Most)	SCM / Causal AI (Emerging)	GNQ Q-BRM
Patient Stratification	⚠ Genomic correlation	⚠ SCM-based	✅ RDG causal pathway profiles
Combination Design	❌ Empirical / trial-and-error	⚠ Manual	✅ Zero-shot quantum prediction
Compound Rescue	❌ No mechanism insight	⚠ Limited	✅ Causal subpopulation discovery
Resistance Prediction	❌ Empirical flags	⚠ Partial	✅ Emergent Neural SDE dynamics
Biomarker Discovery	❌ Correlation-based	⚠ Indirect	✅ Latent causal graph emergence
Off-Target Modeling	❌ Classical force fields	❌ None	✅ DMET+SQD quantum simulation
Data Requirement	❌ Thousands of patients	⚠ Hundreds of patients	✅ Tens — quantum fills the gap
Regulatory Readiness	⚠ Black box	⚠ Limited mechanistic basis	✅ Mechanistic causal rationale

5. Validated Drug Development Applications

5.1 Oncology - Multiple Myeloma,NSCLC

GNQ's lead therapeutic area is oncology. One such example is multiple myeloma, in collaboration with the MMRF. Q-BRM capabilities validated in MM include:

- **Bortezomib resistance profiling:** PSMB5 A49T proteasome resistance modeled via DMET+SQD quantum simulation of binding affinity change — predicting resistance mechanism from first principles, confirmed against CoMMpass outcomes.
- **BCMA pathway combination design:** Apoptosis pathway causal analysis for bispecific antibody combination partners — informing the GNQ application to ELREXFIO (elranatamab) resistance profiling and sequencing strategy.
- **Sequential therapy optimization:** Neural SDE counterfactual simulation of therapy sequencing to minimize cumulative resistance pathway activation across treatment lines.

5.2 Neurodegenerative Diseases - ALS

Q-BRM's RDG-Driven Quantum RCM architecture is indication-agnostic. Active applications include EGFR pathway combination therapy optimization and multi-pathway systems biology combination design in ALS — both demonstrating the platform's generalizability beyond hematologic malignancy.

5.3 Pain Management: MindLab Pharma MLB-001

Q-BRM's DAP module is currently applied to the optimization of MLB-001 — a Morphine + Dextromethorphan + Quinidine combination — through mechanistic pathway analysis of pain signaling, receptor occupancy modeling, and pharmacokinetic interaction prediction via quantum simulation.

5.4 Quantum Drug Development

GNQ's R&D innovation applies Q-BRM's quantum simulation capabilities to off-target effect modeling for drugs with heavy chemical elements — a use case where classical force fields systematically fail and DMET+SQD provides quantum-accurate binding predictions.[2]

6. Engagement Model and Pricing

GNQ engages pharmaceutical and biotech clients under a subscription-based model aligned with the multi-year lifecycle of drug development programs. Standard engagements include:

- **Module A — Feasibility + rNPV Assessment:** Causal pathway feasibility analysis, responder population definition, and go/no-go signal generation for a target compound or indication. Deliverable: mechanistic assessment report with rNPV input recommendations.
- **Module B — Combination Optimization:** Zero-shot combination prediction, pathway complementarity analysis, and resistance escape route coverage assessment for defined drug combination candidates.
- **Module C — Resistance Prediction and Trial Design:** Neural SDE resistance trajectory simulation, biomarker discovery, and counterfactual trial arm modeling for ongoing or planned clinical programs.

Pricing follows a recurring subscription model. All engagements include API access to Q-BRM platform capabilities with black-box IP protection.

7. Conclusion

Q-BRM represents the first drug development platform that generates mechanistic causal insight from quantum physics and systems biology — not just from historical trial data. For pharmaceutical and biotech organizations, this means reliable guidance precisely in the scenarios that matter most: first-in-class compounds, novel combinations, rare patient populations, and resistance prediction before Phase II failure.

The result is not incremental improvement in drug development efficiency — it is a fundamentally different quality of evidence for go/no-go decisions, a new capability for combination design, and a proactive approach to resistance management that current platforms cannot provide.

Engage GNQ Insilico

GNQ Insilico, Inc. | gnq.ai To arrange a platform demonstration, feasibility assessment, or partnership discussion, contact the GNQ business development team.

Glossary of Key Terms

Q-BRM — Quantum Biomedical Reasoning Model. GNQ's proprietary intelligence engine powering DAP, DSP, and DTP. Composed of the Relational Dynamic Graph (RDG), Quantum Relational Causal Model (Quantum RCM), and agentic BRM orchestration layer.

RDG — Relational Dynamic Graph. GNQ's proprietary knowledge graph substrate: 681+ pathway relationships, 20,000+ genes, 2M+ causal links. Typed, weighted, directional biological relationships with continuous temporal dynamics.

Quantum RCM — Quantum Relational Causal Model. The causal inference framework within Q-BRM: DMET+SQD quantum edge weights + Neural ODE/SDE propagation over the RDG. Extends Pearl's SCMs to relational heterogeneous graphs with feedback loops.

DAP — Drug Assessment Platform. GNQ's causal pathway scoring and drug evaluation engine using Integral Variant Scoring (IVS).

DSP — Drug Simulation Platform. GNQ's dynamic causal simulation engine using Neural ODEs and Neural SDEs.

DTP — Digital Twin Platform. GNQ's HIPAA-compliant patient-specific causal modeling and clinical decision support layer.

BRM — Biomedical Reasoning Model. GNQ's agentic orchestration layer built on LangGraph and MCP. Handles natural language intent parsing and orchestrates calls to DAP, DSP, and DTP.

DMET+SQD — Density Matrix Embedding Theory + Sample-based Quantum Diagonalization. IBM's near-term quantum chemistry framework for computing molecular ground states on real quantum hardware without fault-tolerant qubits.

IVS — Integral Variant Scoring. GNQ's proprietary methodology for scoring pathway-level causal impact from patient genomic variant profiles.

Neural ODE — Neural Ordinary Differential Equation. Continuous-time neural architecture for modeling causal state evolution (interventional inference — Pearl Rung 2).

Neural SDE — Neural Stochastic Differential Equation. Extends Neural ODEs with principled stochasticity for uncertainty quantification; enables counterfactual simulation (Pearl Rung 3).

SCM — Structural Causal Model. Judea Pearl's formal framework for causal reasoning using DAGs and structural equations.

DAG — Directed Acyclic Graph. Required by standard SCMs. Cannot represent biological feedback loops — a key limitation addressed by GNQ's RDG.

rNPV — Risk-adjusted Net Present Value. Standard pharma valuation metric for drug programs; GNQ improves rNPV inputs by raising probability of success and accelerating go/no-go timing.

References

[1] **Pearl, J.** "Causality: Models, Reasoning, and Inference." Cambridge University Press, 2nd ed., 2009. ISBN: 978-0-521-89560-6. Foundational framework for Structural Causal Models, do-calculus, and the three-rung Causal Ladder.

[2] **Robledo-Moreno, J., Motta, M., et al.** "Chemistry beyond the scale of exact diagonalization on a quantum-centric supercomputer." *Science Advances* 11(25), eadu9991, June 2025. DOI: 10.1126/sciadv.adu9991. IBM Heron + Fugaku; 45–77 qubits; validates DMET+SQD on real near-term hardware.

[3] **Hager, P., Jungmann, F., et al.** "Evaluation and mitigation of the limitations of large language models in clinical decision-making." *Nature Medicine* 30(9), 2613–2622, 2024. DOI: 10.1038/s41591-024-03097-1. Across 2,400 real cases, LLMs performed significantly worse than physicians on realistic clinical tasks.

[4] **Song, P., et al.** "Large Language Model Reasoning Failures." *arXiv*:2602.06176, February 2026. First comprehensive survey of systemic LLM reasoning failure modes; directly relevant to reliance on LLMs for clinical inference.

[5] **Maier, M., Marazopoulou, K., Arbour, D., Jensen, D.** "A Sound and Complete Algorithm for Learning Causal Models from Relational Data." *Proceedings UAI 2013*, arXiv:1309.6843. Introduces Relational Causal Models (RCM) as a formally sound extension of Pearl's SCMs to heterogeneous relational graphs.

[6] **Chen, R.T.Q., Rubanova, Y., Bettencourt, J., Duvenaud, D.** "Neural Ordinary Differential Equations." *NeurIPS 2018*, pp. 6572–6583. arXiv:1806.07366. Foundational Neural ODE paper; underpins GNQ's continuous-time causal trajectory simulation.